

**Elanco Animal Health**

112 Wharf Road
WEST RYDE NSW 2114
AUSTRALIA
Telephone: (02) 9878 7705
Email: ndavis@lilly.com

July 5 2010

Standards Management Officer
Food Standards Australia New Zealand
PO Box 7186
CANBERRA BC ACT 2610
AUSTRALIA

Dear Sir/Madam,

APPLICATION

Please find enclosed an application to amend the Australian Food Standards Code, Standard 1.3.3 Processing Aids under Clause 12: Permitted bleaching agents, washing and peeling agents, to include 1,3-dibromo-5,5-dimethylhydantoin (DBDMH).

There already exists an entry for the halohydantoin, Bromo-chloro-dimethylhydantoin (BCDMH) and it is proposed that the entry be amended to include the halohydantoin, 1,3-dibromo-5,5-dimethylhydantoin (DBDMH).

At a meeting with Mark Fitzroy in April 2010 there was discussion that the inclusion of DBDMH in the Code may be accomplished during the current round of Code Maintenance. Nevertheless, all required data from Sections 3.1 and 3.3.2 of the Handbook are submitted. The data is included as Appendix 3 to this letter. The statutory declaration and checklist are also attached as Appendix 1 and 2 to this letter.

Please feel free to contact me by phone or email if you wish to discuss this application further.

Yours sincerely,

A handwritten signature in black ink, appearing to be "Noelene Davis".

Noelene Davis
Senior Regulatory Consultant

Appendix 1

STATUTORY DECLARATION*Statutory Declarations Act 1959*

I, Noelene Davis, Senior Regulatory Consultant, Elanco Animal Health, 112 Wharf Rd West Ryde NSW 2114, make the following declaration under the *Statutory Declarations Act 1959*:

1. the information provided in this application fully sets out the matters required
2. the information provided in this application is true to the best of my knowledge and belief
3. no information has been withheld that might prejudice this application, to the best of my knowledge and belief

I understand that a person who intentionally makes a false statement in a statutory declaration is guilty of an offence under section 11 of the *Statutory Declarations Act 1959*, and I believe that the statements in this declaration are true in every particular.

Signature: 

Declared at 112 Wharf Rd West Ryde NSW 2114 on 5th day of July 2010

Before me,

Signature: 

Name: Colin Anderson

Qualifications: Justice of The Peace 168679

Address: 129/8 Savona Drive Homebush Bay NSW 2127

CHECKLIST FOR STANDARDS RELATED TO SUBSTANCES ADDED TO FOOD

This checklist will assist you in determining if you have met the information requirements as detailed in the Application Handbook. Section 3.1 – General Requirements is mandatory for all applications. Sections 3.3.1-3.3.3 are related to the specifics of your application and the information required is in addition to section 3.1.

General Requirements (3.1)

<input checked="" type="checkbox"/> Form of application	<input checked="" type="checkbox"/> Assessment procedure
<input checked="" type="checkbox"/> <i>Executive Summary</i>	
<input checked="" type="checkbox"/> <i>Relevant sections of part 3 identified</i>	
<input checked="" type="checkbox"/> <i>Pages sequentially numbered</i>	
<input checked="" type="checkbox"/> <i>Hard copies capable of being laid flat</i>	
<input checked="" type="checkbox"/> <i>Electronic and hard copies identical</i>	
<input checked="" type="checkbox"/> Applicant details	<input type="checkbox"/> Confidential Commercial Information <input type="checkbox"/> <i>Confidential material separated in both electronic and hard copy</i>
<input checked="" type="checkbox"/> Purpose of the application	<input type="checkbox"/> Exclusive Capturable Commercial Benefit
<input checked="" type="checkbox"/> Justification for the application	<input checked="" type="checkbox"/> International standards
<input checked="" type="checkbox"/> Information to support the application	<input checked="" type="checkbox"/> Statutory Declaration

Food Additives (3.3.1)

<input type="checkbox"/> Nature and technological function information	<input type="checkbox"/> Toxicokinetics and metabolism information
<input type="checkbox"/> Identification information	<input type="checkbox"/> Toxicity information
<input type="checkbox"/> Chemical and physical properties	<input type="checkbox"/> Safety assessments from international agencies
<input type="checkbox"/> Impurity profile	<input type="checkbox"/> List of foods likely to contain the food additive
<input type="checkbox"/> Manufacturing process	<input type="checkbox"/> Proposed levels in foods
<input type="checkbox"/> Specifications	<input type="checkbox"/> Percentage of food group to contain the food additive
<input type="checkbox"/> Food labelling	<input type="checkbox"/> Use in other countries (if applicable)
<input type="checkbox"/> Analytical detection method	

Processing Aids (3.3.2)

<input checked="" type="checkbox"/> Type of processing aid	<input type="checkbox"/> Information on enzyme use on other countries (enzyme only)
<input checked="" type="checkbox"/> Identification information	<input type="checkbox"/> Toxicity information of enzyme (enzyme only)
<input checked="" type="checkbox"/> Chemical and physical properties	<input type="checkbox"/> Information on source organism (enzyme from micro-organism only)

<input checked="" type="checkbox"/> Manufacturing process	<input type="checkbox"/> Pathogenicity and toxicity of source micro-organism (enzyme from micro-organism only)
<input checked="" type="checkbox"/> Specification information	<input type="checkbox"/> Genetic stability of source organism (enzyme from micro-organism only)
<input checked="" type="checkbox"/> Industrial use information (chemical only)	<input type="checkbox"/> Nature of genetic modification (PA from GM micro-organism only)
<input checked="" type="checkbox"/> Information on use in other countries (chemical only)	<input checked="" type="checkbox"/> List of foods likely to contain the processing aid
<input checked="" type="checkbox"/> Toxicokinetics and metabolism information (chemical only)	<input checked="" type="checkbox"/> Anticipated residue levels in foods
<input checked="" type="checkbox"/> Toxicity information (chemical only)	<input checked="" type="checkbox"/> Percentage of food group to use processing aid
<input checked="" type="checkbox"/> Safety assessments from international agencies (chemical only)	<input checked="" type="checkbox"/> Information on residues in foods in other countries (if available)

Nutritive Substances (3.3.3)

<input type="checkbox"/> Identification information	<input type="checkbox"/> Proposed maximum levels in food groups or foods
<input type="checkbox"/> Information on chemical and physical properties	<input type="checkbox"/> Percentage of food group anticipated to contain nutritive substance
<input type="checkbox"/> Impurity profile information	<input type="checkbox"/> Food consumption data for new foods
<input type="checkbox"/> Manufacturing process information	<input type="checkbox"/> Nutritional purpose
<input type="checkbox"/> Specification information	<input type="checkbox"/> Need for nutritive substance in food
<input type="checkbox"/> Analytical detection method	<input type="checkbox"/> Demonstrated potential deficit or health benefit
<input type="checkbox"/> Proposed food label	<input type="checkbox"/> Consumer awareness and understanding
<input type="checkbox"/> Statement that the product being assessed is representative of the commercial product	<input type="checkbox"/> Actual or potential behaviour of consumers
<input type="checkbox"/> Toxicokinetics and metabolism information	<input type="checkbox"/> Demonstration of no adverse effects on any population groups
<input type="checkbox"/> Animal or human toxicity studies	<input type="checkbox"/> Impact on food industry
<input type="checkbox"/> Safety assessments from international agencies	<input type="checkbox"/> Impact on trade
<input type="checkbox"/> List of food groups or foods likely to contain the nutritive substance	

Appendix 3

Food Processing Aid: 1,3-dibromo-5,5-dimethylhydantoin (DBDMH)

Application to amend the Australian Food Standards Code, Standard 1.3.3 Processing Aids under Clause 12: Permitted bleaching agents, washing and peeling agents, to include 1,3-dibromo-5,5-dimethylhydantoin (DBDMH).



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1 General Information on the application

1.1 Executive summary

An application is being made to amend the Australian Food Standards Code, Standard 1.3.3 Processing Aids under Clause 12: Permitted bleaching agents, washing and peeling agents.

There already exists an entry for the halohydantoin bromo-chloro-dimethylhydantoin (BCDMH) and it is proposed that the entry be amended to include the halohydantoin, 1,3-dibromo-5,5-dimethylhydantoin (DBDMH).

Structurally, the halohydantoins consist of a central organic hydantoin ring moiety (either dimethylhydantoin or ethylmethylhydantoin) to which halogen atoms (bromine and/or chlorine) can be attached at both the 1 and 3 positions on the hydantoin ring. In solid form, the halohydantoins are very stable. When used, the halohydantoins are added to water where they rapidly hydrolyze and form hypochlorous and/or hypobromous acid, which are the actual antimicrobial agents. The solution also contains the halogen carrier hydantoin ring, dimethylhydantoin (DMH) and, for certain products, ethylmethylhydantoin (EMH). Accordingly, the halohydantoins are essentially delivery systems for hypochlorous and hypobromous acid.

The proposed use of DBDMH is as a processing aid and antimicrobial treatment in poultry processing to reduce microbial levels on poultry carcasses, parts, trim and organs. The product is added to water and applied via various poultry plant process water systems. Examples of these systems include tanks and spray applications, such as chill tanks, post-chill tanks, pre-chill tanks, inside-outside bird washers (IOBW), on-line reprocessing (OLR), off-line reprocessing and water used in ice making systems for general use in the poultry processing industry. Currently, chlorine is the agent most commonly used on poultry for this purpose mainly through the use of hypochlorites. The use of chlorine, however, has some disadvantages such as difficulty in controlling effective levels with varying pH, corrosion of water systems, high reactivity with organic matter and strong odors due to the formation of chloramines. Another compound that has been widely used in poultry processing is chlorine dioxide. Its disadvantages are worker safety and cost.

The proposed use of DBDMH in meat processing plants is as an antimicrobial treatment on hides, carcasses, heads, trim, parts, and organs. As with the poultry use, DBDMH in meat facilities is added to water and applied via various plant process water systems. Hot water, steam and lactic acid are the most common antimicrobial agents used on meat. The disadvantage to hot water and steam is that these treatments discolour surfaces of the meat. The hot water application uses a high volume of water that adds to its cost. The hot water, steam and lactic acid applications require additional energy for heating. Lactic acid also degrades cement.

This application seeks to include DBDMH in Standard A16 as an alternative antimicrobial agent to these other types of applications.

DBDMH hydrolyzes in water to form hypobromous acid, a safe and widely used compound, and has a unique mode of action that complements pH- and heat-based pathogen interventions.

The US Food and Drug Administration (FDA) and the US Department of Agriculture (USDA) have approved all of the proposed uses for DBDMH. Pre-market notifications called Food Contact Notifications (FCN) were submitted and reviewed by FDA. The list of accepted FCNs is included in Section 3.2. The USDA has listed DBDMH in their FSIS Directive 7120.1. This is included as Attachment 10. The directive identifies the substances that have been approved in 21 Code of Federal Regulations (CFR) for use in meat and poultry products as food additives, approved in

generally recognized as safe (GRAS) notices, approved through pre-market notifications, and approved in letters conveying acceptability determinations (FSIS 2010).

1.2 Applicant Details

1.2.1 Applicant's name

Elanco Animal Health, A division of Eli Lilly Australia Pty Ltd

1.2.2 Company name

Elanco Animal Health, A division of Eli Lilly Australia Pty Ltd

1.2.3 Address

112 Wharf Rd, West Ryde NSW 2114

1.2.4 Telephone

Telephone: 02 9878 7705

Facsimile: 02 9878 7720

1.2.5 Email address

ndavis@lilly.com

1.2.6 Nature of Applicant's business

Elanco is a global research-based animal health and food safety company

1.2.7 Details of other individuals, companies or organisations associated with the application

None

1.3 Purpose of the application

The purpose of the application is to amend the Australian Food Standards Code, Standard 1.3.3 Processing Aids under Clause 12: Permitted bleaching agents, washing and peeling agents.

The proposal is that in the table to Clause 12 the current entry:

Bromo-chloro-dimethylhydantoin	All foods	1.0 (available chlorine) 1.0 (inorganic bromide) 2.0 (dimethylhydantoin)
--------------------------------	-----------	--

be amended to:

Halohydantoin: Bromochloro-dimethylhydantoin and Dibromodimethylhydantoin	All foods	1.0 (available chlorine) 2.0 (inorganic bromide) 2.0 (dimethylhydantoin)
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1.4 Justification for the application

1.4.1 Technological need for the processing aid

For each of the proposed uses, DBDMH is added to water and applied to the meat or poultry as an antimicrobial processing aid. It is applied to carcasses, parts, trim, organs, hides and heads. It is also added to water used in ice making systems for general use in the poultry processing industry. The Australian use pattern will mirror the use as described in the US labels at Attachment 1.

Currently, chlorine is the agent most commonly used on poultry for this purpose mainly through the use of hypochlorites. The use of chlorine, however, has some disadvantages such as difficulty in controlling effective levels with varying pH, corrosion of water systems, high reactivity with organic matter and strong odors due to the formation of chloramines. Another compound that has been widely used in poultry processing is chlorine dioxide. Its disadvantages are worker safety and cost.

Hot water, steam and lactic acid are the most common antimicrobial agents used on meat. The disadvantage to hot water and steam is that these treatments discolour surfaces of the meat. The hot water application uses a high volume of water, which increases the cost of the treatment. The hot water, steam and lactic acid applications require additional energy for heating. Lactic acid also degrades cement.

This application seeks to include DBDMH in Standard A16 as an alternative antimicrobial agent to these other types of applications.

DBDMH hydrolyzes in water to form hypobromous acid, a safe and widely used compound, and has a unique mode of action that complements pH- and heat-based pathogen interventions.

Hypobromous acid (HOBr) is an oxidizing agent that inhibits certain essential bacterial enzymes or causes lysis of cell walls.

DBDMH has proven effective against *E. coli* 0157:H7 and *Salmonella*. For example, testing by the United States Department of Agriculture's (USDA) Agricultural Research Service (ARS) at the U.S. Meat Animal Research Center (MARC) found a 1.5 log to 2.1 log reduction in *E. coli* and a >1 log reduction in *Salmonella* with DBDMH (Kalchayanand 2009)

DBDMH is safe for workers, plant equipment and the environment. It is less corrosive to plant equipment and floors than the current chlorine and acid treatments. DBDMH has been successfully used without meat discoloration and without carcass damage. These effects are associated with high-temperature washes. The DBDMH treated water can be recycled or discharged into public sewer systems. There is no additional cost to heat the DBDMH solution so plants will have reduced energy expense when DBDMH is used to replace hot water, steam and lactic acid interventions.

The use of halohydantoin as an alternative to chlorine disinfection was considered by FSANZ for the listing of BCDMH in the Code and does not need to be reconsidered in detail (ANZFA, 2000).

The use of halohydantoins for microbial control in water and water systems is well established (EPA, 2007). In particular, the halohydantoins are used as disinfectants in commercial and residential

swimming pools, spas and hot tubs; as sanitizers for treatment of toilet bowl water in homes; and for controlling bacterial and fungal contamination in a variety of industrial water systems. (i.e., industrial cooling water systems, pulp and paper mill process water, wastewater treatment systems, air washer water systems, sewage systems, industrial processing water, irrigation systems, and ornamental ponds).

Halohydrantoin is used indirectly in food as a slimicide in the manufacture of food-contact paper and paperboard. (Permitted under FDA regulation 21 C.F.R. Part 176.300).

1.4.2 The safety of the processing aid

DBDMH is safe for workers, plant equipment and the environment.

Toxicological testing shows no concerns and that exposure to DBDMH and its metabolites is low. Refer to Section 3.4.

The breakdown products, DMH and bromide have already been considered with regard to human and environmental safety for the assessment of BCDMH.

1.4.3 The costs and benefits for industry, consumers and government associated with use of the processing aid

Many food processes, including the processing of meat and poultry (relevant to DBDMH) and fruit and vegetables (relevant to BCDMH) require water to wash, cool or transport the product.

The maintenance of antimicrobial activity in process water can have multiple functions, depending on the specific process. These functions include preventing the transfer of pathogenic and spoilage microorganisms between product items within a batch, preventing the transfer of pathogenic and spoilage microorganisms between batches of product, and inactivating a portion of pathogenic and spoilage microorganisms that are attached to the food tissue. If the process is adequately controlled, the net result is a safer food product with a longer shelf life. Antimicrobials can be used at various food processing stages. In practice, these compounds may sometimes be used sequentially in several food processing stages (e.g. pre-chill spray or dip, chiller water immersion, post-chill spray or dip). (FAO/WHO, 2008).

The costs and benefits of DBDMH are similar to those for BCDMH, which is already listed in the Code.

Affected party	Benefit	Cost
Industry	Permitting the use of DBDMH would provide food manufacturers with an alternative antimicrobial agent, which would minimise equipment corrosion, provide treatment without carcass damage associated with high-temperature washes, and provides a reduced energy expense as it does not require heating as does hot water, steam and lactic acid interventions.	No perceived costs
Consumers	<p>The microbiological safety and quality of processed food products has become of increasing importance. Increasing the choice of antimicrobial agents in food processing would be of benefit to consumers. Chlorine is currently the most commonly used antimicrobial agent in poultry processing. Certain chlorine by-products, such as chloramines, are considered undesirable by consumers.</p> <p>Alternatives to the use of chlorine may therefore be seen as a benefit.</p> <p>Hot water, also a common treatment, uses energy in the heating process that some consumers see as damaging to the environment. Hot water can also discolour the meat.</p> <p>Alternatives to hot water treatment may therefore be seen as a benefit</p>	Some consumers may see the use of any chemical as undesirable
Government	No perceived benefit	No perceived cost

1.4.4 Trade impact

The use of DBDMH can have a positive impact on trade if it contributes to the safety of meat and poultry products that are exported.

Currently, water is the only washing treatment that is accepted for meat that is exported to Europe. So DBDMH (or any of the already approved chemical treatments) would not be used in processing of meat destined for European markets. Poultry exports are minor and there is no concern with using chemical treatments in poultry plants.

There are increasing requirements for meat products imported to the US to have received interventions to increase food safety. The addition of DBDMH to the interventions available to processors exporting to the US will be of value.

1.4.5 Support for the application

Australia's food safety is high compared to some other countries but, in the interests of continuous improvement Australian Governments have agreed that food safety should be managed throughout the food supply chain i.e. paddock to plate. The aim is to focus on points in the food chain where hazards are introduced, rather than problem solving down the line (FSANZ, 2010).

The approach builds on Food Safety Standards that already apply mandatory hygiene requirements to manufacturing, retail and food services sectors

In 2002, the Australia and New Zealand Food Regulation Ministerial Council gave FSANZ responsibility to extend its standard-setting process to the primary production sector.

Primary production and processing standards have been developed for the seafood and dairy industry and are currently being assessed for the egg, poultry, meat and meat products industries.

Currently a combination of animal health, welfare, biosecurity and meat safety systems on farms, in abattoirs and at meat and poultry processing plants result in a high standard of safe supply. However, the standards are limited to ready-to-eat meat and poultry products and so FSANZ is looking at incorporating safety requirements for primary production and processing. They will also seek to identify any safety gaps in the supply chain and address those in the standard.

Businesses that process meat and poultry must control their food safety hazards. It is the responsibility of poultry processing businesses to comply with STANDARD 4.2.2 PRIMARY PRODUCTION AND PROCESSING STANDARD FOR POULTRY MEAT. (See Attachment 3. This standard only applies to Australia.)

FSANZ is also examining the meat supply chain with a view to including meat safety measures in the Australia New Zealand Food Standards Code.

Meat processors therefore have an interest in antimicrobial interventions. DAFF recognizes the halogens, including bromine as a major type of antimicrobial treatment available to the poultry production industry.

Producers and consumers in New Zealand, similar to Australia, have a strong interest in safe food, although there is not the same regulatory compulsion by way of existing and proposed primary production and processing standards.

2 Technical information

2.1 Type

The proposed use of DBDMH is as an antimicrobial processing aid applied to meat and poultry carcasses, parts, trim, organs, hides and heads. It is also added to water used in ice making systems for general use in the poultry processing industry.

The purpose of the application is to amend the Australian Food Standards Code, Standard 1.3.3 Processing Aids under Clause 12: Permitted bleaching agents, washing and peeling agents.

The proposal is that in the table to Clause 12 the current entry:

Bromo-chloro-dimethylhydantoin	All foods	1.0 (available chlorine) 1.0 (inorganic bromide) 2.0 (dimethylhydantoin)
--------------------------------	-----------	--

be amended to:

Halohydantoins: Bromochlorodimethylhydantoin and Dibromodimethylhydantoin	All foods	1.0 (available chlorine) 2.0 (inorganic bromide) 2.0 (dimethylhydantoin)
---	-----------	--

2.2 Identity

Dibromodimethylhydantoin (DBDMH)

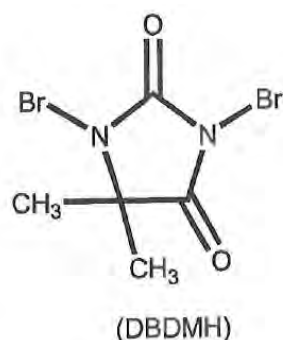
CAS name: 1,3-dibromo-5,5-dimethylhydantoin

IUPAC name: 1,3-dibromo-5,5-dimethylimidazolidine-2,4-dione

CAS Number: 77-48-5

Formula: C₅H₆Br₂N₂O₂

Dibromodimethylhydantoin is a halohydantoin. It consists of a central organic hydantoin ring moiety (dimethylhydantoin) to which halogen atoms (bromine) are attached at the 1 and 3 positions on the hydantoin ring.



The halohydantoins are a group of chemicals comprised of several halogenated compounds.

This group of chemicals includes the following: 1-Bromo-3-chloro-5,5-dimethylhydantoin, 1,3-Dibromo-5,5-dimethylhydantoin, 1,3-Dichloro-5,5-dimethylhydantoin, and 1,3 -Dichloro-5-ethyl-5-methylhydantoin. In addition, the Agency has determined that the 5,5-Dimethylhydantoin (DMH) and 5-Ethyl-5-methylhydantoin (EMH) metabolites of the halogenated hydantoins are appropriate test substances for assessing the toxicity of this group (EPA 2007).

The common names, chemical names, empirical formulas, and CAS numbers of the halohydantoins are presented in the following table.

Common Names, Chemical Names, Empirical Formulas, and CAS Numbers

Common Name	Chemical Name	Empirical Formula	CAS No.
Dichlorodimethylhydantoin	1,3-dichloro-5,5-dimethylhydantoin	$C_5H_6Cl_2N_2O_2$	118-52-5
Bromochlorodimethylhydantoin	1-Bromo-3-Chloro-Dimethylhydantoin	$C_5H_6BrClN_2O_2$	16079-88-2
Dichloroethylmethylhydantoin	1,3-dichloro-5-ethyl-5-methylhydantoin	$C_6H_8Cl_2N_2O_2$	89415-87-2
Dibromodimethylhydantoin	1,3-dibromo-5,5-dimethylhydantoin	$C_5H_6Br_2N_2O_2$	77-48-5
Bromochlorodimethylhydantoin	1-Bromo-3-chloro-5,5-dimethylhydantoin	$C_5H_6BrClN_2O_2$	32718-18-6

(EPA 2007).

2.3 Chemical and physical properties

Specifications

Appearance white to off-white nuggets
 Assay, wt %, min 98.0

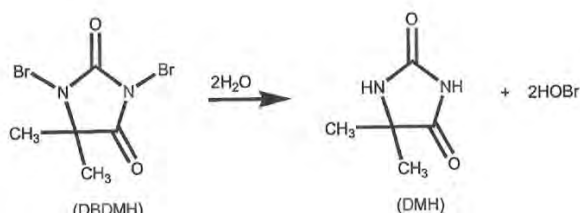
Typical Properties

Size range, approx..... 0.312" x 6 mesh
 Available Bromine, wt % 111
 pH (1% slurry in water) 6.6
 Packed bulk density (at ambient temperature), g/cm..... 1.36
 Melting/decomposition temperature, DSC, °C >190
 Solubility in water, wt %, 68 °F (20 °C)..... 0.1

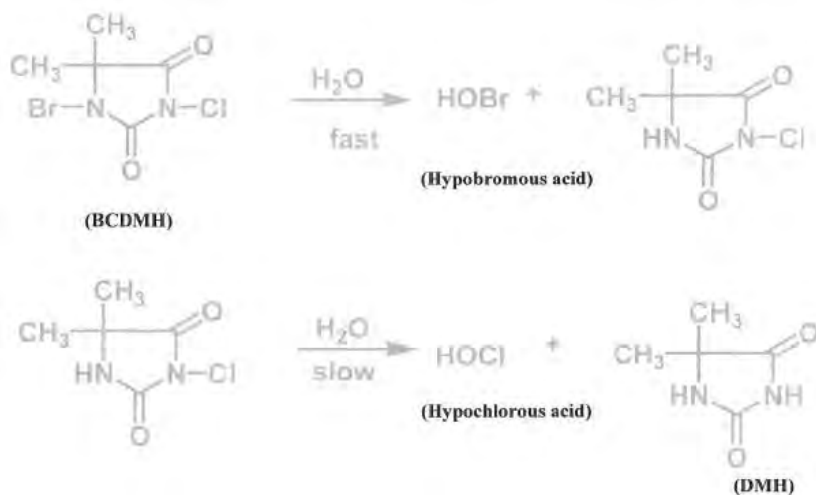
The shelf life of this product is at least two years at normal ambient conditions when properly stored in its original container (Albemarle 2007).

Hydrolysis

In the dry state halohydantoins are stable. Upon usage, which involves addition to water, they rapidly hydrolyze and form hypochlorous and/or hypobromous acid, which are the actual antimicrobial agents. The solution also contains the halogen carrier hydantoin ring, dimethylhydantoin (DMH) and, for certain products, ethylmethylhydantoin (EMH).



Overall each molecule of DBDMH yields 2 molecules of HOBr and 1 molecule of DMH (FAO/WHO 2008).



Overall each molecule of BCDMH yields 1 molecule of hypobromous acid, 1 molecule of hypochlorous acid and 1 molecule of DMH (ANZFA, 2000).

2.4 Manufacturing process

Solid dimethylhydantoin (DMH) is dissolved in water and sodium hydroxide. Bromine is then added to the solution. In this process an excess of bromine is used to ensure that both the 1 and 3 positions on the hydantoin ring are brominated. The wet product is transferred to a drier where it is dried to a powder at low temperature. The powder may then be tableted or granulated.

2.5 Specification for identity and purity

There are no known allergens present in DBDMH

There is no specification for DBDMH in any of the published sources identified in Standard 1.3.4

- DBDMH has an AICS Listing
- ERMA approval code: HSR004136
- DBDMH is one of the isomeric constituents in the APVMA active constituent standard for the equilibrium mix, BCDMH
- DBDMH is listed in Attachment 10 for United States FSIS Directive 7120.1. Attachment 10 identifies the substances that have been approved in 21 Code of Federal Regulations (CFR) for use in meat and poultry products as food additives, approved in generally recognized as

safe (GRAS) notices and approved through pre-market notifications, and approved in letters conveying acceptability determinations (FSIS 2010).

There is a specification for BCDMH in Standard 1.3.4. BCDMH and DBDMH are two of the common forms of halohydantoin

It is proposed that the specification for Bromochlorodimethylhydantoin (BCDMH) be amended to include DBDMH. The following specification is proposed.

Specifications for the halohydantoin

Bromochlorodimethylhydantoin and Dibromodimethylhydantoin

Bromochlorodimethylhydantoin (CAS Number: 126-06-7)

Formula: $C_5H_6BrClN_2O_2$

Dibromodimethylhydantoin (CAS Number 77-48-5)

Formula: $C_5H_6Br_2N_2O_2$

Structurally, the halohydantoin consist of a central organic hydantoin ring moiety, dimethylhydantoin to which halogen atoms (bromine and/or chlorine) can be attached at both the 1 and 3 positions on the hydantoin ring.

Bromochlorodimethylhydantoin and dibromodimethylhydantoin are > 90% pure

Form: Solid or free-flowing, off white granules, tablets

In the dry state halohydantoin are stable. Upon usage, which involves addition to water, the halohydantoin rapidly hydrolyze and form hypochlorous and/or hypobromous acid, which are the actual antimicrobial agents. The solution also contains the halogen carrier hydantoin ring, dimethylhydantoin (DMH).

3 Safety

3.1 Industrial uses

The halohydantoin are used for microbial control in water and water systems. They are used as disinfectants in commercial and residential swimming pools, spas and hot tubs; as sanitizers for treatment of toilet bowl water in homes; and for controlling bacterial and fungal contamination in a variety of industrial water systems (DAFF, 2009).

DBDMH is listed as an industrial chemical on AICS in Australia and is approved by ERMA (HSR004136).

3.2 Overseas use

Halohydantoin are used around the world as antimicrobials. The DBDMH products that are proposed to be introduced by Elanco (AviBrom and BoviBrom) are approved for use in the United States. An application has been made in Canada and various other introductions are planned around the world.

The US approvals for DBDMH are as follows:

Beef Approvals:

FCN 792 – FDA (Food Contact Substance Notification) – March, 2008. Approved for use as an antimicrobial in water applied to beef hides, carcasses, heads, trim, parts, and organs.

No environmental impact statement necessary based on Agency findings.

Poultry Approvals:

FCN 334 – FDA – August, 2003. Chill tank

FCN 357 – FDA – November, 2003. Inside-Outside Bird Washer

FCN 453 – FDA – November 2004. Process water including pre-chill wash system, drag through dip tank, process water anywhere in the plant except scalders

FCN 775 – FDA – December 2007. Water supplied to ice machines to make ice intended for general use in the poultry processing industry

Water Reuse Approval – USDA – June, 2005

Approval for reuse of water within systems allowing water conservation and recycling

Approval for use in poultry for export to Canada and Mexico

The US labels for Elanco-distributed DBDMH products used in beef and poultry are included as Attachment 1 to this submission. The proposed Australian products will have similar labels and equivalent use patterns.

Halohydrantoin is also used as a slimicide in the manufacture of food-contact paper and paperboard. The FDA regulation that permits the halohydrantoin to be used as a slimicide in the manufacture of food-contact paper and paperboard is in 21 C.F.R. Part 176.300 (EPA, 2007).

For Pulp & Paper with food contact, 5 to 25 ppm of halohydrantoin with 1 to 5 ppm of halogen is used at a typical rate of 0.08 to 1.0 kg per tonne of paper. A PLS/PS feeder or PU is used to dispense product in briquette, granular, powder, tablet and gel form (EPA, 2007).

XtraBrom 111 biocide is a free-flowing, bromine-based nugget product. It is used to control the growth of microorganisms in industrial water systems. The active ingredient is 1,3-dibromo-5,5-dimethylhydantoin (DBDMH), providing approximately 111% available bromine. This product is registered with the US EPA for use as a fungicide, algicide, slimicide and microbiocide.

3.3 Metabolism

DBDMH hydrolyzes rapidly upon addition to water to release hypobromous acid, which functions as the active antimicrobial agent. This reaction also yields 5,5-dimethylhydantoin (DMH) as an inactive by-product. The hypobromous acid is ultimately converted to inorganic bromide (Br⁻) ion, after reacting with the microorganisms.

BCDMH similarly produces hypobromous acid upon addition to water. It also produces hypochlorous acid in water. The main stable degradation product in water is 5,5-dimethylhydantoin (DMH) with bromide and chlorine produced at the same time.



3.4 Toxicity

The U.S. Environmental Protection Agency regulates the use of BCDMH and DBDMH as antimicrobial pesticides. These materials are registered for use as industrial water treatment products and recreational water treatment products. With other similar chemistries, EPA grouped them together under the "halohydantoins". Much of the data supporting these products was submitted on the DMH molecule, as this is the persistent component of the halohydantoins. EPA has recently issued a draft Reregistration Eligibility Decision for Halohydantoins. In that document they state: Structurally, the halohydantoins consist of a central organic hydantoin ring moiety (either dimethylhydantoin or ethylmethylhydantoin) to which halogen atoms (bromine and/or chlorine) can be attached at both the 1 and 3 positions on the hydantoin ring.

In solid form, the halohydantoins are very stable. Upon usage, which involves addition to water or a water system, the halohydantoins rapidly hydrolyze and form hypochlorous and/or hypobromous acid, which are the actual antimicrobial agents. The solution also contains the halogen carrier hydantoin ring, dimethylhydantoin (DMH) and, for certain products, ethylmethylhydantoin (EMH). Accordingly, the halohydantoins are essentially delivery systems for hypochlorous and hypobromous acid.

The toxicity data for halohydantoins do not suggest any substantive toxicological concern with regard to the use of DBDMH as proposed here, particularly in light of the fact that DBDMH will not be present as a residue on meat or poultry carcasses, parts and organs.

DBDMH has a similar toxicity profile to the other halohydantoins, including BCDMH, which is already included in the Code. Therefore detailed consideration of the toxicity of DBDMH is not required. Summary information for DBDMH follows.

DBDMH Toxicity Summary (Albemarle, 2009)

Acute Oral - Defined LD50 (Guideline OPPTS 870.1100): The acute oral defined LD50 of XtraBrom 111 biocide is 448 mg/kg of body weight.

DBDMH was administered by single gavage of a water or carboxymethylcellulose suspension to Sprague-Dawley rats (5 male, 5 female) at dose levels of 250, 500, 1000, and 5000 mg/kg. No deaths or abnormal signs occurred in the 250 mg/kg group. Two animals in the 500 mg/kg group died on days 7 and 13 respectively. All animals in the 1000 mg/kg group and all but two of the 5,000 mg/kg group died in the first day. The two remaining 5000 mg/kg animals survived to study end on day 17, but showed either weight loss or signs of hypoactivity.

Acute Dermal - Limit Test (Guideline OPPTS 870.1200): The single dose acute dermal LD50 of DBDMH is greater than 2000 mg/kg of body weight when applied to the skin of Sprague-Dawley rats as a moistened powder. The product was applied to the skin of 5 male and 5 female rats for 24 hours. All animals survived and gained weight during the 14-day observation period. Other than dermal irritation (erythema and edema and/or eschar) there were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior. No gross abnormalities were noted for the animals necropsied at the conclusion of the 14-day observation period.

Primary Skin Irritation - (Guideline OPPTS 870.2500): DBDMH is classified as corrosive to the skin, due to evidence of corrosion to the skin of one of three New Zealand albino rabbits following a 4-hour exposure to moistened powder. Dermal irritation was evaluated by the method of Draize, et al. Because corrosivity had been anticipated, one animal was tested initially, and the other two started only after the first animal did not show corrosion. The first animal showed well-defined erythema

and edema, which decreased from 48 hours to Day 10 of the test. The second and third animals were terminated at the 72-hour observation when the third animal showed severe erythema, edema, eschar and evidence of corrosion. The second animal showed no irritation by 24 hours after exposure. The Primary Dermal Irritation Index (PDII) calculated for this test substance was 4.3.

Dermal Sensitization - Buehler Method (Guideline OPPTS 870.2600): DBDMH is not considered to be a contact sensitizer.

DBDMH (0.75% w/w suspended in distilled water) was applied topically to young adult Hartley albino guinea pigs (20 male, 20 female) once weekly over a three-week induction period. Twenty-seven days after the first induction dose, a challenge dose of the highest nonirritating concentration (0.5% w/w solution in distilled water) was applied to a naive site, and scoring for erythema was made 24 and 48 hours after dosing. A naive control group (ten animals) was treated with the test article at challenge only. No animals had an erythema score of greater than 0.5 at the 24- or 48- hour reading in the test group or naive control group at challenge. Historical response to the positive control substance 1-chloro-2,4-dinitrobenzene (DNCB) showed that the animals were capable of showing sensitization.

The proposed use of DBDMH as an antimicrobial treatment in water and ice and given that it rapidly hydrolyzes in water to hypobromous acid and dimethylhydantoin (DMH), it is not expected to be present on food at the time of consumption. Therefore, there is no direct dietary exposure to DBDMH.

The toxicity of DMH and bromide have already been considered by FSANZ for the inclusion of BCDMH in the Code. No new data is available.

Summary data on the toxicity of halohydantoins follows

In acute toxicity studies the halohydantoins were shown to be of low toxicity by the oral and dermal routes of exposure. Acute toxicity by the inhalation route is more significant (Toxicity category II). The halohydantoins are significant eye and skin irritants (Toxicity category I and II, respectively). Mixed dermal sensitization has also been observed for some of the halohydantoin compounds (EPA, 2007).

Acute Toxicity of Halohydrantoin

Guideline No./ Study Type	MRID No. (TRID No.)	Results	Toxicity Category
5,5-Dimethylhydrantoin			
870.1100 Acute oral (gastric intubation) toxicity (limit test)-Mouse	45738401	LD ₅₀ (combined) > 5,000 mg/kg	IV
1-Bromo-3-chloro-5,5-dimethylhydrantoin			
870.1100 Acute oral toxicity-Rat	93074006, 00128244 (4226-010-01)	LD ₅₀ (males) = 1,350 mg/kg LD ₅₀ (females) = 1,520 mg/kg LD ₅₀ (combined) = 1,390 mg/kg	III
870.1100 Acute oral toxicity-Rat	93077008, 00147325 (4600-950-21)	LD ₅₀ (males) = 1,037 mg/kg LD ₅₀ (females) = 860 mg/kg LD ₅₀ (combined) = 929 mg/kg	III
870.1300 Acute inhalation toxicity-Rat	43654101	LC ₅₀ (males) = 0.157 mg/L LC ₅₀ (females) = 0.213 mg/L LC ₅₀ (combined) = 0.168 mg/L	II
870.2500 Acute dermal irritation-Rabbit	93074011, 93075014, 00128242 (4225-014-10)	severe skin irritant	I
870.2500 Acute dermal irritation-Rabbit	93077009, 00147326 (4600-950-22)	severe skin irritant	I
870.2600 Skin sensitization-Guinea pig	41670001	positive sensitizer	N/A
1,3-Dibromo-5,5-dimethylhydrantoin			
870.1100 Acute oral toxicity-Rat	93076011, 00137105 (4334-012-01)	LD ₅₀ = 760 mg/kg	III
870.1100 Acute oral toxicity-Rat	44988002,)	combined LD ₅₀ = 448 mg/kg	II
870.1200 Acute dermal toxicity-Rabbit	93076025, 00137110 (4334-012-07)	LD ₅₀ cannot be ascertained (study is classified as Unacceptable/non-guideline)	--
870.1200 Acute dermal toxicity-Rat	44988001	LD ₅₀ > 2000 mg/kg	III
870.1300 Acute inhalation toxicity-Rabbit	44988003	LC ₅₀ between 0.51-2.02 mg/L	II

Halohydantoins RED

Guideline No./ Study Type	MRID No. (TRID No.)	Results	Toxicity Category
870.2500 Primary dermal irritation-Rabbit	93076017, 00137109 (4334-012-05)	severe skin irritant	I
870.2500 Primary dermal irritation-Rabbit	44988004	corrosive	I
870.2600 Dermal Sensitization - guinea pig	44988005	non-sensitizer	N/A
1,3-Dichloro-5,5-dimethylhydantoin			
870.1200 Acute dermal toxicity-Rabbit	93076013, 00084176 (2402-448-05)	LD ₅₀ > 20,000 mg/kg	IV
870.2500 Acute dermal irritation-Rabbit	93076017, 00137109 (2402-448-01)	severe skin irritant	I

(EPA, 2007)

FIFRA Table of Toxicity Categories by Hazard Indicator.

Hazard Indicator	I	II	III	IV
Oral LD 50	Up to and including 50 mg/kg	From 50 through 500 mg/kg	From 500 through 5000 mg/kg	Greater than 5000 mg/kg
Inhalation LC 50	Up to and including .2 mg/liter	From .2 through 2 mg/liter	From 2 through 20 mg/liter	Greater than 20 mg/liter
Dermal LD 50	Up to and including 200 mg/kg	From 200 through 2000 mg/kg	From 2000 through 20,000 mg/kg	Greater than 20,000 mg/kg
Eye Effects	Corrosive, corneal opacity not reversible within 7 days	Corneal opacity reversible in 7 days; irritation persisting for 7 days	No corneal opacity; irritation reversible	No irritation
Skin Effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours

3.5 International agency reports

The US EPA RED Decision for Halohydantoins is included at Attachment 7

The joint FAO/WHO Expert Meeting report on the benefits and risks of the use of disinfectants in food processing is included as Attachment 8

The FSIS list of safe ingredients is included as Attachment 10

4 Dietary exposure

4.1 Food groups likely to contain the processing aid and metabolites

The halohydantoin BCDMH, already in the standard, is for use as a processing aid (washing agent) for use in the post-harvest washing of fruits and vegetables and in the manufacture of minimally processed fruits and vegetables. The use of BCDMH is to sanitise the wash waters used and to reduce the microbial load on the produce being treated.

The proposed additional halohydantoin DBDMH, is for use as a processing aid (washing agent) for use as an antimicrobial in water and ice used in the processing of meat and meat products (including poultry and game).

As DBDMH hydrolyzes in water, it is not expected to be present on food at the time of consumption. However, its breakdown product, DMH, would be an expected residue on foods that are not washed or further processed before consumption. In addition, other DBPs, such as organobromine DBPs, bromide and bromate, would also be potential residues on food treated with aqueous solutions of DBDMH (FAO/WHO, 2008).

Food groups likely to contain BCDMH or DBDMH

- None

Food groups likely to contain the metabolites of BCDMH or DBDMH

- Fruits and vegetables
- Meat and meat products (including poultry and game)

4.2 Residues

DBDMH and BCDMH hydrolyze in water to produce hypobromous and (for BCDMH) hypochlorous acids, which would lead to the formation of halides on the treated product and dimethylhydantoin (DMH), with DMH being the major residue.

Addition of BCDMH to the code included the listing of residue limits of 2.0 mg/kg (dimethylhydantoin), 1.0 mg/kg (available chlorine) and 1.0 mg/kg (inorganic bromide) are beside BCDMH in Table II, Group II of Standard A16.

The residues of DBDMH and its metabolites are considered in the publicly available document, *Benefits and risks of the use of chlorine containing disinfectants in food production and food processing*. (Report of a Joint FAO/WHO Expert Meeting. Ann Arbor, MI, USA, 27030 May 2008. See Attachment 8.) The calculations and residue conclusions discussed in the following section are based on similar assumptions. However it should be noted that the calculations in FAO/WHO (2008) use the high levels of 8% water absorption in poultry and 1% in beef. Values of 4% and 0.5% respectively are used in the calculations in the following sections for the Australian situation, based on the industry standards in this country.

4.2.1 DMH

Poultry

The residue of DMH may be calculated by assuming that the poultry carcass will absorb this compound in a proportional amount to the amount of water taken up in the chill tank. The

industry standard for water uptake in poultry in Australia is 4%. Assuming the density of the poultry is roughly equivalent to that of the chiller water, the concentration of DMH in the chilled carcass may be estimated as 4 % of the carcass weight multiplied by the DMH concentration in the chilled water.

It is estimated that the maximum DBDMH addition level that might ever be needed in the chiller water would be 90 ppm i.e. that needed to provide an active bromine level of 100 ppm. The corresponding level of the DMH by product in the chiller water is 40 ppm. On this basis the maximum migration of DMH to the poultry is calculated as $40 \text{ ppm} \times 4\% = 1.6 \text{ ppm}$.

Beef

The theoretical maximum levels of DMH produced from the use of 270 ppm DBDMH is 121 ppm. Using a worst-case moisture uptake of 0.5%, the maximum residue level theoretically in beef is $121 \text{ ppm} \times 0.005 = 0.61 \text{ ppm}$

4.2.2 Bromide

Poultry

Similar calculations may be carried out for the remaining by-products of DBDMH. The active antimicrobial agent, hypobromous acid, is not expected to be present as such as a residue on the poultry carcass. Rather, as discussed previously, the hypobromous acid will be converted to bromide ion in the disinfection process. Analysis for the ultimate by-product, bromide ion, were not conducted. Therefore, as a worst-case, it is assumed that all of the bromine originally added ultimately may be present in the chiller water as bromide ion. The maximum actual amount of bromine added will amount to 50 ppm. Thus the worst-case uptake of bromide by the poultry will be $4\% \times 50 \text{ ppm} = 2 \text{ ppm}$.

Beef

The theoretical maximum levels of bromide ion produced from the use of 270 ppm DBDMH is 155.2 ppm. Using a worst-case moisture uptake of 1%, the maximum residue level theoretically in beef is $155.2 \text{ ppm} \times 0.01 = 0.75 \text{ ppm}$

4.2.3 Trichloromethanes

Poultry

Chloroform is not expected to be present in the poultry or poultry processing water or ice above levels normally observed in potable water produced using accepted disinfection processes. However, the US FDA estimated a bromoform concentration of approximately $0.005 \text{ } \mu\text{g/g}$ raw chicken and dibromochloromethane (DBCM) or bromodichloromethane (BDCM) concentrations of less than $0.0004 \text{ } \mu\text{g/g}$ raw chicken. For DBCM and BDCM the residues values are data from the USFDA indicating that DBCM and BDCM were not detected in the poultry process water above the LOD of $5 \text{ } \mu\text{g/l}$ (FAO/WHO, 2008).

Beef

Chloroform is also not expected to be present in the beef or beef processing water above levels normally observed in potable water produced using accepted disinfection processes. However, the average concentration of bromoform found in the spray used to treat beef was $5.5 \text{ } \mu\text{g/kg}$.

The above assumptions give a residual bromoform level of 0.00006 µg/g beef. The presence of DBCM and BDCM on beef is related to the method used to generate the potable water used in the beef processing water and to the use of DBDMH. Data from the US FDA (2008b) indicate that these compounds were not detected in the process water above the LOD of 5 µg/kg. Using the assumptions above and the LOD, the concentration of either DBCM or BDCM would be less than 0.00005 µg/g raw beef (FAO/WHO, 2008).

4.2.4 Discussion

In Standard 1.3.3 Processing Aids Clause 12, the Code includes maximum permitted levels listed against BCDMH of:

- 1.0 ppm (available chlorine)
- 1.0 ppm (inorganic bromide)
- 2.0 ppm (dimethylhydantoin)

Based on the calculations presented for DBDMH maximum permitted levels appropriate for the proposed use are:

- 2.0 ppm (inorganic bromide)
- 2.0 ppm (dimethylhydantoin)

It is most likely that the calculations lead to a considerable over-estimation of residues in food. However, there is no actual residue data available for the proposed use.

It is proposed that the entry in the code should therefore be amended to:

Halohydantoins: Bromochlorodimethylhydantoin and Dibromodimethylhydantoin	All foods	1.0 (available chlorine) 2.0 (inorganic bromide) 2.0 (dimethylhydantoin)
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4.3 Market

DBDMH has been available in the US for several years. Antimicrobial interventions are used in most meat processing facilities. For beef the intervention is currently, often only a hot water spray. In poultry processing, chlorine is the most common intervention. It is expected that the use of antimicrobial interventions will increase, as there is an increased government and industry focus on multiple interventions along the food supply chain to improve food safety.

It is expected that DBDMH will reach a peak of 20% of the Australian market for antimicrobials with the proposed use patterns.

4.4 Residues in foods in other countries

Note that bromochlorodimethylhydantoin, as a biocide for fruits, vegetables and ornamentals is in Table 5 of the Australian MRL Standard.

Overseas MRLs for bromide are included as Attachment 2.

No CODEX or overseas maximum residue levels (MRLs) have been established for halohydantoins.

5 Attachments

	Attachment	Page	Volume
US labels for DBDMH products used in beef and poultry	1	26	1
Bromide MRL lists	2	29	1
STANDARD FOR POULTRY MEAT. Food Standards Australia New Zealand.	3	37	1
Albermarle (2009). 1,3-Dibromo-5,5-Dimethylhydantoin (DBDMH). Information sheets	4	46	1
ANZFA (2000). Full Assessment Report And Regulatory Impact Statement, Application A393, Bromo-Chloro-Dimethylhydantoin (BCDMH) As A Processing Aid	5	63	1
DAFF (2009). National Water Biosecurity Manual, Poultry Production. Department of Agriculture Fisheries & Forestry, August 2009	6	89	1
EPA (2007). Reregistration Eligibility Decision for Halohydantoins (Case 3055). United States Environmental Protection Agency. EPA 739-R-07-001	7	126	1
FAO/WHO (2008). Benefits and Risks of the Use of Chlorine-containing Disinfectants in Food Production and Food Processing. Report of a Joint FAO/WHO Expert Meeting. MI, USA, 27–30 May 2008	8	283	2
FSANZ (2010). FINAL ASSESSMENT REPORT PROPOSAL P282 PRIMARY PRODUCTION & PROCESSING	9	572	3
FSIS (2010). FSIS Directive 5120. 1. Safe and Suitable ingredients used in the production of meat, poultry and egg products. USDA, April 12 2010	10	671	3
Kalchayanand N <i>et al.</i> (2009). Reduction of <i>Escherichia coli</i> O157:H7- and <i>Salmonella</i> -Inoculated Fresh Meat. Journal of Food Protection, Vol 72, No. 1, 2009, Pages 151-156	11	713	3

Attachment 1



(1,3-dibromo-5,5-dimethylhydantoin)

**A poultry carcass antimicrobial
for pathogen reduction.**

**KEEP OUT OF REACH OF CHILDREN
DANGER**

SAFETY

Causes irreversible eye damage and skin burns. Do not get in eyes, on skin or on clothing. Wear chemical goggles or safety glasses, protective clothing and rubber gloves. May be fatal if swallowed. Wash thoroughly with soap and water after handling and before eating, drinking or using tobacco. Harmful if absorbed through skin. Harmful if inhaled. Avoid breathing dust. Remove contaminated clothing and wash clothing separately before reuse. Consult MSDS and follow directions.

PHYSICAL AND CHEMICAL HAZARDS

AviBrom™ is a strong oxidizing and brominating agent. Do not mix with other chemicals. Mix only with water. Do not add this product to any dispensing device containing remnants of another product. Such use may lead to a violent reaction leading to fire or explosion. Avoid contact with aldehydes, strong reducing agents, acids and ammonia-containing products.

STORAGE AND DISPOSAL

Keep this product dry in original tightly closed container when not in use. Store in a cool, dry, well-ventilated area away from heat and flame.

Sweep or shovel spills into appropriate container for disposal. Material that can't be used according to label directions should be disposed of in a properly permitted industrial landfill. Do not reuse container. Rinse thoroughly before discarding in trash.

Distributed by:



2001 West Main Street • P.O. Box 708 • Greenfield, IN 46140
(800) 428-4441 • www.ElancoFoodSolutions.com

FIRST AID

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

IF SWALLOWED: Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a poison control center or doctor. Do not give anything by mouth to an unconscious person.

IF INHALED: Move person to fresh air. If person is not breathing, call 9-1-1 or ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

FOR INDUSTRIAL USE ONLY

DIRECTIONS FOR USE

This product should only be used in applications and in a manner specified on the label.

This product is an effective antimicrobial poultry carcass wash when used in **chill tanks, scalders, plant process water or inside-outside bird washers.**

This product must be dissolved in water in an appropriate feeder before being used in any application.

Water containing a maximum of 100 ppm available (total) bromine may be reused on raw poultry product at its point of origin or upstream from its point of origin in the process and must be in compliance with 9 CFR 416.2(g).

The concentration of this product should never exceed 100 ppm available (total) bromine in the water supply line feeding either the chill tank, the inside-outside bird washer (IOBW), scalding or in the plant process water. Product should be fed to chill tank, IOBW, scalding or plant process water to maintain the desired residual. Bromine levels should be monitored periodically during the day using a suitable bromine test kit.

FDA- and USDA-reviewed and -accepted for use as a poultry carcass antimicrobial for pathogen reduction.

AviBrom is a trademark of Albemarle.
Elanco® and the diagonal bar are trademarks of Eli Lilly and Company.
Manufactured for Elanco by Albemarle.

Manufactured by:

 **ALBEMARLE®**

451 Florida Street • Baton Rouge, LA 70801

AH0560
01 83 41 00



(1,3-dibromo-5,5-dimethylhydantoin)

**A post-harvest antimicrobial for
pathogen reduction on beef hides,
carcasses, heads and organs.**

**KEEP OUT OF REACH OF CHILDREN
DANGER**

FIRST AID

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

IF SWALLOWED: Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a poison control center or doctor. Do not give anything by mouth to an unconscious person.

IF INHALED: Move person to fresh air. If person is not breathing, call 9-1-1 or ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

SAFETY

Causes irreversible eye damage and skin burns. Do not get in eyes, on skin or on clothing. Wear chemical goggles or safety glasses, protective clothing and rubber gloves. May be fatal if swallowed. Wash thoroughly with soap and water after handling and before eating, drinking or using tobacco. Harmful if absorbed through skin. Harmful if inhaled. Avoid breathing dust. Remove contaminated clothing and wash clothing separately before reuse. Consult MSDS and follow directions.

PHYSICAL AND CHEMICAL HAZARDS

BoviBrom is a strong oxidizing and brominating agent. Do not mix with other chemicals. Mix only with water. Do not add this product to any dispensing device containing remnants of another product. Such use may lead to a violent reaction leading to fire or explosion. Avoid contact with aldehydes, strong reducing agents, acids and ammonia-containing products.

STORAGE AND DISPOSAL

Keep this product dry in original tightly closed container when not in use. Store in a cool, dry, well-ventilated area away from heat and flame.

Sweep or shovel spills into appropriate container for disposal. Material that can't be used according to label directions should be disposed of in a properly permitted industrial landfill. Do not reuse container. Rinse thoroughly before discarding in trash.

Distributed by:



2001 West Main Street • P.O. Box 708 • Greenfield, IN 46140
(800) 428-4441 • www.ElancoFoodSolutions.com

FOR INDUSTRIAL USE ONLY

DIRECTIONS FOR USE

This product should only be used in applications and in a manner specified on the label.

This product is an effective post-harvest antimicrobial wash when applied to beef hides, carcasses, heads and organs.

This product must be dissolved in water in an approved feeder before being used in any application.

The concentration of this product should never exceed 300 ppm available (total) bromine in the water being directly applied to beef products.

Water containing a maximum of 300 ppm available (total) bromine may be reused on raw beef product at its point of origin or upstream from its point of origin in the process and must be in compliance with 9 CFR 416.2 (g).

Total bromine levels should be monitored periodically during the day using a suitable bromine test kit to ensure desired residuals are maintained.

BoviBrom is a trademark of Albemarle.
Elanco® and the diagonal bar are trademarks of Eli Lilly and Company.
Manufactured for Elanco by Albemarle.

Manufactured by:

 **ALBEMARLE®**

451 Florida Street • Baton Rouge, LA 70801

Attachment 2

NZ

Methyl Bromide 74-83-9 Considered as inorganic bromide
and calculated as total bromide

Nuts200

Spices400

Any other food50

EU

Pesticide residues and maximum residue levels (mg/kg)

(*) Indicates lower limit of analytical determination

Pesticides - Web Version - EU MRLs (File created on 12/04/2010 14:13)		
Code number	Groups and examples of individual products to which the MRLs apply (a)	Bromide ion
1000000	10. PRODUCTS OF ANIMAL ORIGIN- TERRESTRIAL ANIMALS	0,05*
1010000	(i) Meat, preparations of meat, offals, blood, animal fats fresh chilled or frozen, salted, in brine, dried or smoked or processed as flours or meals other processed products such as sausages and food preparations based on these	0,05*
1011000	(a) Swine	0,05*
1011010	Meat	0,05*
1011020	Fat free of lean meat	0,05*
1011030	Liver	0,05*
1011040	Kidney	0,05*
1011050	Edible offal	0,05*
1011990	Others	0,05*
1012000	(b) Bovine	0,05*
1012010	Meat	0,05*
1012020	Fat	0,05*
1012030	Liver	0,05*
1012040	Kidney	0,05*
1012050	Edible offal	0,05*
1012990	Others	0,05*
1013000	(c) Sheep	0,05*
1013010	Meat	0,05*
1013020	Fat	0,05*
1013030	Liver	0,05*
1013040	Kidney	0,05*

1013050	Edible offal	0,05*
1013990	Others	0,05*
1014000	(d) Goat	0,05*
1014010	Meat	0,05*
1014020	Fat	0,05*
1014030	Liver	0,05*
1014040	Kidney	0,05*
1014050	Edible offal	0,05*
1014990	Others	0,05*
1015000	(e) Horses, asses, mules or hinnies	0,05*
1015010	Meat	0,05*
1015020	Fat	0,05*
1015030	Liver	0,05*
1015040	Kidney	0,05*
1015050	Edible offal	0,05*
1015990	Others	0,05*
1016000	(f) Poultry -chicken, geese, duck, turkey and Guinea fowl-, ostrich, pigeon	0,05*
1016010	Meat	0,05*
1016020	Fat	0,05*
1016030	Liver	0,05*
1016040	Kidney	0,05*
1016050	Edible offal	0,05*
1016990	Others	0,05*

Japan

Table of MRLs for Agricultural Chemicals

Agricultural Chemical : BROMIDE

Note : Bromine refers to inorganic bromine.

Food	MRLs(ppm)	Note	MRLs(ppm) Time limit for application
Rice (brown rice)	50		
Wheat	50		
Barley	50		
Rye	50		
Corn (maize, including pop	80		

corn and sweet corn)			
Buckwheat	180		
Other cereal grains	50		
Soybeans, dried	200		
Beans, dried	200		
Peas	50		
Broad beans	200		
Peanuts, dried	200		
Other legumes/pulses	200		
Potato	60		
Taro	50		
Sweet potato	60		
Yam	50		
Konjac	50		
Other Potatoes	40		
Sugar beet	40		
Sugarcane	50		
Japanese radish, roots (including radish)	200		
Japanese radish, leaves (including radish)	50		
Turnip, roots (including rutabaga)	200		
Turnip, leaves (including rutabaga)	1000		
Horseradish	40		
Watercress	50		
Chinese cabbage	50		
Cabbage	100		
Brussels sprouts	100		
Kale	50		
KOMATSUNA (Japanese mustard spinach)	50		
KYONA	50		
Qing-geng-cai	50		
Cauliflower	100		
Broccoli	110		
Other cruciferous vegetables	50		
Burdock	50		
Salsify	40		

Artichoke	50		
Chicory	50		
Endive	50		
SHUNGIKU	50		
Lettuce (including cos lettuce and leaf lettuce)	100		
Other composite vegetables	400		
Onion	50		
Welsh (including leek)	50		
Garlic	50		
NIRA	50		
Asparagus	100		
Multiplying onion (including shallot)	50		
Other liliaceous vegetables	50		
Carrot	40		
Parsnip	40		
Parsley	50		
Celery	300		
MITSUBA	50		
Other umbelliferous vegetables	50		
Tomato	75		
Pimento (sweet pepper)	150		
Egg plant	40		
Other solanaceous vegetables	150		
Cucumber (including gherkin)	150		
Pumpkin (including squash)	200		
Orinetal pickling melon (vegetable)	50		
Water melon	100		
Melons	230		
MAKUWAURI melon	50		
Other cucurbitaceous vegetables	50		
Spinach	50		
Bamboo shoots	50		
Okra	200		
Ginger	400		
Peas, immature (with pods)	50		
kidney beans, immature (with	50		

pods)			
Green soybeans	110		
Button mushroom	50		
SHIITAKE mushroom	50		
Other mushrooms	50		
Other vegetables	500		
UNSHU orange, pulp	30		
Citrus NATSUDAIDAI, whole	30		
Lemon	30		
Orange (including navel orange)	30		
Grapefruit	30		
Lime	30		
Other citrus fruits	30		
Apple	20		
Japanese pear	20		
Pear	20		
Quince	20		
Loquat	20		
Peach	20		
Nectarine	20		
Apricot	20		
Japanese plum (including prune)	20		
Mume plum	20		
Cherry	20		
Strawberry	30		
Raspberry	20		
Blackberry	20		
Blueberry	20		
Cranberry	20		
Huckleberry	20		
Other berries	20		
Grape	20		
Japanese persimmon	20		
Banana	20		
Kiwifruit	30		
Papaya	20		
Avocado	75		
Pineapple	20		

Guava	20		
Mango	20		
Passion fruit	20		
Date	20		
Other Fruits	60		
Sunflower seeds	50		
Sesam seeds	110		
Safflower seeds	50		
Cotton seeds	130		
Rapeseeds	50		
Other oil seeds	400		
Ginkgo nut	200		
Chestnut	200		
Pecan	200		
Almond	200		
Walnut	200		
Other nuts	200		
Tea	50		
Coffee beans	60		
Cacao beans	50		
Hop	400		
Other spices	500		
Other herbs	500		
Cattle, muscle	50		
Pig, muscle	50		
Other terrestrial mammals, muscle	50		
Cattle, fat	50		
Pig, fat	50		
Other terrestrial mammals, fat	50		
Cattle, liver	50		
Pig, liver	50		
Other terrestrial mammals, liver	50		
Cattle, kidney	50		
Pig, kidney	50		
Other terrestrial mammals, kidney	50		
Cattle, edible offal	50		
Pig, edible offal	50		
Other terrestrial mammals,	50		

edible offal			
Milk	50		
Chicken, muscle	50		
Other poultry, muscle	50		
Chicken, fat	50		
Other poultry, fat	50		
Chicken, liver	50		
Other poultry, liver	50		
Chicken, kidney	50		
Other poultry, kidney	50		
Chicken, edible offal	50		
Other poultry, edible offal	50		
Chicken eggs	50		
Other poultry, eggs	50		
Salmoniformes (such as salmon and trout)	50		
Anguilliformes (such as eel)	50		
Perciformes (such as bonito, horse mackerel, mackerel, sea bass, sea bream and tuna)	50		
Other fish	50		
Shelled molluscs	50		
Crustaceans	50		
Other aquatic animals	50		
Honey (including royal-jelly)	50		
Wheat flour (limited to whole grain)	50		
Peach, dried	50		
Plum, dried	20		
Fig, dried	250		
Raisin	100		
Date, dried	100		
Fruits, dried	30	except peach, plum, grape, date and fig	
Other herbs, dried	400		

Attachment 3

STANDARD 4.2.2

PRIMARY PRODUCTION AND PROCESSING STANDARD FOR POULTRY MEAT

To commence on 20 May 2012

(Australia only)

Purpose and commentary

This Standard sets out a number of food safety requirements for the primary production and processing of poultry, and poultry carcasses and poultry meat for human consumption. At the primary production stage, businesses that produce poultry must implement measures to control the food safety hazards and must be able to trace their products. Businesses that process poultry must control their food safety hazards and must be able to trace their products.

It is the responsibility of these businesses not only to comply with this Standard but also to be able to demonstrate compliance. This Standard is, in part, intended to reduce the contamination of poultry, poultry carcasses and poultry meat by pathogenic *Campylobacter* and *Salmonella*.

Table of Provisions

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- 2 Application

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- 4 Inputs
- 5 Waste disposal
- 6 Health and hygiene requirements
- 7 Skills and knowledge
- 8 Design, construction and maintenance of premises, equipment and transportation vehicles
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- 11 Application
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- 13 Receiving birds for processing
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Clauses

Division 1 – Preliminary

1 Interpretation

(1) Unless the contrary intention appears, and subject to Standard 4.1.1, the definitions in Chapter 3 of this Code apply in this Standard.

(2) The definition of ‘condition’ in Standard 3.2.2 does not apply in this Standard.

(3) In this Standard –

carcass means the whole dressed body of slaughtered poultry, but excludes any part that has been removed from the dressed body, for example, the head, feathers, viscera and blood.

food safety management statement means a statement, which at a minimum, has been approved or recognised by the relevant authority and subjected to ongoing verification activities by a poultry producer or poultry processor and the relevant authority.

Editorial note:

‘Authority’ is defined in draft Standard 4.1.1 as –

the State, Territory or Commonwealth agency or agencies having the legal authority to implement and enforce primary production and processing Standards.

poultry means chicken, turkey, duck, squab (pigeons), geese, pheasants, quail, guinea fowl, muttonbirds and other avian species (except ratites).

poultry handler means a person who handles or supervises the handling of poultry.

poultry meat means the parts of the poultry carcass intended for human consumption.

poultry producer means a business, enterprise or activity that involves –

- (a) growing; or
- (b) live transporting;

of poultry for human consumption.

poultry processor means a business, enterprise or activity that involves the processing or transporting of poultry product for human consumption.

poultry product means the carcass of poultry, poultry meat or poultry meat product, as the case may be.

premises means a poultry primary production or processing premises.

processing of poultry or poultry product includes the –

- (a) holding before stunning; or
- (b) stunning; or
- (c) bleeding; or
- (d) scalding; or
- (e) defeathering; or
- (f) removing of head or feet; or
- (g) processing of feet; or
- (h) removing of viscera; or
- (i) processing of offal; or
- (j) trimming; or
- (k) washing; or
- (l) chilling; or
- (m) spin chilling; or
- (n) freezing; or
- (o) thawing; or
- (p) deboning or portioning; or
- (q) mincing or dicing; or
- (r) marinating; or
- (s) injecting or massaging; or
- (t) partial cooking; or
- (u) crumbing; or
- (v) packaging; or
- (w) storage, associated with processing;

of poultry or poultry product, as the case may be, for human consumption.

unsuitable means unsuitable as defined in Standard 3.1.1, but includes poultry or poultry product that is in a condition, or contains a substance a person would ordinarily regard as making the poultry, after processing, or poultry product unfit for human consumption.

Editorial note:

‘Suitable’ are defined in Standard 3.1.1. Clause 2 of Standard 3.1.1 provides –

Food is not suitable if it –

- (a) is damaged, deteriorated or perished to an extent that affects its reasonable intended use; or
- (b) contains any damaged, deteriorated or perished substance that affects its reasonable intended use; or

- (c) is the product of a diseased animal or an animal that has died otherwise than by slaughter, and has not been declared by or under another Act to be safe for human consumption; or
- (d) contains a biological or chemical agent, or other matter or substance, that is foreign to the nature of the food.

However, food is not unsuitable for the purposes of the Food Safety Standards merely because –

- (a) it contains an agricultural or veterinary chemical in an amount that does not contravene the *Australia New Zealand Food Standards Code*; or
- (b) it contains a metal or non-metal contaminant (within the meaning of the *Australia New Zealand Food Standards Code*) in an amount that does not contravene the permitted level for the contaminant as specified in the *Australia New Zealand Food Standards Code*; or
- (c) it contains any matter or substance that is permitted by the *Australia New Zealand Food Standards Code*.

2 Application

This Standard does not apply to poultry retail sale activities or poultry product retail sale activities.

Division 2 – Primary production of poultry

3 General food safety management

- (1) A poultry producer must systematically examine all of its primary production operations to identify potential hazards and implement control measures to address those hazards.
- (2) A poultry producer must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.
- (3) A poultry producer must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.

4 Inputs

A poultry producer must take all reasonable measures to ensure inputs do not make the poultry unsuitable.

Editorial note:

See the definition of ‘inputs’ in Standard 4.1.1 which includes feed, litter, water and chemicals used in or in connection with the primary production activity.

5 Waste disposal

- (1) A poultry producer must store, handle or dispose of waste in a manner that will not make the poultry unsuitable.
- (2) For subclause 5(1), waste includes sewage, waste water, litter, dead poultry and garbage.

6 Health and hygiene requirements

- (1) A poultry handler must exercise personal hygiene and health practices that do not make the poultry unsuitable.
- (2) A poultry producer must take all reasonable measures to ensure that poultry handlers, personnel and visitors exercise personal hygiene and health practices that do not make the poultry unsuitable.

7 Skills and knowledge

A poultry producer must ensure that poultry handlers have –

- (a) skills in food safety and food hygiene; and
- (b) knowledge of food safety and food hygiene matters;

commensurate with their work.

8 Design, construction and maintenance of premises, equipment and transportation vehicles

A poultry producer must –

- (a) ensure that premises, equipment and transportation vehicles are designed and constructed in a way that minimises the contamination of poultry, allows for effective cleaning and sanitisation and minimises the harbourage of pests and vermin; and
- (b) keep premises, equipment and transportation vehicles effectively cleaned, sanitised and in good repair to ensure poultry is not made unsuitable.

9 Traceability

A poultry producer must be able to identify the immediate recipient of the poultry handled by the poultry producer.

10 Sale or supply of poultry

A poultry producer must not sell or supply poultry for human consumption if the producer ought reasonably know or ought reasonably suspect that the poultry is unsuitable.

Editorial note:

‘Supply’ is defined in Standard 4.1.1 as including intra company transfers of product.

Division 3 – Processing of poultry

11 Application

- (1) Subject to subclause (2), and to avoid doubt, Standards 3.2.2 and 3.2.3 apply to a poultry processor.
- (2) In areas where poultry is slaughtered –
 - (a) paragraph 17(1)(d) of Standard 3.2.2 does not apply; and
 - (b) paragraph 24(1)(a) of Standard 3.2.2 does not apply in relation to the poultry intended for slaughter.

12 General food safety management

- (1) A poultry processor must systematically examine all of its processing operations to identify potential hazards and implement control measures to address those hazards.
- (2) A poultry processor must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.
- (3) A poultry processor must verify the effectiveness of the control measures.
- (4) A poultry processor must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.

13 Receiving

A poultry processor must not process poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

14 Inputs

A poultry processor must take all reasonable measures to ensure inputs do not make the poultry product unsuitable.

Editorial note:

See Standard 4.1.1 for the definition of ‘inputs’.

For guidance on what constitutes acceptable water in processing see the *Australian Drinking Water Guidelines 2004* of the National Health and Medical Research Council of Australia.

15 Waste disposal

- (1) A poultry processor must store, handle or dispose of waste in a manner that will not make the poultry product unsuitable.
- (2) For subclause 15(1), waste includes unsuitable poultry and unsuitable poultry product, sewage, waste water and garbage.

16 Skills and knowledge

A poultry processor must ensure that persons engaged in poultry processing have –

- (a) skills in food safety and food hygiene; and
- (b) knowledge of food safety and food hygiene matters; and
- (c) skills and knowledge to detect a condition that would render poultry or poultry product unsuitable;

commensurate with their work.

17 Traceability

A poultry processor must ensure that it can identify the immediate supplier and immediate recipient of poultry product handled by the poultry processing business.

18 Sale or supply

A poultry processor must not sell or supply poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

Editorial note:

See Standard 1.3.3 for requirements relating to the use of water as a processing aid.

See Standard 1.2.4 for labelling requirements where water is an ingredient in the final poultry product at a level of 5% or more.

19 Requirements for producers of ready-to-eat poultry meat

Division 3 of Standard 4.2.3 applies to the producers of ready-to-eat poultry meat.

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Attachment 4

BOVIBROM®

Material Safety Data Sheet

Revision Date 25-Jun-2009
Supersedes New

1. PRODUCT AND COMPANY IDENTIFICATION

Product Name BOVIBROM®
Chemical Name 1,3-Dibromo-5,5-dimethylhydantoin
CAS-No 77-78-5
Formula C₅H₆Br₂N₂O₂
Recommended use Beef carcass antimicrobial

Company Albemarle Corporation
 451 Florida Street
 Baton Rouge, LA 70801

Emergency Telephone Numbers 225-344-7147

For Non-Emergency 800-535-3030

	NFPA	HMIS
Health	3	3
Flammability	1	1
Physical Hazards	1	1

2. HAZARDS IDENTIFICATION

Emergency Overview

Corrosive - causes irreversible eye damage
 Causes skin burns
 Harmful in contact with skin
 May be fatal if swallowed

Potential Health Effects

Eyes Possible risks of irreversible effects.
Skin Harmful in contact with skin. Causes burns.
Inhalation Harmful by inhalation.
Ingestion May be fatal if swallowed.

See Section 11 for additional Toxicological information.

Occupational Exposure Limit See Section 8

3. COMPOSITION/INFORMATION ON INGREDIENTS

Component	CAS-No	Weight %
1,3-Dibromo-5,5-dimethyl hydantoin	77-48-5	100

4. FIRST AID MEASURES

Ad Lib	If medical advice is needed: Have product container or label at hand
Eye contact	If in eyes, hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
Skin Contact	If on skin or clothing, take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.
Inhalation	If inhaled, move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for further treatment advice.
Ingestion	If swallowed, call a physician or Poison Control Centre immediately. Have person sip a glass of water if able to swallow. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Combustion/explosion hazards	Not available.
Suitable Extinguishing Media	Use water fog, foam, dry chemical or carbon dioxide (CO2) to extinguish flames.
Hazardous Combustion Products	Oxides of carbon. Bromine.
Protective Equipment and Precautions for Firefighters	Toxic fumes may be present; use of respirator suggested.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions	Avoid contact with skin, eyes and clothing. Avoid dust formation. Ensure adequate ventilation.
Environmental Precautions	Prevent further leakage or spillage if safe to do so.
Methods for Clean-up	Sweep up and shovel into suitable containers for disposal.

7. HANDLING AND STORAGE

Handling	Avoid contact with skin, eyes and clothing. Wear personal protective equipment. Avoid dust formation.
Storage	Store in well-ventilated, cool (<120F), dry area, away from heat or flame. Store in containers made of HDPE, LDPE, or PP. Do not store in metal or fiberboard containers. Close container when not in use.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls Use in a well-ventilated area.

Personal Protective Equipment

Eye/face Protection Chemical goggles. Face-shield.

Skin Protection Wear protective clothing.

Hand protection Rubber gloves resistant to chemical permeation.

Respiratory protection NIOSH approved dust/mist respirator under dusty or irritating conditions.

9. PHYSICAL AND CHEMICAL PROPERTIES

Flash point	Not applicable.	Flammable limits (LEL, UEL)	No data available
Form	Solid	Vapor pressure	No data available
Color	White/Off-white	Density	No data available
Odor	Halogen	Vapor density	No data available
pH	6.0-6.5(1% slurry in pH 7 water)	Water Solubility	~0.1%
Boiling Point	No data available	Melting/freezing point	>190 °C(Decomposes)
Molecular Weight	286	Viscosity, dynamic	No data available
Viscosity, kinematic	No data available	Partition Coefficient (log Pow)	No data available
Flammability (solid, gas)	No data available	Oxidizing Properties	Oxidizer
Explosive Properties	No data available		

10. STABILITY AND REACTIVITY

Stability Stable.

Conditions to Avoid Avoid extremely high heat and flame.

Materials to avoid This product is a strong oxidizing and brominating agent. Avoid contact with reducing agents, acids, ammonia-containing products, organic materials (such as aldehydes and alcohols) and other oxidizing agents (such as calcium hypochlorite). Avoid contact with common metals such as aluminum, iron, copper, brass and steel. Contact with incompatible materials can promote the exothermic decomposition of the product.

Hazardous decomposition products Carbon oxides. Bromine.

Hazardous Polymerization None under normal processing.

11. TOXICOLOGICAL INFORMATION

Acute Effects

Eye contact
Skin contact
Ingestion
Inhalation

Possible risks of irreversible effects.
Causes burns. Harmful if absorbed through skin.
May be fatal if swallowed.
Harmful by inhalation.

LD50 Oral
LD50 Dermal:

448mg/kg of body weight (rat) (Albino Sprague-Dawley)
>2,000mg/kg of body weight (rat) (Albino Sprague-Dawley)

Other data

SKIN IRRITATION, Rabbit (albino New Zealand): Product is considered corrosive to the skin.

12. ECOLOGICAL INFORMATION

Ecotoxicity

EC50
EC50

EC50/48h/daphnia :0.7mg/L
EC50/48h/Rainbow Trout = 0.4mg/L

Ecotoxicity effects

No information available.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method

Dispose in a safe manner in accordance with local/national regulations.

14. TRANSPORT INFORMATION

DOT

Proper Shipping Name Oxidizing Solid, N.O.S. (1,3-Dibromo-5,5-dimethylhydantoin)
Hazard Class 5.1
UN No. 1479
Packing Group II
Description UN 1479, Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

IMDG/IMO

IMO Class 5.1
Packing Group II
UN-No 1479
IMO Labelling and Marking 5.1
Proper Shipping Name Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin)
EmS F-A, S-Q
Marpol - Annex II Not applicable
Marpol - Annex III Unregulated
Transport Description UN 1479 Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

IATA/ICAO

IATA/ICAO Class 5.1
Packing Group II
UN-No 1479
IATA/ICAO Labelling 5.1
Passenger Aircraft Passenger Aircraft
Cargo aircraft only Cargo aircraft only
Proper shipping name Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin)
Transport Description UN 1479 Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

15. REGULATORY INFORMATION

International Inventories	TSCA	DSL	NDSL	AICS	ENECS	ELINCS	ENCS	KECL	PICCS	CHINA	NZIoC
BOVIBROM®	X	X	-	X	X	-	X	X	X	X	X

(X) Complies (-) Does not Comply

TSCA Statement

THIS MATERIAL IS EXEMPT FROM THE TOXIC SUBSTANCES CONTROL ACT (15 USC 2601-2629)..

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazardous Categorization

Chronic Health Hazard No
Acute Health Hazard Yes
Fire Hazard No
Sudden Release of Pressure Hazard No
Reactive Hazard Yes

Reportable and Threshold Planning Quantities

No ingredients have RQs or TPQs under SARA or CERCLA

State Regulations

No components subject to "Right-To-Know" legislation in the following States; California, Massachusetts, New Jersey, and Pennsylvania.

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all the information required by the CPR.

WHMIS Hazards

E Corrosive material

D2B Toxic materials

16. OTHER INFORMATION

Prepared By

Health & Environment Department
Albemarle Corporation

FOR ADDITIONAL NONEMERGENCY PRODUCT INFORMATION, CONTACT:

HEALTH AND ENVIRONMENT DEPARTMENT
ALBEMARLE CORPORATION
451 FLORIDA ST.
BATON ROUGE, LA. 70801
(800) 535-3030

The information contained herein is accurate to the best of our knowledge. The Company makes no warranty of any kind, express or implied, concerning the safe use of this material in your process or in combination with other substances.

AVIBROM®

Material Safety Data Sheet

Revision Date 25-Jun-2009
Supersedes New

1. PRODUCT AND COMPANY IDENTIFICATION

Product Name AVIBROM®
Chemical Name 1,3-Dibromo-5,5-dimethylhydantoin
CAS-No 77-78-5
Formula C₅H₆Br₂N₂O₂
Recommended use Poultry carcass antimicrobial

Company Albemarle Corporation
 451 Florida Street
 Baton Rouge, LA 70801

Emergency Telephone Numbers 225-344-7147

For Non-Emergency 800-535-3030

	NFPA	HMIS
Health	3	3
Flammability	1	1
Physical Hazards	1	1

2. HAZARDS IDENTIFICATION

Emergency Overview

Corrosive - causes irreversible eye damage
 Causes skin burns
 Harmful in contact with skin
 May be fatal if swallowed

Potential Health Effects

Eyes	Possible risks of irreversible effects.
Skin	Harmful in contact with skin. Causes burns.
Inhalation	Harmful by inhalation.
Ingestion	May be fatal if swallowed.

See Section 11 for additional Toxicological information.

Occupational Exposure Limit See Section 8

3. COMPOSITION/INFORMATION ON INGREDIENTS

Component	CAS-No	Weight %
1,3-Dibromo-5,5-dimethyl hydantoin	77-48-5	100

4. FIRST AID MEASURES

Ad Lib	If medical advice is needed: Have product container or label at hand
Eye contact	If in eyes, hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
Skin Contact	If on skin or clothing, take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.
Inhalation	If inhaled, move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for further treatment advice.
Ingestion	If swallowed, call a physician or Poison Control Centre immediately. Have person sip a glass of water if able to swallow. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Combustion/explosion hazards	Not available.
Suitable Extinguishing Media	Use water fog, foam, dry chemical or carbon dioxide (CO2) to extinguish flames.
Hazardous Combustion Products	Oxides of carbon. Bromine.
Protective Equipment and Precautions for Firefighters	Toxic fumes may be present; use of respirator suggested.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions	Avoid contact with skin, eyes and clothing. Avoid dust formation. Ensure adequate ventilation.
Environmental Precautions	Prevent further leakage or spillage if safe to do so.
Methods for Clean-up	Sweep up and shovel into suitable containers for disposal.

7. HANDLING AND STORAGE

Handling	Avoid contact with skin, eyes and clothing. Wear personal protective equipment. Avoid dust formation.
Storage	Store in well-ventilated, cool (<120F), dry area, away from heat or flame. Store in containers made of HDPE, LDPE, or PP. Do not store in metal or fiberboard containers. Close container when not in use.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls	Use in a well-ventilated area.
Personal Protective Equipment	
Eye/face Protection	Chemical goggles. Face-shield.
Skin Protection	Wear protective clothing.
Hand protection	Rubber gloves resistant to chemical permeation.
Respiratory protection	NIOSH approved dust/mist respirator under dusty or irritating conditions.

9. PHYSICAL AND CHEMICAL PROPERTIES

Flash point	Not applicable.	Flammable limits (LEL, UEL)	No data available
Form	Solid	Vapor pressure	No data available
Color	White/Off-white	Density	No data available
Odor	Halogen	Vapor density	No data available
pH	6.0-6.5(1% slurry in pH 7 water)	Water Solubility	~0.1%
Boiling Point	No data available	Melting/freezing point	>190 °C(Decomposes)
Molecular Weight	286	Viscosity, dynamic	No data available
Viscosity, kinematic	No data available	Partition Coefficient (log Pow)	No data available
Flammability (solid, gas)	No data available	Oxidizing Properties	Oxidizer
Explosive Properties	No data available		

10. STABILITY AND REACTIVITY

Stability	Stable.
Conditions to Avoid	Avoid extremely high heat and flame.
Materials to avoid	This product is a strong oxidizing and brominating agent. Avoid contact with reducing agents, acids, ammonia-containing products, organic materials (such as aldehydes and alcohols) and other oxidizing agents (such as calcium hypochlorite). Avoid contact with common metals such as aluminum, iron, copper, brass and steel. Contact with incompatible materials can promote the exothermic decomposition of the product.
Hazardous decomposition products	Carbon oxides. Bromine.
Hazardous Polymerization	None under normal processing.

11. TOXICOLOGICAL INFORMATION

Acute Effects

Eye contact
Skin contact
Ingestion
Inhalation

Possible risks of irreversible effects.
Causes burns. Harmful if absorbed through skin.
May be fatal if swallowed.
Harmful by inhalation.

LD50 Oral
LD50 Dermal:

448mg/kg of body weight (rat) (Albino Sprague-Dawley)
>2,000mg/kg of body weight (rat) (Albino Sprague-Dawley)

Other data

SKIN IRRITATION, Rabbit (albino New Zealand): Product is considered corrosive to the skin.

12. ECOLOGICAL INFORMATION

Ecotoxicity

EC50
EC50

EC50/48h/daphnia :0.7mg/L
EC50/48h/Rainbow Trout = 0.4mg/L

Ecotoxicity effects

No information available.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method

Dispose in a safe manner in accordance with local/national regulations.

14. TRANSPORT INFORMATION

DOT

Proper Shipping Name Oxidizing Solid, N.O.S. (1,3-Dibromo-5,5-dimethylhydantoin)
Hazard Class 5.1
UN No. 1479
Packing Group II
Description UN 1479, Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

IMDG/IMO

IMO Class 5.1
Packing Group II
UN-No 1479
IMO Labelling and Marking 5.1
Proper Shipping Name Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin)
EmS F-A, S-Q
Marpol - Annex II Not applicable
Marpol - Annex III Unregulated
Transport Description UN 1479 Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

IATA/ICAO

IATA/ICAO Class 5.1
Packing Group II
UN-No 1479
IATA/ICAO Labelling 5.1
Passenger Aircraft Passenger Aircraft
Cargo aircraft only Cargo aircraft only
Proper shipping name Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin)
Transport Description UN 1479 Oxidizing solid, N.O.S. (1,3-Dibromo-5,5-dimethyl hydantoin), 5.1, II

15. REGULATORY INFORMATION

International Inventories	TSCA	DSL	NDSL	AICS	ENECS	ELINCS	ENCS	KECL	PICCS	CHINA	NZIoC
AVIBROM®	X	X	-	X	X	-	X	X	X	X	X

(X) Complies (-) Does not Comply

TSCA Statement

THIS MATERIAL IS EXEMPT FROM THE TOXIC SUBSTANCES CONTROL ACT (15 USC 2601-2629)..

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazardous Categorization

Chronic Health Hazard No
Acute Health Hazard Yes
Fire Hazard No
Sudden Release of Pressure Hazard No
Reactive Hazard Yes

Reportable and Threshold Planning Quantities

No ingredients have RQs or TPQs under SARA or CERCLA

State Regulations

No components subject to "Right-To-Know" legislation in the following States; California, Massachusetts, New Jersey, and Pennsylvania.

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all the information required by the CPR.

WHMIS Hazards

E Corrosive material

D2B Toxic materials

16. OTHER INFORMATION

Prepared By

Health & Environment Department
Albemarle Corporation

FOR ADDITIONAL NONEMERGENCY PRODUCT INFORMATION, CONTACT:

HEALTH AND ENVIRONMENT DEPARTMENT
ALBEMARLE CORPORATION
451 FLORIDA ST.
BATON ROUGE, LA. 70801
(800) 535-3030

The information contained herein is accurate to the best of our knowledge. The Company makes no warranty of any kind, express or implied, concerning the safe use of this material in your process or in combination with other substances.

Toxicity Data

Description of product: XtraBrom 111 biocide is a bromine-based fungicide, algicide, slimicide and microbicide for commercial and industrial recirculating cooling water systems and decorative fountains. The active ingredient is 1,3-dibromo-5,5-dimethylhydantoin (DBDMH).

Acute Oral - Defined LD₅₀ (Guideline OPPTS 870.1100): The acute oral defined LD₅₀ of XtraBrom 111 biocide is 448 mg/kg of body weight. XtraBrom 111 biocide was administered by single gavage of a water or carboxymethylcellulose suspension to Sprague-Dawley rats (5 male, 5 female) at dose levels of 250, 500, 1000, and 5000 mg/kg. No deaths or abnormal signs occurred in the 250 mg/kg group. Two animals in the 500 mg/kg group died on days 7 and 13 respectively. All animals in the 1000 mg/kg group and all but two of the 5,000 mg/kg group died in the first day. The two remaining 5000 mg/kg animals survived to study end on day 17, but showed either weight loss or signs of hypoactivity.

Acute Dermal - Limit Test (Guideline OPPTS 870.1200): The single dose acute dermal LD₅₀ of XtraBrom 111 biocide is greater than 2000 mg/kg of body weight when applied to the skin of Sprague-Dawley rats as a moistened powder. The product was applied to the skin of 5 male and 5 female rats for 24 hours. All animals survived and gained weight during the 14-day observation period. Other than dermal irritation (erythema and edema and/or eschar) there were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior. No gross abnormalities were noted for the animals necropsied at the conclusion of the 14-day observation period.

Primary Skin Irritation - (Guideline OPPTS 870.2500): XtraBrom 111 biocide is classified as corrosive to the skin, due to evidence of corrosion to the skin of one of three New Zealand albino rabbits following a 4-hour exposure to moistened powder. Dermal irritation was evaluated by the method of Draize, et al. Because corrosivity had been anticipated, one animal was tested initially, and the other two started only after the first animal did not show corrosion. The first animal showed well-defined erythema and edema, which decreased from 48 hours to Day 10 of the test. The second and third animals were terminated at the 72-hour observation when the third animal showed severe erythema, edema, eschar and evidence of corrosion. The second animal showed no irritation by 24 hours after exposure. The Primary Dermal Irritation Index (PDII) calculated for this test substance was 4.3.

Dermal Sensitization - Buehler Method (Guideline OPPTS 870.2600): XtraBrom 111 biocide is not considered to be a contact sensitizer. XtraBrom 111 biocide (0.75% w/w suspended in distilled water) was applied topically to young adult Hartley albino guinea pigs (20 male, 20 female) once weekly over a three-week induction period. Twenty-seven days after the first induction dose, a challenge dose of the highest non-irritating concentration (0.5% w/w solution in distilled water) was applied to a naive site, and scoring for erythema was made 24 and 48 hours after dosing. A naive control group (ten animals) was treated with the test article at challenge only. No animals had an erythema score of greater than 0.5 at the 24- or 48- hour reading in the test group or naive control group at challenge. Historical response to the positive control substance 1-chloro-2,4-dinitrobenzene (DNCB) showed that the animals were capable of showing sensitization.

Static Aquatic Toxicity Data

Oncorhynchus mykiss Rainbow Trout: The 48-hour EC₅₀ value for rainbow trout tested under static conditions was 0.178 mg Cl₂/L (0.4 mg of material/L). Five concentrations of XtraBrom 111 biocide (0.0588, 0.118, 0.235, 0.470, & 0.940 mg Cl₂/L) were tested using moderately hard fresh water (130-160 mg/L as CaCO₃) in 10 L aquaria. A minimum of 10 rainbow trout (5 per replicate) were tested per concentration; with instantaneous biomass loading of 0.0567 grams of fish/liter. No mortality was observed during the 96-hour test in concentrations lower than 0.235 mg Cl₂/L; 100% mortality was observed at 24 hours in the concentrations of 0.470 and 0.940 mg Cl₂/L. In the 0.235 mg Cl₂/L concentration, one replicate had 80% mortality at 24 hours and the other replicate had 100% mortality. No further deaths occurred after the 24-hour observation.

Daphnia Magna Waterflea: The estimated 48-hour EC₅₀ value for *Daphnia magna* under static conditions was 0.321 mg Cl₂/L (0.7 mg of material/L). Five concentrations of XtraBrom 111 biocide (0.0588, 0.118, 0.235, 0.470, & 0.940 mg Cl₂/L) were tested in moderately hard water (130-160 mg/L as CaCO₃). Ten daphnids were used per concentration replicate. Observations of immobility/mortality were made at 24 and 48 hours. No deaths nor abnormal signs occurred at 0.0588 mg Cl₂/L. One animal in one replicate died in the 0.118 mg Cl₂/L group at 24 hours. No animals died in the 0.235 mg Cl₂/L test group, but three animals in one replicate were observed to be quiescent at 48 hours. All animals in the 0.470 mg Cl₂/L were dead at 24 hours, and all animals in the 0.940 mg Cl₂/L died, half at 24 hours, and half by 48 hours.

For further information, please refer to the technical data sheet, material safety data sheet and startup document.

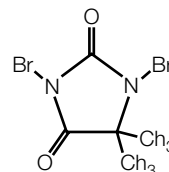
The information presented herein is believed to be accurate and reliable, but is presented without guarantee or responsibility on the part of Albemarle Corporation. It is the responsibility of the user to comply with all applicable laws and regulations and to provide for a safe workplace. The user should consider any health or safety hazards or information contained herein only as a guide, and should take those precautions which are necessary or prudent to instruct employees and to develop work practice procedures in order to promote a safe work environment. Further, nothing contained herein shall be taken as an inducement or recommendation to manufacture or use any of the herein materials or processes in violation of existing or future patents.



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Description

DBDMH is a white powder with a faint characteristic bromine odor. It is used as a brominating reagent and is a suitable alternative to n-bromosuccinimide. For further information on the use of DBDMH as a brominating agent see Z. E. Jolles, Ed., *Bromine and its Compounds*, (Orlando, Z. E. Academic Press, 1966) 393-394, 407.



(DBDMH)
CAS 77-48-5
 $C_5H_6Br_2N_2O_2$

Specifications

Appearance	powder with a faint, characteristic bromine odor, free of foreign matter
Color.....	white to off-white
Assay, wt %	98.0
Volatiles, wt %	0.5
Bromine, wt %	54.0
Chlorine, wt %	0.1

Typical Properties

Molecular weight	285.93
Packed bulk density (at ambient temperature), g/cm ³	1.36
Melting/decomposition temperature, DSC, °C	197 - 203
Solubility in water, wt %, 68 °F (20 °C)	0.1

The shelf life of this product is indefinite at normal ambient conditions when properly stored in its original container.

Compatibility

DBDMH is an oxidizing and brominating agent. Contact in the neat form with organic materials such as alcohols and aldehydes, strong reducing agents, acids and ammonia-containing products should be avoided. DBDMH should be stored in high density polyethylene (HDPE), low density polyethylene (LDPE) or polypropylene (PP). Do not store this product in metal and fiberboard containers. In its neat form, this product is expected to be compatible with Teflon[®], polyvinyl chloride (PVC), Viton[®], Kynar[®], chlorobutyl rubber, Hypalon[®], titanium and Hastelloy[®] C. In its neat form, this product is not compatible with nylon and most common metals such as brass, copper, carbon steel, stainless steel, galvanized steel and aluminum.

Shipping Information**Container Information**

30-Liter fiber drums with inner PE liners. 18 drums per CP3 pallet
 Net weight per drum 25 kg
 Net weight per pallet 450 kg
 Drum dimensions DIAM: 360MM, H:360MM
 Pallet dimensions 1140MM x 1140MM x 140MM

Shipping Classification

Proper shipping name: OXIDIZING SOLID, N.O.S.
 (1,3-dibromo-5,5-dimethylhydantoin)
 Hazard classification: 5.1
 ID number: UN1479
 Packing Group: II
 Label: Oxidizer
 Placard: Oxidizer

Safety Handling Information

DBDMH causes burns to the skin and eyes. It is harmful if swallowed or if inhaled.
 For specific handling information, please refer to the current material safety data sheet,
 which is available on request.

Chemical Registration Numbers

CAS: 77-48-5
 EINECS: 201-030-9

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Attachment 5



20 September 2000

05/01

FULL ASSESSMENT REPORT AND REGULATORY IMPACT STATEMENT

APPLICATION A393

BROMO-CHLORO-DIMETHYLHYDANTOIN (BCDMH) AS A PROCESSING AID

EXECUTIVE SUMMARY

- ANZFA received an application on 29 June 1999 from Wobelea Pty Ltd to amend the *Food Standards Code* so as to permit the use of bromo-chloro-dimethylhydantoin (BCDMH) as a processing aid in Standard A16.
- Five submissions were received in response to the preliminary assessment (section 14) notice. Three of these supported the application while the other two reserved their position pending a full toxicological and technical assessment by ANZFA.
- The scientific evaluations indicated that there are no public health and safety concerns with the use of BCDMH as a washing agent and its use is technologically justified. The New Food Standards Code proposes changes to Standard A16 are consistent with ANZFA's section 10 objectives. The requested changes should be implemented and commence on gazettal.
- The Regulatory Impact Statement supports the requested amendments and concludes that the preferred option is Option 2, to permit BCDMH as a processing aid in Standard A16.

OBJECTIVES AND BACKGROUND OF THE APPLICATION

This application seeks approval of bromo-chloro-dimethylhydantoin (BCDMH) as a processing aid in Standard A16 of the Australian *Food Standards Code*. Standard A16 regulates water-disinfecting agents (such as chlorine, ozone and chlorine dioxide), in Table II, Group II - Bleaching Agents, Washing and Peeling Agents and in Table VI-Processing Aids Used in Packaged Water and in Water Used as an Ingredient in Other Foods.

The proposed use of BCDMH is for sanitising water used to wash fruit and vegetables, both post harvest and in the production of minimally processed fruit and vegetable products. Currently, chlorine is the agent most commonly used for this purpose mainly through the use of hypochlorites. The use of chlorine, however, has some disadvantages such as difficulty in controlling effective levels with varying pH, corrosion of water systems, and product tainting and spotting. Other compounds, which have also been widely used for water sanitation, are ozone and chlorine dioxide but they also present disadvantages such as worker safety and cost. This application seeks to include BCDMH in Standard A16 as an alternative washing agent to these compounds.

RELEVANT PROVISIONS

Australian Food Standards Code:

- **Standard A16** – Processing Aids.

There are no provisions in the New Zealand Food Regulations for processing aids.

Codex does not regulate the use of processing aids but does maintain an Inventory of Processing Aids. BCDMH is not included in this inventory, though nor are other water treatment agents such as chlorine, ozone and chlorine dioxide.

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) evaluated BCDMH and registered its use in post-harvest wash systems as an agricultural chemical. It is currently listed in Table 5 of the NRA's *MRL Standard* – Uses of substances where maximum residue limits are not necessary.

PUBLIC CONSULTATION

A notice requesting public comment was posted on 15 September 1999 and submissions closed on 27 October 1999.

Submissions were received from the New Zealand Ministry of Health, Food Technology Association of Victoria, InforMed Systems, National Council of Women of New Zealand and the Western Australian Food Advisory Committee (WAFAC). The main issues raised are summarised below.

Western Australia Food Advisory Committee

WAFAC had previously requested information as to whether there is a withholding period (WHP) for BCDMH, as the information provided at preliminary assessment suggested that BCDMH is registered for use in situations where the residues are identical or indistinguishable from natural food components. The Committee suggested that claims of low residue levels detailed in the preliminary assessment report should be considered in regard to the effect of a WHP.

The Committee was concerned that only a comparative assessment against hypochlorite and not against other bactericidal compounds such as quaternary ammonium compounds or chlorine dioxide solution had been made. However, WAFAC also noted the claim that BCDMH has a very low phytotoxicity and remains active over a wide pH range when compared to calcium hypochlorite and **supported the application** on this basis.

InforMed Systems Ltd

InforMed Systems were of the view that this was not a simple application and that the safety of BCDMH should be established before any recommendation is made.

New Zealand Ministry of Health

The NZ Ministry of Health's submission raised concern as to whether the correct classification of BCDMH is as a processing aid and not a food additive. Further comment on this application was not provided as the Ministry of Health wishes to consider ANZFA's assessment of the technical and toxicological data before making a more informed response.

National Council of Women of New Zealand

The National Council of Women of New Zealand noted the benefits BCDMH may provide over products such as calcium hypochlorite, and would not oppose the application provided the toxicological report determined no safety concerns.

Food Technology Association of Victoria Inc.

The Food Technology Association of Victoria supported the application, providing the toxicology report was acceptable.

OPTIONS

1. Maintain the *status quo* and not permit the use of BCDMH as processing aid.
2. Amend Standard A16 to permit the use of BCDMH as a processing aid (washing agent).

SCIENTIFIC ASSESSMENT

Toxicological Report (Refer to Attachment 3)

There appears to be limited toxicological concerns from the use of BCDMH as a processing aid for use as sanitising water used to wash fruit and vegetables. A provisional ADI for DMH (the major residue of BCDMH) was established using the NOEL from the best available sub-chronic study and using a safety factor of 2000. Based on this ADI, dietary intakes calculations show that only 42% of the ADI would be reached.

ANZFA also performed a dietary exposure calculation (using DIAMOND) based on residues in fruit and vegetables of DMH and conservative values in other commodities for inorganic bromide (50 mg/kg for cereal grains and 400 mg/kg for spices). A total dietary exposure was calculated at 0.16mg/kg bw/day (16% of ADI for bromide) for average consumers and 0.39mg/kg bw/day (38% of ADI for bromide) for high consumers (95th percentile).

In conclusion, considering the available toxicological and dietary exposure data and the current Table 5¹ entry in the NRA's *MRL Standard*, there are no toxicological grounds not to approve BCDMH as a processing aid in Standard A16.

¹ Table 5 – Uses of substances where maximum residue limits are not necessary, is used in situations where residues do not or should not occur in foods or animal feeds; or where the residues are identical to or indistinguishable from natural food components; or are otherwise of no toxicological significance.

Food Technology Report (Refer to Attachment 4)

At present there are a number of agents which may be used for the disinfection of water used in the food industry such as chlorine (hypochlorites), chlorine dioxide and ozone. The sanitisers used primarily for both the postharvest washing of fruit and vegetables and in fruit and vegetable processing are hypochlorites. However, while providing a relatively cheap and effective means of controlling the microbiological quality of wash waters, the use of hypochlorites (particularly calcium hypochlorite) has several disadvantages. These include:

- difficulty in maintaining an effective concentration at pH levels above pH 7.5;
- corrosion of water and packaging systems;
- problems with use in heated water systems; and
- calcium spotting and tainting of produce.

The use of chlorine dioxide can overcome some of the disadvantages of hypochlorites in that it is effective within a broader pH range (pH 6.0-8.0), and it is non-tainting and non-corrosive at the levels used. However, because it is unstable and needs to be generated on site it is a more expensive option than hypochlorites. Ozone is also relatively unaffected at pH range 6.0-8.0 and is very effective at low concentrations. It is also unstable and, like chlorine dioxide, needs to be generated on site. Occupational health and safety concerns with the use of ozone in the food industry may be a determining factor in its use.

BCDMH is a stable compound, effective across a broad pH range and at much lower concentrations than chlorine. BCDMH would provide a viable alternative to the use of other disinfecting agents such as hypochlorites, chlorine dioxide and ozone, presently listed in Group II of Standard A16.

Residues

BCDMH breaks down to produce hypobromous and hypochlorous acids (which would lead to the formation of halides on the treated produce) and dimethylhydantoin (DMH), with DMH being the major residue. Based on the available residue data supplied by the NRA, residues of DMH would be lower than 1 mg/kg on produce passing through dip solutions of BCDMH at the proposed levels of use. Theoretical “maximum” residues of 2 mg/kg may result in vegetables such as broccoli.

Standard A14 of the *Food Standards Code* sets residue levels for inorganic bromide of 20 mg/kg in fruits and vegetables. Residues of inorganic bromide resulting from the use of BCDMH would be far below this value. Chlorine residues should be, similarly, quite low and well below the 1.0 mg/kg (available chlorine) limit applied to other chlorine compounds listed in Table II, Group II processing aids in Standard A16.

Based on the available residue data and to be consistent with existing residue limits, it is proposed that residue limits of 2.0 mg/kg (dimethylhydantoin), 1.0 mg/kg (available chlorine) and 1.0 mg/kg (inorganic bromide) are listed beside BCDMH in Table II, Group II of Standard A16.

EVALUATION OF ISSUES RAISED IN PUBLIC SUBMISSIONS

- **Withholding period for BCDMH**

BCDMH is already registered for use as an agricultural chemical by the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) and can legally be used on fruits and vegetables in post-harvest wash systems. ANZFA approached the NRA with respect to information on the withholding period (WHP). The NRA advised ANZFA that there was some limited residue data however, because of the products listing in Table 5 of the *MRL Standard* (where residues do not or should not occur in foods; or where the residues are identical or indistinguishable from natural food components; or are otherwise of no toxicological significance), there was no allocated WHP.

- **Assessment of BCDMH against other washing agents**

A comparison of BCDMH against chlorine, ozone and chlorine dioxide was made in the Food Technology Report. This report concluded that BCDMH was a viable alternative to these washing agents.

- **Safety of BCDMH**

Before recommending changes to the *Food Standards Code* any public health and safety concerns are identified and addressed. The toxicological report concluded that there were no toxicological concerns and that exposure to BCDMH is low (even in high consuming individuals) when estimates were made of total dietary intakes from residues that may occur in fruit and vegetables.

- **Classification of BCDMH as a processing aid**

A processing aid is defined in Standard A16 – Processing Aids of the *Food Standards Code* as “a substance used in the processing of raw materials, foods or ingredients, to fulfil a technological purpose relating to treatment or processing, but does not perform a technological function in the final food”. One of the proposed uses of BCDMH is to sanitise the wash waters used for the production of minimally processed fruits and vegetables and to reduce the microbial load on the produce being treated. There are no residues of BCDMH on the final product that would have any technological effect. The use of BCDMH as a washing agent fulfils the definition of a processing aid.

REGULATORY IMPACT ANALYSIS

1. Issue identification

Alternatives to regulation are not considered appropriate with regard to the use of BCDMH as a water treatment agent. Currently, processing aids permitted for use in Australia are listed in Standard A16 of the *Food Standards Code*. New entries in the Tables to Standard A16 are required to undergo an evaluation to determine efficacy and to ensure that there are no public health and safety concerns with permitting their use. The standard is intended to reflect current use and to prohibit inappropriate use of processing aids.

Parties likely to be affected by the possible options as listed above are consumers, manufacturers and State/Territory and New Zealand Health Departments.

Option 1

- Maintain the *status quo* and not permit the use of BCDMH as processing aid.

AFFECTED PARTY	BENEFITS	COSTS
Government	No perceived benefits	No perceived costs
Industry	No perceived benefits	There are other washing agents permitted for use, such as chlorine, which industry can currently use. The use of BCDMH, however, may result in lower treatment costs and less corrosion of equipment. Maintaining the status quo would deny industry any advantages that the use of BCDMH may give.
Consumers	No perceived benefits other than for individuals that wish to avoid all chemical residues that may be present in food and would therefore object to the use of any new agent.	An alternative water sanitiser to chlorine which should result in lower residues may be seen as desirable to consumers. Denying the use of BCDMH could be perceived as a cost in this context.

Option 2

- Amend Standard A16 to permit the use of BCDMH as a processing aid.

AFFECTED PARTY	BENEFITS	COSTS
Government	No perceived benefit	No perceived cost
Industry	Permitting the use of BCDMH would provide food manufacturers with an alternative washing agent which could lower treatment costs and help minimise equipment corrosion.	Providing industry with a greater choice of washing agents would incur no costs.
Consumers	The microbiological safety and quality of minimally processed fruit and vegetable products has become of increasing importance. Increasing the choice of washing agents, which may assist this, would be of benefit to consumers. Chlorine is currently the most commonly used water treatment agent. Certain chlorine by-products, such as chloramines, are considered undesirable by consumers. Alternatives to the use of chlorine may therefore been seen as a benefit.	No perceived costs apart from the objection some individuals may have to the increase in number of chemical agents permitted for use on food.

2. Evaluation

Maintaining the *status quo* (Option 1) appears to provide no benefit to government, industry and consumers. Option 1 denies industry access to an alternative washing agent which is of low toxicity, is effective at lower concentrations than commonly used chlorine agents, and may contribute to lower production costs.

Option 2, which proposes to amend the *Food Standards Code* to permit the use of BCDMH as a processing aid, appears to impose no significant costs on government, industry or consumers and may be of benefit to industry and consumers.

Assessment of the costs and benefits of Options 1 and 2 indicates that there would be a net benefit in permitting the use of BCDMH as a processing aid.

ASSESSMENT OF ANZFA'S SECTION 10 OBJECTIVES

(a) the protection of public health and safety

Toxicological evaluation of BCDMH indicates that there are no significant public health and safety concerns associated with its use as a processing aid for water treatment.

(b) the provision of adequate information relating to food to enable consumers to make informed choices and to prevent fraud and deception

There is no requirement for labelling of processing aids in the *Food Standards Code*. Provision of this information would not be meaningful to consumers.

(c) the promotion of fair trading in food

If approved, BCDMH may be used by all members of the industry and no issues in relation to fair trading were raised. To not allow approval may disadvantage manufacturers.

(d) the promotion of trade and commerce in the food industry

The approval of BCDMH will provide industry with an alternative washing agent that may provide benefits over existing agents. This could facilitate trade and commerce in the food industry.

(e) the promotion of consistency between domestic and international food standards where these are at variance.

There is currently no approval for use of BCDMH as a processing aid in other countries. Codex does not have a processing aid standard but do maintain an Inventory of Processing Aids. Bromo-chloro-dimethylhydantoin is not included in this inventory, though nor is other washing agents such as chlorine dioxide, ozone and chlorine.

CONCLUSIONS

The full assessment report concludes that permitting the use of BCDMH as a washing agent is technologically justified and poses no significant risk to public health and safety.

Approval of BCDMH as a washing agent in Standard A16 will provide manufacturers with an alternative processing aid for the disinfection of water, which is non-corrosive at the levels used, remains effective at high pH (to pH 8.5), is more effective at lower concentrations and has a very low phytotoxicity.

WORLD TRADE ORGANISATION (WTO) NOTIFICATION

Australia and New Zealand are members of the WTO and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the agreement between the Governments of Australia and New Zealand on Uniform Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

In conclusion, the proposed variation to the Code constitutes a minor change to the Code and is not expected to impact on trade issues for either technical or sanitary or phytosanitary reasons. Therefore a notification to the World Trade Organization on grounds relating to the WTO **is not** required.

Attachments to the Report:

1. Draft Variation to the Australian *Food Standards Code*
2. Explanatory Notes
3. Toxicological Report
4. Food Technology Report

ATTACHMENT 1

DRAFT VARIATION TO THE AUSTRALIAN FOOD STANDARDS CODE

To commence: On gazettal

Standard A16 of the Food Standards Code is varied by:-

- (a) inserting in the Schedule Bromo-chloro-dimethylhydantoin in column 1 of Group II and 1.0 (available chlorine), 1.0 (inorganic bromide), 2.0 (dimethylhydantoin) in column 2.

Standard A11 of the Food Standards Code is varied by:-

Inserting-

Addendum 8 means *Addendum 8* to this standard;

Inserting in columns 1 and 2 respectively of the Schedule-

Bromo-chloro-dimethylhydantoin Addendum 8; *and*

inserting immediately after Addendum 7-

Addendum 8**SPECIFICATIONS FOR BROMO-CHLORO-DIMETHYLHYDANTOIN**

Bromo-chloro-dimethylhydantoin (CAS Number: 126-06-7)

Formula: $C_5H_6BrClN_2O_2$

Formula weight: 241.5

Chemical Properties

Appearance: Solid or free flowing granules

Colour: White

Odour: Faint halogenous odour

Melting Point $163-164^{\circ}C$

Specific gravity 1.8-2

Solubility in water 0.2g/100g at $25^{\circ}C$

Stability

Stable when dry and uncontaminated

Chemical Tests:

Manufacturing process:

Solid dimethylhydantoin (DMH) is dissolved in water with bromine and chlorine. The reaction is 0.5 mole bromine and 1.5 mole chlorine for one mole DMH. During the reaction the pH is kept basic by the addition of caustic soda. The wet product is transferred to a drier where it is dried to a powder at low temperature. The powder may then be tableted or granulated.

Assay:

Procedure:

Various analytical methods exist for analysis, namely, GLC, HPLC, UV and NMR. HPLC offers the best sensitivity.

ATTACHMENT 2**EXPLANATORY NOTES - DRAFT****APPLICATION A 393 - Bromo-chloro-dimethylhydantoin (BCDMH) as a processing aid****FOR RECOMMENDING A VARIATION TO STANDARD A16-PROCESSING AIDS**

The Australia New Zealand Food Authority has before it application **A 393** (received on 29 June 1999) from Wobelea Pty Ltd to amend the *Food Standards Code* so as to approve the use of bromo-chloro-dimethylhydantoin (BCDMH) as a processing aid (washing agent) in Standard A16. ANZFA has completed a full assessment of the application and has prepared draft variations to the Australian *Food Standards Code*.

At present there are a number of agents, which may be used for the disinfection of water used in the food industry such as chlorine (hypochlorites), chlorine dioxide and ozone. The sanitisers used primarily for both the postharvest washing of fruit and vegetables and in fruit and vegetable processing are hypochlorites. However, while providing a relatively cheap and effective means of controlling the microbiological quality of wash waters, the use of hypochlorites does present several disadvantages. These include:

- difficulty in maintaining an effective concentration at pH levels above pH 7.5;
- corrosion of water and packaging systems;
- problems with use in heated water systems; and
- calcium spotting and tainting of produce.

The use of other agents such as chlorine dioxide can overcome some of the disadvantages of hypochlorites in that it is effective within a broad pH range (pH 6.0-8.0), and is non-tainting and non-corrosive at the levels used. However, because it is unstable and needs to be generated on site it is a more expensive option than hypochlorites. Ozone is also relatively unaffected at pH range 6.0-8.0 and is very effective at low concentrations. It is also unstable and, like chlorine dioxide, needs to be generated on site. Occupational health and safety concerns with the use of ozone in the food industry may be a determining factor in its use.

BCDMH is a stable compound, effective across a broad pH range and at much lower concentrations than chlorine (proposed levels of use of BCDMH are 5-15 ppm). The approval of BCDMH as a washing agent in Group II of Standard A16 will provide manufacturers with an alternative processing aid for the disinfection of water, which may provide advantages over the agents currently used.

The toxicological evaluation of BCDMH concluded that, based on available toxicological and dietary exposure data, there were no health and safety concerns from the proposed use. Residue limits of 1.0 mg/kg available chlorine, 1.0 mg/kg inorganic bromine and 2 mg/kg dimethylhydantoin are proposed, based on the available residue data and consistent with good manufacturing practice.

PROPOSED DRAFT VARIATION TO THE AUSTRALIAN FOOD STANDARDS CODE (refer to drafting at Attachment 1)

REGULATION IMPACT ANALYSIS

The Authority develops food regulations suitable for adoption in Australia and New Zealand. It is required to consider the impact, including compliance costs to business, of various regulatory (and non-regulatory) options on all sectors of the community, which includes the consumers, food industry and governments in both countries. The regulation impact assessment will identify and evaluate, though not be limited to, the costs and benefits of the regulation, and its health, economic and social impacts. In the course of assessing the regulatory impact, the Authority is guided by the *Australian Guide to Regulation* (Commonwealth of Australia 1997) and *New Zealand Code of Regulatory Practice*.

Consideration of the Regulatory Impact for this application concludes that the amendment to the Code is cost effective, of benefit to both producers and consumers, and is the preferred regulatory option.

WORLD TRADE ORGANIZATION (WTO) NOTIFICATION

Australia and New Zealand are members of the WTO and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the agreement between the Governments of Australia and New Zealand on Uniform Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

This matter does not need to be notified to the WTO as a Sanitary or Phytosanitary (SPS) notification or a Technical Barriers to Trade (TBT) notification because it does not impact on human or animal health and will not have significant effect on the trade of other members.

FOOD STANDARDS SETTING IN AUSTRALIA AND NEW ZEALAND

The Governments of Australia and New Zealand entered an Agreement in December 1995 establishing a system for the development of joint food standards. The Australia New Zealand Food Authority is now developing a joint *Australia New Zealand Food Standards Code*, which will provide compositional and labelling standards for food in both Australia and New Zealand.

Until the joint *Australia New Zealand Food Standards Code* is finalised the following arrangements for the two countries apply:

- **Food imported into New Zealand other than from Australia** must comply with either the *Australian Food Standards Code*, as gazetted in New Zealand, or the *New Zealand Food Regulations 1984*, but not a combination of both. However, in all cases maximum

residue limits for agricultural and veterinary chemicals must comply solely with those limits specified in the New Zealand *Food Regulations 1984*.

- **Food imported into New Zealand from Australia** must comply with either the Australian *Food Standards Code* or the New Zealand *Food Regulations 1984*, but not a combination of both. However, in all cases maximum residue limits for agricultural and veterinary chemicals must comply solely with those limits specified in the New Zealand (Maximum Residue Limits of Agricultural Compounds) Mandatory Food Standard 1999
- **Food imported into New Zealand from Australia** must comply with either the Australian *Food Standards Code* or the New Zealand *Food Regulations 1984*, but not a combination of both.
- **Food imported into Australia from New Zealand** must comply with the Australian *Food Standards Code*. However, under the provisions of the Trans-Tasman Mutual Recognition Arrangement, food may be imported into Australia from New Zealand if it complies with the New Zealand *Food Regulations 1984* or *Dietary Supplements Regulations 1985*.
- **Food manufactured in Australia and sold in Australia** must comply solely with the Australian *Food Standards Code*, except for exemptions granted in Standard T1.

In addition to the above, all food sold in New Zealand must comply with the New Zealand *Fair Trading Act 1986* and all food sold in Australia must comply with the Australian *Trade Practices Act 1974*, and the respective Australian State and Territory *Fair Trading Acts*.

Any person or organisation may apply to ANZFA to have the *Food Standards Code* amended. In addition, ANZFA may develop proposals to amend the Australian *Food Standards Code* or to develop joint Australia New Zealand food standards. ANZFA can provide advice on the requirements for applications to amend the *Food Standards Code*.

INVITATION FOR PUBLIC SUBMISSIONS

The Authority has completed a full assessment of the application, prepared draft variations to the Australian *Food Standards Code* and will now conduct an inquiry to consider the draft variations and its regulatory impact.

Written submissions containing technical or other relevant information which will assist the Authority in undertaking a full assessment on matters relevant to the application, including consideration of its regulatory impact, are invited from interested individuals and organisations. Technical information presented should be in sufficient detail to allow independent scientific assessment.

Submissions providing more general comment and opinion are also invited. The Authority's policy on the management of submissions is available from the Standards Liaison Officer upon request.

The processes of the Authority are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of the Authority and made available for inspection. If you wish any confidential information contained in a submission to remain confidential to the Authority, you should clearly identify the sensitive information and provide justification for treating it in confidence. The *Australia New Zealand Food Authority Act 1991* requires the Authority to treat in confidence trade secrets relating to food and any other information relating to food, the commercial value of which would be or could reasonably be expected to be, destroyed or diminished by disclosure.

All correspondence and submissions on this matter should be addressed to the **Project Manager - Application A393** at one of the following addresses:

Australia New Zealand Food Authority	Australia New Zealand Food Authority
PO Box 7186	PO Box 10559
Canberra Mail Centre ACT 2610The Terrace	WELLINGTON 6036
AUSTRALIA	NEW ZEALAND
Tel (02) 6271 2222 Fax (02) 6271 2278	Tel (04) 473 9942 Fax (04) 473 9855

Submissions should be received by the Authority by **18 October 2000**.

General queries on this matter and other Authority business can be directed to the Standards Liaison Officer at the above address or by Email on <slo@anzfa.gov.au>. Submissions should not be sent by Email as the Authority cannot guarantee receipt. Requests for more general information on the Authority can be directed to the Information Officer at the above address or by Email <info@anzfa.gov.au>.

ATTACHMENT 3**TOXICOLOGICAL REPORT**

The National Registration Authority (NRA) provided a toxicological report on BCDMH (technical) produced in 1993 by the, then, Chemical Assessments Units of the Therapeutic Goods Administration (TGA). This was based on data that was submitted at the time of registration for approval for use of BCDMH in swimming pools, spas and hot tubs.

Following this initial registration for use and subsequent submission of appropriate new data, BCDMH was registered with the NRA for use as a biocide for fruits, vegetables and ornamentals in August 1997 (Table 5 entry). Under the NRA Table 5 regulations BCDMH is allowed only in situations where residues do not or should not occur in foods; or where the residues are identical or indistinguishable from natural food components; or are otherwise of no toxicological significance.

Metabolism

BCDMH (technical) is the source material used in Wobleleas' YM-FAB Nylate Halogen-based Broad Spectrum Biocide. BCDMH produces hypobromous acid (650 g/kg available bromine) and hypochlorous acid (260g/kg available chlorine) in water. The main stable degradation product in water is 5,5-dimethyl-2,4-imidazolidinedione (DMH) with bromide and chlorine produced at the same time.

DMH is considered to be the major residue in BCDMH treated produce.

Acute studies

Acute oral LD50s of BCDMH were 1037 and 860 mg/kg bw in male and female rats, respectively. Acute oral LD50s were cited as 7,800 mg/kg bw, 12,650 mg/kg bw and 8430 mg/kg bw in rats, rabbits and in guinea pigs, respectively.

Sub-chronic studies

Charles River CD rats (20/sex/group) received 0, 500, 5000 or 50,000 ppm DMH in drinking water for 13 weeks.

Ten males and 3 females in the high-dose group died. At high-dose animals showed thinness and emaciation, urogenital staining, hunching, decreased motor activity, ataxia, irritability and reduced bodyweight gains and food and water consumption. Histo-pathological changes in high-dose animals included atrophy of the thymus, spleen and lymph nodes, renal necrosis of the tip of the papilla, pelvic transitional cell hyperplasia, hyperplasia of the epithelial lining of the renal papilla, atrophy of the uterine wall and gastric necrotic inflammation.

The NOEL of 500 ppm was determined which corresponded to approximately 50mg/kg bw/day in the diet.

Based on this sub-chronic study and using a safety factor of 2000, an ADI of 0.025mg/kg bw/day can be established for DMH.

Genotoxicity studies

BCDMH was not mutagenic in *Salmonella typhimurium* strains at concentrations of 5-5000µg/plate, with or without S9 mix. However, the compound did induce base-pair substitutions in *E coli* at concentrations of 25-3000ug/plate, with or without metabolic activation.

DMH did not induce chromosome aberrations in CHO cells at concentrations of 10-800ug/ml, with or without metabolic activation, and did not induce unscheduled DNA repair in cultured human epithelioid cells at concentrations of 10-480ug/ml.

Other available studies

The applicant provided summaries of 2 other long-term carcinogenicity studies that have been undertaken on DMH in 1996 by Bromine Compounds Pty Ltd, Israel.

In an 18 month dietary study in mice and a 24 month study in rats it was concluded that tumour incidences were similar between the control and treated groups and did not reveal any changes related to the administration of DMH. The NOEL for both studies was greater than 1000mg/kg bw/day.

Dietary calculations and residue data

Presently no existing MRLs or residue definitions exist for BCDMH. However, MRLs for inorganic bromide for fruits and vegetables have been set at 20 mg/kg. The ADI for bromide is 1 mg/kg bw/day.

The NRA evaluated the available residue data provided by the applicant in various treated fruits and vegetables and concluded that maximum residues in treated vegetables were 2 mg/kg and in fruits 0.2 mg/kg (based on residues of the major degradation product DMH).

Based on the provisional ADI of 0.025mg/kg bw/day, the maximum residues of DMH in treated fruits and vegetables would result in a Theoretical Maximum Daily Intake (TMDI) of 42% of the ADI.

ANZFA has also performed a dietary exposure calculation (using DIAMOND) based on the above maximum residues in fruit and vegetables of DMH and conservative values in other commodities for inorganic bromide (50 mg/kg for cereal grains and 400 mg/kg for spices). A total dietary exposure was calculated at 0.16mg/kg bw/day (16% of ADI for bromide) for average consumers and 0.39mg/kg bw/day (38% of ADI for bromide) for high consumers (95th percentile).

Interactions with other chemicals (drugs)

Hydantoins are used therapeutically, particularly as antiepileptic agents (diphenylhydantoins). The most widely used of these is phenytoin, marketed in Australia as the preparation Dilantin. Information obtained from the 1998 edition of MIMS indicated that the oral dosage for adults of Dilantin is 4 to 5 mg/kg bw/day in two to three divided doses and in children 5 mg/kg bw/day.

Phenytoin is extensively bound to plasma proteins and can be displaced by drugs competing for protein-binding sites, such as some analgesics. Drugs may also interact with phenytoin by inhibiting its metabolism – phenytoin hydroxylation is saturable and is therefore readily inhibited by agents, which compete for its metabolic pathways (this has been reported, for example, with some antibacterial agents). There is no information to indicate whether dimethylhydantoin (DMH) would interact with phenytoin in these ways. Looking at possible dietary exposure, however, shows that for high consumers of fruits and vegetables (worst case scenario), the intake of residues of DMH would be less than 0.39 mg/kg bw/day. Therefore, there would appear to be a >10-fold safety factor between consumption of BCDMH residues and levels of diphenylhydantoin which are used therapeutically (4 to 5 mg/kg bw/day).

Conclusions

There appears to be limited toxicological concerns from the use of BCDMH as a processing aid for use as sanitising water used to wash fruit and vegetables. A provisional ADI for DMH (the major degradation product of BCDMH) was established using the NOEL from the best available sub-chronic study and using a safety factor of 2000. Based on this ADI, dietary intakes calculations show that only 42% of the ADI would be reached.

In conclusion, considering the available toxicological data and the current Table 5 entry in the MRL standard there are no toxicological grounds not to approve BCDMH as a processing aid in Standard A16.

ATTACHMENT 4

BCDMH – Food Technology Evaluation

Bromo-chloro-dimethylhydantoin (BCDMH) is proposed for use as a processing aid (washing agent) for use in the post-harvest washing of fruits and vegetables and in the manufacture of minimally processed fruits and vegetables. The use of BCDMH is to sanitise the wash waters used and to reduce the microbial load on the produce being treated.

Fresh fruits and vegetables

Many fruits and vegetables are washed after harvest to remove dirt and organic debris prior to packing and storage. Fungicides may also be applied after washing. The quality of the water used in these washing, dipping or rinsing systems is paramount as wash water can harbour many fruit and vegetable pathogens.

Although many bacteria and fungi can cause postharvest rot of fruit and vegetables, the major postharvest losses are caused by species of the fungi *Alternaria*, *Botrytis*, *Diplodia*, *Monilinia*, *Mucor*, *Penicillium*, *Phomopsis*, *Rhizopus* and *Sclerotinia* and of the bacteria *Erwinia* and *Pseudomonas*. Postharvest infection results when these micro-organisms are able to invade produce via any break (often microscopic) in the skin, though it can also occur through direct penetration of the skin (eg. *Sclerotinia*).

Control of postharvest wastage is achieved through using specific storage temperatures (low or high depending on the produce), modified atmospheres, correct humidity, good sanitation and development of wound barriers. For some produce the application of fungicides may be used. When fruits and vegetables are subject to wash systems, disinfection of the wash water is critical for minimising exposure of the produce to fruit and vegetable pathogens.

A processing aid is defined in Standard A16 – Processing Aids of the Food Standards Code as “a substance used in the processing of raw materials, foods or ingredients, to fulfil a technological purpose relating to treatment of processing, but does not perform a technological function in the final food”. The post-harvest washing of fruits and vegetables does not meet the definition of a food processing operation in this context and therefore the use of BCDMH in post-harvest washing is as an agricultural chemical. The National Registration Authority for Agricultural and Veterinary Chemicals have evaluated BCDMH and registered its use in post-harvest wash systems as an agricultural chemical.

Minimally processed fruits and vegetables

For the purposes of this report, minimally processed fruits and vegetables are those that have undergone a minimal processing step such as trimming, peeling, slicing, shredding, washing or a combination of these. Such products include salad mixes, stir-fry mix, vegetable florets and pieces, diced fruits and bean shoots. These products are generally prepared and packaged for convenient consumption.

One of the main features of minimally processed fruits and vegetables include the presence of cut surfaces or damaged plant tissues which compromise shelf life by leading to enzymatic browning, white surface discolouration, senescence, degradation in texture and flavour, and microbial spoilage. Minimising these physiological activities is achieved through reducing physical damage, ensuring correct storage conditions and the use of chemical agents where permitted.

The rinsing of produce during the production of minimally processed fruits and vegetables is an important step in minimising physical damage. Washing with chlorinated water removes the enzymes and nutrients that are released during minimal processing and which coat exposed surfaces. If left, these exudates would result in rapid degradation. Washing also eliminates the majority of micro-organisms present, contributing to improved shelf life and, potentially, removing pathogenic bacteria that may be present.

A wide range and number of micro-organisms have been associated with minimally processed fruit and vegetable products including *Pseudomonas*, *Erwinia*, *Enterobacter* and *Bacillus* bacteria; yeasts such as *Cryptococcus*, *Rhodotorula* and *Candida*, and a wide range of moulds including *Fusarium*, *Alternaria*, *Mucor* and *Rhizopus*. Potential food-borne pathogens such as *Salmonella*, *Listeria monocytogenes*, *Escherichia coli* and *Clostridium botulinum* have also been isolated from a variety of these products.

Wash water quality

It is essential to maintain an effective concentration of a broad-spectrum antimicrobial agent in water used for washing fruit and vegetables to minimise the microbial load in the wash water and prevent re-contamination of product and to reduce as much as possible the microbial flora on the fruits and vegetables being treated. Several disinfecting compounds are available though chlorine compounds are the most widely used disinfectants for this purpose, being active across a wide microbial spectrum and relatively inexpensive. Tabled below are the main disinfecting compounds that may be used as washing agents, currently permitted by Standard A16 – Processing Aids.

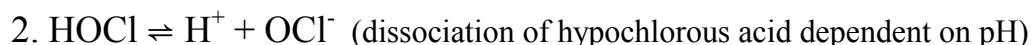
Disinfecting Agent	Standard A16 permission
Chlorine	Group II – Bleaching Agents, Washing and Peeling agents
Chlorine dioxide	
Calcium hypochlorite	
Sodium chlorite	
Sodium hypochlorite	
Hydrogen peroxide	
Peracetic acid	
Ozone	
Sodium hydroxide	Generally permitted processing aids
Phosphoric & sulphuric acids	

An evaluation of the most commonly used water sanitising compounds – chlorine, ozone and chlorine dioxide – is provided below, along with an assessment of BCDMH.

Chlorine compounds

Calcium and sodium hypochlorites are the compounds most widely used for chlorination of wash waters. Sodium hypochlorites are generally sold as liquids, containing 10 to 14% available chlorine, and calcium hypochlorites are sold in powder form, containing about 30% available chlorine. When the hypochlorites are added to water they produce hypochlorous acid (HOCl), which is considered to be the germicidal agent. Germicidal activity is directly proportional to the concentration of unionised HOCl in the solution. The mode of action through which HOCl kills micro-organisms has not been clearly defined but involves it binding with cell proteins, interfering with cell metabolism and inhibiting enzymes.

The level of active chlorine (HOCl level) generally accepted, as the level to achieve disinfection in wash waters for fruit and vegetable processing is 100mg/kg. This level may vary depending on the produce and the likely pathogen load and on exposure time. Citrus fruit, for example, is very susceptible to decay by *Penicillium* and a chlorine concentration of 200 mg/kg is recommended to achieve sterilisation in wash water and dips. Maintaining an effective concentration of chlorine, however, is not easy. When hypochlorites dissolve in water both HOCl and hypochlorite ions are produced, the proportion of each being dependent on the pH of the solution.



At a pH of about 7.5, the proportion of HOCl drops significantly with increasing pH, decreasing the effective chlorine level. Keeping an effective concentration of HOCl in the wash water means, therefore, keeping effective pH control. Generally for disinfection purposes this is pH 7.2 to 7.6 where HOCl represents 47 to 69% of free available chlorine.

While the use of chlorine provides a relatively inexpensive and extremely effective means of disinfecting (if used correctly), it does have disadvantages. As discussed, the concentration of chlorine can be difficult to maintain. As water used in wash water systems for post-harvest washes may need to be sourced from a variety of sources including creeks, rivers and bore waters in which conditions may be alkaline (pH 8.2 +), this can decrease the effectiveness of chlorine. The continual dosing of wash systems with hypochlorites to maintain an effective concentration may also cause the accumulation of chloramines on fruit which cause tainting. In addition, the amount of debris present on produce can add to the formation of chlorinated by-products that can cause tainting and increase the demand on the biocide.

The use of hypochlorites can also cause corrosion in fruit bins, water systems and in-line packing equipment as chlorine is a strong oxidising agent. Calcium hypochlorite can be a particular problem in heated water systems such as tomato dump tanks where the deposition of calcium can effect the heater controls. Calcium spotting of produce, particularly dark fruits, can also result from the use of calcium hypochlorite.

Ozone

Ozone (O₃) is a strong antimicrobial agent, active in the gaseous or aqueous phase against bacteria, moulds, yeasts, parasites and viruses. It has been used for decades for the treatment of drinking water and municipal and industrial wastewater. When compared with chlorine and other disinfectants, lower concentrations of ozone and shorter contact times are sufficient in controlling or reducing microbial populations. It has, for example, been shown to be more effective against micro-organisms at concentrations of 0.64 – 1.11 ppm compared to Cl₂ at 100ppm.

Ozone decomposes in solution in a stepwise fashion, producing hydroperoxyl (·HO₂), hydroxyl (·OH) and superoxide (·O₂⁻) radicals. The reactivity of ozone is attributed to the strong oxidising power of these free radicals. Having a high oxidation potential, ozone reacts with micro-organisms fast, resulting in a high death rate. This high reactivity, however, is also a disadvantage in using ozone as a disinfectant in the food industry because its instability makes it difficult to predict how ozone may react in the presence of organic matter. It is difficult to generalise that a particular concentration of ozone at a given rate will always be effective in inhibiting a definite concentration of micro-organisms in a food product.

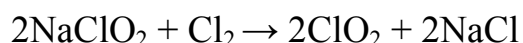
The susceptibility of micro-organisms to ozone may vary depending on the pH of the medium, temperature, the presence of additives and the organic matter surrounding the cells. The stability of aqueous ozone increases with decreasing pH and ozone inactivation of micro-organisms seems to be enhanced at acidic pH values. Its effectiveness, however, is relatively unaffected at pH 6.0 to 8.0. Ozone decomposition is accelerated as temperatures increase and its solubility increases with decreasing temperature.

As ozone is extremely unstable, when it is used in industry it is usually generated at the point of application and in closed systems, largely through photochemical and electric discharge methods such as with a corona discharge ozone generator. Because of its extremely toxic effects when inhaled, ozone detection and destruction systems and respirators are also needed on site for the safety of workers. Other disadvantages that may result from using ozone include the surface oxidation of foods resulting in changes in the surface colour of some fruits and vegetables.

Chlorine dioxide

Chlorine dioxide (ClO₂) is a powerful oxidising agent, which readily dissolves in water to form a solution which is biocidal to a wide range of micro-organisms. Its applications in the food industry have included the sterilisation of fluming and can-cooling water and the control of taste and odour in process water used in soft drink bottling, brewing and distilling.

Chlorine dioxide is unstable and so is generated on site by reacting sodium chlorite with chlorine to form chlorine dioxide and sodium chloride:

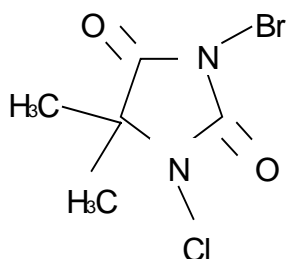


Chlorine dioxide does not hydrolyse in water to form hypochlorous acid but remains dissolved as a gas and may decompose to its chlorite and chlorate ionic forms. There have been health concerns with the production of chlorate and chlorite by-products however recent technological advances have been able to overcome this by producing ClO_2 from the reaction of tetrachlorodecaoxide with HOBr (hypobromous acid).

Chlorine dioxide is largely unaffected by pH (is effective over the pH range 3 to 13) and is effective in waters with high organic levels. It acts by dissolving the cell wall of micro-organisms and has a much shorter kill time than liquid chlorine. ClO_2 is effective at much lower concentrations than chlorine (1-3 ppm) and does not cause problems with tainting and corrosion.

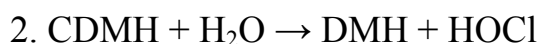
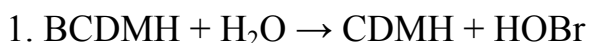
Bromo-chloro-dimethylhydantoin (BCDMH)

Bromo-chloro-dimethylhydantoin (BCDMH) has been used as an alternative compound to Cl_2 for water sanitising such as for spas, heated pools and cooling towers. When dissolved in water, BCDMH releases hypobromous (HOBr) and hypochlorous (HOCl) acids, which work synergistically in achieving sterilisation of water dips. BCDMH, however, has a low solubility and requires an erosion feeder to dissolve it in water.



Structural formula of BCDMH

The Br-N bond of BCDMH is weaker than that of the Cl-N bond so that Br^+ is first displaced from BCDMH when reacting with water:



This gives a quicker build up of HOBr than HOCl , contributing to a stronger immediate concentration of HOBr and a quicker killing effect against micro-organisms. After the dissociation of bromine, there is a slower release of chlorine from BCDMH, giving longer-term disinfection. After a period of time, an accumulation of DMH (dimethyl hydantoin) occurs because of the hydrolysis of the N-halogen bonds. If the DMH concentration builds to a level which impedes further reaction, the longer term disinfection activity of BCDMH is compromised. This may be addressed by draining off some water and adding fresh water.

Bromine enhances the disinfectant activity of chlorine, allowing less chlorine to be used. BCDMH is therefore more active at lower concentrations than, for example, calcium hypochlorite. The levels of use for both post-harvest washing and use on minimally processed fruit and vegetables is proposed at between 5 – 15 mg/L, much less than that needed with hypochlorites.

BCDMH has been shown to be completely effective at eliminating high concentrations of *Penicillium* spores (up to 10^7 cfu²/ml) at concentrations of 5 to 7 mg/L BCDMH with a contact time of 10 to 15 minutes. Evaluations testing the effectiveness of BCDMH against test suspensions (inoculum density $10^5 - 10^6$ organisms per ml) of *Staphylococcus aureus*, *Escherichia coli*, *Listeria monocytogenes* and *Salmonella kahla* have shown a 99.9% kill rate using BCDMH concentrations of 10 ppm (measured as chlorine) and contact times less than 5 minutes³.

As the level of use of BCDMH is much less than that of hypochlorites, there are fewer problems with equipment corrosion and tainting. In addition, the disinfectant activity of BCDMH is not as affected by pH changes as chlorine so that its use in alkaline wash waters (e.g. pH 8.5) does not decrease its effectiveness.

Conclusions

At present there are a number of agents, which may be used for the disinfection of water used in the food industry such as chlorine (hypochlorites), chlorine dioxide and ozone. The sanitisers used primarily for both the postharvest washing of fruit and vegetables and in fruit and vegetable processing are hypochlorites, particularly calcium hypochlorite. However, while providing a relatively cheap and effective means of controlling the microbiological quality of wash waters, the use of hypochlorites does present several disadvantages. These include:

- difficulty in maintaining an effective concentration at pH levels above pH 7.5;
- corrosion of water and packaging systems;
- problems with use in heated water systems; and
- calcium spotting and tainting of produce.

The use of chlorine dioxide can overcome some of the disadvantages of hypochlorites in that it is effective within a broad pH range (pH 6.0-8.0), and is non-tainting and non-corrosive at the levels used. However, because it is unstable and needs to be generated on site it is a more expensive option than hypochlorites. Ozone is also relatively unaffected at pH range 6.0-8.0 and is very effective at low concentrations. It is also unstable and, like chlorine dioxide, needs to be generated on site. Occupational health and safety concerns with the use of ozone in the food industry may be a determining factor in its use.

BCDMH is a stable compound, effective across a broad pH range and at much lower concentrations than chlorine. BCDMH would provide a viable alternative to the use of other disinfecting agents such as hypochlorites, chlorine dioxide and ozone, presently listed in Group II of Standard A16.

² Colony forming units

³ Microbiological evaluations supplied by the applicant and conducted by Microtech Laboratories Pty Ltd.

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Attachment 6

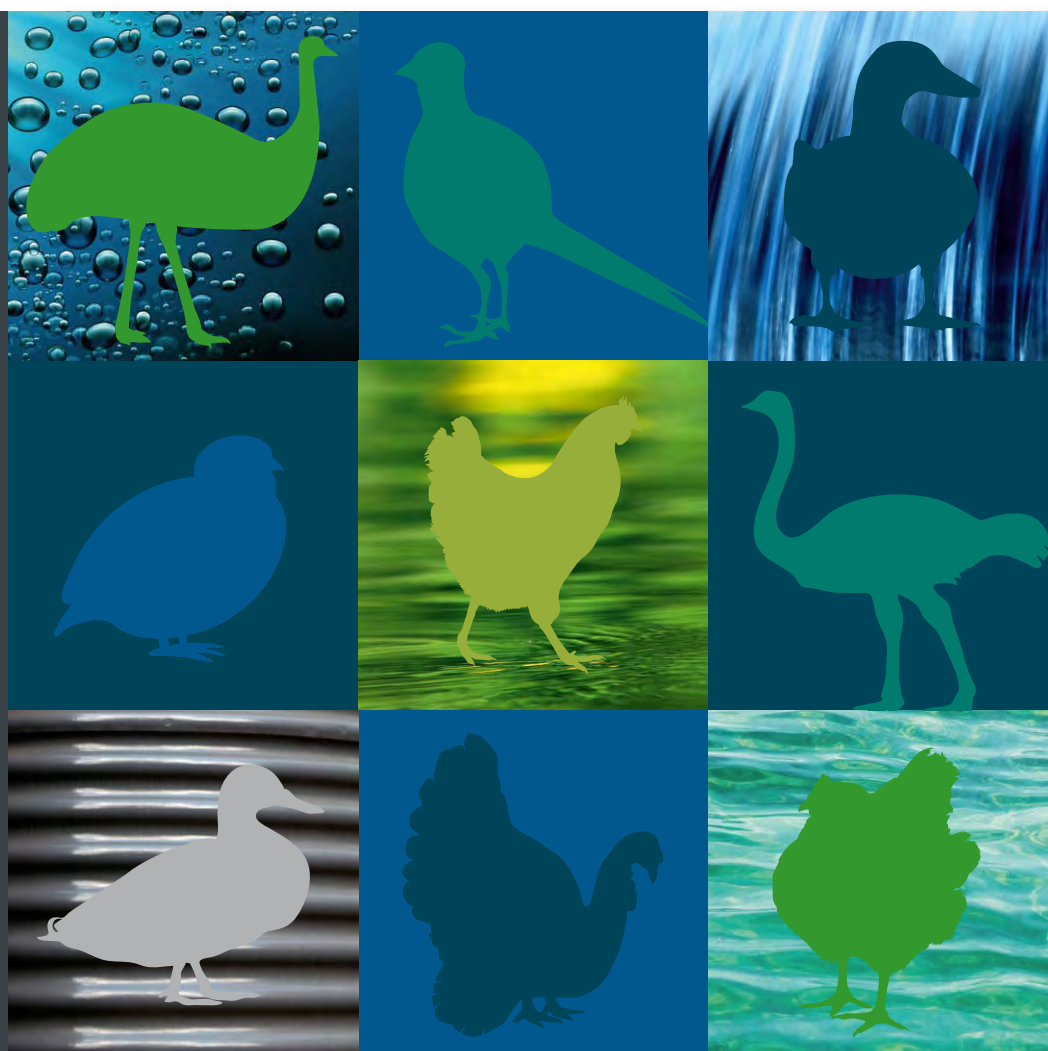


Australian Government
Department of Agriculture,
Fisheries and Forestry



National **Water Biosecurity** Manual

P O U L T R Y P R O D U C T I O N



This report was commissioned by the Department of Agriculture Fisheries & Forestry at the request of the Biosecurity Consultative Group—established as a resolution of the 2007 Government-Industry Avian Influenza Forum.

Contributions to the development of this manual are gratefully acknowledged:

Dr Peter C. Scott and Dr Tim Ahern, Scolexia Animal and Avian Health Consultancy (authors)

Illustrations by Fernando Ferreira

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8/19 Norwood Crescent

Moonee Ponds VIC 3039

Telephone: +61 (0) 3 9326 0106

Facsimile: +61 (0) 3 9372 7576

Email: info@scolexia.com.au

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Water sources used by the Australian poultry industry are varied, and include town water, underground water, surface water and rain water. Whatever the source, water provided to poultry farms must be free from microbial contamination that could cause disease in poultry, or lead to food safety issues.

This report describes the water sources most commonly used by the Australian poultry industry, and water sanitation systems applicable for use on commercial poultry farms.

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SUMMARY

The use of untreated surface water that has been contaminated by waterfowl has been implicated in outbreaks of highly pathogenic avian influenza (HPAI) in commercial poultry in Australia and overseas. This report describes methods for the treatment of surface water to reduce the risks of introduction of avian influenza (AI) viruses to commercial poultry farms in Australia.

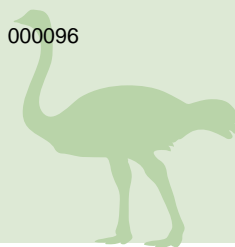
Fortunately, Australia is not in the high-risk migratory pathways for waterfowl (ducks, swans and geese), the recognised reservoirs for AI viruses in the northern hemisphere. However, migratory shore birds still present a low risk of introducing overseas AI strains to Australian birds when they mix with local waterfowl, and the latter share water sources with commercial poultry. Wild bird surveillance programs in Australia have also detected low pathogenicity AI (LPAI) viruses in resident Australian populations of wild water birds.

This report describes the water sources most commonly used by the Australian poultry industry, and water sanitation systems applicable for use on commercial poultry farms. These primary sources of water are mains water, bore or underground water, surface water and rain water.

The highest risk of contamination is associated with the use of surface water (including bore water stored in dams), particularly surface waters that provide habitat for waterfowl. Mains water is identified as the most biosecure water source for poultry.

Chicken meat farms mostly use mains water, however commercial layer farms may use other sources because of their distance from mains water supplies. Other poultry farms rely on either mains or a mix of mains and non-mains water supply.

This report provides a description of various methods of surface water sanitation, and the advantages and disadvantages associated with each method.



Effective sanitation requires:

- effective pre-treatment of water (to reduce organic load)
- correct dosage of sanitiser
- an adequate duration of chemical concentration level in water (contact time)
- reliable operation of equipment
- accurate monitoring (of flow rates, dosing volumes and other parameters)
- avoiding contamination of water after it has been sanitised
- adequate water storage facilities.

The most common deficiencies seen in water sanitation are

- intermittent use of sanitation systems
- no sanitation of surface water
- minimal monitoring of sanitiser levels
- open storage systems
- incorrect dosing of sanitiser
- inadequate pre-treatment of water
- problematic equipment (or poor maintenance)
- ineffective products
- mixing of unsanitised rainwater or recycled water with sanitised water
- inadequate contact time.

The poultry industry should identify and use water sanitisers and application systems that are reliable and effective, economical, user-friendly and with technical support readily available.



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INTRODUCTION

The incursion of an avian pathogen into a commercial poultry flock can occur by vertical transfer¹ or through a variety of horizontal contacts between livestock, personnel, equipment, fomites², feed and water.

Water is an essential nutrient and it is important that drinking water is free from microbial contamination that may result in disease in the poultry flock or cause food safety issues.

Contaminated water supplies have been implicated in the introduction and persistence of endemic pathogens³ such as *Escherichia coli* (*E. coli*), *Salmonella spp.*, *Campylobacter spp.*, infectious bursal disease virus (IBDV) or egg drop syndrome (EDS), and in the introduction of emergency animal diseases (EADs) such as virulent Newcastle disease virus (vNDV) or avian influenza (AI).

This publication focuses on the risks of introduction of AI viruses through the use of surface water contaminated by wild waterfowl.

This paper will also predominantly focus on the commercial Australian poultry industry and types of poultry housing and husbandry normally practiced.

1 Vertical transfer—via the egg

2 Fomite: an inanimate object that may be contaminated with infectious organisms, e.g. clothing, buckets, tools

3 Endemic pathogens are those that are known to occur in a population or region, for example, in the Australian poultry population



1 SOURCES OF WATER FOR POULTRY

Water sources used by the Australian poultry industry are varied and also differ between states and territories and between rural and urban localities. Primary water sources for supply to poultry include:

- mains or town water
- bore or underground water
- surface water
- rain water.

1.1 Mains or town water

Unlike chicken meat farms, commercial layer farms tend not to be centrally located and tend not to use (or have access to) mains or town water supplies. For poultry species other than chickens, mains or non-mains water supply may be used.

Mains water is generally treated and sanitised prior to distribution and is therefore the preferred and most biosecure water for poultry. Sanitation of mains water at the farm site is uncommon, although some producers may choose to use a sanitiser to control biofilm and other non-specific microbial build-up in drinking or cooling systems. On occasion, mains water has been found to have high levels of coliforms requiring treatment (such as treating the mains supply with chlorination). With reduced water availability in many areas of Australia, restrictions have been put on some intensive livestock and industrial facilities to reduce mains water use. This has necessitated the use of alternatives such as bore or surface water.

Some water authorities also mandate that poultry farms can only access prescribed flow rates (litres per second) from the mains supply. This requires producers to use farm water storage with site distribution via pumps, in order to provide additional water in times of higher demand.

1.2 Bore water (underground water)

The use of underground water is common in Australia, particularly where the quality (especially the salinity) is suitable for use in poultry. The suitability of bore water varies significantly between localities, with some areas such as south-east Queensland generally being favourable, while others such as North and North-central Victoria are variable. The state departments of primary industry can provide information on water quality for some localities.

Underground water is usually considered to have a very low risk of containing avian pathogens, so on-farm sanitation is uncommon for this water source. Shallow bores or spring water, however, may be affected by surface run-off and can, particularly after heavy rains, contain levels of coliforms including *E. coli*. The presence of *E. coli* indicates faecal matter, such as from grazing animals, has contaminated the bore through surface run-off.



The treatment of bore water by methods including desalination (reverse osmosis) to reduce high salinity can be undertaken using existing and improving technology. However, a thorough knowledge of the technical aspects of water treatment technology, bore operation and environmental aspects is essential. Access to bore water generally requires a license from the local catchment or water authority, an extraction permit and an allocation allowance. Often this allocation may need to be traded or offset against existing allowances from other supply sources.

It is also necessary to maintain farm storage of bore water, particularly where flow rates are below peak demand or the water has been previously treated. This storage may be sealed or, in some cases, pumped directly into open water storage such as a dam. Bore water stored in the open should be considered a non-secure source of water that can be contaminated with avian pathogens such as AI viruses.

1.3 Surface water (dams, reservoirs, channel, rivers and streams)

Surface water provides the highest risk for potential contamination with avian pathogens, particularly those associated with aquatic water birds such as AI and EDS viruses and bacteria associated with water run-off, such as *E. coli*, *Campylobacter spp.* and *Salmonella spp.* Effective sanitation of surface water is required to reduce the risk of an EAD in poultry.

Surface water that provides a permanent or transient habitat for waterfowl, particularly the *Anseriformes* (ducks, geese, swans) or *Charadriiformes* (shorebirds), is at highest risk of contamination with AI virus.

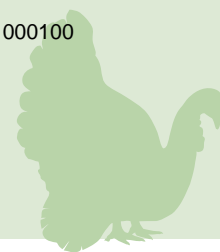
The methods required to effectively sanitise surface water and eliminate avian pathogens are generally more technically complex than thought by water users. Factors influencing the effectiveness of surface water sanitation include:

- the avian pathogen involved
- the quality of the water and its organic load, pH and solutes
- the sanitiser used
- the contact time between the sanitiser and the water
- the turbidity of the water.

Even after these aspects are considered and addressed there are mechanical, maintenance and monitoring factors that can also influence the effectiveness of water sanitation.

1.4 Other sources (rain water, carted water, recycled water)

The origin of alternative water sources should be identified in order to evaluate their biosecurity risk. For instance, water carted from a secure mains supply is associated with much lower risk than water from a lake or dam. With this knowledge, the necessary actions should be taken to ensure that the water is a secure and biologically safe supply for poultry. Other horizontal contacts such as vehicular and personnel movements should also be assessed for their biosecurity risk.



2 AVIAN INFLUENZA AND WATER SUPPLY TO POULTRY FARMS

To understand and appreciate the risk that surface water poses to poultry it is necessary to understand the epidemiology of AI viruses in waterfowl (Arzey 2004; East, Hamilton, & Garner 2008; Khalenkov, Laver, & Webster R.G 2008; Leung et al. 2007; Senne 2003; Stallknecht et al. 1990b) and the ability of the viruses to persist in surface water and ambient conditions (De Benedictis, Beato, & Capua 2007; Doyle, Schultz-Cherry, & Robach 2007; McFerran 1997; Ogata & Shibata 2008; Rice et al. 2007). Readers are referred to the various publications for further detail on these subjects.

Wild bird surveillance programs have detected LPAI viruses in the Australian wild water bird population.

While Australia is not in the high-risk migratory waterfowl pathways for H5N1 HPAI virus, there is still a low risk of viruses being introduced from overseas where migrating shorebirds, waterfowl and commercial poultry share close proximity. There are a few localities in Australia where such an association occurs (East, Hamilton, & Garner 2008). There is also a risk from Australian AI strains for poultry farms located close to water bodies that host wild waterfowl. The risk is through the potential for the supply of contaminated surface water, physical association of these waterfowl or their fomites with commercial poultry, and possibly through other horizontal contacts.

Contaminated surface water and/or the presence of wild waterfowl have been implicated in previous AI outbreaks in Australia (East, Hamilton, & Garner 2008; Selleck et al. 2003; Senne 2003; Westbury 2003). The persistence of the AI virus in water is an important component of the epidemiology of the spread of AI virus from waterfowl to commercial poultry via surface water. Low water temperatures combined with prolonged shedding of virus by waterfowl can result in particular strains of AI virus persisting in the environment for up to 200 days. This may account for the generational cycling of the virus in ducks returning to water habitats for breeding purposes (Stallknecht, Shane, Kearney, & Zwank 1990b; Stallknecht 2003).

AI viruses have also demonstrated tolerance and stability at a pH range from neutral to 8.5, with infectivity declining below a pH of 6.0. Under saline conditions, infectivity is inversely related to salt concentration (Stallknecht et al. 1990a).



3 OPERATIONAL ASPECTS OF SURFACE WATER USE IN AUSTRALIAN POULTRY FARMS

Surface water is used in Australian commercial poultry farms where alternative economical supplies of water are not available. There may be circumstances where different types of water supply are used in combination with surface water. On some properties, different types of water supply may be used for different purposes. Combined sources of water may be used:

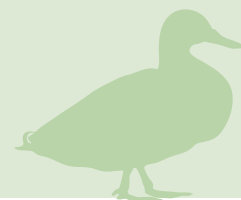
- when mixing moderately saline bore water with surface water to reduce salinity, making the water more suitable for use
- when quality water from the mains supply or bore is used for drinking purposes while surface water is used for cooling (evaporative or fogging)
- when surface water use is seasonal. While mains or bore water supply may be adequate during the winter, the higher demands for water for cooling in summer requires on-farm stored surface (dam) water
- when excess bore water is stored in a dam during winter for use on the poultry farm during times of high water demand in summer
- when poultry gain opportunistic access to surface water after heavy rain periods.

Most commonly, surface water is pumped into holding tanks and distributed throughout the farm by further pumping or gravitation. Storage facilities may have constant inflows proportional to water demand or be fed from a primary storage that is filled when needed. Total farm water storage (tanks) can vary from a few hours' to a week's supply. Smaller tanks can be plastic, fibreglass or steel with larger tanks made from concrete or steel, with plastic liners. On newer farms, storage tanks are also required by planning laws to be able to serve a secondary purpose—that of a fire fighting water supply.

Surface water, other than that delivered in piped irrigation distribution systems, is accessible by waterfowl within the boundary of the property housing the poultry. This proximity provides a further risk of horizontal contact between waterfowl or their waste with commercial poultry.

Even in situations where there is adequate mains water or quality bore water for drinking water and cooling use, planning authorities often require the building of retention or dry basin dams on new poultry developments to ensure farm run-off is kept within the boundaries of the property. Similarly, dams may be created on a new poultry development site to provide the necessary material for earthworks in constructing the shed foundations or pads. As earthworks are expensive, the cost is minimised by obtaining earth immediately adjacent to the sheds rather than carting it from a more distant location.

If these dams are frequented by waterfowl, they can pose some risk through attracting waterfowl closer to poultry sheds. This problem is further exacerbated if cereal grain cropping is undertaken on the land immediately surrounding the sheds. In such situations, risk can be reduced by bird aversion activities and using clean footwear and foot baths prior to entry to the sheds. In free range facilities, poultry should be denied access to surface water, and attractants to wild waterfowl must be minimised.



4 SANITATION OF SURFACE WATER

The ability to effectively eliminate poultry pathogens from surface water is dependent on a number of factors, including the type of pathogen, the quality of the surface water, the sanitiser used and the operational aspects of the dosing equipment and storage facilities used. A critical component of good water sanitation is to have clean water and achieving this may require pretreatment such as filtration. Dirty water cannot be effectively sanitised no matter which generic sanitiser is used.

4.1 Microbial contaminants

Potential avian pathogens include bacteria, protozoa, fungi and viruses. The sensitivity of these various microbial contaminants to chemicals and treatments is extremely varied. Sensitivity is further affected by the growth stage of the organism and whether or not it is protected by organic material. Agents such as cryptosporidia are particularly resistant to most water sanitisers, IBD virus is resistant to inactivation by many sanitisers, while the *Enterobacteriaceae* (including *E. coli* and *salmonellae*) are moderately sensitive to most. Fortunately for the poultry industry, AI virus as an enveloped virus is relatively sensitive to the majority of sanitisers. Poor quality water of high salinity and pH's divergent from neutral are by themselves capable of limiting the persistence of AI virus.

In contrast, EDS is caused by an adenovirus which is more stable than AI virus, able to remain viable even in a pH range of 3 to 10. Sporadic outbreaks of EDS can be associated with inadequately sanitised surface water to which wild waterfowl have had access.

4.2 Water sanitisers

There are many brands of water sanitisers available to the poultry producer, although they are predominantly derived from only a few chemical groups. In some cases, water may need treatment prior to sanitation.

The choice of sanitiser should primarily be based on efficacy, followed by other factors such as application method, cost and safety. Poultry producers are not specialists in the science of sanitisers and are thus usually dependent on company technical advisors, veterinarians or sales people to provide the necessary information.

Some sanitisers are marketed based on information only about their effectiveness to inactivate bacteria, usually under non-commercial situations such as distilled water with serum. The failure to produce data on viral inactivation is usually because such testing is expensive and technically difficult to undertake. The major types of water sanitisers that are available include the following categories:

- the halogens—including chlorine, bromides and iodines (iodophors), chloramines, and potassium permanganates
- other oxidisers, including chlorine dioxide, hydrogen peroxide, ozone and peracetic acid
- organic acids, usually short chain fatty acids
- quaternary ammonium compounds
- ultraviolet (UV) light
- other products such as citric acid, copper-silver ionisation, etc.

The more commonly used water sanitisers are discussed below.



4.2.1 Halogens

Of these, **chlorine** (hypochlorous acid/chlorite ion) is the most commonly recognised and used. The activity is mediated by hypochlorous acid produced at acid pH and the efficacy of chlorines declines as pH increases (optimum around pH 6.7). Hypochlorous acid denatures proteins by oxidation and it is this property as an oxidiser that confers its biocidal activity. Chlorine is available in liquid form as sodium hypochlorite and in solid form as calcium hypochlorite. Sodium hypochlorite is usually available at a concentration of 10 to 12% (De Benedictis, Beato, & Capua 2007). Chlorine (usually as liquid hypochlorite) has a broad spectrum of activity, is minimally affected by hard water and acts rapidly. Its use is limited by its corrosive nature. The efficacy of chlorine is affected by organic material and turbidity, UV light and heat and its limited residual activity. Chlorine has a very low cost and application systems involve only small capital outlay.

While some earlier reports had demonstrated the effectiveness of chlorine on AI virus, it was not until 2007 (Rice, Adcock, Sivaganesan, Brown, Stallknecht, & Swayne 2007) that specific work was undertaken demonstrating chlorine's effectiveness against H5N1. Studies demonstrated that once the chlorine demand was met, the maintenance of free residual chlorine at around 1 part per million (ppm) was sufficient to inactivate the virus.

Iodines, or formulated variations such as iodophor, are similar in effectiveness to chlorine, showing some advantage in ability to cope with organic load.

Bromine is more stable than chlorine as it has a higher evaporative point. Bromine continues to be effective even after reacting with organic compounds. Hypobromous acid is the active form that inactivates the pathogens. After reacting, the hypobromous acid is reduced back to bromide ions. The addition of an oxidizer will convert the bromide back to hypobromous acid. This is done by adding fresh oxygenated water, for example, in an evaporative cooling pad recirculating water tank.

4.2.2 Other oxidisers

Amongst oxidisers, **chlorine dioxide** is becoming popular for water sanitation in the poultry industry. It is broad spectrum, sporidical and fast acting. It disinfects by oxidation but does not chlorinate. It is also significantly more resistant than chlorine to organic quenching and less affected by pH. This allows for more effective sanitation of water using levels of chlorine dioxide as low as 0.1 ppm.

Chlorine dioxide assists in reducing biofilm build-up in drinker systems and, unlike halogens, does not form complexes like chloramines which are potentially carcinogenic. The cost of the chemical is much higher than chlorine and there is the added requirement for a chemical activator such as phosphoric acid. Application systems are also significantly more expensive than those required for chlorine. With new technology, the lower cost precursor compound sodium chlorite can be used to generate chlorine dioxide using an electro-discharge plate that generates hydrogen gas. The capital outlay for this equipment is high.



Hydrogen peroxide has similar inactivation properties to chlorine dioxide and can be used in the solution or vapour phase. However it is corrosive, inactivated by heat and organic material, and needs to be used at high concentrations. This oxidiser also has limited residual activity.

Peracetic acid is similar in activity to chlorine dioxide and is effective in the presence of organic matter. Compared with chlorine, its limitations—besides cost—are that it is corrosive to soft metals, unstable at high ambient temperatures and is an irritant, particularly in its concentrated form.

Ozone is generated from electrical discharge units and bubbled into the water supply. Ozone sanitises water either by direct oxidation and disruption of cell membranes of microbes by molecular ozone or by free radical-mediated destruction of microbes. Also, through indirect oxidation reactions of ozone, the ozone molecule decomposes to form free radicals which react quickly to oxidise organic and inorganic compounds. Generally the efficacy and activity of ozone are similar to chlorine dioxide. Set up capital costs can be high, as are maintenance costs due to discharge tubes requiring replacement every few years.

4.2.3 Ultraviolet light

UV light is used minimally in the poultry industry and generally for the sanitation of low volumes of clean water in hatchery mister sprays. UV light has proved unable to inactivate HPAI virus after 45 minutes exposure (De Benedictis, Beato, & Capua 2007). UV water treatment is not effective for sanitising surface water unless the water is clean. It has a relatively low cost but its usefulness is limited under situations where there are very high volumetric demands and it has no residual activity. Its efficacy is not affected by pH.

4.2.4 Organic and inorganic acids

Acids have a high viricidal activity and through the correct choice of acid, or acid mixture, this class of disinfectants can be used for several purposes from liquid effluent treatment to decontamination of structures. There are two categories of acids that can be used in disinfection procedures: organic acids (formic, citric, lactic, mallic, glutaric and propionic acids) and inorganic acids (nitric, hydrochloric, sulphuric, phosphoric, sulphamic acids). Both are effective, especially against viruses that are sensitive to low pH, but they are generally slow-acting (Jeffrey D.J. 1995). Inorganic acids are able to inactivate viruses only through decreasing pH values. These acids are more typically used in research, for example, in sanitising clean water for specific pathogen free (SPF) birds. In contrast, organic acids inactivate viruses also through the interaction of lipophilic structures with membranes of enveloped viruses (Haas et al. 1995).

Organic acids were originally introduced to the poultry industry as an aid to improving flock performance rather than as a generic water sanitiser. Their ability to inactivate microbial contamination varies depending on the agent. Their cost is high when compared to chlorine, and high levels of organic acids in poultry drinking water may decrease water intake and reduce performance. This latter effect is due to the organic acids affecting the taste of the water. Acidifiers do not replace sanitisers but are used to reduce high water pH to levels of 6.0 to 6.7 to improve the efficacy of sanitisers such as chlorine.



4.3 Application systems and facilitation for water sanitation

To achieve and sustain effective water sanitation, application equipment and its correct use are just as important as the type of sanitiser used. Effective water sanitation requires:

- effective pretreatment of the water
- correct dosage of sanitiser
- adequate contact time
- reliable operation
- accurate monitoring in real time
- avoiding contamination post-sanitation
- adequate water storage and appropriate configuration of storage.

4.3.1 Pretreatment of water

High organic load is an impediment to effective sanitation of surface water, which can be further compounded by the presence of other chemicals such as mineral salts, nitrogenous compounds, iron and colloids (silicates). The pH of water and the level of oxygenation will also influence the efficacy of sanitation. Seasonal factors may also affect water quality, for example additional rainfall or low rainfall requiring admixtures of bore water. These factors will affect the need to pre-treat the water and will have some bearing on the type of sanitiser used.

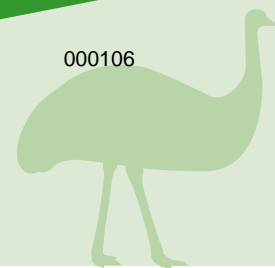
Before any technical decision is made about water pretreatment, it is essential that a complete analysis of the surface water is done. The testing should include a complete chemical analysis (pH, total dissolved solids (TDS), chloride, nitrate, nitrite, sulphate, iron, copper, magnesium, manganese, zinc, sodium, and calcium), turbidity, biochemical oxygen demand (BOD) and a microbiological analysis (total coliforms, *E.coli*, faecal coliforms). Pretreatment by desalination does not remove microbial pathogens, so sanitation of the treated water is still required.

Other pretreatments include sand filters and flocculants to remove solids and organic loads (see Appendix). Removal of high levels of iron can be achieved by aerating or treating the water with an oxidiser (chemicals which flocculate⁴ the iron), followed by the use of settling tanks. There may also be the need for pH adjustment using hydrochloric or phosphoric acids.

Biofilms are an impediment to effective sanitation and should be cleared from lines with flushing and the use of oxidizing sanitisers such as chlorine dioxide and peracetic acid. In some cases where biofilms have been long standing and associated with water pipe corrosion, it is necessary to replace the water lines.

All of these pretreatments require an understanding of the science involved and an investment in capital to achieve the required outcome.

4 Flocculate means the process whereby a solute comes out of solution in the form of flakes.



4.3.2 Dosage of sanitiser

The correct dosage of chemical is essential to achieve effective sanitation of surface water. For liquid addition, dosage equipment must be able to deliver the correct amount of sanitiser to a measured quantity of water. This can be done either via mechanical flow detection pumps, electronic pulsating digital solenoid driven diaphragms, or peristaltic pumps (see Appendix). For the addition of chlorine dioxide, ozone and crystalline iodine systems, the technical aspects of application and dosage are more complicated and require the support of an adequately qualified and trained distributor.

The ongoing maintenance of such equipment is critical. The choice of applicator is influenced by availability of power and cost.

4.3.3 Adequate contact time

Adequate contact time is essential to ensure that microbial pathogens are inactivated prior to the delivery of water to poultry. The duration of contact time is dependent on the contaminant, the quality of the water, the type of sanitiser used and the temperature of the water. Such detailed information is not always available in the field situation and producers therefore need to be conservative about contact time. While different sanitisers act at different rates to inactivate particular avian pathogens, **two hours** at the **recommended sanitiser concentrations** is suggested as the minimum contact time. Achieving this benchmark will ensure a high level of confidence for achieving effective water sanitation for most systems and conditions.

Ultimately the only way to ensure that contact time has been adequate is to undertake monitoring for microbial contaminants. While it is not usually practical to test for viruses, bacteria can be used as an indicator.

4.3.4 Reliable operation of equipment

The continuous use of water by poultry operations necessitates continuously effective sanitation of surface water. Even temporary failure of effective sanitation increases the risk of incursion of a water-associated avian pathogen. The purchase of better quality equipment is a small capital outlay considering the importance of the required outcome. While operational aspects of the equipment may fail (such as electronic mechanisms, seals, and casings) there are also maintenance issues (such as air locks, corrosion and filter blockages) that need to be routinely attended to. For more sophisticated set-ups, a maintenance contract from the supplier is often necessary, and the assurance that there are readily available replacement parts.

When buying equipment from overseas, it is important to ensure that it is compatible with Australian standard fitting sizes and electrical input requirements.

4.3.5 Monitoring

It is essential that the effectiveness of equipment can be monitored. This can be done using inbuilt sensing equipment with remote readouts, or through manual measurements of flow rates and dosing volumes. Monitors can also be alarmed to warn the producer of a failure. Simple manual checks to ensure that the correct amount of sanitiser is being used can provide an effective cross-check.



4.3.6 Avoidance of contamination post-sanitation

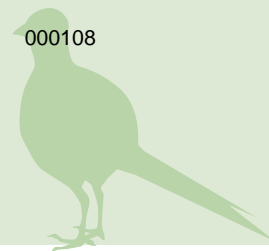
Effective water sanitation can be undone by allowing recontamination after treatment. Treated water should be transferred in sealed systems and into sealed tanks. There should be no other source of water entering the treated water, such as untreated rainwater. If the system is closed, then falling sanitiser levels in the stored water are of no consequence as the avian pathogens will already have been inactivated and there is no opportunity for recontamination. The principle of maintaining measurable chlorine at the drinker level is not of paramount importance if the water has been effectively pretreated. The presence of a measurable level of sanitiser at the level of the drinker does give the producer more confidence that effective sanitation is being carried out and also aids in controlling the non-specific build up of coliforms, algae and biofilms. Residual activity is particularly important for water distribution systems.

4.3.7 Water storage

Effective sanitation, adequate contact time, sealed storage and reliable equipment operation can only be achieved with the correct (and coordinated) configuration of untreated water delivery, treatment, storage and treated water delivery (Appendix). This means that where the treatment of surface water is required, installation of a number of storage tanks of appropriate size that can store and deliver the treated water in a strategic manner will be required. The procedure of injecting chlorine directly into the main water supply line to the shed does not allow adequate contact time. However, with chlorine dioxide the contact time may be adequate.

In addition, the use of only one water tank for sanitising and holding stored water is inadequate, particularly under periods of high water demand, as there will be a replenishment of raw water entering the system that will have inadequate contact time with the sanitising chemical. It is preferable, if not essential, to have a two tank storage system that is solenoid⁵ controlled with high and low level ball valves (Appendix). This allows the delivery of sanitised water after a guaranteed minimum contact time. Alternatively, this may be done manually by draining sanitised water from the main storage tank into secondary storage tanks that supply the daily demand of the sheds. It is also critical that all water supplied to the sheds is sanitised. Sanitising only the drinking water and not the water used for cooling increases the risk of incursion by water-borne pathogens.

⁵ An electromechanical valve that is controlled by the starting and stopping of an electrical current and usually used as a switch to control the flow of fluid.



4.4 Monitoring to ensure effective water sanitation

The monitoring and disciplined record keeping of sanitiser levels and other parameters including pH and oxidation and reduction potential (ORP) are critical in ensuring effective microbial inactivation potential in treated water.

Monitoring sanitised water is not straightforward and the use of chlorine test strips alone may not give a true indication of the disinfection potential of the chlorinated water. Technical assistance must be sought, particularly when dealing with halogens other than chlorine and with oxidising compounds such as chlorine dioxide. This advice should preferably come from a competent technical advisor.

Most methods for testing for effective water sanitation look at the level of the particular sanitiser in the water as an indicator (e.g. chlorine at 1 to 2 ppm at the drinker level) and if this is achieved then it is assumed that the water is effectively sanitised. This is true for reasonable quality water, but for poor quality water the effectiveness of the sanitiser may be compromised despite its level appearing to be correct. ORP does not measure the chemical—instead, it measures the capacity of the sanitised water to kill microorganisms.

Determination of the ORP has become the procedure of choice for monitoring, and can be performed with incorporated systems or a hand-held apparatus. The quality of the testing unit should be evaluated prior to purchase. ORP, measured in millivolts (mV), operates much like a digital thermometer or pH probe and ORP sensors allow easy monitoring and tracking of critical disinfectant levels in water systems. ORP for water system monitoring provides the operator with a rapid and single-value assessment of the disinfection potential of water. Research has shown that at an ORP value of 650 to 700 mV, spoilage bacteria and bacteria such as *E. coli* and salmonellae are killed within a few seconds. Other microorganisms such as protozoa and viruses are inactivated over longer contact times, generally measured in minutes.

The ORP is a valuable tool where water quality is poor. For example, where water pH is high, measurable chlorine levels may be high but the level of active sanitising agent, hypochlorous acid, may be below effective levels, resulting in an ORP measurement significantly below 650. The routine measurement of ORP in mV is not a linear relationship at typical use rates. In chlorine sanitation systems, increasing pH will lower the ORP and decreasing the pH will increase ORP, reflecting the increased availability of hypochlorous acid. In 1972, the World Health Organisation adopted an ORP standard for drinking water disinfection of 650 mV. At this level the sanitiser in the water is active enough to destroy harmful organisms almost instantaneously.



4.5 Common deficiencies seen with water sanitation in the poultry industry

Despite the importance of effective sanitation of surface water in the Australian poultry industry, deficiencies can occur that may increase the risk of incursion of a disease such as AI. Given that effective sanitation of surface water is not achieved under all circumstances, poultry flocks in Australia may be exposed to surface water that has been ineffectively treated. Epidemiological links have been made between contaminated drinking water and a number of past HPAI outbreaks in Australia and overseas.

Some producers may not recognise the importance of water sanitation in their overall biosecurity program, or may lack the necessary combination of available technical skills and knowledge to ensure an effective surface water sanitation system in their poultry operation. Deficiencies which may be seen within the poultry industry include:

- no intention to sanitise surface water due to either
 - noncompliance due to various motivations
 - some organic farms wishing to avoid chemical use
- use of equipment, sanitisers and systems that fail to ensure the reliable and sustainable effective sanitation of water through any of the following
 - ineffective products
 - inadequate contact time
 - open storage systems
 - mixing of unsanitised rainwater or recycled water
 - incorrect dosing
 - no maintenance program
 - problematic equipment
 - inability to accommodate for changed demands in water quality
 - inadequate pretreatment
- insufficient monitoring through
 - absence of, or inadequate, testing programs
 - inability to test system operational status in real time (alarms)
 - inadequate frequency of monitoring
 - use of only microbiological testing
- intermittent use of sanitation systems due to
 - avoiding sanitation during vaccination or with young stock
 - modification of facilities
 - insufficient stocks of chemicals.



4.5.1 No sanitation of surface water

The failure to sanitise surface water is relatively uncommon in the Australian poultry industry. Vertically integrated companies are generally comprehensively audited and supply sanitised water to poultry. Industry- and company-based quality assurance programs and state regulatory authorities encourage water biosecurity in all poultry industry sectors.

Organic farming organisations state that there are no accreditation problems with using water chlorination, so water chlorination systems can be used on organic poultry farms. For those not wishing to use chlorine-based sanitisers, there are alternatives that can be considered and technical advice should be sought.

4.5.2 Use of equipment, sanitisers and systems that fail to ensure effective sanitation of water

New products for water sanitation should be carefully assessed. Products should claim effective water sanitation, rather than just improved bird performance, and should provide some data related to the inactivation of microbial contaminants.

Inadequate contact time may be observed when a one-tank system is used. When water demand is high in a one-tank system, water sanitised with chlorine is replenished with a significant amount of raw water, with the mix of treated and untreated water then leaving the storage tank before adequate contact time with the sanitiser. The direct injection of chlorine into the main water input line also results in inadequate contact time. In these situations chlorine dioxide may be a suitable alternative sanitiser.

A similar situation may arise when rain water or other catchment waters (including recycled water) gain entry to the storage tank without prior sanitation. While rain water carries a lower risk, roof surfaces frequented by wild birds, and in some cases ducks, can result in faecal contamination of this water. Similarly, open water tanks can be contaminated by free flying and roosting birds and possibly even by contaminated dust-laden aerosols.

Non-operational dosing systems can be caused by:

- air locks⁶ in dispensing lines (particularly during hot weather if dosing systems do not have an automatic bleeding system)
- broken and/or defective pump mechanisms
- corroded pump internals (medication pumps are often unsuitable for use with chlorine)
- fractured doser housings after frosts and other damage.

6 Trapped air



- Where there has been heavy rainfall with run-off into dams, the increased organic load demand can significantly impact on the level of effective sanitiser in the system. This is not an issue where there is automatic monitoring, as the dosing will increase automatically or an alarm will sound.

Water from creeks, dams and channels can be of poor standard, particularly during drought. It is often poorly aerated, its oxygen demand is high and, despite the addition of copious amounts of chlorine, its ability to inactivate pathogens is limited. This is where measuring ORP is a useful adjunct. Pretreatment of this water is often required.

Some producers use manual dosing with either liquid or solid chlorine but this approach is haphazard and unreliable, with resultant wide fluctuations in chlorine levels. While considered economical, this is a false economy as it does not consider the time taken and repeated labor required.

Underlying many of these dosing and system failures is the inability of the poultry farmer to identify or correct the mechanical failure. Compounding the problem, local plumbers often cannot be obtained at short notice and may lack both the understanding of precision pumps and/or the science of water sanitation.

4.5.3 Insufficient monitoring

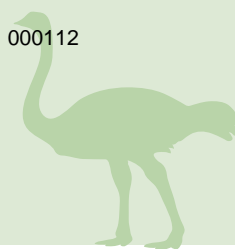
Producers who are part of audited quality assurance programs are usually mandated to complete monitoring sheets to record water testing information. All producers should place priority on testing water frequently (i.e. daily to bi-weekly) and recording this information.

Some of the sanitisers, particularly the novel ones, have no readily available test for real-time farm testing, which is clearly a disadvantage. As previously indicated, testing for the primary chemical alone, particularly chlorine, may not give a true indication of sanitising efficacy, particularly where input water is poor. Farmers in this situation need to also test for pH and ORP.

Actual microbiological monitoring of drinking water within the poultry industry is not a common routine. When undertaken, the presence and quantification of total bacteria, coliforms and *E. coli* act as a marker of effective water sanitation. Sample collection, handling and delivery of the water sample to the testing laboratories can be problematic for producers, as there is a need to use sterile collection bottles and to get these to the testing laboratory within 24 hours and under chilled conditions.

4.5.4 Intermittent use of sanitation

Some farm managers turn the water sanitation system off during the administration of live vaccines, with the intention of not harming the vaccine. However, this approach opens up the possibility of contaminated water reaching birds. The correct procedure is to sanitise the water as usual and then run it into the medication tank, allow it stand overnight (or at least several hours) with skim milk powder and then add the vaccine in the normal manner. The use of medication pumps for vaccination complicates this matter of chlorinated water and vaccination because of the nature of the direct injection system. The authors of this document prefer medication tanks to dosators for vaccination and medication.



The practice of discontinuing sanitising water during facility upgrades and re-plumbing of the site opens up a risk window. On occasions farm managers find that they have depleted their stocks of sanitiser and are unable to replace this stock immediately. Again there is a period of risk until this sanitiser is replaced. To avoid the problem of depleted stocks monitor the stocks of sanitiser and usage rate and always have replacement sanitiser available.

It is necessary to sanitise water for birds of all ages, including young hatchlings.

5 OVERVIEW AND RECOMMENDATIONS FOR THE BIOSECURITY OF WATER FOR POULTRY

Numerous publications, trials and field observations clearly identify drinking water as a biosecurity risk for poultry. For EADs such as AI, surface water that has been contaminated by waterfowl provides one of the highest risks. For the Australian poultry industry to reduce the likelihood of an outbreak of AI in a commercial poultry flock, it is essential that effective sanitation of surface water is undertaken where such water is used for drinking or cooling purposes.

Because effective water sanitation is so important, the industry needs education programs that cover the use of water sanitisers and application systems, and promote the use of sanitation that is:

- reliable and effective
- economical both in capital set-up and cost of sanitiser
- easy to use
- has readily available technical support.



APPENDIX WATER CHLORINATION SYSTEMS

The schematic technical drawings illustrate a typical set-up for the chlorination of surface water being supplied to commercial poultry sheds for drinking water and cooling purposes. The system illustrated can be modified for delivery of other recognized water sanitisers, and specialized application systems can be used to replace the dosing pump for use with iodine, chlorine dioxide, ozone or other agents. As individual farm requirements vary, producers are advised to seek technical advice from their service providers for specific details on water sanitation and the delivery and storage systems that are applicable to their farm.

Explanatory Notes

Input water

Input water requiring sanitation, typically surface water (dams, streams, channels, rainwater, untreated reticulated water), should be first analysed for electrolytes, heavy metals, turbidity, organic load, pH and microbiological contamination (coliforms, *E. Coli*) to determine

- its suitability for poultry drinking water
- its suitability for effective chlorination.

This information determines what type of water pretreatment is required. Such testing should be repeated at least twice a year, or whenever there are changes in water source or quality. For chlorination to be effective the water needs to be clean and around neutral pH, so pretreatment, when required, is pivotal to effective chlorination.

Pretreatment and filtration (A1)

The type of pretreatment system required will depend on the quality of the input water. It may vary from a simple physical filter to a sand filter with an automatic back-flush mechanism. For heavy organic loads a flocculation system may be required and where the input water is alkaline the water will need to be acidified. See figures 1, 2, and 3.



Figure 1 Schematic water reticulation system, large capacity water storage

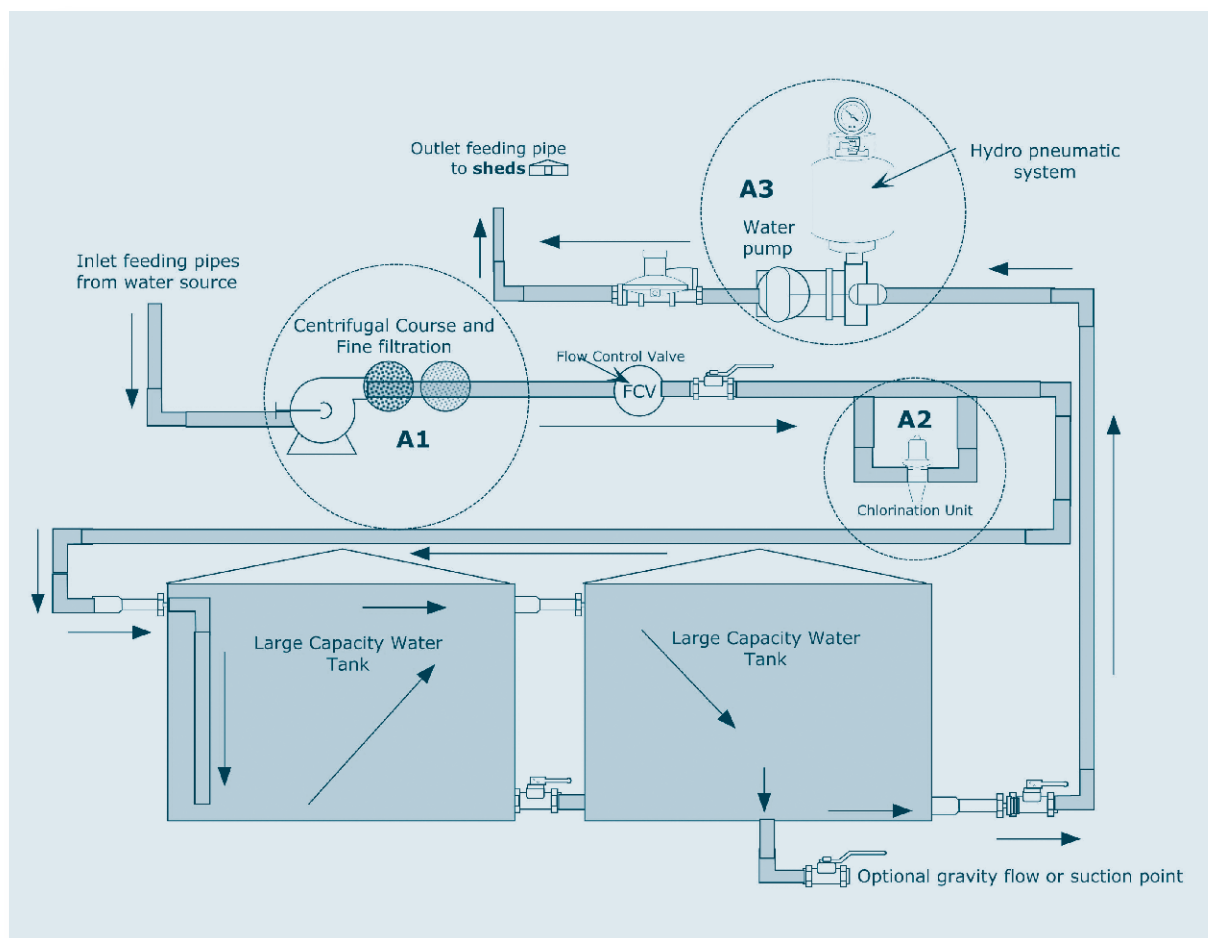


Figure 2 Schematic Water Reticulation System

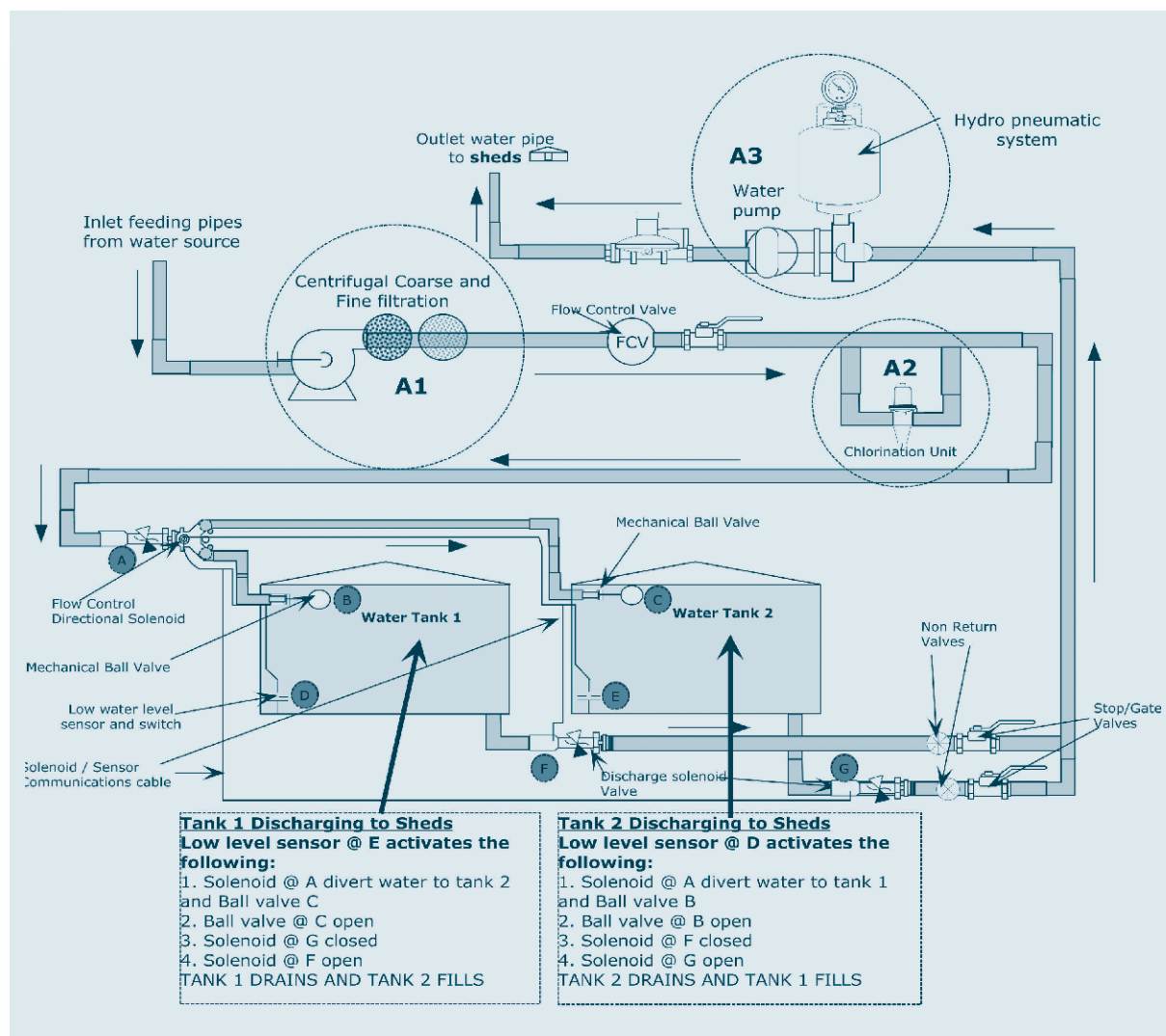
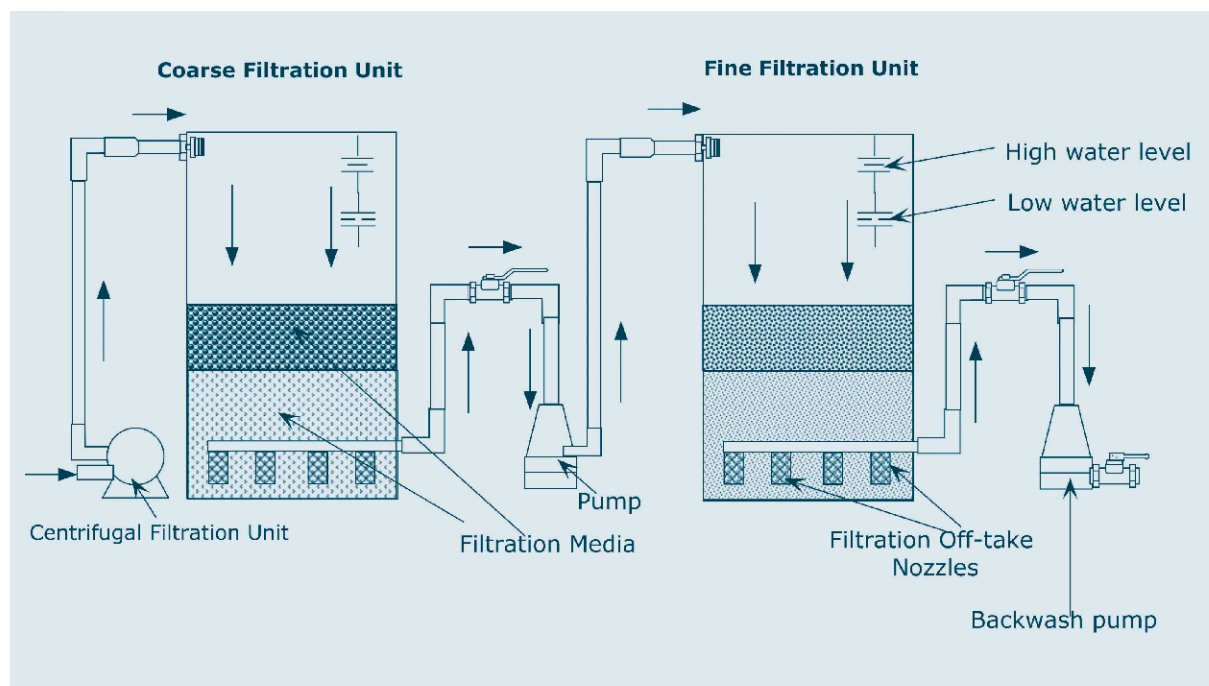




Figure 3 Mechanical Filtration Unit (A1)





Chlorination unit (A2)

Chlorine dosing pumps, typically supplying 12.5% sodium hypochlorite, can either be mechanical (operated by physical water flow—figure 4 (A2.1)) or electronic (requiring electrical power—figure 5 (A2.2)). These dosing pumps need to have internal parts that are resistant to corrosion and degradation by chlorine and capable of resisting ambient weather conditions including extreme cold, heat and UV light, or otherwise be placed in protective housing. There are numerous suppliers of dosing pumps suitable for poultry farms. Equipment should be obtained from suppliers who can provide good technical back-up and service including spare parts. Plumbing fittings must be compatible with those used in Australia.

The dosing rate required will vary according to the quality of water and the farm usage rate and will require some initial trials to establish the desired results.

Storage tanks

The configuration of water storage on the farm should ensure there is adequate contact time between the fresh water and the required level of chlorine, before the treated water is supplied to the sheds and poultry. The delivery of chlorine directly into the shed water supply line, or the use of small capacity holding tanks that directly supply the sheds will not allow adequate contact time, particularly during periods of high demand for drinking and cooling water. Inadequate contact time between the chlorine and water increases the risk of the introduction of water-borne avian pathogens.

A two-storage tank system is the most acceptable configuration to ensure adequate contact time when chlorinating surface water. A primary storage tank can be filled with chlorinated water and, after a minimum retention period, manually drained into the secondary sealed tank supplying the poultry sheds. This is low cost but requires ongoing intervention by the poultry farm manager.

The schematic diagrams outline two possible storage tank set-ups.

Large capacity water tanks (figure 1)

Where large storage tanks are used (with the capacity to store two or more days' water supply for the farm at peak demand) and the water usage output is a proportionally low ratio to the total storage volume, then a system can be used where the chlorinated water enters the primary tank at the bottom and the chlorinated water enters the secondary supply tank from the high level outflow. In this set up, the dilution rate of the fresh water is low and the bottom of the tank input and the top of the tank output ensures the water is effectively sanitised. The certainty of this can be enhanced by adjusting the chlorine dosing pump to ensure that the chlorine level in the second tank is maintained between 1 to 5 ppm, achieving 1 to 2 ppm at the drinker level.



Smaller capacity water tanks (figure 2)

Figure 2 outlines a more sophisticated but still relatively simple set-up, in which each tank delivers chlorinated water to the sheds only after a specified holding period, which is predetermined by the time the paired tank takes to empty. The minimum retention period will be determined by the size of the tanks as they relate to water usage on farm under peak demand. This should be around a minimum of two hours for chlorine, but in most existing set-ups extends to 12 or more hours.

Measurement of chlorine levels

The measurement of free chlorine levels can be done manually using test strips, colour kits or indirectly using portable ORP meters which read in mV. In establishing a chlorination system, these measurements are made and the dosing rate of chlorine adjusted until the desired free chlorine levels are achieved at the location being measured.

Alternatively this can be done automatically using electronic sensing and recording equipment (ORP/mV) which may include feedback to the dosing pump and/or low chlorine level alarms. These systems provide the flexibility to accommodate sudden changes in water quality, for example after heavy rain or dramatic changes in inflow water requirements. They also allow the immediate detection of chlorination system failures and reduce the window of opportunity for birds to receive untreated surface water.

Farm/shed water pump (A3)

Chlorinated water is delivered to the sheds by a hydro-pneumatic water pump (figure 6). Often, two or three variable speed pumps are used in series to allow efficiency of power use, back-up contingencies and extending pump life.

To limit biofilm build-up, it is advisable from time to time to flush the farm water reticulation system at various discharge points around the farm (taps and hydrants). For significant biofilm build-up it is advisable to use a higher concentration flush with an oxidizing sanitiser during batch turnarounds. The effectiveness of chlorine is limited by biofilms, and chlorine does not remove existing biofilms.



Figure 4 Mechanical Pump (A2.1)

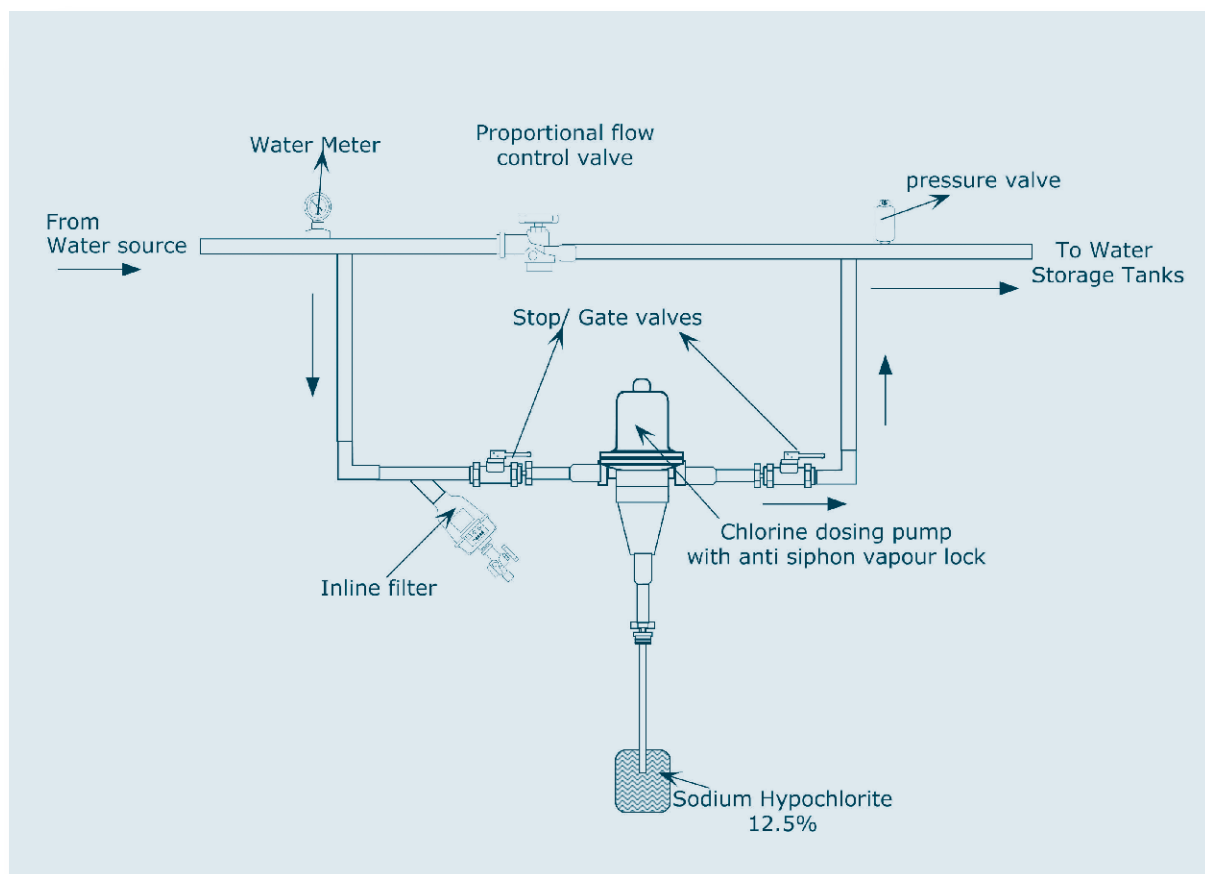




Figure 5 Electronic Dosing Pumps (A2.2)

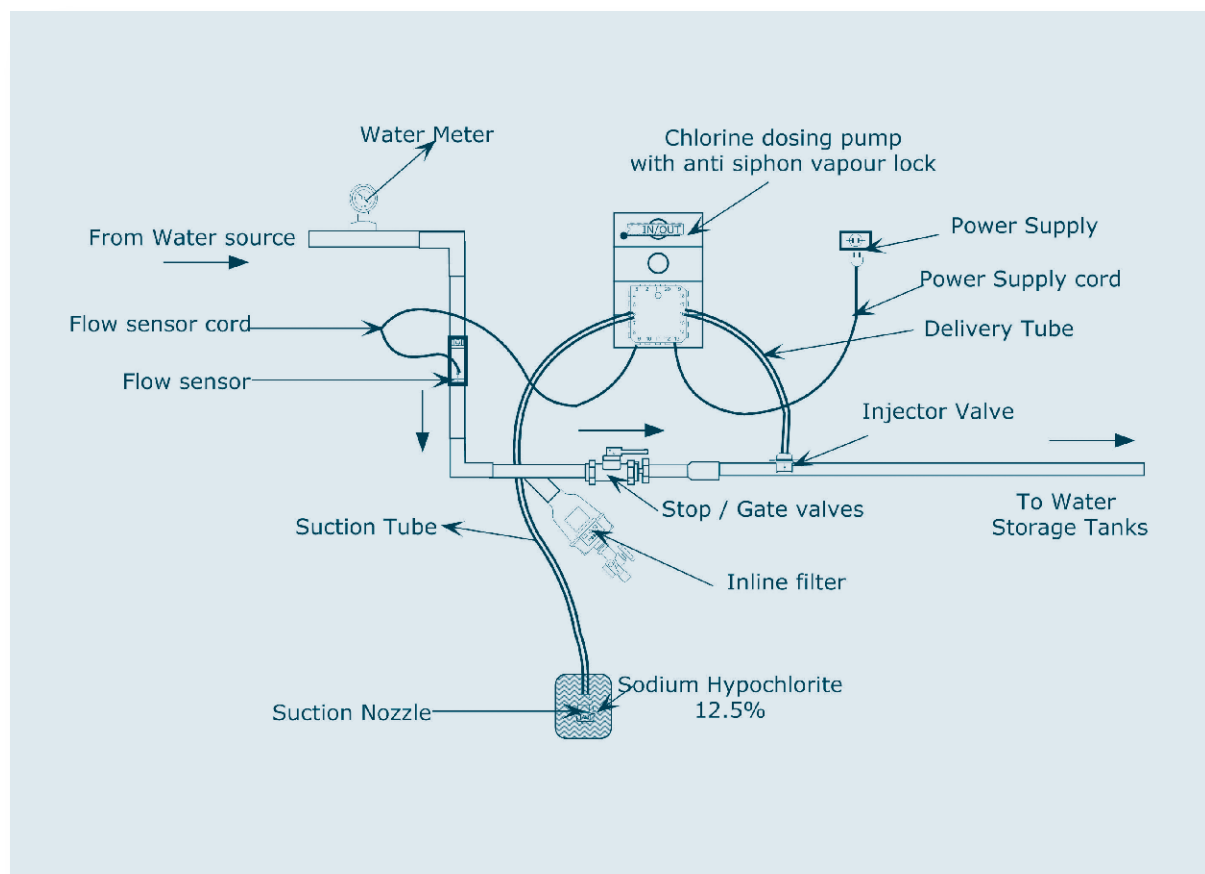
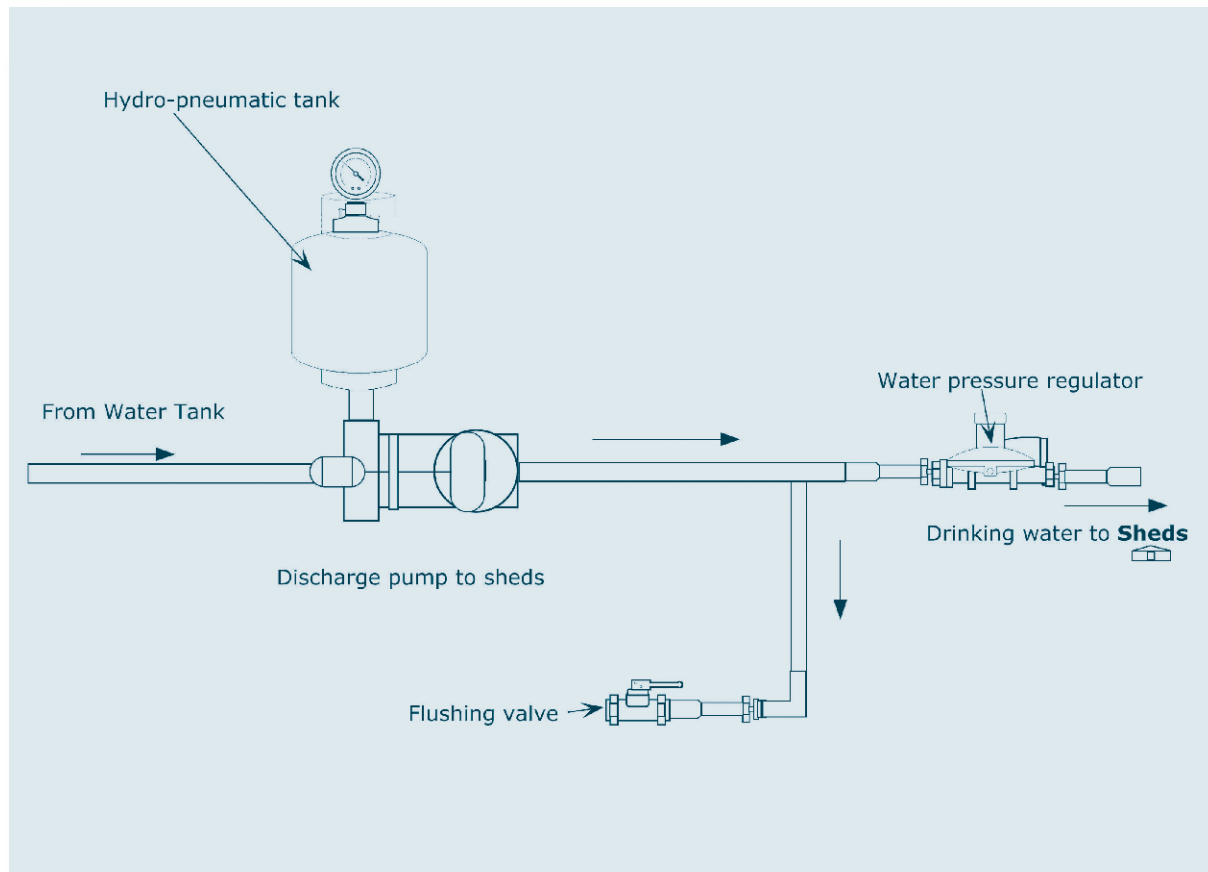




Figure 6 Hydro-pneumatic system (A3)





ABBREVIATIONS

AI	avian influenza
BOD	biochemical oxygen demand
E. coli	Escherichia coli
EAD	emergency animal disease
EDS	egg drop syndrome
HPAI	highly pathogenic avian influenza
IBDV	infectious bursal disease virus
LPAI	low pathogenicity avian influenza

mV	millivolt
ORP	oxidation-reduction potential
ppm	parts per million
SPF	specific pathogen free
spp	species
TDS	total dissolved solids
UV	ultraviolet
vNDV	virulent Newcastle disease virus

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Attachment 7



United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
(7510P)

Halohydantoins RED
EPA 739-R-07-001
September 2007

Reregistration Eligibility Decision for Halohydantoins (Case 3055)

Halohydantoins RED

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

This is to inform you that the Environmental Protection Agency (hereafter referred to as EPA or the Agency) has completed its review of the available data and public comments received related to the preliminary risk assessments for the antimicrobial halohydantoins. The Reregistration Eligibility Decision (RED) was approved in the form of a decision memorandum which summarized the regulatory decision for halohydantoins on September 30, 2004. Public comments and additional data received were considered in this decision.

Based on its review, EPA is now publishing its Reregistration Eligibility Decision (RED) and risk management decision for halohydantoins and its associated human health and environmental risks. A Notice of Availability will be published in the *Federal Register* announcing the publication of the RED.

The RED and supporting risk assessments for the halohydantoins are available to the public in EPA's Pesticide Docket EPA-HQ-OPP-2004-0303 at: <http://www.regulations.gov>.

The halohydantnoins RED was developed through EPA's public participation process, published in the Federal Register on July 20, 2005, which provides opportunities for public involvement in the Agency's pesticide tolerance reassessment and reregistration programs. Developed in partnership with USDA and with input from EPA's advisory committees and others, the public participation process encourages robust public involvement starting early and continuing throughout the pesticide risk assessment and risk mitigation decision making process. The public participation process encompasses full, modified, and streamlined versions that enable the Agency to tailor the level of review to the level of refinement of the risk assessments, as well as to the amount of use, risk, public concern, and complexity associated with each pesticide. Using the public participation process, EPA is attaining its strong commitment to both involve the public and meet statutory deadlines.

Please note that the halohydantoins risk assessment and the attached RED document concern only this particular pesticide. This RED presents the Agency's conclusions on the dietary, drinking water, occupational and ecological risks posed by exposure to halohydantoins alone. This document also contains both generic and product-specific data that the Agency intends to require in Data Call-Ins (DCIs). Note that DCIs, with all pertinent instructions, will be sent to registrants at a later date. Additionally, for product-specific DCIs, the first set of required

Halohydantoins RED

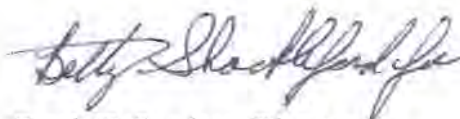
responses will be due 90 days from the receipt of the DCI letter. The second set of required responses will be due eight months from the receipt of the DCI letter.

As part of the RED, the Agency has determined that halohydantoins will be eligible for reregistration provided that all the conditions identified in this document are satisfied, including implementation of the risk mitigation measures outlined in Section IV of the document. Sections IV and V of this RED document describe labeling amendments for end-use products and data requirements necessary to implement these mitigation measures. Instructions for registrants on submitting the revised labeling can be found in the set of instructions for product-specific data that accompanies this document.

Should a registrant fail to implement any of the risk mitigation measures outlined in this document, the Agency will continue to have concerns about the risks posed by halohydantoins. Where the Agency has identified any unreasonable adverse effect to human health and the environment, the Agency may at any time initiate appropriate regulatory action to address this concern. At that time, any affected person(s) may challenge the Agency's action.

If you have questions on this document or the label changes necessary for reregistration, please contact the Chemical Review Manager, ShaRon Carlisle, at (703) 308-6427. For questions about product reregistration and/or the Product DCI that accompanies this document, please contact Emily Mitchell at (703) 308-8583.

Sincerely,

A handwritten signature in dark ink, appearing to read "Frank T. Sanders", is positioned above the printed name.

Frank T. Sanders, Director
Antimicrobials Division (7510C)

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CHEMICAL TEAM

Science Team

Tim McMahon

Michelle Centra

Najm Shamim

Timothy Leighton

Jonathan Chen

Kathryn Montague

Sanyvette Williams-Foy

Regulatory Team

ShaRon Carlisle

Heather Garvie

Diane Isbell

GLOSSARY OF TERMS AND ABBREVIATIONS

a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
APHIS	Animal and Plant Health Inspection Service
ARTF	Agricultural Re-entry Task Force
BCF	Bioconcentration Factor
CDC	Centers for Disease Control
CDPR	California Department of Pesticide Regulation
CFR	Code of Federal Regulations
ChEI	Cholinesterase Inhibition
CMBS	Carbamate Market Basket Survey
cPAD	Chronic Population Adjusted Dose
CSFII	USDA Continuing Surveys for Food Intake by Individuals
CWS	Community Water System
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DL	Double layer clothing {i.e., coveralls over SL}
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
EXAMS	Tier II Surface Water Computer Model
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FOB	Functional Observation Battery
FQPA	Food Quality Protection Act
FR	Federal Register
GL	With gloves
GPS	Global Positioning System
HIARC	Hazard Identification Assessment Review Committee
IDFS	Incident Data System
IGR	Insect Growth Regulator
IPM	Integrated Pest Management
RED	Reregistration Eligibility Decision
LADD	Lifetime Average Daily Dose
LC ₅₀	Median Lethal Concentration. Statistically derived concentration of a substance expected to cause death in 50% of test animals, usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LCO	Lawn Care Operator
LD ₅₀	Median Lethal Dose. Statistically derived single dose causing death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation), expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEC	Lowest Observed Adverse Effect Concentration
LOAEL	Lowest Observed Adverse Effect Level
LOC	Level of Concern
LOEC	Lowest Observed Effect Concentration
mg/kg/day	Milligram Per Kilogram Per Day
MOE	Margin of Exposure

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MP	Manufacturing-Use Product
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
MRL	Maximum Residue Level
N/A	Not Applicable
NASS	National Agricultural Statistical Service
NAWQA	USGS National Water Quality Assessment
NG	No Gloves
NMFS	National Marine Fisheries Service
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
NPIC	National Pesticide Information Center
NR	No respirator
OP	Organophosphorus
OPP	EPA Office of Pesticide Programs
ORETF	Outdoor Residential Exposure Task Force
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDCI	Product Specific Data Call-In
PDP	USDA Pesticide Data Program
PF10	Protections factor 10 respirator
PF5	Protection factor 5 respirator
PHED	Pesticide Handler's Exposure Data
PHI	Pre-harvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
PRZM	Pesticide Root Zone Model
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RPA	Reasonable and Prudent Alternatives
RPM	Reasonable and Prudent Measures
RQ	Risk Quotient
RTU	(Ready-to-use)
RUP	Restricted Use Pesticide
SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
SL	Single layer clothing
SLN	Special Local Need (Registrations Under Section 24C of FIFRA)
STORET	Storage and Retrieval
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TRAC	Tolerance Reassessment Advisory Committee
UF	Uncertainty Factor
USDA	United States Department of Agriculture
USFWS	United States Fish and Wildlife Service
USGS	United States Geological Survey
WPS	Worker Protection Standard

ABSTRACT

The Environmental Protection Agency (EPA or the Agency) has completed the human health and environmental risk assessments for halohydantoins and is issuing its risk management decision and tolerance reassessment. The risk assessments, which are summarized below, are based on the review of the required target database supporting the use patterns of currently registered products and additional information received through the public docket. After considering the risks identified in the revised risk assessments, comments received, and mitigation suggestions from interested parties, the Agency developed its risk management decision for uses of halohydantoins that pose risks of concern. As a result of this review, EPA has determined that the halohydantoin groups of chemicals are eligible for reregistration, provided that risk mitigation measures are adopted and labels are amended accordingly. That decision is discussed fully in this document.

I. INTRODUCTION

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all submitted data to the U.S. Environmental Protection Agency (referred to as EPA or “the Agency”). Reregistration involves a thorough review of the scientific database underlying a pesticide’s registration. The purpose of the Agency’s review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the “no unreasonable adverse effects” criteria of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. This Act amends FIFRA to require tolerance reassessment. The Agency has decided that, for those chemicals that have tolerances and are undergoing reregistration, the tolerance reassessment will be accomplished through this reregistration process. The Act also required that by 2006, EPA must review all tolerances in effect on the day before the date of the enactment of the FQPA. FQPA also amends the Federal Food, Drug, and Cosmetic Act (FFDCA) to require a safety finding in tolerance reassessment based on factors including consideration of cumulative effects of chemicals with a common mechanism of toxicity. At this time, the Agency has not identified any other chemical substances that have a mechanism of common toxicity with that of the halohydantoins group. For reregistration purposes, EPA has assumed that the halohydantoins do not have a common mechanism of toxicity and will not perform a cumulative risk assessment as part of the tolerance reassessment for these pesticidal chemicals. This document presents the Agency’s revised human health and ecological risk assessments and the reregistration eligibility decision for the halohydantoins.

These antimicrobial chemicals are registered for use in indoor food and non-food, indoor residential, aquatic non-food residential, aquatic food, aquatic non-food, and aquatic non-food industrial sites for control of bacteria, fungi, and algal slimes.

The Agency has concluded that the FQPA Safety Factor for the halohydantoins should be removed (equivalent to 1X). Although there is quantitative evidence of increased sensitivity of neonatal rabbits, the Agency considered this effect not indicative of susceptibility, based upon the very high dose level at which the effect occurred, the minimal nature of the effect, and the likelihood that the effect was due to a greater dose received by pups from ingestion of both milk and feed during the lactation period. Therefore, the Agency determined that the special hazard-based FQPA safety factor could be removed for the halohydantoins and that the use of a standard uncertainty factor of 100 would be sufficient.

Risks summarized in this document are those that result only from the use of the active ingredient, halohydantoins. The FFDCA requires that the Agency consider available information concerning the cumulative effects of a particular pesticide’s residues and other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic

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effect by a common toxic mechanism could lead to the same adverse health effect that would occur at a higher level of exposure to any of the substances individually. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding for the halohydantoins and any other substances. The halohydantoins do not appear to produce a toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that the halohydantoins have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative>.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of halohydantoins. In an effort to simplify the RED, the information presented herein is summarized from more detailed information, which can be found in the technical supporting document for halohydantoins referenced in this RED. The revised risk assessments and related addenda are not included in this document, but are available in the Public Docket at <http://www.regulations.gov> (Docket ID #EPA-HQ-OPP-2004-0303).

This document consists of six sections. Section I is the introduction. Section II provides a chemical overview, a profile of the use and usage of halohydantoins, and its regulatory history. Section III, Summary of Halohydantoins Risk Assessments, gives an overview of the human health and environmental assessments, based on the data available to the Agency. Section IV, Risk Management, Reregistration, and Tolerance Reassessment Decision, presents the reregistration eligibility and risk management decisions. Section V, What Registrants Need to Do, summarizes the necessary label changes based on the risk mitigation measures outlined in Section IV. Finally, the Appendices list all use patterns eligible for reregistration, bibliographic information, related documents and how to access them, and Data Call-In (DCI) information.

II. CHEMICAL OVERVIEW

A. Regulatory History

The halohydantoins were first registered in October 1961. There are currently 114 active products containing a halohydantoin registered under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In 1987, EPA issued a Data Call-In (DCI) for antimicrobial products, which covered the halohydantoins. In response to this DCI, generic toxicology, environmental fate and ecotoxicity data were submitted. Generic data were developed on the breakdown products, dimethylhydantoin (DMH) and ethylmethylhydantoin (EMH). The primary reason for developing generic data on DMH and EMH rather than the entire halohydantoin molecule is that these ring structures represent the persistent component of the halohydantoins. A secondary reason for evaluating the halohydantoin moieties is that the corrosive properties of the released halogens would limit the amount of chemical that could be administered to laboratory animals; thereby precluding a meaningful evaluation of the halohydantoin moieties. The Agency also determined that data developed on DMH was applicable to EMH and vice versa. The basis for this decision was the similarity of the chemical structure of these two chemicals and the similarity of results from studies conducted on both the DMH and EMH compounds.

B. Chemical Identification

The halohydantoins are a group of chemicals comprised of several halogenated compounds. This group of chemicals includes the following: 1-Bromo-3-chloro-5,5-dimethylhydantoin, 1,3-Dibromo-5,5-dimethylhydantoin, 1,3-Dichloro-5,5-dimethylhydantoin, and 1,3-Dichloro-5-ethyl-5-methylhydantoin. In addition, the Agency has determined that the 5,5-Dimethylhydantoin (DMH) and 5-Ethyl-5-methylhydantoin (EMH) metabolites of the halogenated hydantoins are appropriate test substances for assessing the toxicity of this group. However, since the hydroxymethylhydantoins as listed above have the potential for release of formaldehyde, the risks associated with this release need to be assessed. The Agency has determined that the risks from exposure to formaldehyde via the hydroxymethylhydantoins will be addressed when registration review is conducted on hydroxymethylhydantoin.

The common names, chemical names, empirical formulas, and CAS numbers of the halohydantoins are presented in Table 1.

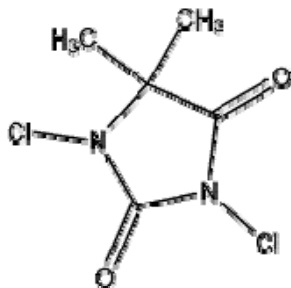
Table 1. Common Names, Chemical Names, Empirical Formulas, and CAS Numbers

Common Name	Chemical Name	Empirical Formula	CAS No.
Dichlorodimethylhydantoin	1,3-dichloro-5,5-dimethylhydantoin	C ₅ H ₆ Cl ₂ N ₂ O ₂	118-52-5
Bromochlorodimethylhydantoin	1-Bromo-3-Chloro-	C ₅ H ₆ BrClN ₂ O ₂	16079-88-2

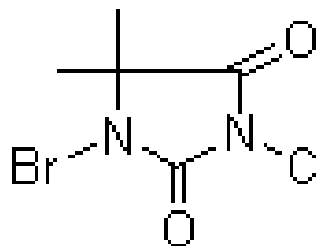
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Common Name	Chemical Name	Empirical Formula	CAS No.
	Dimethylhydantoin		
Dichloroethylmethylhydantoin	1,3-dichloro-5-ethyl-5-methylhydantoin	$C_6H_8Cl_2N_2O_2$	89415-87-2
Dibromodimethylhydantoin	1,3-dibromo-5,5-dimethylhydantoin	$C_5H_6Br_2N_2O_2$	77-48-5
Bromochlorodimethylhydantoin	1-Bromo-3-chloro-5,5-dimethylhydantoin	$C_5H_6BrClN_2O_2$	32718-18-6

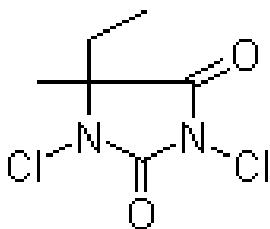
Structures of the halohydantoins considered in this document are below:



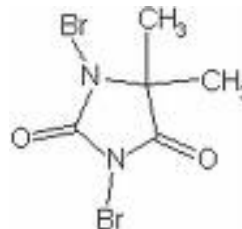
1,3 Dichloro-5,5-Dimethylhydantoin



1-Bromo-3-Chloro-Dimethylhydantoin

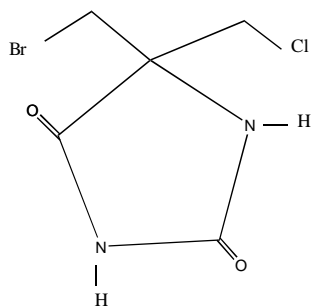


1,3-Dichloro-5-Ethyl-5-Methylhydantoin



1,3,-dibromo-5,5-dimethylhydantoin

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1-bromo-3-chloro-5,5-dimethylhydantoin

Physical and chemical properties of a typical halohydantoin are shown in Table 2.

Table 2. Physical and Chemical properties of a typical Halohydantoin product

Parameter	Value
Color	Off-white
Physical State	Solid
Odor	Slight halogen odor
Stability	Stable in the dry state. It decomposes exothermally at 180°C. It is attacked by strong alkali's, acids, and moisture.
Oxidation/Reduction	Oxidizer
pH of water solution, 1% slurry at 25°C	6.5
Melting point	between 120 and 148°C
K _{ow}	unknown
Water solubility at 25°C	0.54 g / 100 g
Vapor Pressure	NA

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Structurally, the halohydantoins consist of a central organic hydantoin ring moiety (either dimethylhydantoin or ethylmethylhydantoin) to which halogen atoms (bromine and/or chlorine) can be attached at both the 1 and 3 positions on the hydantoin ring.

In concentrated form, the halohydantoins are very stable. Upon usage, which involves dilution in water or a water system, the halohydantoins rapidly decompose to release chlorine and/or bromine and dimethylhydantoin (DMH) and, for certain products, ethylmethylhydantoin (EMH). These released halogens react with water to form either hypochlorous or hypobromous acid, which is the actual biocidal agent. Accordingly, the halohydantoins are essentially delivery systems for hypochlorous and hypobromous acid.

a. Use Profile

The halohydantoins are used for microbial control in water and water systems. In particular, the halohydantoins are used as disinfectants in commercial and residential swimming pools, spas and hot tubs; as sanitizers for treatment of toilet bowl water in homes; and for controlling bacterial and fungal contamination in a variety of industrial water systems. (i.e., industrial cooling water systems, pulp and paper mill process water, wastewater treatment systems, air washer water systems, sewage systems, industrial processing water, irrigation systems, and ornamental ponds).

The only food-use for the halohydantoins is as a slimicide in the manufacture of food-contact paper and paperboard. The 1998 Antimicrobial Regulation Technical Corrections Act (ARTCA) gave the U.S. Food and Drug Administration (FDA) jurisdiction for regulating dietary residues of food-contact slimicides under Section 409 of the Federal Food, Drug and Cosmetic Act (FFDCA). In addition, EPA is responsible for registering the slimicide product under FIFRA. The FDA regulation that permits the halohydantoins to be used as slimicides in the manufacture of food-contact paper and paperboard is in 21 C.F.R. Part 176.300.

USE SITES:

Indoor Non-Food

Hydrostatic Sterilizer Water Systems
Pasteurizer/Warmer/Cannery/Retort Water Systems
Transportation Cleaning

Indoor Residential

Toilet Bowls and Urinals
Bathroom Premises/Hard Surfaces

Non-Food Residential

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Swimming Pool Water Systems
 Air Conditioner
 Hot Tubs & Spas

Indirect Food

Pulp and Paper Mill Water (food contact paper)

Aquatic Nonfood

Ornamental Ponds/Aquaria
 Irrigation Systems

Aquatic Non-Food Industrial

Air Washer Water Systems (includes air scrubbing and washing)
 Evaporative Condenser Water Systems
 Pulp and Paper Mill Systems
 Sewage/Wastewater Treatment Systems
 Commercial/Industrial Water Cooling Tower Systems
 Heat Exchanger Water Systems
 Industrial Processing Water
 Photo Processing Water
 Secondary Oil Recovery Injection Water
 Oil Recovery Drilling Muds and Packer Fluids
 Recirculating Cooling Water (Greenhouses & Nurseries)

APPLICATION RATES AND METHODS:

Indoor Non-Food

For *recirculating cooling water systems* the typical rate of application ranges from 0.1 to 0.75 lbs per 1,000 gallons of water with 5-70 ppm halohydantoins with 0.5 - 5 ppm halogen by method of Place Solid (PLS), Pour Solid (PS) Feeders, Pour Liquid (PL) and Pour Undiluted (PU). End Use pack size ranges from 25 to 2,200 lb. for briquettes, tablets and in granular form. The end-use pack size for gels range from 22 oz to 400 pounds.

For *transportation cleaning*, 1 to 5 ppm of halohydantoins with 1 to 3 ppm halogen is used at a typical rate of .025 to 0.1 lbs per 1,000 gallons of water. PLS or PS feeder is used for briquettes and tablets in end use pack sizes that range from 20 to 50 pounds.

Indoor Residential

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For *toilet bowls and urinals*, 1 to 5 ppm of halohydantoins with 2 to 10 ppm of halogen is used by method of Place Solid at a typical rate of 17 to 25 grams per month in briquette and tablet form.

For *bathroom premises and hard surfaces*, 588 ppm of halohydantoins with 1,125 ppm of halogen is used at a typical rate of 0.45 ounces per every 3 gallons of water applied by mop and brush. For bathroom and hard surface use, the product is in granular and tablet form; end use pack sizes range from 1 to 50 pounds.

Non-food Residential

For *residential and commercial pools*, 50 to 300 ppm of halohydantoins with 1 to 4 ppm of halogen is used at a weekly rate of 0.5 to 2.5 pounds per 10,000 gallons of water. Product is dispensed through a PLS/PS feeder in tablet, briquette and granular form from end use packs that range from 20 to 50 pounds.

For *residential and commercial spas*, 30 to 100 ppm of halohydantoins with 2 to 6 ppm of halogen is used at a weekly rate of 0.1 to 0.5 pounds per 1,000 gallons of water. Product is dispensed through a PLS/PS feeder in tablet, briquettes and granular form from end use packs that range from 1 to 50 pounds.

For use in *air conditioner and dehumidifier basin/drip pans*, one or more 20 gram tablets are placed in the basin or drip pan from end use pack sizes of 25 or 50 pounds.

Indirect Food

For *Pulp & Paper* with food contact, 5 to 25 ppm of halohydantoins with 1 to 5 ppm of halogen is used at a typical rate of 0.16 to 2.0 pounds per ton of paper. A PLS/PS feeder or PU is used to dispense product in briquette, granular, powder, tablet and gel form. End use product pack sizes range from 25 to 2,200 lbs. for briquettes, tablets and granular formulations. The end-use pack size for gel products range from 22 oz to 400 pounds.

Aquatic Non-Food

For *Decorative Waters* without fish, 50 to 260 ppm of halohydantoins with 1 to 3 ppm of Halogen is used at a weekly rate of 0.5 to 1.4 pounds per 10,000 gallons of water. A PLS/PS feeder is used to dispense product in briquette, granular, tablet and gel form. End use product pack size ranges from 22 oz to 400 pounds for gel and 20 to 50 pounds for all other forms.

For *irrigation and automatic water distribution systems* (not for use on food crops) 8 to 24 ppm of halohydantoins with 5 to 15 ppm of halogen is used at a typical rate of 15 to 45 grams per 1,000 gallons of water. A PLS/PS feeder, PU, or PL is used to dispense product in granular, powder and tablet form. End use products are packaged in 3 and 25 pound containers.

Aquatic Non-Food Industrial

For ***Recirculating cooling systems***, 5 to 70 ppm of halohydantoins with 0.5 to 5 ppm of halogens is used at a typical rate of 0.1 to 0.75 pounds per 1,000 gallons of water dependent on level of biological control. A PLS/ PS feeder, PU, or PL is used to dispense product in granular, briquettes, tablet and gel form. End use product package sizes range from 22 oz to 400 pounds for the gel formulation and 25 to 2,200 pounds for all other formulations.

For ***once through cooling systems***, 5 to 35 ppm of halohydantoins with 0.5 to 5 ppm of halogen is used at a typical application rate of 0.1 to 0.3 pounds per 1,000 gallons of water. A PLS/ PS feeder, PU, or PL is used to dispense product in granular, briquettes, tablet and gel form. End use product package sizes range from 22 oz to 400 pounds for the gel formula and 25 to 2,200 pounds for all other formulations.

For ***Pulp and Paper***, 5 to 25 ppm of halohydantoins with 1 to 5 ppm of halogen is used at a typical application rate of 0.16 to 2.0 pounds per ton of paper. A PLS/ PS feeder or PU is used to dispense the product in granular, powder, tablet and gel form. End use product package sizes range from 22 oz to 400 pounds for gel formulations and 25 to 2,200 pounds for all other formulations.

For ***sewage and wastewater treatment systems***, 5 to 35 ppm of halohydantoins with 0.5 to 5 ppm of halogen is used at a typical application rate of 0.1 to 0.75 pounds per 1,000 gallons of water. A PLS/ PS feeder, PU, or PL is used to dispense product in briquette, granular, tablet and gel forms. End use product package sizes range from 22 oz to 400 pounds for gel formulations and 25 to 2,200 pounds for all other formulations.

For ***photo processing***, 1 to 5 ppm of halohydantoins with 1 to 3 ppm of halogen is used at a typical application rate of 0.006 to 0.02 pounds per 1,000 gallon of water. A PLS/ PS feeder is used to dispense product in granular, briquettes and tablet forms. End use product package sizes range from 1 to 50 pounds.

For ***secondary oil recovery injection water***, 300 ppm of halohydantoins with 280 ppm of halogen is used at a typical application rate of 2.3 pounds per 1,000 gallons of water. A PLS/ PS feeder is used to dispense the product in granular and tablet forms. End use pack sizes range from 25 to 2,200 pounds.

For ***oil recovery drilling mud & packer fluids***, 940 ppm of halohydantoins with 1,800 ppm of halogen is used at a typical application rate of 15 pounds per 1,000 gallons of water. A PLS/ PS feeder is used to dispense the product in granular and tablet form. End use product package sizes range from 25 to 2,200 pounds.

For ***recirculating cooling water for greenhouses and nurseries***, 8 to 24 ppm of halohydantoins with 5 to 15 ppm of halogen is used at a typical rate of 15 to 45 grams per

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1,000 gallons of water. A PLS/ PS feeder is used to dispense product in granular, powder and tablet forms. End use product package sizes are 3 and 25 pounds.

TARGET PESTS:

Slime-forming bacteria and fungi; pathogens in swimming pools, spas, hot tubs, toilet bowls and urinals; mollusks and algae.

FORMULATION TYPES:

Powder, granular, tablets (including nuggets), briquettes and gel.

III. Summary of Halohydantoins Risk Assessments

The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments, and to help the reader better understand the conclusions reached in the assessments. The human health and ecological risk assessment documents and supporting information listed in Appendix C were used to formulate the safety finding and regulatory decision for halohydantoins. While the risk assessments and related addenda are not included in this document, they are available to the public in EPA's Pesticide Docket EPA-HQ-OPP-2004-0303 at <http://www.regulations.gov>. Hard copies of these documents may be found in the OPP public docket. The OPP public docket is located in Room S-4900, One Potomac Yard, 2777 South Crystal Drive, Arlington, VA 22202, and is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m.

A. Human Health Risk Assessment

The halohydantoins are a group of chemicals comprised of several halogenated compounds. This group of chemicals includes the following: 1-Bromo-3-chloro-5,5-dimethylhydantoin, 1,3-Dibromo-5,5-dimethylhydantoin, 1,3-Dichloro-5,5-dimethylhydantoin, and 1,3-Dichloro-5-ethyl-5-methylhydantoin. In addition, the Agency has determined that the 5,5-Dimethylhydantoin (DMH) and 5-Ethyl-5-methylhydantoin (EMH) metabolites of the halogenated hydantoins are appropriate test substances for assessing the toxicity of this group. However, since the hydroxymethylhydantoins as listed above have the potential for release of formaldehyde, the risks associated with this release need to be assessed. The Agency has determined that the risks from exposure to formaldehyde via the hydroxymethylhydantoins will be addressed when registration review is conducted on hydroxymethylhydantoin. Therefore, this reregistration eligibility decision (RED) document assesses the eligibility of the halohydantoins and their metabolites for reregistration.

The Agency's use of human studies in the halohydantoins risk assessment is in accordance with the Agency's Final Rule promulgated on January 26, 2006, related to Protections for Subjects in Human Research, which is codified in 40 CFR Part 26.

1. Toxicity of Halohydantoins

A brief overview of the toxicity studies used for determining endpoints in the dietary risk assessments are outlined in this section; other toxicity endpoints will be presented later in this document. Further details on the toxicity of halohydantoins can be found in the *Halohydantoins Revised Risk Assessment for the Reregistration Eligibility Decision*, dated June 25, 2007. This document is available to the public in EPA's Pesticide Docket EPA-HQ-OPP-2004-0303 at: <http://www.regulations.gov>

The Agency has reviewed all toxicity studies submitted for halohydantoins and has determined that the toxicological database is sufficient for reregistration. The studies have been submitted to support guideline requirements. Major features of the toxicology profile are presented below. In acute toxicity studies, summarized in Table 3 below, the halohydantoins were shown to be of low toxicity by the oral and dermal routes of exposure (Toxicity categories III and

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IV, respectively). Acute toxicity by the inhalation route is more significant (Toxicity category II). The halohydantoins are significant eye and skin irritants (Toxicity category I and II, respectively). Mixed dermal sensitization has also been observed for some of the halohydantoin compounds. See Table 4 for the studies and toxicity endpoints that were used in the dietary risk assessment.

Table 3. Acute Toxicity of Halohydantoins

Guideline No./ Study Type	MRID No. (TRID No.)	Results	Toxicity Category
5,5-Dimethylhydantoin			
870.1100 Acute oral (gastric intubation) toxicity (limit test)-Mouse	45738401	LD ₅₀ (combined) > 5,000 mg/kg	IV
1-Bromo-3-chloro-5,5-dimethylhydantoin			
870.1100 Acute oral toxicity-Rat	93074006, 00128244 (4226-010-01)	LD ₅₀ (males) = 1,350 mg/kg LD ₅₀ (females) = 1,520 mg/kg LD ₅₀ (combined) = 1,390 mg/kg	III
870.1100 Acute oral toxicity-Rat	93077008, 00147325 (4600-950-21)	LD ₅₀ (males) = 1,037 mg/kg LD ₅₀ (females) = 860 mg/kg LD ₅₀ (combined) = 929 mg/kg	III
870.1300 Acute inhalation toxicity-Rat	43654101	LC ₅₀ (males) = 0.157 mg/L LC ₅₀ (females) = 0.213 mg/L LC ₅₀ (combined) = 0.168 mg/L	II
870.2500 Acute dermal irritation-Rabbit	93074011, 93075014, 00128242 (4225-014-10)	severe skin irritant	I
870.2500 Acute dermal irritation-Rabbit	93077009, 00147326 (4600-950-22)	severe skin irritant	I
870.2600 Skin sensitization-Guinea pig	41670001	positive sensitizer	N/A
1,3-Dibromo-5,5-dimethylhydantoin			
870.1100 Acute oral toxicity-Rat	93076011, 00137105 (4334-012-01)	LD ₅₀ = 760 mg/kg	III
870.1100 Acute oral toxicity-Rat	44988002,)	combined LD ₅₀ = 448 mg/kg	II
870.1200 Acute dermal toxicity-Rabbit	93076025, 00137110 (4334-012-07)	LD ₅₀ cannot be ascertained (study is classified as Unacceptable/non-guideline)	--
870.1200 Acute dermal toxicity-Rat	44988001	LD ₅₀ > 2000 mg/kg	III
870.1300 Acute inhalation toxicity-Rabbit	44988003	LC ₅₀ between 0.51-2.02 mg/L	II

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Guideline No./ Study Type	MRID No. (TRID No.)	Results	Toxicity Category
870.2500 Primary dermal irritation-Rabbit	93076017, 00137109 (4334-012-05)	severe skin irritant	I
870.2500 Primary dermal irritation-Rabbit	44988004	corrosive	I
870.2600 Dermal Sensitization - guinea pig	44988005	non-sensitizer	N/A
1,3-Dichloro-5,5-dimethylhydantoin			
870.1200 Acute dermal toxicity-Rabbit	93076013, 00084176 (2402-448-05)	LD ₅₀ > 20,000 mg/kg	IV
870.2500 Acute dermal irritation-Rabbit	93076017, 00137109 (2402-448-01)	severe skin irritant	I

Table 4. Summary of Toxicological Dose and Endpoints for the Halohydantoins for Use in Human Risk Assessment

Exposure Scenario	Dose Used in Risk Assessment, UF		Study and Toxicological Effects
Acute Dietary <u>females 13-50 years of age</u>	NOAEL = 100 mg/kg/day UF = 100 Acute RfD = 1 mg/kg	FQPA SF = 1 aPAD = <u>acute RfD</u> FQPA SF = 1 mg/kg/day	developmental toxicity - rabbit developmental LOAEL = 500 mg/kg/day based on skeletal variations. (MRID 42413101)
Chronic Dietary ^a <u>all populations</u>	NOAEL= 300 mg/kg/day UF = 100 Chronic RfD (gen Pop.) = 3 mg/kg/day	FQPA SF = 1 cPAD = <u>chr RfD</u> FQPA SF = 3 mg/kg/day	chronic toxicity/carcinogenicity - rats LOAEL = 1000 mg/kg/day based on decreased body weight/weight gain and lymph node hyperplasia. (MRID 43397702)
Chronic Dietary ^a <u>females 13-50 years of age</u>	NOAEL= 100 mg/kg/day UF = 100 Chronic RfD (females 13-50) = 1 mg/kg/day	FQPA SF = 1 cPAD = <u>chr RfD</u> FQPA SF = 1 mg/kg/day	developmental toxicity - rabbit developmental LOAEL = 500 mg/kg/day based on skeletal variations. (MRID 42413101)

UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest

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observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure

^aThe HIARC selected separate chronic RfDs for females, ages 13-50, and the general population. A separate endpoint for the general population was selected because this was an unusual case where the developmental toxicity NOAEL was lower than the NOAEL from the chronic toxicity studies. The chronic RfD for the general population provides a more appropriate endpoint for individuals other than females

General Toxicity Observations

Non-acute toxicity testing of halohydantoins (DMH/EMH) (including subchronic, developmental, reproductive, and chronic toxicity testing) all show the presence of non-specific toxicity only at relatively high doses of the test chemical. Developmental and reproductive toxicity data demonstrate no increase in susceptibility to the toxic effects of 5,5-dimethylhydantoin with the exception of one study, where fetal and litter effects (increased incidence of 27th presacral vertebrae) in rabbits were observed at a lower dose level than that which resulted in maternal toxicity (decreased body weight and food consumption during the dosing period) following treatment. The increase of 27th presacral vertebrae is a common variation found in rabbit developmental toxicity studies and was not considered an adverse effect. In a prenatal developmental toxicity study conducted in rabbits with 5-ethyl-5-methylhydantoin, there was no increased susceptibility of the fetuses observed.

Available metabolism data indicate that DMH and EMH are excreted unchanged in the rat. However, it is known that hydroxymethylhydantoins are formaldehyde releasers. The DMH portion of the molecule is assumed to behave the same as the hydantoins from the halohydantoin compounds. Any risk associated from the formaldehyde portion of the hydroxymethylhydantoin molecule will be addressed in the registration review of the hydroxymethylhydantoins.

Uncertainty Factors

Although there is quantitative evidence of increased sensitivity of neonatal rabbits, the Agency does not consider this effect indicative of susceptibility, based upon the very high dose level at which the effect occurred, the minimal nature of the effect, and the likelihood that the effect was due to a greater dose received by pups from ingestion of both milk and feed during the lactational period. Therefore, the Agency recommended that the special hazard-based FQPA safety factor could be removed for the halohydantoins and that the use of a standard uncertainty factor of 100 would be protective for offspring.

Dietary

Acute and chronic dietary endpoints were selected using the no observed adverse effect level (NOAEL) of 100 mg/kg/day for females 13-50 based on a developmental toxicity study on rabbits, in which skeletal variations were seen at 500 mg/kg/day. A chronic dietary endpoint of 300 mg/kg/day was selected for the general population based on a chronic toxicity study on rats, in which decreased body weight, weight gain, and lymph node hyperplasia were observed.

Incidental Oral

The incidental short-term oral endpoint was selected using a NOAEL of 500 mg/kg/day, based a developmental toxicity study on rabbits, in which decreased body weight gain in maternal rabbits at 1000 mg/kg/day. The intermediate- term oral endpoint was selected using a NOAEL of

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300 mg/kg/day, based on a subchronic oral toxicity study in which decreased body weight and liver weight were observed at 1000 mg/kg/day.

Short-, Intermediate- and Long-term Dermal

An endpoint for dermal toxicity (all times exposure durations) was selected using a NOAEL of 390 mg/kg/day based on the results of a 90-day dermal subchronic toxicity study (MRID 43173901) in which no systemic toxicity was found at the highest dose tested. The LOAEL is greater than 390 mg/kg/day.

Inhalation (all durations)

The short-term inhalation endpoint was selected to be the same as the oral endpoint of 100 mg/kg/day, due to skeletal effects in the offspring at 500 mg/kg/day in a developmental toxicity study in rabbits. For inhalation exposures, a 100% inhalation absorption value is used for route-to-route extrapolation.

Carcinogenicity

Cancer studies in rats and mice indicated no systemic effects other than decreased body weight and body weight gains in females (rats) and males (mice) and increased hyperplasia of submandibular lymph nodes in males (rats). No evidence of carcinogenicity of the test material was reported. 5,5-dimethylhydantoin is classified as ‘not likely’ to be a carcinogen based upon the negative evidence for carcinogenicity in both the rat and mouse studies as well as the negative evidence of mutagenicity.

Mutagenicity

The data on mutagenicity of dimethylhydantoin shows, in large part, negative responses in the studies conducted. Literature reports indicate a positive effect for 2 in vitro mammalian cytogenetic assays in Chinese Hamster Ovary cells.

Endocrine Disruption Potential

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency’s EDSP have been developed, the halohydantoins may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

2. FQPA Safety Factor

The FQPA Safety Factor (as required by the Food Quality Protection Act of 1996) is intended to provide an additional 10-fold safety factor (10X), to protect for special sensitivity in infants and children to specific pesticide residues in food, drinking water, or residential exposures, or to compensate for an incomplete database. The database for reproductive or developmental toxicity testing of 5,5-dimethylhydantoin is complete. Based on the overall examination of the effects of DMH, the HIARC concluded that there was some evidence for increased susceptibility, because a developmental endpoint was selected for dietary risk assessment, an additional safety factor to address FQPA concerns is not necessary.

3. Population Adjusted Dose (PAD)

Dietary risk is characterized in terms of the Population Adjusted Dose (PAD), which reflects the reference dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA Safety Factor (SF). This calculation is performed for each population subgroup. A risk estimate that is less than 100% of the acute or chronic PAD is not of concern. The Agency has conducted a dietary exposure and risk assessment for the use of halohydantoins as a slimicide in food contact paper and paperboard, and for use as a preservative in inorganic slurries which are used as fillers for food contact paper and paperboard.

a. Acute PAD

Acute dietary risk is assessed by comparing acute dietary exposure estimates (in mg/kg/day) to the acute Population Adjusted Dose (aPAD). Acute dietary risk is expressed as a percent of the aPAD. The aPAD is the acute reference dose (1 mg/kg/day) modified by the FQPA safety factor. The acute reference dose was derived from a developmental toxicity study in rabbits in which both the NOAEL (100 mg/kg/day) and the LOAEL (500 mg/kg/day) were determined. Acute dietary exposure was estimated for females ages 13-50 only since the endpoint chosen is based on a developmental effect. The halohydantoins aPAD is 1 mg/kg/day. Uncertainty factors were included for inter-species extrapolation (10x) and intra-species variation (10x).

b. Chronic PAD

Chronic dietary risk for halohydantoins was assessed by comparing chronic dietary exposure estimates (in mg/kg/day) to the chronic Population Adjusted Dose (cPAD). Chronic dietary risk is expressed as a percent of the cPAD. The cPAD is the chronic reference dose (1 mg/kg/day females 13-50 and 3 mg/kg/day all populations) modified by the FQPA safety factor. The cPAD was derived from a developmental toxicity study in rabbits and a chronic toxicity in rats; in which both the NOAELs and LOAELs were determined. The halohydantoins cPAD is 3 mg/kg/day based on a reference dose of 3 mg/kg/day for the general populations group and 1 mg/kg/day for females age 13-50; which includes the incorporation of the FQPA safety factor (1X) for the overall U.S. population or any population subgroups. Uncertainty factors were also included for inter-species extrapolation (10x) and intra-species variation (10x).

4. Dietary Exposure Assumptions

Dietary exposure to the halohydantoins occurs from the slimicide use in the manufacture of paper and paperboard. Acute and chronic dietary exposures were assessed for these indirect food-contact uses. No pesticide tolerances have been established for halohydantoins. The Agency has used available methods to estimate halohydantoin residues on food due to migration of these chemicals or their breakdown products, when these substances come into contact with food-contact paper and paperboard. In this regard, the Food and Drug Administration (FDA) has developed guidelines to estimate the residues of pesticides used as slimicides on food contact paper and paperboard. The Agency has decided to use FDA methodology to estimate the residues of such chemicals and/or their breakdown products on food items and also to determine the Estimated Daily Intake (EDI) of these pesticides.

EPA used two methods to calculate dietary exposure for adult populations. In the first method, the following assumptions were made:

- Food contact surface could be a onetime use/day or repeat use material/day;
- The amount of food that comes into contact with the treated paper is based on an FDA default value;
- 100 percent of the active material present in the paper migrates into the food.

In the second (alternative) method, additional consideration is given to the type of food that is being contained in the treated paper, and factors such as the quantity of active ingredient in the paper are not considered.

The concentration of halohydantoins in the paper slurry was calculated assuming that the chemical was used both as a slimicide and as a preservative in paper. Although two types of use involve different moieties (halohydantoin for slimicide, hydroxymethylhydantoin for material preservative), the concentrations were summed together to determine a total concentration of hydantoins (EMH and DMH) in the slurry. The EDI was then calculated based on this concentration for both adults and children. The results of the calculations are shown in Tables 5 and 6.

For more details on the exposure estimates and dietary risk, see Dietary Risk Assessment of Halohydantoins, dated October 12, 2004, available under docket number EPA-HQ-OPP-2004-0303 on <http://www.regulations.gov>.

5. Dietary Risk Assessment

a. Dietary Risk from Food

Generally, a dietary risk estimate that is less than 100% of the acute or chronic PAD does not exceed the Agency's risk concerns. A summary of acute and chronic risk estimates are shown in Tables 5 and 6.

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The Agency has determined that the acute dietary risk estimates do not exceed the Agency's level of concern (less than 100% of the aPAD) for females between 13-50 years, the pertinent sub-population tested. The acute dietary exposure for an adult female is 0.533% of the acute PAD using method #2 for estimating exposure.

The chronic dietary risk assessment concluded the chronic risk estimates are also below the Agency's level of concern (less than 100% of the cPAD) for the general U.S. population (0.533% of the cPAD) and all population subgroups. The highest exposed population subgroup was children 3-5 years old at 1.6% of the cPAD using method #2 for estimating exposure.

Table 5. Summary of Dietary Exposure and Risk for Halohydantoins (1st Method)

Population Subgroup	EDI mg/day	Acute Dietary		Chronic Dietary	
		Dietary Exposure ^a (mg/kg/day)	% aPAD ^b	Dietary Exposure (mg/kg/day) ^a	% cPAD ^b
Adult Male	0.0276	--	--	3.94×10^{-4}	0.0131
Adult Female	0.0276	4.60×10^{-4}	0.046	4.60×10^{-4}	0.0153
Children	0.0138	--	--	1.38×10^{-3}	0.046

a-- acute and chronic exposure analysis based on daily consumption of 0.00276 mg/person/day for adults and body weights of 70 kg and 60 kg for males and females, respectively. For infants/children, exposure based on daily consumption of 0.0138 mg/person/day; and a 10 kg body weight.

b--%PAD = dietary exposure (mg/kg/day) * 100 / aPAD or cPAD, where aPAD for females between 13-50 years of age = 1.0 mg/kg/day and cPAD for the general population = 3.0 mg/kg/day

Table 6. Summary of Dietary Exposure and Risk for Halohydantoins (2nd Method)

Population Subgroup	EDI mg/day	Acute Dietary		Chronic Dietary	
		Dietary Exposure ^a (mg/kg/day)	% aPAD ^b	Dietary Exposure (mg/kg/day) ^a	% cPAD ^b
Adult Male	0.96	--	--	0.0137	0.457
Adult Female	0.96	0.016	1.6	0.016	0.533
Children	0.48	--	--	0.048	1.6

a-- acute and chronic exposure analysis based on daily consumption of 0.96 mg/person/day for adults and body weights of 70 kg and 60 kg for males and females, respectively. For infants/children, exposure based on daily consumption of 0.48 mg/person/day; and a 10 kg body weight.

b--%PAD = dietary exposure (mg/kg/day) * 100 / aPAD or cPAD, where aPAD for females between 13-50 years of age = 1.0 mg/kg/day and cPAD for the general population = 3.0 mg/kg/day

b. Dietary Risk from Drinking Water

Drinking water exposure to pesticides can occur through surface and groundwater contamination. The Agency is presently relying on predicted environmental concentrations (PECs) of pesticides in surface water to estimate drinking water exposures to halohydantoins. Considering all of the uses of this pesticide, the once-through cooling tower water system can be expected to have the greatest impact on water, since the scenario has the greatest quantity of effluent being produced and has the greatest chance of bacterial fouling, needing a pesticide application. Using the PDM4 model, the short-term Estimated Environmental Concentration (EEC) in surface water use was estimated to be 36 ug/L. The chronic maximum EEC using this model was determined to be 313 ug/L.

6. Residential Exposure Assessment

The residential exposure assessment considers all potential pesticide exposure, other than exposure due to residues in food or in drinking water. Residential exposure may occur while using household cleaning products, paint, adhesives, and deodorizers. For the purposes of this screening level assessment, handler scenarios have been developed that encompass multiple products but represent a worst-case scenario for all products represented in the assessment. Each route of exposure (oral, dermal, inhalation) is assessed, where appropriate, and risk is expressed as a Margin of Exposure (MOE), which is the ratio of estimated exposure to an appropriate No Observed Effect Level (NOAEL) dose.

a. Residential Toxicity

The toxicity endpoints and associated uncertainty factors used for assessing the non-dietary risks for halohydantoins are listed in Table 7. Although the dermal endpoint represents short-, intermediate-, and long-term durations, the exposure duration of most homeowner applications of cleaning products is believed to be best represented by the short-term duration. The inhalation endpoint used in the assessment represents the short-term duration. The calculated dermal and inhalation MOEs are not of concern for any of the scenarios (MOE greater than 10,000 for all scenarios).

However, since the hydroxymethylhydantoins have the potential for release of formaldehyde, the risks associated with this release need to be assessed. The Agency has determined that the risks from exposure to formaldehyde via the hydroxymethylhydantoins will be addressed when registration review is conducted on hydroxymethylhydantoin.

Table 7. Toxicological Endpoints

Exposure Scenario	Dose Used in Risk Assessment, UF		Study and Toxicological Effects
Short-Term Oral (1-30 days) (Incidental)	oral study NOAEL= 500 mg/kg/day UF = 100	Residential, includes the 1x FQPA SF	developmental toxicity - rabbit maternal LOAEL = 1000 mg/kg/day based on decreased body weight gain in maternal rabbits. (MRID 42413101)
Intermediate-Term Oral (1 to 6 months) (Incidental)	oral study NOAEL= 300 mg/kg/day UF = 100	Residential, includes the 1x FQPA SF	subchronic oral toxicity - rat LOAEL = 1000 mg/kg/day based on decreased body weight and liver weight. (MRID 42009201)
<u>Dermal- all time periods</u> Short-, (1-30 days), Intermediate-, (1 to 6 months), Long-term (>6 months) (Occupational/ Residential)	dermal study NOAEL= 390 mg/kg/day (HDT) UF = 100 for all populations	MOE = 100 (Occupational) Residential, includes the 1x FQPA SF	subchronic dermal toxicity - rats No systemic toxicity at the highest dose tested (MRID 43173901)
Short-Term Inhalation (1-30 days) (Occupational/ Residential)	Oral NOAEL= 100 mg/kg/day (inhalation absorption rate = 100%) UF = 100 for all populations	Residential, includes the 1x FQPA SF	developmental toxicity - rabbit developmental LOAEL = 500 mg/kg/day based on skeletal effects in offspring. (MRID 42413101)

It should be noted that this exposure assessment identifies short-term (1-30 days) and intermediate-term (1-6 months) noncancer exposure doses based on the reported toxicology endpoints for Halohydantoin. Because of the shorter exposure durations of these toxicological endpoints, conservative event-based exposure assumptions are used to calculate upper bound daily dose estimates. The noncancer doses are not amortized over a lifetime. However, MOEs for all scenarios are much greater than the target MOE of 100 and are not of concern.

b. Residential Handler Exposure

i. Exposure Scenarios, Data and Assumptions

Halohydantoins may be added to residential-use products as disinfectants and sanitizers in in-tank toilet bowl, swimming pool and spa products. The pool/spa and air conditioner drip pan uses are represented by the application to residential (i.e., backyard) swimming pools and spas.

Hydroxymethylhydantoins may be added as a material preservative to control bacteria and fungi (EPA Reg No. 6836-271) in residential-use products such as household cleaning products, paints, adhesives, and deodorizers. For the purposes of this screening-level assessment, handler scenarios have been assessed for residential uses that represent high-end exposures for the wide variety of products. Therefore, not all products are assessed individually. Table 8 presents the handler scenarios considered to represent the high end conservative estimates of exposure for the residential assessment.

Table 8. Residential Handler Scenarios	
Handler Scenario	Typical Products Represented (but not limited to)
Handling of liquid general purpose cleaner	Household cleaning products, carpet shampoo, deodorizer
Solid placement of in-tank toilet cleaner	In-tank toilet tablet
Painting of a house using brush, roller, or airless sprayer	Paint, adhesives, caulk
Solid placement into swimming pools & spas	Pools/spas and air conditioner drip pans

ii. Residential Handler Risk

Based on toxicological criteria and potential for exposure, the Agency has conducted dermal and inhalation exposure assessments. A summary of the residential handler exposures and risks for the representative scenarios are presented in Table 9. Although the dermal endpoint represents short-, intermediate-, and long-term durations, the exposure duration of most homeowner applications of cleaning products is believed to be best represented by the short-term duration. The inhalation endpoint used in the assessment represents only the short-term duration. The calculated dermal and inhalation MOEs indicate that risks are not of concern for any of the scenarios (MOE greater than 1,000 for all scenarios). Further details on the residential risk can be found in the *Halohydantoins Revised Risk Assessment for the Reregistration Eligibility Decision*, dated June 25, 2007. This document is available to the public in EPA's Pesticide Docket EPA-HQ-OPP-2004-0303 at: <http://www.regulations.gov>. As stated previously, formaldehyde is a metabolite of hydroxymethylhydantoins and there may be risk associated with this exposure. Any

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risks associated with formaldehyde will be in the Registration Review Document for hydroxymethylhydantoins.

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Table 9. Calculation of Short-term Dermal and Inhalation MOE for Residential Handlers

Exposure Scenario	Method of Application	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE ^b
Household Cleaning Products	Wipes	0.014	28,000	0.00033	300,000
	Mopping	0.0053	73,000	0.00018	570,000
Toilet Bowl Tablets	Solid Placed	0.036	11,000	0.00091	110,000
Painting	Brush/ Roller	0.69	570	0.00084	120,000
	Airless Sprayer	1.8	220	0.019	5,400
Swimming Pools / Spas					
Swimming Pools (Residential – backyard)	Solid Place	0.12	3200	0.000015	6500000
	Solid Pour	0.85	460	0.00046	220000
Spas	Solid Place	0.396	984	0.0000506	1,970,000
	Solid Pour	2.8	139	0.00151	66,500

c. Residential Post-application
i. Exposure Scenarios, Data and Assumptions

Residential postapplication exposures result when adults and children come into contact where pesticide end use products have recently been applied (e.g., treated hard surface floors), or when children incidentally ingest the pesticide residues through mouthing the treated products/treated articles, through hand-to-mouth or object-to-mouth contact. For the purposes of this screening level assessment, postapplication scenarios have been developed that represent high-end exposure scenarios for all products represented. Table 10 presents the postapplication scenarios considered in this assessment. Three scenarios have been considered: (1) exposure to residue from hard floors that have been cleaned/mopped with a general cleaner preserved with hydroxymethylhydantoin, (2) exposure to residue on clothing that has been treated with halohydrantoin during textile processing, and (3) exposure to swimmers in treated pools. For this screening-level assessment, fabric softeners have been grouped with textile processing chemicals for calculating exposure.

Table 10. Residential Postapplication Scenarios

Handler Scenario	Products Represented
Toddler exposed to residue from a hard floor	Hard surface cleaner/floor
Adult and toddler exposed to residue on clothing	Textile processing chemicals, fabric softener
Adult and Children exposed to residue in a swimming pool	Pool and spa products

ii. Post Application Risk

a. Residential Post Application Risk (Hard Surfaces)

There is the potential for toddlers playing on treated floors to be exposed to hydantoins contributed by the hydroxymethylhydantoin material preservatives. Due to limited data, the following assumptions have been made to determine toddler exposure while playing on treated hard floors:

- Toddlers (3 years old) are used to represent the 1 to 6 year old age group.
- As a conservative estimate, it has been assumed that one gallon of mopping solution can treat 1000 ft² of floor surface.
- No data could be found regarding the quantity of treatment solution residue left on the floor after treatment. It has been assumed that 25% of the solution remains after the final mop.
- No leaching data were available that could be used to estimate the residue transfer

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from the hard surface (i.e., floor). Therefore, the Residential SOP estimate of 10 percent of the amount on the floor is available for dermal transfer.

The short- and intermediate-term dermal MOE calculated is 700, which is above the target MOE of 100. See the Occupational Residential Exposure Chapter for a more detailed review, available under docket number EPA-HQ-OPP-2004-0303 on <http://www.regulations.gov>.

In addition to the dermal exposure from toddlers playing on treated floors, there is the potential for incidental oral exposure via hand-to-mouth activities. Although residential floors are believed to be washed/mopped on an intermittent basis, facilities such as day care centers may clean the floors more frequently; therefore, both the short- and intermediate-term incidental oral endpoints are provided to assess the potential risks. Due to limited data, the following assumptions from the Residential SOPs (in addition to the assumptions listed above) have been made to estimate hand-to-mouth exposures for toddlers playing on treated carpets:

- The surface area of the portion of the hand-to-mouth per event is 20 cm²;
- The number of hand-to-mouth events per hour is 20;
- Exposure time is 4 hours/day;
- Saliva extraction efficiency is 50 percent

Based on these assumptions, the potential dose rate using these assumptions is 0.07 mg/kg/day resulting in a hand-to-mouth MOE for toddlers of 7100 (short-term) and 4300 (intermediate-term) and thus, are not a concern to the Agency.

b. Residential Post Application Risk (Clothing)

Although hydroxymethylhydantoin has been listed for use in textile processing, it is unclear in what capacity the chemical is to be used. It has been assumed, for this risk assessment, that the chemical is impregnated into the material in the same manner as a dye would impregnate. Data on which these calculations could be based were generally unavailable; therefore, a number of conservative assumptions have been made:

- Toddlers (3 years old) are used to represent the 1 to 6 year old age group and are assumed to weigh 15 kg, the median for male and female toddlers (USEPA, 2000b). The median surface area for a 3 year old, minus the head, is 0.657 m². Median values for body weights and surface areas for adults have been used (70 kg and 1.69 m², not including head surface area).
- Based on rough estimates provided by the American Association of Textile Chemists and Colorists (AATCC), dyes are used on fabric at a rate of about 4% by weight (AATCC, 2003). A medium-sized polo cotton shirt of regular knit construction weighs about 250 g. Assuming that the shirt covers 0.659 m² of the body's surface area (based on the mean adult surface area for the torso, including the neck (USEPA, 1997)), the cloth weight to surface area ratio is 379 g/m². If an adult wears clothing of a similar weight over all parts of the body, minus the head (1.69 m² (USEPA, 1997)),

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then the weight of clothing worn by an adult is 641 g. Using the same cloth weight to surface area ratio, the weight of clothing worn by a toddler is 214 g. Area mouthed, for lack of data, is assumed to be equivalent to the area of fingers used in the hand-to-mouth exposure estimates (i.e., 20 cm^2 or $20 \text{ cm}^2 / 10,000 = 0.002 \text{ m}^2$).

- No leaching data were available that could be used to estimate a flux rate of the chemical from clothing. It has been conservatively assumed that, over the course of a day, the amount of chemical transferred is the full quantity of chemical present in the clothing. This is a conservative assumption and should not be considered as representative of the true rate at which the chemical would be transferred. However, as a screening-level assessment the risks are not of concern.

The dermal MOE's calculated for both toddler and adult scenarios are not of concern (MOE's = 119 and 185 for toddlers and adults, respectively). The short-term incidental oral MOE, as a result of mouthing treated fabric, is not of concern (MOE = 45,000). The short-term NOAELs were used instead of the intermediate-term NOAELs because all of the residues were assumed to be available for exposure in one day (for lack of any residue data). See the Occupational Residential Exposure Chapter for a more detailed review, available under docket number EPA-HQ-OPP-2004-0303 on <http://www.regulations.gov>.

c. Residential Post Application Risk (Swimming)

There are potential postapplication exposures to halohydrantoin associated with use of swimming pools and spas. Because the amount of exposure will most likely be much greater for swimming pools than for spas, based on the amount of time spent in the water, only swimming pool scenarios have been considered.

The SWIMODEL 3.0 was developed by EPA as a screening tool to conduct exposure assessments of pesticides found in swimming pools and spas (Dang, 2003). The SWIMODEL uses well-accepted screening exposure assessment equations to calculate the total worst-case exposure for swimmers expressed as a mass-based intake value (mg/event). The model focuses on potential chemical intakes only and does not take into account metabolism or excretion of the chemical of concern. Detailed information and the downloadable executable file are available at <http://www.epa.gov/oppad001/swimodel.htm>.

It should be noted that this exposure assessment identifies short-term (1-30 days) and intermediate-term (1-6 months) noncancer exposure doses based on the reported toxicology endpoints for halohydantoins. Because of the shorter exposure durations of these toxicological endpoints, conservative event-based exposure assumptions are used to calculate upper bound daily dose estimates. The noncancer doses are not amortized over a lifetime. However, as shown below in Table 11, MOEs for all scenarios are much greater than the target MOE of 100 and are not of concern.

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Table 11. Margins of Exposure for Swimming Pool^a

Age	Type of Swimmer	Dermal MOE	Inhalation MOE	Ingestion MOE
Adult	Competitive	3,100,000	47,000	190,000
Adult	Non-competitive	1,900,000	90,000	56,000
Child 7-10 yrs	Competitive	7,100,000	100,000	60,000
Child 7-10 yrs	Non-competitive	1,400,000	38,000	12,000
Child 7-10 yrs	Non-competitive	1,400,000	38,000	12,000
Child 11-14 yrs	Competitive	4,100,000	81,000	96,000
Child 11-14 yrs	Non-competitive	2,800,00	100,000	32,000

^aMOE = NOAEL (mg/kg/day)/Dose(mg/kg/day). Dermal route is based on an absorbed dose, and therefore, the oral endpoint is used to estimate risk. The inhalation and ingestion NOAELs are 100 mg/kg/day and 300 mg/kg/day (intermediate-term), respectively. Target MOE = 100.

7. Aggregate Risk

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require “that there is a reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information.” Aggregate exposure will typically include exposures from food, drinking water, residential uses of a pesticide, and other non-occupational sources of exposure. Results of the aggregate risk assessment are summarized here, and are discussed more extensively in the document, Revised Halohydantoins Risk Assessment, dated June 25, 2007, which is available in the public docket at <http://www.regulations.gov> (Docket ID #EPA-HQ-OPP-2004-0303).

a. Acute Dietary Aggregate Risk

The acute aggregate assessment includes dietary and drinking water exposures only. The acute dietary risk estimates from indirect food uses (i.e., use in food-contact packaging and treated articles) are less than 2% of the aPAD in all considered scenarios. Thus, the acute dietary (food) risk estimate associated with halohydantoins is below the Agency’s level of concern.

Drinking water exposure could occur from application of the pesticide to industrial water systems but is not expected. Drinking water monitoring data are not available; therefore, the Agency calculated a drinking water level of comparison (DWLOC) to account for potential drinking water exposures from the exposure from once-through cooling tower uses. The short-term EEC for halohydantoin in surface was 36 ppb, or 36 ug/L. See the Ecological Hazard Chapter for a more detailed review, available under docket number EPA-HQ-OPP-2004-0303 on <http://www.regulations.gov>. As shown in Table 12, the acute DWLOCs are greater than the EEC, indicating that acute aggregate food and drinking water exposure do not exceed the Agency’s level of concern.

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Table 12. Acute Aggregate Exposure and Risk

Population Subgroup	aPAD mg/kg/day	Acute Food Exp ¹ mg/kg/day	Max Acute Water Exp ² mg/kg/day	Surface Water EEC ³ mg/L	Acute DWLOC ⁴ mg/L	Potential Risk Concern
Females 13-50 years	1.0	4.6x10 ⁻⁴	0.999	0.036	29986	No
Females 13-50 years (alternate FDA method)		0.016	0.984		29520	No

¹Acute food exposure = estimated daily intake (mg/person/day) / body weight (70 kg)

²Maximum acute water exposure (mg/kg/day) = [(aPAD (mg/kg/day) - acute food exposure (mg/kg/day)]

³Based on PDM4 model.

⁴Acute DWLOC(μg/L) = $\frac{\text{maximum acute water exposure (mg/kg/day)} \times \text{body weight (kg)}}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$

b. Short-and Intermediate-term Aggregate Risk

Only dermal and inhalation aggregate risks were considered for the short-term duration in the aggregate risk evaluation. This is because homeowner cleaning scenarios are considered short-term exposures only and thus do not involve intermediate or long-term exposure. Further, not all of the non -dietary scenarios mentioned in this risk assessment have been aggregated, as it is unlikely that all of the scenarios mentioned in the exposure assessment have a reasonable probability of occurring together. For purposes of this aggregate assessment, the dietary exposure (food + water) is aggregated only with the cleaning scenarios involving wiping of hard surfaces, mopping, and cleaning of toilets for adults. Table 13 presents a summary of the aggregate dermal and inhalation short-term risk for adults. As shown, the aggregate MOE for both the dermal and inhalation exposure was is not of concern.

For toddlers, the dietary exposure is aggregated with the single dermal scenario of floor contact, and the dietary exposure is aggregated separately with the single incidental oral floor scenario. These scenarios are aggregated separately because exposures and MOEs for short- and intermediate-term aggregate exposure risk assessment (oral, dermal, and inhalation exposures) cannot be combined due to the lack of a common endpoint of toxicity from the different routes of exposure. Clothing is not included in the aggregate risk because a screening level assessment was performed in which it was assumed that, over the course of a day, the amount of chemical transferred is the full quantity of chemical present in the clothing. This is a conservative assumption and should not be considered as representative of the true rate at which the chemical would be transferred.

Calculation of aggregate MOE's for toddlers from dietary exposure and either dermal or inhalation exposure from the floor treatment also showed no risk of concern. Short-term aggregate MOE's were calculated as 1000 and 5000 for the dermal and inhalation exposure scenario, while intermediate-term aggregate MOE's were calculated as 909 and 3333 for the dermal and inhalation exposure scenario respectively.

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Table 13 Short-Term Aggregate Risk and DWLOC Calculations for Adults										
Population	Short-Term Scenario									
	Target Aggreg. MOE	MOE food ¹	MOE dermal ²	MOE inhalation ³	Short-Term Aggregate MOE (food and dermal residential) ⁴	Short-term Aggregate MOE (food + inhalation residential) ⁵	MOE water ⁶	Allowable water exposure ⁷ (mg/kg/day)	Surface Water EEC ⁸ (µg/L)	DWLOC ⁹ (µg/L)
Adult	100	36496	7090	196000	5988	31250	101	4.9	4	147000

¹ MOE food = [(short-term oral NOAEL)/(chronic dietary exposure)] Oral NOAEL of 500 mg/kg/day with chronic exposure of 0.0137.

² MOE dermal = [(short-term dermal NOAEL)/(dermal residential exposure)] dermal NOAEL of 390 mg/kg/day used with total exposure of 0.055 mg/kg/day from cleaning scenarios.

³ MOE inhalation = [(inhalation NOAEL)/(high-end inhalation residential exposure)] Inhalation NOAEL of 100 mg/kg/day used with total exposure of 0.00051 mg/kg/day

⁴ Aggregate MOE (food and dermal residential) = $1 \div [(1 \div \text{MOE food}) + (1 \div \text{MOE dermal})]$

⁵ Aggregate MOE (food and inhalation residential) = $1 \div [(1 \div \text{MOE food}) + (1 \div \text{MOE inhalation})]$

⁶ Water MOE = $1 \div [(1 \div \text{Target Aggregate MOE}) - (1 \div \text{Aggregate MOE (food and residential)})]$

⁷ Allowable water exposure = Short or Intermediate Term Oral NOAEL \div MOE water

⁸ using PDM4 model

⁹ DWLOC(µg/L) = $\frac{\text{allowable water exposure (4.9mg/kg/day)} \times \text{body weight (60kg)}}{[\text{water consumption (2L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$

c. Chronic Dietary Aggregate Risk

Table 14 presents the total chronic dietary exposure estimate for halohydantoins, and the chronic DWLOCs. The chronic PAD and the chronic dietary (food) exposure for that subgroup were used to calculate the chronic DWLOC. Two methods were used to calculate dietary exposure, and calculations are presented using both methods. Based on the use of the PDM4 model the chronic maximum EEC for dihalodialkylhydantoin in surface water was calculated as 313 ppb, or 313 ug/L. As shown in Table 14, the chronic DWLOCs are greater than the EEC, indicating that aggregate food and drinking water exposure do not exceed the Agency's level of concern.

Table 14. Chronic Aggregate Exposure and Risk

Population Subgroup	cPAD mg/kg/day	Chronic Food Exp ¹ mg/kg/day	Max Chronic Water Exp ² mg/kg/day	Surface Water EEC ³ mg/L	Chronic DWLOC ⁴ mg/L
General Population	3.0	3.94×10^{-4}	2.999	0.3	104986
General Population (alternate FDA method)		0.0137	2.986		104520
Females 13-50 years	1.0	4.60×10^{-4}	0.999		29986
Females 13-50 years (alternate FDA method)		0.016	0.984		29520

¹Chronic food exposure = estimated daily intake (mg/person/day) / body weight (70 kg [M]; 60kg[F])

²Maximum chronic water exposure (mg/kg/day) = [(cPAD (mg/kg/day) - chronic food exposure (mg/kg/day))]

³Based on PDM4 model.

⁴Chronic DWLOC(μ g/L) = $\frac{[\text{maximum chronic water exposure (mg/kg/day)} \times \text{body weight (kg)}]}{[\text{water consumption (L)} \times 10^{-3} \text{ mg}/\mu\text{g}]}$

8. Occupational Exposure and Risk

Workers can be exposed to a pesticide through mixing, loading, and/or applying a pesticide, or re-entering treated sites. Occupational handlers of halohydantoins products use them in a variety of industrial applications, including recirculating cooling water, once-through cooling tower water, pulp and paper process water, photo processing water, and transportation cleaning systems. Concentrations of halohydantoin in these products range from 90% to 98%, and are generally formulated as tablets, pellets, briquettes, or granules. The remaining formulations are gels, powders, or ready-to-use solutions, and all may be considered as solid (as opposed to liquid) formulations.

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Occupational risk for all of these potentially exposed populations is measured by a Margin of Exposure (MOE), which determines how close the occupational exposure comes to a No Observed Adverse Effect Level (NOAEL) from toxicological studies. In the case of halohydantoins, MOEs greater than 100 are not of concern to the Agency. For workers entering a treated site, MOEs are calculated for each day after application to determine the minimum length of time required before workers can safely re-enter.

For more information on the assumptions and calculations of potential risk of halohydantoins to workers, see the Occupational Exposure Assessment (Section 6) in the *Revised Halohydantoins Risk Assessment*, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

a. Occupational Toxicity

The toxicological endpoints used in the occupational assessment can be found in Table 7 above.

b. Occupational Handler Exposure

EPA has assessed the exposures and risks to occupational workers that handle and apply halohydantoin in the Occupational Exposure Assessment in the *Revised Halohydantoins Risk Assessment*, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303). This section summarizes the results of the occupational exposure/risk assessment. The following handler exposure scenarios were assessed and represent high-end exposures to industrial uses of the formulated product:

- Placing the halohydantoin tablets/pellets into cooling and process water systems, and
- Pouring halohydantoin granules/powders into a feeder for cooling and process water systems.

These two types of exposure scenarios were assessed for each of the water systems in question. The methods for applying gels, briquettes, and ready-to-use solutions are nearly identical to at least one of the two methods described above, based on the directions on the label. Therefore, although the two exposure scenarios considered include only products that are tablets, pellets, granules, or powders, these scenarios should be sufficient to describe the risks associated with all formulations.

i. Industrial Process (Handlers)

Occupational handler risk estimates have been assessed for halohydantoins using surrogate unit exposure data from the Chemical Manufacturers Association (CMA) database, application rates from labels, and EPA estimates of daily amount handled. The handlers were identified as those individuals who use dihalodialkylhydantoin in industrial/commercial water systems (recirculating cooling water, once-through cooling tower water, pulp and paper process water, photo processing water, and transportation cleaning systems) to limit microbial growth. The application rates were assumed to be the maximum rates listed on the product labels. The amounts of pesticide handled were based on a report containing use information for selected

scenarios related to antimicrobials (Dang, 1996).

For industrial use, the short- and intermediate-term dermal and inhalation MOEs for the primary were determined. Dermal MOEs range from a high of 151,000 for solid pour in photo processing water systems, to 76 for solid place in once-through cooling tower water systems. Except for once-through cooling tower water systems, all MOEs are above the target margin of exposure (100). For more information, see the Revised Halohydantoin Risk Assessment, dated December 15, 2004, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

Material Preservatives and Commercial/Institutional/Industrial Premises and Equipment and Swimming Pools

Use of dihalodialkylhydantoin in a commercial setting is similar in purpose to industrial use; used to prevent-slime formation in water systems. In addition, it is used as a material preservative in paints. Six scenarios have been identified to represent potential high-end exposures for these uses.:

- Liquid pour of product into paint during manufacturing as a material preservative;
- Solid place of product in air conditioner / humidifier drip pans,;
- Solid place of product in ornamental fountains,;
- Solid place of product for use in transportation cleaning water systems,;
- Commercial painters (brush/airless sprayer); and
- Solid place/pour of product in commercial swimming pools and spas.

The occupational material preservative use assessed for paints is believed to be representative of the other preservative uses on the labels such as detergents, fabric softeners, household cleaning products, surfactants, etc. Therefore, a separate commercial use of household cleaning products has not been conducted.

Very little data are available at this time regarding typical amounts of product handled by workers. For a-workers performing air conditioning maintenance in a large institution, it has been assumed that 3 air-conditioner units were maintained one day. A large ornamental fountain was assumed to be the same size as an average residential swimming pool. Assumptions for the in-bay car wash are based on information from the International Carwash Association and from anecdotal evidence. The EPA calculated the exposures for workers at a commercial/public swimming pool, using the assumption that a large commercial/public swimming pool size is 200,000 gallons, and that a large commercial spa's volume is approximately 1000 gallons.

For commercial uses, the short- and intermediate term dermal MOEs for the handlers wearing PPE range from 140 to 151,000. An MOE lower than the target MOE was found for only one scenario; placing tablets into public swimming pools ungloved (MOE=46). However, the product labels state that gloves should be worn when placing tablets into swimming pools. When gloves are used risks are mitigated for the placing of tablets (MOE = 7,500). For more information, see the Revised Halohydantoin Risk Assessment, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

Metal Working Fluids

Potential inhalation and dermal exposures to occupational handlers may exist when using treated metal working fluid. The Agency conducted the screening level assessment for metal working fluids using the Chemical Engineering Branch (CEB) model (U.S. EPA, 1991). Exposure assumptions used in the model are presented in Dang, 1997. The CEB model uses measured and/or assumed airborne oil mist concentrations for metal working operations. Since no measured concentrations are available for halohydantoins, the high-end oil mist concentration is based on the OSHA's Permissible Exposure Limit (PEL) of 5 mg/m³ (NIOSH, 1998). The label indicates that 0.45% (i.e., 0.0045) of the product is added to metal working fluids and of that, only 52.4% is the active ingredient. Therefore, the upper bound air concentration of halohydantoins that a worker is exposed to is 5 mg/m³ x 0.0045 x 0.524 or an air concentration of 0.012 mg/m³. Additionally, the following assumptions were made in the assessment: the inhalation rate for adults is 1.25 m³/hr; the exposure duration is 8 hours; and body weight is 70 kg. Using these assumptions, the long-term dose was calculated to be 0.0017 mg/kg/day, resulting in a long-term MOE of 59,000. Therefore, the calculated MOE indicates that the inhalation risks do not exceed the Agency's level of concern for a machinist exposure to metal working fluid that is treated with halohydantoins.

A screening-level long-term dermal exposure estimate was derived from the 2-Hand Dermal Immersion in Liquid Model in ChemSTEER (EPA/OPPT). The model is available at www.epa.gov/opptintr/exposure/docs/chemsteer.htm. The weight fraction of halohydantoin in metal working fluids is 0.0024 (0.0045 formulated product added to oil x 0.524 ai in formulated product = 0.0024). Based on the model for emersion of hands in metal working fluids, the long-term dermal dose is estimated at 0.3 mg/kg/day. The long-term dermal MOE is 1,300 (i.e., dermal NOAEL of 390 mg/kg/day / potential dose of 0.3 mg/kg/day). The dermal MOE is above the target MOE of 100, and therefore, the risk is not of concern. For more information, see the Revised Halohydantoins Risk Assessment, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

ii. Agricultural Premises and Aquatic Area Uses (Handlers)

For occupational handlers, one agricultural premise use and one aquatic area use have been identified.

- Solid pour/place of product into chemigation systems,
- Solid pour of product into vehicle and foot baths at greenhouse entrances.

Use of halohydantoin in chemigation systems is via loading of a brominator feed system, through which the product is dispensed via dissolution as feed water is passed through the tank. The amount of halohydantoin that will be used in the irrigation systems will depend greatly on the size of the greenhouse/nursery and the amount of irrigation necessary for the particular crop/climatic conditions. The amount of footbaths that should be used for the assessment is also in question. From anecdotal evidence, 1 gallon of water is used for each footbath, and 1" of water use for irrigation can be assumed. It has also been assumed that, for chemigation, the product

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will be used on 10 acres of crop. From these assumptions, the total amount of water applied for chemigation is 270,000 gallons. This scenario is not representative of the available exposure data and the uncertainty level is deemed high. The exposures maybe overestimated because of the extrapolation to such a high amount of water applied. All MOEs calculated are of concern (i.e., MOEs less than the target MOE of 100). No postapplication exposures were considered. For more information, see the Revised Halohydantoins Risk Assessment, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

c. Postapplication Exposure (All Occupational Uses)

Postapplication inhalation exposures may occur in the industrial settings around the water systems via inhalation, and dermal exposures may occur while maintaining industrial equipment. However, occupational postapplication dermal and inhalation exposures to halohydantoins are likely to be minimal compared to handler exposure because of dilution during processing. No postapplication exposures were evaluated for the agricultural premise use and aquatic area use as this exposure is anticipated to be negligible. No postapplication exposure data have been submitted to the agency to determine the extent of postapplication exposures in the industrial settings. Inhalation exposures are expected to be minimal because aerosol generation is not expected and the vapor pressure of dihalodialkylhydantoin is low.

d. Human Incident Data

Halohydantoins are active ingredients used in a variety of products (e.g. for treatment of swimming pools, spas and hot tubs, and toilet bowl water). The purpose of this chapter is to review the evidence of health effects in humans resulting from exposure to Halohydantoins.

Two approaches are used in this section:

- The potential health effects of halohydantoins in humans, reported as incident reports from different sources, are summarized.
- A literature search of chronic health effects associated with halohydantoin exposure, including results of epidemiological studies, is summarized.

There are many incidences that have been reported associated with exposure to end-use products containing halohydantoins. Dermal, ocular, and inhalation are the primary routes of exposure. Most of the incidences are related to irritation and/or allergic type reaction. The most common symptoms reported for cases of dermal exposure were skin irritation/burning, rash, itching, skin discoloration/redness, blistering, allergic type reactions including hives/welts, allergic contact dermatitis, and bleeding also have been reported. The most common symptoms reported for cases of ocular exposure were eye irritation/burning. Eye pain and swelling of eyes also has been reported in some incidences.

The most common symptoms reported for cases of inhalation exposure were respiratory irritation/burning, irritation to mouth/throat/nose, coughing/choking, shortness of breath, dizziness, flu-like symptoms, and headache. Seizure and heart palpitation also have been

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reported.

Although oral exposure is considered a minor route of exposure for halohydantoin use, irritation to mouth/throat/nose, vomiting/nausea/abdominal pain have been reported in the cases of ingestion.

B. Environmental Risk Assessment

The following environmental risk characterization is intended to describe the magnitude of the estimated environmental risks associated with halohydantoin use. For more information, see the Revised Halohydantoin Risk Assessment, dated June 25, 2007, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

1. Environmental Fate and Transport

The Agency does not have a complete database for environmental fate studies on dihalodialkylhydantoin. However, hydrolysis appears to be the major route for dissipation. Dihalodialkylhydantoin has been shown to hydrolyze relatively rapidly. It also degrades rapidly in an anaerobic aquatic environment with an observed half-life of less than 4 hours; there are indications that this short half-life appeared to be independent of aerobic or anaerobic conditions. The rapid hydrolysis, under abiotic conditions, show half-lives of less than 30 days in pH 5, pH 7, and pH 9 (in buffered solutions), which indicated that hydrolysis is an early step in the degradation process. However, the major degradate, dimethylhydantoin (DMH), was hydrolytically stable at pH 5, 7, and 9, and may possibly leach in the soil profile or move with surface water runoff and may pose environmental concerns. An aqueous photolytic study on dimethylhydantoin, conducted at pH 7 and at $25 \pm 1^\circ\text{C}$ in the presence of xenon arc as light source, yielded a first order rate constant of $7.89 \times 10^{-4}/\text{day}$ which translates into a half life of 878 days. Aqueous photolytic stability means that surface water runoff of DMH can be a source of concern for drinking water contamination. The Agency lacks any data on halohydantoin as far as mobility (soil column leaching) is concerned, as well as binding constants to soils to indicate if dihalodialkylhydantoin will be persistent in soils. Because of lack of data, the Agency cannot assess if halohydantoin are bioaccumulative and if these can be potentially a source of concern for the aquatic organisms.

Dihalodialkylhydantoin degrades relatively rapidly in water under abiotic conditions. However, there is environmental concern for soil or surface water contamination from the major degradate DMH, as DMH is hydrolytically and photolytically stable. DMH is also stable under aerobic conditions and shows a moderate tendency toward binding with soils (K_d 's). If present in the environment, it may cause a concern for ground- and surface water contamination.

2. Ecological Risk

Most of the halohydantoin uses are considered indoor uses. However, there is potential environmental exposure from the once-through cooling tower use. Halogenated halohydantoin show varying toxicity, depending on the number of halogens (bromine or chlorine) on the molecule. The halogens dissociate from the DMH core upon exposure to water; therefore, DMH was considered to be the moiety of concern for environmental exposure and ecological toxicity. A summary of ecotoxicological endpoints for DMH is provided in the Table 15. As indicated in the table, DMH demonstrates low toxicity to terrestrial and aquatic animals.

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Table 15: Summary of Ecotoxicity Endpoints

Test type	Species	% a.i.	Endpoint	EPA MRID #	Toxicity Category
Avian acute oral (71-1/850.2100)	Northern bobwhite (<i>Colinus virginianus</i>)	96	LD50 = 1839mg/kg NOEL = 1350 mg/kg	147319	Slightly toxic
Avian dietary (71-2/850.2200)	Northern bobwhite (<i>Colinus virginianus</i>)	96	LC50 > 5620 ppm	147321	Practically non-toxic
Avian dietary (71-2/850.2200)	Mallard (<i>Anas platyrhynchos</i>)	97.2	>5000 ppm NOEC = 5000 ppm	432899-03	Practically non-toxic
Freshwater fish acute (72-1/850.1075)	Rainbow trout (<i>Oncorhynchus mykiss</i>)	97.1	LC50 >972 mg/L NOEC = 972 mg/L	423736-01	Practically non-toxic
Freshwater fish acute (72-1/850.1075)	Bluegill (<i>Lepomis macrochirus</i>)	97.1	LC50 > 1,017 mg/L NOEC = 1,017 mg/L	423685-01	Practically non-toxic
Fish early life-stage (72-4/850.1300)	Fathead minnow (<i>Pimephales promelas</i>)	99.9	NOEC = 14 mg/L(dry weight) LOEC = 29 mg/L	427217-02	(chronic endpoints are not assigned a toxicity category)
Freshwater invertebrate acute (72-2/850.1010)	<i>Daphnia magna</i>	97.1	EC50 > 1070 mg/L NOEC = 1070 mg/L	423736-03	Practically non-toxic
Marine/estuarine fish acute (72-3a/850.1075)	Sheepshead minnow (<i>Cyprinodon variegatus</i>)	97.1	LC50 > 1006 mg/L NOEC = 1006 mg/L	423747-01	Practically non-toxic
Marine/estuarine invertebrate acute (72-3c/850.1045)	Mysid (<i>Mysidopsis bahia</i>)	97.1	LC50 > 921mg/L (limit test)	423736-02	Practically non-toxic
Marine/estuarine bivalve acute (72-3b/850.1025)	Eastern oyster (<i>Crassostrea virginica</i>) shell deposition	97.2	EC50 > 125 mg/L NOEC = 125 mg/L	432899-02	Practically non-toxic

3. Environmental Exposure Modeling

The PDM4 Model was used to estimate exposure from once-through cooling tower uses. A low-flow power plant (100 ± 10 million gallons per day) was used as the scenario providing the maximum concentrations of DMH in the receiving water, e.g., the “worst case” scenario. Actual concentrations in receiving waters are likely lower, and will likely not show the increasing trend indicated in Table 16, due to higher flow rates and possible degradation/dissipation of DMH by mechanisms other than hydrolysis. Based on the modeling, a summary of the estimated environmental concentrations (EECs) over time is provided below:

Table 16: Summary of Estimated Environmental Concentrations of DMH in Rivers Receiving Outfall from Low-Flow Power Plants Using Once-through cooling tower Systems

Time Period Modeled	Peak Concentration of DMH (EEC)	Duration of Peak Concentration
4 days	36.0 ppb	24 hours
30 days	210 ppb	24 hours
60 days	313 ppb	24 hours

The model was also used to determine the percent of days per year various “concentrations of concern” were exceeded for several power plant scenarios. For more information, see the Revised Halohydantoin Risk Assessment, dated December 15, 2004, available at <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303).

a. Terrestrial Organisms:

No model is available to estimate exposure and risk to birds and mammals from discharge of once-through cooling tower system effluents into surface waters. The low EECs, coupled with the generally low toxicity of DMH to birds and mammals, indicate that risks to these organisms are unlikely. There are no data available to assess the phytotoxicity of DMH at this time; therefore, the risk to terrestrial/semi-aquatic plants cannot currently be assessed.

b. Aquatic Organisms:

Using the worst-case scenario of a low-flow power plant using halohydantoins for once-through cooling tower system treatment, the following risk quotients (RQ) were calculated for aquatic organisms in Table 17.

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Table 17: Aquatic Organism Risk Quotients for DMH Used in Once-through cooling tower of Low-Flow Power Plants

Endpoint Type	Species	Value	EEC (from Table 16)	RQ (EEC/LC50)
Freshwater Fish Acute	Rainbow trout (<i>Oncorhynchus mykiss</i>)	LC50 >972 mg/L (MRID - 423736-01)	36.0 ppb (0.036 mg/L)	0.000037
Freshwater Invertebrate Acute	<i>Daphnia magna</i>	EC50 > 1070 mg/L NOEC = 1070 mg/L (MRID 423736-03)	36.0 ppb (0.036 mg/L)	0.000034
Freshwater Fish Chronic	Fathead minnow (<i>Pimephales promelas</i>)	NOEC = 14 mg/L LOEC = 29 mg/L (MRID - 427217-02)	313 ppb (0.313 mg/L)	0.022

Using the very conservative EECs provided by modeling the once-through cooling tower, no LOCs are exceeded. Expressed as number of days exceedance, using the most sensitive parameter of 14.0 mg/L (14000 ppb) (freshwater fish chronic NOEC) as the “concentration of concern” and the exceedance curve generated by modeling, the chance of this concentration being exceeded by any of the once-through plant scenarios is extremely low, less than once every two years. Other uses of halohydantoin products are indoor or contained (e.g., swimming pool) uses, and should not result in appreciable environmental exposure when products are used as labeled. As indicated in Table 16 above, risks to freshwater fish and aquatic invertebrates are not anticipated from the use of halohydantoins in once-through cooling tower systems as the RQs do not exceed the Agency’s level of concern. Marine/estuarine fish are generally less sensitive than freshwater fish to halohydantoins, and marine/estuarine invertebrates are comparably as sensitive to DMH as freshwater invertebrates. Therefore, the freshwater RQs are presumed to be protective of marine/estuarine species. Risks to aquatic plants cannot be assessed due to the lack of phytotoxicity data.

4. Listed Species Consideration

a. The Endangered Species Act

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an “action” that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means “to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species.” 50 C.F.R. § 402.02.

To facilitate compliance with the requirements of the Endangered Species Act subsection (a) (2), the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA 2004). After the Agency’s screening-level risk assessment is performed, if any of the Agency’s Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

For certain use categories, the Agency assumes there will be minimal environmental exposure, and only a minimal toxicity data set is required (Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs U.S. Environmental Protection Agency - Endangered and Threatened Species Effects Determinations, 1/23/04, Appendix A, Section II B, pg.81). Chemicals in these categories therefore do not undergo a full screening-level risk assessment, and are considered to fall under a “no effect” determination. Based on low toxicity and the use of halohydrantoin products low exposure, risk to endangered birds and mammals is not anticipated. Calculated RQs for fish and aquatic invertebrates from the once-through cooling tower use are well below LOCs for Endangered species; other uses of halohydrantoin products are indoor or contained (e.g., swimming pool) uses, and should not result in appreciable environmental exposure when products are used as labeled. Therefore, risk to Endangered fish and aquatic invertebrate species is not anticipated from the use of halohydrantoin products. Risk to Endangered plants cannot be addressed due to the lack of phytotoxicity data.

IV. Risk Management, Reregistration, and Tolerance Reassessment Decision

A. Determination of Reregistration Eligibility

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether or not products containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic (i.e., active ingredient-specific) data required to support reregistration of products containing halohydantoins as active ingredients. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all supported products containing halohydantoins.

The Agency has completed its assessment of the dietary, occupational, drinking water and ecological risks associated with the use of pesticide products containing the active ingredient halohydantoins. Based on a review of these data and on public comments on the Agency's assessments for the active ingredient halohydantoin, the Agency has sufficient information on the human health and ecological effects of halohydantoins to make decisions as part of the tolerance reassessment process under FFDCA and reregistration process under FIFRA, as amended by FQPA. The Agency has determined that products containing halohydantoins are eligible for reregistration provided that: (i) current data gaps and confirmatory data needs are addressed; (ii) the risk mitigation measures outlined in this document are adopted; and (iii) label amendments are made to reflect these measures. Label changes are described in Section V. Appendix A summarizes the uses of halohydantoins that are eligible for reregistration. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of halohydantoins and lists the submitted studies that the Agency found acceptable. Data gaps are identified as generic data requirements that have not been satisfied with acceptable data.

Based on its evaluation of halohydantoins, the Agency has determined that halohydantoins products, unless labeled and used as specified in this document, would present risks inconsistent with FIFRA. Accordingly, should a registrant fail to implement any of the risk mitigation measures identified in this document, the Agency may take regulatory action to address the risk concerns from the use of halohydantoins. If all changes outlined in this document are incorporated into the product labels, then all current risks for halohydantoins will be substantially mitigated for the purposes of this determination.

B. Public Comments and Responses

Through the Agency's public participation process, EPA worked with stakeholders and the public to reach the regulatory decisions for halohydantoins. During the public comment period on the risk assessments, which closed on September 29, 2004, the Agency received comments from the ACC Brominated Biocides Panel and other interested parties. These comments in their entirety are available in the public docket; <http://www.regulations.gov> (EPA-HQ-OPP-2004-0303). The Agency's responses to these comments are incorporated into the revised risk assessment, which is also available in the public docket.

C. Regulatory Position

1. Food Quality Protection Act (FQPA) Considerations

a. “Risk Cup” Determination

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with this pesticide. The Agency has concluded that the tolerance exemption for halohydantoins meets the FQPA safety standards and that the risk from dietary (food sources only) exposure is within the “risk cup.” An aggregate assessment was conducted for exposures from food and residential use. The Agency has determined that the human health risks from these combined exposures are within acceptable levels provided that the mitigation contained in this document is implemented. In reaching this determination, EPA has considered the available information on the special sensitivity of infants and children, as well as aggregate exposure from food, water and residential exposures.

b. Determination of Safety to U.S. Population

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with halohydantoins. The Agency has determined that, the established tolerance exemptions for halohydantoins with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(D) of the FFDCa, and that there is a reasonable certainty no harm will result to the general population or any subgroup from the use of halohydantoins. In reaching this conclusion, the Agency has considered all available information on the toxicity, use practices and exposure scenarios, and the environmental behavior of halohydantoins. As discussed in Section III, the acute and chronic dietary (food and drinking water) risks from halohydantoins are below the Agency’s level of concern.

c. Determination of Safety to Infants and Children

EPA has determined that the tolerance exemptions for halohydantoins meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCa, that there is a reasonable certainty of no harm for infants and children. The safety determination for infants and children considers toxicity, use practices, and environmental behavior noted above for the general population, but also takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of halohydantoins in this population subgroup.

In determining whether infants and children are particularly susceptible to toxic effects from exposure to residues of halohydantoins, the Agency considered the completeness of the hazard database for developmental and reproductive effects, the nature of the effects observed, and other information. On the basis of this information, the FQPA safety factor has been reduced

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to 1X for halohydantoins. The rationale for the decisions are based on: the developmental endpoint is sufficiently protective of effects that may occur in infants and children from exposure to dimethylhydantoin. Even though, there is quantitative evidence of increased sensitivity of neonatal rabbits, the Agency considered this effect not indicative of susceptibility, based upon: (1) the very high dose level at which the effect occurred; (2) the minimal nature of the effect and (3) the likelihood that the effect was due to a greater dose received by pups from ingestion of both milk and feed during the lactation period.

d. Endocrine Disruptor Effects

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency’s Endocrine Disrupting Screening Program (EDSP) have been developed, halohydantoins may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

e. Cumulative Risks

Risks summarized in this document are those that result only from the use of halohydantoins. The Food Quality Protection Act (FQPA) requires that the Agency consider “available information” concerning the cumulative effects of a particular pesticide’s residues and “other substances that have a common mechanism of toxicity.” The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the substances individually. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding for halohydantoins. For information regarding EPA’s efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA’s Office of Pesticide Programs concerning common

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mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

2. Tolerance Summary

No pesticide tolerances have been established for the halohydantoins. The Agency has determined that, the established tolerance exemptions for halohydantoins with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(D) of the FFDCA, and that there is a reasonable certainty no harm will result to the general population or any subgroup from the use of halohydantoins.

3. Codex Harmonization

No CODEX maximum residue levels (MRLs) have been established for halohydantoins.

D. Regulatory Rationale

The Agency has determined that the halohydantoins are eligible for reregistration provided that additional required data confirm this decision, the risk mitigation measures outlined in this document are adopted, and label amendments are made to reflect these measures.

The following is a summary of the rationale for managing risks associated with the use of halohydantoins. Where labeling revisions are warranted, specific language is set forth in the summary tables of Section V of this document.

1. Human Health Risk Management

a. Dietary (Food) Risk Mitigation

Generally, a dietary risk estimate that is less than 100% of the acute or chronic PAD does not exceed the Agency's risk concerns. For all supported uses, acute and chronic dietary risk estimates are not of concern. Therefore, no risk mitigation measures are required.

b. Drinking Water Risk Mitigation

Based on modeling, the once-through cooling tower use of the halohydantoins is not likely to result in risks to drinking water. Therefore, no risk mitigation is required.

c. Residential Risk Mitigation

Residential risks for handlers were calculated for short- and intermediate-term dermal and inhalation exposures. For all supported uses, residential exposure risk estimates are not of

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concern. However, as formaldehyde is a metabolite of dihalodialkylhydantoins, there may be risk associated with this exposure, particularly for use of products that produce a greater chance of inhalation exposure to formaldehyde, such as air fresheners. Risks associated with the exposure to formaldehyde via the hydroxymethylhydantoins will be addressed when registration review is conducted on hydroxymethylhydantoin. Therefore, no risk mitigation measures are necessary.

d. Occupational Risk Mitigation

i. Handler Mitigation

Dermal and Inhalation Risk for Agricultural Premises

Dermal and inhalation risk concerns have been identified for occupational handlers treating agricultural premises. All MOEs calculated are of concern (i.e. scenarios are of concern with MOEs less than the target MOE of 100). No postapplication exposures were considered.

To reduce occupational exposure, the following label language will be required:

- For irrigation/chemigation rates that are greater than 35,000 gallons per day, applicators must use “solid pour.” For smaller applications less than 35,000 gallons per day, applicators can “place” the solids.
- Confirmatory exposure data will be required

Dermal Risk for Swimming Pools

Occupational risks of concern were identified for handlers placing tablets into public swimming pools ungloved (MOE=46). However, the product labels state that gloves should be worn when placing tablets into swimming pools. When gloves are used for the placing of tablets the MOE is not of concern (MOE = 7,500). The risk will be mitigated by requiring the use of gloves.

Once-through Cooling Tower

Occupational risks of concern were identified for handlers applying halohydantoins to once-through cooling towers. To reduce exposure and mitigate risks, handlers will be required to use gloves when applying these products to once-through cooling towers.

ii. Post-Application Risk Mitigation

Post-application inhalation exposures may occur in the industrial settings around the water systems via inhalation. Dermal exposures may occur while maintaining industrial equipment. However, occupational postapplication dermal and inhalation exposures to dihalodialkylhydantoin are likely to be minimal compared to handler exposure because of dilution

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during application. No exposure data has been submitted to the Agency to determine the extent of post-application exposures in the industrial settings. Inhalation exposures are expected to be minimal because aerosol generation is not expected and the vapor pressure of dihalodialkylhydantoin is low. The Agency does not believe that any mitigation is necessary at this time.

2. Environmental Risk Management

Most of the halohydantoins uses are considered indoor uses. However, there is potential environmental exposure from the once-through cooling tower use. Risks to freshwater fish and aquatic invertebrates are not anticipated from the use of halohydantoins in once-through cooling tower systems as the RQs do not exceed the Agency's level of concern. Marine/estuarine fish are generally less sensitive than freshwater fish to halohydantoins, and marine/estuarine invertebrates are comparably as sensitive to DMH as freshwater invertebrates. No risk mitigation is required.

3. Other Labeling Requirements

In order to be eligible for reregistration, various use and safety information will be included in the labeling of all end-use products containing halohydantoins. For the specific labeling statements and a list of outstanding data, refer to Section V of this RED document.

4. Listed Species Considerations

a. The Endangered Species Act

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an "action" that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species" (50 C.F.R. ' 402.02).

To facilitate compliance with the requirements of the Endangered Species Act subsection (a)(2) the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA 2004). After the Agency's screening-level risk assessment is performed, if any of the Agency's Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify

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if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

For certain use categories, the Agency assumes there will be minimal environmental exposure, and only a minimal toxicity data set is required (Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs U.S. Environmental Protection Agency - Endangered and Threatened Species Effects Determinations, 1/23/04, Appendix A, Section IIB, pg.81). Chemicals in these categories therefore do not undergo a full screening-level risk assessment, and are considered to fall under a no effect determination. The current active ingredient uses of halohydantoins fall into this category. Risks to endangered birds and mammals are not anticipated from the use of hydantoin products due to low exposure and low toxicity. Calculated RQ's for fish and aquatic invertebrates from the once-through cooling tower use are well below LOCs for endangered species; other use of hydantoin products are indoor or contained (e.g., swimming pool) uses, and should not result in appreciable environmental exposure when products are used as labeled. Therefore, risk to endangered fish and aquatic invertebrate species is not anticipated from the use of hydantoin products. Risk to endangered plants cannot be addressed due to the lack of phytotoxicity data.

V. What Registrants Need to Do

The Agency has determined that halohydantoins are eligible for reregistration provided that: (i) additional data that the Agency intends to require confirm this decision; and (ii) the risk mitigation measures outlined in this document are adopted, and (iii) label amendments are made to reflect these measures. To implement the risk mitigation measures, the registrants must amend their product labeling to incorporate the label statements set forth in the Label Changes Summary Table in Section B below (Table 17). The additional data requirements that the Agency intends to obtain will include, among other things, submission of the following:

For halohydantoins technical grade active ingredient products, the registrant needs to submit the following items:

Within 90 days from receipt of the generic data call in (DCI):

1. completed response forms to the generic DCI (i.e., DCI response form and requirements status and registrant's response form); and
2. submit any time extension and/or waiver requests with a full written justification.

Within the time limit specified in the generic DCI:

1. cite any existing generic data, which address data requirements or submit new generic data responding to the DCI.

Please contact ShaRon Carlisle at (703) 308-6427 with questions regarding generic reregistration.

By US mail:
Document Processing Desk (DCI/AD)
(DCI/AD)
ShaRon Carlisle
US EPA (7510P)
1200 Pennsylvania Ave., NW
Washington, DC 20460

By express or courier service:
Document Processing Desk

ShaRon Carlisle
Office of Pesticide Programs (7510P)
One Potomac Yard (South Building),
2777 South Crystal Drive
Arlington, VA 22202

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For end use products containing the active ingredient halohydantoins, the registrant needs to submit the following items for each product.

Within 90 days from the receipt of the product-specific data call-in (PDCI):

1. completed response forms to the PDCI (i.e., PDCI response form and requirements status and registrant's response form); and
2. submit any time extension or waiver requests with a full written justification.

Within eight months from the receipt of the PDCI:

1. two copies of the confidential statement of formula (EPA Form 8570-4);
2. a completed original application for reregistration (EPA Form 8570-1). Indicate on the form that it is an "application for reregistration";
3. five copies of the draft label incorporating all label amendments outlined in Table 13 of this document;
4. a completed form certifying compliance with data compensation requirements (EPA Form 8570-34); and
5. if applicable, a completed form certifying compliance with cost share offer requirements (EPA Form 8570-32); and
6. the product-specific data responding to the PDCI.

Please contact Emily Mitchell at (703) 308-8583 with questions regarding product reregistration and/or the PDCI. All materials submitted in response to the PDCI should be addressed as follows:

By US mail:
Document Processing Desk (PM-32)
Emily Mitchell
US EPA (7510P)
1200 Pennsylvania Ave., NW
Washington, DC 20460

By express or courier service:
Document Processing Desk (PM-32)
Emily Mitchell
Office of Pesticide Programs (7510P)
One Potomac Yard (South Building),
2777 South Crystal Drive
Arlington, VA 22202

A. Manufacturing Use Products

1. Additional Generic Data Requirements

The generic database supporting the reregistration of halohydantoins has been reviewed and determined to be substantially complete. However, the following additional data requirements have been identified by the Agency as confirmatory and included in the generic DCI for this RED.

The risk assessment noted deficiencies in the surrogate dermal and inhalation exposure data available from the Chemical Manufacturers Association (CMA) data base. Therefore, the Agency is requiring confirmatory data to support the uses assessed with the CMA exposure data within this risk assessment. The risk assessment also noted that many of the use parameters (e.g., amount handled and duration of use) were based on professional judgments. Therefore, descriptions of human activities associated with the uses assessed are required as confirmatory.

The following ecological effects data are required to support the once through cooling tower system uses for halohydantoin products:

- 72-4/850.1400 Aquatic invertebrate life-cycle test with DMH

In addition, the following phytotoxicity studies are needed to address the Endangered Species Act identified by the Agency:

- 122-1 Seedling emergence/vegetative vigor in rice (at 1 ppm DMH, mixed in the soil and applied to the foliage in the same test)
- 122-2 Tier I Aquatic plant toxicity using *Lemna* sp. (at 1 ppm DMH)
- 122-2 Tier 1 Algal toxicity using the green alga *Selenastrum capricornutum* (at 1 ppm DMH)

Reserved data requirements (**pending the results of the plant tests described above**):

- 123-1/850.4225 and 850.4250 Tier II (dose-response) seedling emergence/vegetative vigor with rice
- 123-2/850.4400 Tier II (dose-response) aquatic plant toxicity using *Lemna* sp.
- 123-2/850.5400 Tier II (dose-response) algal toxicity, 4 species (green alga, freshwater diatom, marine diatom, and blue-green cyanobacteria)

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Table 18. Confirmatory Data Requirements for Reregistration

Guideline Study Name	New OPPTS Guideline No.	Old Guideline No.
Dermal Indoor Exposure	875.1200, 875.1600	233 and 236
Inhalation Indoor Exposure	875.1400, 875.1600	234 and 236
Descriptions of Human Activity	875.2800	133-1
Aquatic invertebrate life-cycle test with DMH	850.1400	72-4
Seedling emergence/vegetative vigor in rice (at 1 ppm DMH, mixed in the soil and applied to the foliage in the same test)		122-1
Tier I Aquatic plant toxicity using <i>Lemna</i> sp. (at 1 ppm DMH)		122-2
Tier 1 Algal toxicity using the green alga <i>Selenastrum capricornutum</i> (at 1 ppm DMH)		122-2
Studies Held in Reserve		
Tier II (dose-response) seedling emergence/vegetative vigor with rice	850.4225 and 850.4250	123-1
Tier II (dose-response) aquatic plant toxicity using <i>Lemna</i> sp.	850.4400	123-2
Tier II (dose-response) algal toxicity, 4 species (green alga, freshwater diatom, marine diatom, and blue-green cyanobacteria)	850.5400	123-2

2. Labeling for Technical and Manufacturing Use Products

To ensure compliance with FIFRA, technical and manufacturing use product (MP) labeling should be revised to comply with all current EPA regulations, PR Notices and applicable policies. The Technical and MP labeling should bear the labeling contained in Table 19, Label Changes Summary Table.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. The Registrant must review previous data submissions to ensure that they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then the study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product.

A product-specific data call-in, outlining specific data requirements, will follow this

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RED be sent to the registrants at a later date. The PDCI will be based upon current efficacy-related requirements for antimicrobial pesticide products, claims, or use patterns.

2. Labeling for End-Use Products

Labeling changes are necessary to implement measures outlined in Section IV above. Specific language to incorporate these changes is specified in Table 19.

Registrants may generally distribute and sell products bearing old labels/labeling for 26 months from the date of the issuance of this Reregistration Eligibility Decision document. Persons other than the registrant may generally distribute or sell such products for 52 months from the approval of labels reflecting the mitigation described in this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to “Existing Stocks of Pesticide Products; Statement of Policy,” *Federal Register*, Volume 56, No. 123, June 26, 1991.

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a. Label Changes Summary Table

In order to be eligible for reregistration, amend all product labels to incorporate the risk mitigation measures outlined in Section IV. The following table describes how language on the labels should be amended.

Table 19. Labeling Changes Summary Table

Description	Amended Labeling Language	Placement on Label
Manufacturing Use Product		
Supported Use Sites	<p>“Only for formulation into antimicrobial products for use in: agricultural/farm premises, structures, buildings, and equipment; dairy farm milk handling facilities, equipment, storage rooms, houses, and sheds; food processing plants, food handling, food distribution equipment and premises; eating establishments premises and equipment; commercial, institutional, and industrial premises and equipment (floors, walls, storage areas); domestic dwellings, food handling areas, indoor premises; and medical institutional critical care and non-critical care premises, human water systems, swimming pools and industrial processes and water systems.”</p> <p>For Formulation into antimicrobial products for use in: animal transport vehicles, carpets, fountains/water displays/decorative ponds/, once- through and recirculating industrial commercial cooling water systems, pulp/paper mill water systems, and swimming pools, mushroom facilities/premises and equipment, egg handling equipment and rooms, egg washing treatment, chick room, poultry houses chiller water/carcass spray, food processing plants/equipment, dairies/breweries and bottling plants/equipment, fruit and vegetable rinse/process water and tank lines, potable drinking water, water storage systems (aircrafts boats, RVs, off-shore oil rigs), water filtration systems, ventilation systems.</p>	Directions for Use
End Use Products Intended for Occupational Use		

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Description	Amended Labeling Language	Placement on Label
Application Restrictions-For Occupational Handler -Dermal (Tablets into public swimming pools)	“Must wear chemical resistant gloves while placing the tablet in the swimmingpool”	Precautionary Statements under: Hazards to Humans and Domestic Animals (Immediately Following Engineering Controls
Application Restrictions-For Occupational Handler -Dermal (Once through cooling tower – “solid place”)	“Must wear chemical resistant gloves while placing the tablet in the once through cooling tower system”	Precautionary Statements under: Hazards to Humans and Domestic Animals (Immediately Following Engineering Controls
Application Restrictions-For Residential Handler -Dermal (Tablets into public swimmingpools)	“Must wear chemical resistant gloves while placing the tablet in the swimmingpool/spas”	Precautionary Statements under: Hazards to Humans and Domestic Animals (Immediately Following Engineering Controls

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Description	Amended Labeling Language	Placement on Label
Application Restrictions-For Occupational Handler (<i>Greenhouse Irrigation</i>)	<ol style="list-style-type: none"> 1) Must have label language that states for application rates greater than 35, 000 gallons per day applicators must use “solid pour” and for smaller applications less than 35,000 gallons per day, applicators can must “place solids” into a metered feeding system 2) “Occupational handler must wear chemical resistant gloves while placing granules and tablets in nursery and greenhouse irrigation systems” 	Precautionary Statements under: Hazards to Humans and Domestic Animals (Immediately Following Engineering Controls

VI. APPENDICES

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
Residential and public access premises				
Hard non-porous non-food contact surfaces, such as bathrooms, flooring, walls, garbage cans. Etc.	6836-324 (soluble solid)	Spray, brush, mop or sponge	1gram of product per 7.8 gallons of water. Preclean areas. 10 minute contact time.	Avoid breathing spray.
Kennels	6836-324 (soluble solid)	Spray, brush, mop or sponge	1gram of product per 7.8 gallons of water. Preclean areas. 10 minute contact time.	Avoid breathing spray.
In- Tank- Sanitizer	777-106 777-107 5185-446 5185-469 5813-65 5813-66 6836-255 6836-256 6836-263 6836-264 6836-265 6836-272 6836-273 6836-274 6836-275 6836-279	Place tablet in tank	Clean toilet bowl thoroughly and flush the toilet. When water level is low and valve closed, place tablet into the right corner of the tank. When tablet dissolved replace it with a new tablet. Tablets should be used in toilets flushed daily.	Do not touch tablet directly. Wash hands thoroughly if there is any skin contact.

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
	6836-287 6836-288 6836-291 6836-299 6836-300 (Tablet)			
In Tank Sanitizer/Necktie	5813-84 (Tablet)	Place tablet in tank	Clean toilet bowl thoroughly including under rim. Flush toilet and remove toilet tank lid. Hang unit(s) on toilet tank wall with tablet holder on inside of tank and fragrance gel (holder) on the outside of the tank.	Immediately wash your hands after handling unit.
Industrial Process and Water Systems				
Air Gas Scrubber Systems	3377-62 3377-71 (Ready to Use)	Open Pour/Ready to Use	<u>Initial Dose:</u> When system is noticeably fouled add product to achieve a residual bromine level of 0.5-5ppm or as needed to maintain control. Repeat until control is achieved. <u>Subsequent Dose:</u> When	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			microbial control is evident apply product to achieve a residual bromine level of 0.5-5ppm or as needed to maintain control.	
Pulp and Paper Systems	1448-356 1448-428 5785-63 6836-282 63838-4 75361-1 83451-4 (Tablet)	Place tablet in the system at a point where sufficient mixing can occur	When system is noticeably fouled add at a of 12 to 20 ppm When biological control is evident: 12 to 90 ppm. 0.5-2.0 lbs of product per ton.	Do not exceed 2.2lbs of this product per dry metric ton fiber when this product is used in the manufacture of paper and paperboard products that contain food.
Pulp and Paper Systems	6836-297 (Tablet)	Place tablet in the system at a point where sufficient mixing can occur	0.5-2.0 lbs of product per ton. To produce 0.1-1.0 ppm of available halogen as chlorine.	May be used in the manufacture of food contact paper and paperboard products.
	1448-420 3377-62 3377-63 3377-71 5785-57	Open Pour/ready to use	When system is noticeably fouled add at a rate of 0.5 to 120ppm. When biological control is evident add at a rate of 12	Do not exceed 1.0 kilograms per 1,000kg per dry metric ton fiber in paper and paperboard components that contact food.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	(Ready to Use)		to 90 ppm.	
	8622-29 83451-3 5785-65 (Granular)	Open Pour/Granules	When system is noticeably fouled add 12 to 20 ppm. When biological control is evident add 12 to 90 ppm.	Used in the manufacture of paper and paperboard products that does not contact food.
	8622-28 (wetable powder)	Open Pour/Powder	When system is noticeably fouled add 12 to 20 ppm. When biological control is evident add 12 to 90 ppm.	Used in the manufacture of paper and paperboard products that do not contact food
	83451-10 (Soluble Concentrate)	Open Pour/Soluble Concentrate	When system is noticeably fouled add 28.8 to 288ppm. When biological control is evident add 28.8 to 216 ppm.	Used in the manufacture of paper and paperboard products that does not contact food.
	83451-11 (Gel)	Open Pour/Gel	When system is noticeably fouled add 32.9 to 329ppm. When biological control is	Used in the manufacture of paper and paperboard products that contact food.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			evident add 32.9 to 247 ppm	
Paper and Paperboard Process Water (Continued)	6836-113 6836-115 6836-314 (Tablet)	Place tablet in system	<p><u>Initial Dose:</u> When system is noticeably fouled apply 0.5 to 2.0 lbs per ton of paper produced to achieve 0.1- 1.0 ppm total available halogen as chlorine. Repeat treatment until residual is achieved.</p> <p><u>Subsequent Dose:</u> When microbial control is evident apply 0.5-2.0 lbs per ton of paper produced to achieve 0.1-1.0 ppm total available halogen as chlorine. Repeat periodically as needed to maintain control.</p>	None listed
	6836-317 (Tablet)	Place tablet in system	<p><u>Initial Dose:</u> When system is noticeably fouled apply 0.1-10lbs of tablets to 1,000 gallons (0.1 to 1.0 lbs of tablets per dry metric ton of paper produced) Repeat treatment until residual of up to 5 ppm bromine is achieved.</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Paper and Paperboard Process Water (Continued)			<u>Subsequent Dose:</u> When microbial control is evident apply 0.1 to 0.75 lbs of this product to 1,000 gallons of water. (0.1 to 0.75 lbs of tablets per dry metric ton of paper produced). Repeat treatment until achieve 0.1-1.0 ppm _{total} available. Repeat treatment until residual of up to 1 ppm is achieved.	
	83451-10 (Soluble Concentrate)	Open Pour/Soluble Concentrate	<u>Initial Dose:</u> When system is noticeably fouled add 0.0238 to 0.238 gallons to 1,000 gallons of water in the system. <u>Subsequent Dose:</u> When biological control is evident add 0.0238 to 0.179 gallons to 1,000 gallons of water in the system.	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Paper and Paperboard Process Water (Continued)				
	6836-237 6836-280 6836-281 6836-296 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When system is noticeably fouled apply 0.5-2.0lbs per _{ton} of paper produced to achieve 0.1-1.0 ppm total available halogen as chlorine. Repeat treatment until residual is achieved. <u>Subsequent Dose:</u> When microbial control is evident apply 0.5-2.0 lbs per _{ton} of paper produced to achieve 0.1-1.0 ppm _{total} available halogen as chlorine. Repeat periodically as needed to maintain control.	None listed.
	6836-312 6836-315 6836-319	Open Pour/ Powder	<u>Initial Dose:</u> When system is noticeably fouled apply 0.1-2.0lbs per ton of paper	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	(Wettable Powder)		<p>produced to achieve 0.1-1.0 ppm total available halogen as chlorine. Repeat treatment until residual is achieved.</p> <p><u>Subsequent Dose:</u> When microbial control is evident apply 0.1-2.0 lbs per ton of paper produced to achieve 0.1-1.0 ppm total available halogen as chlorine. Repeat periodically as needed to maintain control.</p>	
Pasteurizer, Can Warmer, Cannery, Retort Water Systems	1448-356 1448-428 5185-420 69681-16 83451-4 (Tablet)	Place tablet in system	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Pasteurizer, Can Warmer, Cannery, Retort Water Systems (Continued)			gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	
	1448-420 (Ready to Use)	Open Pour/Ready to Use	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.</p>	None listed
	83451-3 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Pasteurizer, Can Warmer, Cannery, Retort Water Systems (Continued)			<p>/1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.</p>	
	83451-10 (Soluble Concentrate)	Open Pour/ Soluble Concentrate	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.0477 to 0.143 gallons /1,000 gallons of water. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.0238 to 0.072 gallons /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	83451-12 (Ready to Use)	Open Pour/ Ready to Use	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.</p>	None listed.
	83451-11 (Gel)	Open Pour/Ready to Use	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.0545 to 0.1634 gallons /1,000 gallons of water. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.0272 to 0.0823 gallons /1,000 gallons of water.</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	
Evaporative Cooler	1448-356 1448-428 5785-63 5785-100 5185-420 69681-16 75361-1 83451-4 (Tablet)	Place tablet in system	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	None listed.
Evaporative Cooler (Continued)	1448-420 83451-12 (Ready to Use)	Open Pour/Ready to Use	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Evaporative Cooler (Continued)			control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	
	83451-12 (Wettable Powder)	Open Pour/Powder	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	
	83451-10 (Ready to Use)	Open Pour/Ready to Use	<u>Initial Dose:</u> When system is noticeably fouled add 0.0477 to 0.143 gallons/1,000 gallons of water in the system. Repeat initial dose until 1 to 3 ppm bromine residual is established for at least 4	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			hours. <u>Subsequent Dose:</u> When microbial control is evident add 0.0238 to 0.072 gallons/1,000 gallons of water in the system. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	
	75361-1 (Tablet)	Place tablet in the system	Place tablets into condensate line dispenser or floatation device into reservoir. Maintain 1 to 4 ppm active bromine.	Do not place tablet on metal surfaces.
	83451-3 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	
	83451-11 (Gel)	Open Pour/Gel	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.0545 to 0.1634 gallons /1,000 gallons of water. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.0272 to 0.0823 gallons /1,000 gallons of water. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours</p>	None listed.
Recirculating Cooling Water	1448-356 1448-428 5185-420	Place tablet in system.	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds	None listed

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	5185-421 5785-63 5785-100 63838-4 6836-314 6836-315 6836-317 69681-16 83451-4 (Tablet)		/1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	
	8622-77 63838-7 (powder)		<u>Initial Dose:</u> When the system is noticeably fouled add 1.7 to 6.0 pounds /10,000 gallons. Repeat until 1 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.8 to 3.0 pounds /10,000 gallons. Repeat as needed to maintain 1-3 ppm bromine residual for at least 4 hours	
	1448-420 (Ready to Use)	Open Pour/Ready to Use	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Recirculating Cooling Water (Continued)			<p>/1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours</p>	
	8622-30 (Tablet)	Place tablet in system	<p><u>Initial Dose:</u> When system is noticeably fouled, add 0.75 to 6.0 lbs/1000 gallons of water. Repeat in dosage until one ppm halogen residual, measured as free chlorine for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When system is noticeably fouled, add 0.1 to 3.0 lbs/1000 gallons of water. Repeat as needed to maintain one ppm halogen</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Recirculating Cooling Water (Continued)			residual, measured as free chlorine for at least 4 hours.	
	5785-62 66397-1 75361-1 8622-73 (Tablet)	Place tablet in system	<p><u>Initial Dose:</u> When system is noticeably fouled, add 0.75 to 6.0 lbs/1000 gallons of water. Repeat in dosage until one ppm halogen residual, measured as free chlorine for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When system is noticeably fouled, add 0.1 to 3.0 lbs/1000 gallons of water. Repeat as needed to maintain one ppm halogen residual, measured as free chlorine for at least 4 hours.</p>	None listed.
	5785-69	Place tablet in	<u>Initial Dose:</u> When system	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Recirculating Cooling Water (Continued)	(Tablet)	system.	is noticeably fouled use 1 to 2 tablets for each 100 gallons of water. Add additional tablets until a residual of 10 to 35 ppm bromine is established. Maintain treatment until system is free from microbial fouling. <u>Subsequent Dose:</u> Use tabs as needed to maintain a residual of 5 to 15 ppm bromine.	
	5785-65 6836-315 6836-316 83451-3 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When the system is noticeably fouled ass 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			least 4 hours	
	6836-237 6836-280 6836-324 (Granular)	Open Pour/Granules	<p><u>Initial Dose:</u> When system is noticeably fouled add 0.1 to 1.0 lbs to 1,000 gallons of water. Repeat until control is achieved.</p> <p><u>Subsequent Dose:</u> When microbial control is evident add 0.1 to 0.75 lbs to 1,000 gallons of water every 3 days or as needed to maintain control.</p>	None listed.
	83451-12 (Wettable Powder)	Open Pour/Powder	<p><u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm</p>	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Recirculating Cooling Water (Continued)			bromine residual for at least 4 hours.	
	1448-420 3876-150 5785-57 6836-113 6836-115 6836-116 6836-120 6836-121 6836-122 6836-123 6836-124 6836-210 (Ready to Use Solution)	Intermittent, slug or continuous feed method.	<p><u>Initial Dose:</u> When system is noticeably fouled add 0.1 to 1.0 lbs to 1,000 gallons of water. Repeat until control is achieved.</p> <p><u>Subsequent Dose:</u> When microbial control is evident add 0.1 to 0.75 lbs to 1,000 gallons of water every 3 days or as needed to maintain control.</p>	None listed.
	5785-70 (Granular)	Open Pour/Granules	<p><u>Initial Dose:</u> Use 1oz per 100 gallons of water. Add additional granules until residual of 1 to 35 ppm is established.</p> <p><u>Subsequent Dose:</u> Use as needed to maintain residual 5 to 15 ppm bromine.</p>	Do not mix granules with pesticide or fertilizer concentrates.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	3377-62 3377-71 (Ready to Use)	Intermittent, slug or continuous method.	<u>Initial Dose:</u> When system is noticeably fouled add 0.5 to 5ppm as needed to maintain control. Applying ½ ounce to 1,000 gallons of water yields theoretical average 4 ppm available bromine. Repeat as until control is evident. <u>Subsequent Dose:</u> When microbial control is evident add 05 to 5 ppm as needed to maintain control.	None listed.
	83451-10 (Soluble Concentrate)	Open Pour/Soluble Concentrate	<u>Initial Dose:</u> When system is noticeably fouled add 0.0477 to 0.143 gallons /1000 gallons of water. Repeat initial dose until bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When microbial control is evident add 0.0238 to 0.072 gallons/1,000 gallons of water. Repeat as needed to maintain 1 to 3 ppm bromine residual for at	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			least 4 hours.	
	83451-11 (Gel)	Open Pour/Gel	<u>Initial Dose:</u> add 0.0545 to 0.1634 gallons/ 1000 gallons of water. Repeat initial dosage until 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> add 0.0272 to 0.0823 gallons/ 1000 gallons of water. Repeat as needed until 1 to 3 ppm bromine residual is established for at least 4 hours.	None listed.
Once Through Cooling Water System	1448-356 1448-428 5785-63 63838-4 6836-115 69681-16 83451-4 8622-30 (Tablet)	Place tablet in system	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Once Through Cooling Water System (Continued)			to maintain 1 to 3 ppm bromine.	
	5785-62 (Tablet)	Place tablet in system	<u>Initial Dose:</u> When system is noticeably fouled, add 0.75 to 2.25lbs/1000 gallons of water. Repeat in dosage until one ppm halogen residual, measured as free chlorine for at least 4 hours <u>Subsequent Dose:</u> When system is noticeably fouled, add 0.4 to 1.25 lbs/1000 gallons of water. Repeat as needed to maintain one ppm halogen residual, measured as free chlorine for at least 4 hours.	None listed.
	63838-4 75361-1 8622-73 (Tablet)	Place tablet in system	<u>Initial Dose:</u> When noticeably fouled add 2-6 lbs per 10,000gallons of water. Repeat initial dosage until at least one ppm of active residual bromine is established for at least 4 hours. <u>Subsequent Dose:</u> When	None listed. None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			microbial control is evident add 1 to 3lbs per 10,000 gallons of water. Repeat as needed to maintain one ppm of active residual bromine for at least 4 hours.	
	1448-420 3876-150 5785-57 6836-210 6836-113 6836-317 (Ready to Use)	Open Pour/Ready to Use	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	None listed.
	5785-65 6836-237 6836-280 6836-315 83451-3 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Once Through Cooling Water System (Continued)			hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours	
	8622-29 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When noticeably fouled add 2-6 lbs per 10,000 gallons of water. Repeat initial dosage until at least one ppm of active residual bromine is established for at least 4 hours. <u>Subsequent Dose:</u> When microbial control is evident add 1 to 3lbs per 10,000 gallons of water. Repeat as needed to maintain one ppm of active residual bromine for at least 4 hours.	None listed.
	6836-316 83451-12 (Wettable)	Open Pour/Powder	<u>Initial Dose:</u> When the system is noticeably fouled add 0.2 to 0.6 pounds	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Once Through Cooling Water System (Continued)	Powder)		/1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine	
	8622-28 (Wettable Powder)	Open Pour/Powder	<u>Initial Dose:</u> When noticeably fouled add 2-6 lbs per 10,000 gallons of water. Repeat initial dosage until at least one ppm of active residual bromine is established for at least 4 hours. <u>Subsequent Dose:</u> When microbial control is evident add 1 to 3lbs per 10,000 gallons of water. Repeat as needed to maintain one ppm of active residual bromine for at least 4 hours.	None listed.
	83451-10 (Soluble	Open Pour/Soluble	<u>Initial Dose:</u> When system is noticeably fouled add	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	Concentrate)	Concentrate	0.0477 to 0.143 gallons /1000 gallons of water. Repeat initial dose until bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When microbial control is evident add 0.0238 to 0.072 gallons/1000 gallons of water. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	
	83451-11 (Gel)	Open Pour/Gel	<u>Initial Dose:</u> When system is noticeably fouled add 0.0545 to 0.1634 gallons/ 1000 gallons of water. Repeat initial dosage until 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When microbial control is evident add 0.0272 to 0.0823 gallons/1000 gallons of water. Repeat as needed to	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			maintain 1 to 3 ppm bromine residual for at least 4 hours.	
Auxiliary Water and Waste Water System	1448-356 5185-420 5785-63 6836-314 6836-317 69681-16 83451-4 (Tablet)	Place tablet in system	Add 0.1 to 0.6 lbs /1,000 gallons of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection point in the disinfection contact chamber. Adjust this product's dosage to achieve disinfection and minimize the halogen concentration at the exit of the contact chamber.	Do not use treated wastewater to irrigate crops.
Auxiliary Water and Waste Water System (Continued)	5785-65 (Granular)	Open Pour/Granules	Add 0.1 to 0.6 lbs /1,000 gallons of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection point in the disinfection contact chamber. Adjust this product's dosage to achieve disinfection and minimize the halogen concentration at the exit of the contact chamber.	Do not use treated wastewater to irrigate crops.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	1448-420 5785-57 (Ready to Use)	Open Pour/Ready to Use	Add 0.1 to 0.6 lbs /1,000 gallons of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection point in the disinfection contact chamber. Adjust this product's dosage to achieve disinfection and minimize the halogen concentration at the exit of the contact chamber.	Do not use treated wastewater to irrigate crops.
	3377-62 3377-71 (Ready to Use)	Open Pour/Ready to Use	The quantity required varies with degree of fouling. Add sufficient amount to achieve residual bromine levels 0.5 -5ppm. Applying ½ounce to 1,000 gallons of water yields a theoretical average of 4 ppm of available bromine. Higher dosages may be necessary depending upon the system.	None listed

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Auxiliary Water and Waste Water System (Continued)	83451-10 (Soluble Concentrate)	Open Pour/Soluble Concentrate	Add 0.0238 to 0.143 gallons of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection point in the contact chamber. Adjust this product's dosage to achieve sanitization and minimize the halogen concentration at the exit of the contact chamber.	Do not use treated wastewater to irrigate crops.
	6836-316 (Wettable Powder)	Open Pour/Powder	Add 0.1 to 0.6 lbs /1,000 gallons of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection of water treated to maintain 0.5 to 5.0 ppm bromine residual at the injection point in the contact chamber.	Do not use treated wastewater to irrigate crops.
	83451-11 (Gel)	Open Pour/Gel	Add 0.0272 to 0.1634 gallons /1,000 gallons of water treated to maintain	Do not use treated wastewater to irrigate crops

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			0.5 to 5.0 ppm bromine residual at the injection point in the contact chamber. Adjust this product's dosage to achieve sanitization and minimize the halogen concentration at the exit of the contact chamber.	
Industrial air washer systems	6836-113 6836-115 6836-210 6836-314 6836-316 (Tablet)	Place tablet in system	<u>Initial Dose:</u> When system is noticeably fouled add to airwasher sump or chill water sump to insure uniform mixing. Add 0.1 to 1.0 lbs per 1,000 gallons of water. <u>Subsequent Dose:</u> When microbial control is evident add 0.1 to 0.6 lbs per 1,000 gallons of water.	None listed.
Industrial air washer systems	6836-314 6836-316	Place tablet in system	<u>Initial Dose:</u> When the system is noticeably fouled	Badly fouled systems should be cleaned before treatment is done.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
(Continued)	(Tablet)		add 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours. <u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.	
	6836-237 6836-280 6836-324 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When system is noticeably fouled add to airwasher sump or chill water sump to insure uniform mixing. Add 0.1 to 1.0 lbs per 1,000 gallons of water. <u>Subsequent Dose:</u> When microbial control is evident add 0.1 to 0.6 lbs per 1,000 gallons of water.	Badly fouled systems should be cleaned before treatment is done.
	6836-315 (Granular)	Open Pour/Granules	<u>Initial Dose:</u> When the system is noticeably fouled	Badly fouled systems should be cleaned before treatment is done.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Industrial air washer systems (Continued)			<p>ass 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at least 4 hours.</p>	
	6836-316 (Wettable Powder)	Open Pour/Powder	<p><u>Initial Dose:</u> When the system is noticeably fouled ass 0.2 to 0.6 pounds /1,000 gallons. Repeat in 1 to 3 ppm bromine residual is established for at least 4 hours.</p> <p><u>Subsequent Dose:</u> When control is evident add 0.1 to 0.3 pounds /1,000 gallons. Repeat as needed to maintain 1 to 3 ppm bromine residual for at</p>	Badly fouled systems should be cleaned before treatment is done.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			least 4 hours	
	3377-62 3377-63 3377-71 (Ready to Use)	Open Pour/Ready to Use	<p><u>Initial Dose:</u> When system is noticeably fouled, add sufficient amount to achieve a residual bromine level of 0.5 -5ppm or as needed to maintain control. Apply ½ ounce to 1,000 gallons of water. Yields a theoretical average 4ppm available bromine. Repeat until control is achieved.</p> <p><u>Subsequent Dose:</u> When microbial control is evident, apply sufficient amount to achieve area residual bromine level 0.5 to 5ppm or as needed to maintain control.</p>	None listed.
Photo Processing Water	6836-115	Place in system	Place tabs with the	Do not use water from this line to mix

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
	6836-317 6836-314 69681-16 83451-4 (Tablet)		regulating valve at a low setting. If biological growth is observed increase the flow in small increments until growth is controlled. 1.0 to 3.0 ppm of residual bromine should be introduced into water supply line. Three to (3) to 9 grams of tabs will introduce 1.0 to 3.0 ppm residual bromine in 1,000 gallons of water.	chemicals.
	6836-237 6836-315 6836-324 (Granular)	Open Pour/Granules	It is intended that 0.5 to 3.0 ppm of residual bromine should be introduced into water supply line. Three to (3) to 12 grams of tabs will introduce 1.0 to 3.0 ppm residual bromine in 1,000 gallons of water.	Do not use water from this line to mix chemicals.
	6836-316 (Wettable Powder)	Open Pour/Powder	Adjust pH between 7.2 to 7.6 when using other products as outlined in directions for other products. A bromine or	Do not use water from this line to mix chemicals.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			chlorine residual of 1-2 ppm must first be established in the water. When bromine residual reaches 1-2 ppm adjust feeder accordingly. To maintain bromine residual adjust the feeder feed rate to assure constant treatment level of 1-3 ppm.	
Automobile wash water systems	6836-210 (Tablet)	Place tablet in system	Initial Dose: If a heavily fouled system exists and physical cleaning is not possible add 0.05 to 0.2 lbs per 1,000 gallons of water for two weeks. Then reduce maintenance levels. Maintenance Dose: Effective control under normal circumstances is maintained by adding 0.025 to 0.1 pounds per 1,000 gallons of water.	None listed.
Commercial, Institutional and Industrial Premises and Equipment				

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
Air Conditioner/Humidifier Drip Pans	1448-356 5785-63 5785-100 5185-420 69681-16 83451-3 (Granular)	Open Pour/Granules	Place this product in the basin or drip pan close to the outlet drain. Use one or more tablets as necessary to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	Do not place tablets directly onto metal surfaces.
Air Conditioner/Humidifier Drip Pans (Continued)	75361-1 (Tablet)	Place tablet in system	Place tablet into condensate line dispenser or floatation device into reservoir. Maintain 1-4 ppm active bromine. Check once every month or more often as required. The life of the tablet will vary depending on atmospheric conditions and temperature requirements.	Do not place tablets directly onto metal surfaces
	83451-4 8622-30 (Tablet)	Place tablet in system	Place this product in the basin or drip pan close to the outlet drain. Use one or more tablets as necessary	None listed

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	
	1448-420 8622-30 (Ready to Use)	Open Pour/ Ready to Use	Place this product in the basin or drip pan close to the outlet drain. Use one or more tablets as necessary to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	None listed.
	83451-3 (Granular)	Open Pour/Granules	Place this product in the basin or drip pan close to the outlet drain. Use one or more tablets as necessary to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	None listed.
	8622-29 (Granular)	Open Pour/Granules	Place this product in the basin or drip pan close to	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Air Conditioner/Humidifier Drip Pans (Continued)			the outlet drain. Use one or more tablets as necessary to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	
	8622-29 (Granular)	Open Pour/Granules	Place this product in the basin or drip pan close to the outlet drain. Use one or more tablets as necessary to maintain cleanliness of the system. The amount of tablets needed will vary with temperature humidity, and condensate volume.	None listed.
Swimming Pools, Spas, Hot Tubs				
Swimming Pools	1448-428 3377-72 57787-24 63838-4 66397-1 66397-2 67262-23	Place tablet into system	<u>Initial Application:</u> Adjust ph to 7.2-7.8. Adjust the feeder flow of water according to the manufacturer's directions to maintain bromine residual between 1-4 ppm	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Swimming Pools (Continued)	6836-116 6836-118 6836-197 6836-211 6836-314 6836-317 69681-16 7124-102 7124-104 75361-1 (Tablet)		in the pool per 1,000 gallons. <u>Continued Application:</u> Check feeder periodically a refill with additional product. Adjust feeder flow water according to manufacturer's directions to maintain bromine levels between 1-4 ppm in pool.	
	8622-41 8622-70 8622-73 (Tablet)	Place tablet into system	Newly Filled Pools: Establish an effective active bromine residual of between 2-3 ppm. Residential: Add 17 tablets per 10,000 gallons every 5- 7 days as needed to maintain a bromine residual of 2-3 ppm at all times. Commercial: Add 31	Keep pH between 7.2-7.6 and never allow it to fall below 7.0.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Swimming Pools (Continued)			tablets per 10,000 gallons every 5-7 days or as needed to maintain and achieve bromine residual between 3-5 ppm at all times.	
	3377-61 6836-211 (Soluble Concentrate)	Open Pour/Soluble Concentrate	<p><u>Initial Application:</u> Chemically balance calcium hardness to 200 ppm and total alkalinity to 100 to 150 ppm. Adjust pH to 7.2-7.8. Adjust the flow of water into feeder according to manufacturer's directions to maintain active bromine residual between 1-4 ppm.</p> <p><u>Continued Application:</u> Check the feeder weekly and refill with additional product. Adjust the flow of water into feeder according to manufacturer's directions to maintain an active bromine level</p>	Do not mix this product in concentrated form w any other chemicals. Do not add other chemicals to the feeding device when using this product. A violent reaction leading to fire and explosion could result.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			between 1-4 ppm.	
	42177-74 6836-123 (Ready to Use)	Open Pour/Ready to Use	Balance calcium and alkalinity and then adjust pH to between 7.2-7.6. Superoxidate to 1020ppm bromine. Water is safe when bromine is below 5 ppm. If bromine residual content is below 1-3 ppm, add 0.2-2.0 oz per 1000 as needed to maintain	Do not mix with other chemicals. Always add product to large quantities of water.
	6836-316 (Wettable Powder)	Open Pour/Powder	Adjust pH between 7.2-7.6. A bromine or chlorine residual of 1 to 3 ppm must first be established in the pool. To maintain bromine residual adjust feeder feed rate to assure a constant treatment level.	None listed
	6836-250 6836-251 5185-490 (Granular)	Open Pour/Granules	Add product to maintain 1- 3 ppm as bromine. Use a reliable test kit to monitor for bromine regularly. Maintain the pool water pH between 7.2-7.8.	None listed.

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
Spas and Hot Tubs	1448-428 3377-72 5185-420 5185-421 63838-4 66397-1 66397-2 6836-116 6836-196 6826-211 6836-242 6836-243 (Tablet)	Place tablet in system	Adjust the feeder according to manufacturer's directions to maintain a bromine level between 1-4 ppm in residential spas and 3-6 ppm in commercial spas. Check feeder regularly and add additional product as needed.	Do not heat above manufacturer's recommended temperature.
Spas and Hot Tubs (Continued)	6836-314 6836-317 69681-16 7124-102 7124-103 7124-104 71654-13 75361-1 75562-1 (Tablet)	Place tablet in system	Adjust the feeder according to manufacturer's directions to maintain a bromine level between 1-4 ppm in residential spas and 3-6 ppm in commercial spas. Check feeder regularly and add additional product as needed.	Do not heat above manufacturer's recommended temperature.
	6836-316 (Wettable Powder)	Open Pour/Powder	Adjust the feeder according to manufacturer's directions to maintain a bromine level between 1-4 ppm in residential spas and	Do not heat above manufacturer's recommended temperature.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Spas and Hot Tubs (Continued)			3-6 ppm in commercial spas. Check feeder regularly and add additional product as needed.	
	57787-24 8622-41 8622-70 (Tablet)	Place tablet in system	Introduce 3 tablets per 300 gallons of spa water with the use of floating tablet feeder or automatic brominator. Adjust tablet feeder or brominator to obtain an active bromine residual of at least 2 ppm. Maintain spa by adding 3 tablets per 300 gallons every 5-7 days or as needed to maintain an active bromine residual of 2ppm at all times.	Keep pH between 7.2-7.6 and never allow it to fall below 7.0.
	5185-490 6836-251 (Granular)	Open Pour/Granules	Adjust the feeder according to manufacturer's directions to maintain a bromine level between 2-4 ppm in residential spas and 3-6 ppm in commercial spas. Check feeder regularly and add	Do not heat above manufacturer's recommended temperature.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Spas and Hot Tubs (Continued)			additional product as needed.	
	3377-61 6836-211 (Soluble Concentrate)	Open Pour/ Soluble Concentrate	Adjust the feeder according to manufacturer's directions to maintain a bromine level between 1-4 ppm in residential spas and 3-6 ppm in commercial spas. Check feeder regularly and add additional product as needed.	Do not mix this product in concentrated form with any other chemicals. Do not add other chemicals to the feeding device when using this product. A violent reaction leading to fire and explosion could result.
	5185-433 (Soluble Concentrate)	Open Pour/Soluble Concentrate	Use one dispenser per 350 gallons of spa or hot tub water. Under heavy bather loading or reduced water circulation, additional dispensers may be used to maintain constant active bromine residuals of 2 to 4 ppm in residential spas.	None listed.
	42177-75 67262-23 6836-123	Open Pour/ Ready to Use	Adjust the feeder according to manufacturer's directions to maintain a	Do not heat above manufacturer's recommended temperature.

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Use Site	Reg. no./ Formulation n	Method of Application	Application Rate/ No. of applications	Use Limitations
	(Ready to use)		bromine level between 1-4 ppm in residential spas and 3-6 ppm in commercial spas. Check feeder regularly and add additional product as needed.	
	53735-10 (Ready to use)	Open Pour/Ready to Use	Use one dispenser per 350 gallons of spa or hot tub water. Under heavy bather loading or reduced water circulation, additional dispensers may be used to maintain constant active bromine residuals of 2 to 4 ppm in residential spas.	None listed
	5185-480 (cartridge)	Install Cartridge in Spa feeder	Adjust pH to between 7.2-7.6. Place this product in spa feeder. To Install insert canister into opening lining up canister tabs with key ways. While pushing canister rotate counter clockwise, pull to remove from opening.	This product can only be used in conjunction with polaris precis spa feeder.
Foot Spas	3377-61	Place tablet in	Add one tablet to the foot	None listed.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	75562-1 (Tablet)	system	spa water and agitate to dissolve. One tablet in 1-1.25 gallons of spa water will provide an active bromine concentration of 40 ppm.	
Aquatic Areas				
Chemigation	5785-69 (Tablet)	Open Pour/Tablet	Maintain residual between 5-15 ppm bromine in the water. To insure even distribution of tablets, it is important to level treated mats. If microbial growth develops add additional tablets until bromine residual reaches 10-35 ppm. Continue until fouling is eliminated, then resume treatment between 5-15ppm bromine.	Do not mix with pesticide or fertilizer concentrates
Chemigation (continued)	5785-70 (Granular)	Open Pour/Granules	Maintain residual between 5-15 ppm bromine in the water. To insure even distribution of granules, it is important to level treated mats. If microbial growth develops add additional	Do not mix with pesticide or fertilizer concentrates

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
			granules until bromine residual reaches 10-35 ppm. Continue until fouling is eliminated, then resume treatment between 5-15ppm bromine.	
Ornamental Fountains	1448-356 1448-428 3377-71 3377-72 5185-420 63838-4 6836-115 83451-4 (Tablet)	Place tablet in system	Adjust pH to 7.2-7.6. A bromine residual of 1-2 ppm must be established in the water. To maintain a bromine residual adjust the brominator feed rate to assure a constant treatment of 1-3ppm.	None listed.
	63838-4 6836-115 (Tablet)	Place tablet in system	<u>Initial Dose:</u> Add 0.1 to 6lbs per 10,000 gallons of water. Repeat initial dose until control is achieved. <u>Subsequent Dose:</u> Add 0.1 to 3lbs per 10,000 gallons daily or as needed to maintain control.	None listed.
	3377-72 (Tablet)	Place tablet in system	Add sufficient amount to achieve and maintain a bromine residual 0.5-5ppm or as needed to control the system. If using a	Do not mix this product in concentrated form w any other chemicals. Do not add other chemicals to the feeding device when using this product. A violent reaction leading to fire and explosion could result.

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Ornamental Fountains (Continued)			dispensing device adjust the device feed _{rate} to assure a constant treatment between 0.5-5ppm residual bromine.	
	5785-70 (Granular)	Open Pour/Granules	Maintain residual between 5-15 ppm bromine in the water. To insure even distribution of granules, it is important to level treated mats. If microbial growth develops add additional granules until bromine residual reaches 10-35 ppm. Continue until fouling is eliminated, then resume treatment between 5-15ppm bromine.	Do not mix with pesticide or fertilizer concentrates.
	5185-490 (Granular)	Open Pour/Granules	A bromine or chlorine residual of 1-2ppm must be established. To maintain bromine residual, adjust brominator feed rate to assure a constant treatment level of 1-3 ppm.	None listed.
	3377-61 3377-62	Open Pour/ Soluble	Add sufficient amount to achieve and maintain a	Do not mix this product in concentrated form with any other chemicals. Do not add other

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
Ornamental Fountains (Continued)	(Soluble Concentrate)	Concentrate	bromine residual 0.5-5ppm or as needed to control the system. If using a dispensing device adjust the device feed rate to assure a constant treatment between 0.5-5ppm residual bromine.	chemicals to the feeding device when using this product. A violent reaction leading to fire and explosion could result
	83451-10 (Soluble Concentrate)	Open Pour/Soluble Concentrate	A bromine or chlorine residual of 1-2ppm must be established. To maintain bromine residual, adjust brominator feed rate to assure a constant treatment level of 1-3 ppm.	None listed.
	1448-420 (Ready to Use)	Open Pour/Ready to Use	A bromine or chlorine residual of 1-2ppm must be established. To maintain bromine residual, adjust brominator feed rate to assure a constant treatment level of 1-3 ppm.	None listed
	3377-71 (Ready to	Open Pour/Ready to	Add sufficient amount to achieve and maintain a	Do not mix this product in concentrated form w any other chemicals. Do not add other

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Use Site	Reg. no./ Formulation	Method of Application	Application Rate/ No. of applications	Use Limitations
	Use)	Use	bromine residual 0.5-5ppm or as needed to control the system. If using a dispensing device adjust the device feed _{rate} to assure a constant treatment between 0.5-5ppm residual bromine.	chemicals to the feeding device when using this product. A violent reaction leading to fire and explosion could result

APPENDIX B: Dihalodialkylhydantoins (case 3055)

Appendix B lists the **generic** (not product specific) data requirements which support the re-registration of dihalodialkylhydantoins. These requirements apply to dihalodialkylhydantoins in all products, including data requirements for which a technical grade active ingredient is the test substance. The data table is organized in the following formats:

1. **Data Requirement** (Columns 1 and 2). The data requirements are listed by Guideline Number. The first column lists the new Part 158 Guideline numbers, and the second column lists the old Part 158 Guideline numbers. Each Guideline Number has an associated test protocol set forth in the Pesticide Assessment Guidance, which are available on the EPA website.

2. **Guideline Description** (Column 3). Identifies the guideline type.

3. **Use Pattern** (Column 4). This column indicates the standard Antimicrobial Division use patterns categories for which the generic (not product specific) data requirements apply. The number designations are used in Appendix B.

(1) **Agricultural premises and equipment**

(3) **Commercial, institutional and industrial premises and equipment**

(4) **Residential and public access premises**

(7) **Materials preservatives**

(8) **Industrial processes and water systems**

(11) **Swimming pools**

(12) **Aquatic areas**

3. **Bibliographic Citation** (Column 5). If the Agency has data in its files to support a specific generic Guideline requirement, this column will identify each study by a "Master Record Identification (MRID) number. The listed studies are considered "valid" and acceptable for satisfying the Guideline requirement. Refer to the Bibliography appendix for a complete citation of each study.

DATA REQUIREMENT	CITATION(S)
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New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
TECHNICAL GRADE ACTIVE INGREDIENT (TGAI) CHEMISTRY				
830.1550	61-1	Product Identity and Composition	1,3,4,7,8,11,12	MRID# 35011701
830.1600 830.1620 830.1650	61-2 A	Starting Materials and Manufacturing Process	1,3,4,7,8,11,12	MRID# 35011701
830.1670	61-2 B	Formation of Impurities	1,3,4,7,8,11,12	MRID# 35011701
830.1700	62-1	Preliminary Analysis	1,3,4,7,8,11,12	MRID# 41952701 MRID# 41952801 MRID# 42478501
830.1750	62-2	Certification of Limits	1,3,4,7,8,11,12	MRID# 43315902
830.1800	62-3	Analytical Method	1,3,4,7,8,11,12	MRID# 41952701 MRID# 41952801
830.6302	63-2	Color	1,3,4,7,8,11,12	MRID# 35011701
830.6303	63-3	Physical State	1,3,4,7,8,11,12	MRID# 35011701
830.6304	63-4	Odor	1,3,4,7,8,11,12	MRID# 35011701
830.7200	63-5	Melting Point	1,3,4,7,8,11,12	MRID# 35011701
830.7220	63-6	Boiling Point	1,3,4,7,8,11,12	N/A
830.7300	63-7	Density	1,3,4,7,8,11,12	MRID# 35011701
830.7840 830.7860	63-8	Solubility	1,3,4,7,8,11,12	MRID# 35011701
830.7950	63-9	Vapor Pressure	1,3,4,7,8,11,12	N/A
830.7370	63-10	Dissociation Constant in Water	1,3,4,7,8,11,12	N/A

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
830.7550 830.7560 830.7570	63-11	Partition Coefficient (Octanol/Water)	1,3,4,7,8,11,12	Data Gap
830.7000	63-12	pH	1,3,4,7,8,11,12	MRID# 35011701
830.6313	63-13	Stability	1,3,4,7,8,11,12	MRID# 35011701
830.6314	63-14	Oxidizing/Reducing Action	1,3,4,7,8,11,12	MRID# 35011701
830.6316	63-16	Explodability	1,3,4,7,8,11,12	N/A
830.6317	63-17	Storage Stability	1,3,4,7,8,11,12	MRID# 35011701
830.6320	63-20	Corrosion Characteristics	1,3,4,7,8,11,12	MRID# 35011701
ECOLOGICAL EFFECTS				
850.2100	71-1 A	Avian Acute Oral Toxicity Test - Quail/duck	1,3,4,7,8,11,12	Acc# 253966 Acc# 253972 Acc# 253071 Acc# 253073 Acc# 252719 Acc# 137088 Acc# 147319 MRID# 43289905
850.2200	71-2 A	Avian Acute Dietary - Quail	1,3,4,7,8,11,12	Acc# 147321 Acc# 253071 MRID# 43289904

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
850.2200	71-2 B	Avian Acute Dietary – Duck	1,3,4,7,8,11,12	Acc# 147321 Acc# 253071 Acc# 253073 Acc# 253966 Acc# 253972 MRID# 43289903
850.1075	72-1 A	Fish Acute Toxicity - Bluegill	1,3,4,7,8,11,12	Acc# 145356 Acc# 147322 Acc# 252719 Acc# 253071 Acc# 253072 Acc# 253074 MRID# 42368501 MRID# 42373601 MRID# 42374702 MRID# 43179706
850.1075	72-1 B	Fish Acute Toxicity - Minnow	1,3,4,7,8,11,12	MRID# 46053 MRID# 42374702
850.1075	72-1 C	Fish Acute Toxicity - Rainbow Trout	1,3,4,7,8,11,12	Acc# 145358 Acc# 147322 Acc# 147323 Acc# 252719 Acc# 253071 Acc# 253072 Acc# 253074 MRID# 46053 MRID# 42373601 MRID# 43179705

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
850.1010	72-2 A	Acute Aquatic Invertebrate Toxicity	1,3,4,7,8,11,12	Acc# 252719 Acc# 253071 Acc# 253072 Acc# 253074 Acc# 147324 Acc# 145357 MRID# 46053 MRID# 42373603 MRID# 43179707
850.1025	72-3 A	Estu/Mari tox. Fish	1,3,4,7,8,11,12	MRID# 40993103 MRID# 42076102 MRID# 42374701 MRID# 43687301
850.1035?	72-3 B	Estu/Mari tox. Mollusk	1,3,4,7,8,11,12	MRID# 40993101 MRID# 42076101 MRID# 43289902 MRID# 43687302
850.1045?	72-3 C	Estu/Mari tox. Shrimp	1,3,4,7,8,11,12	MRID# 40993101 MRID# 42076103 MRID# 43687303 MRID# 42373602
850.1300	72-4 A	Early Life Stage Fish	1,3,4,7,8,11,12	MRID# 42721702
850.1400	72-4 B	Life Cycle Invertebrate	1,3,4,7,8,11,12	Data Gap
850.4225	123-1	Seedling emergence dose-response in rice	1,3,4,7,8,11,12	Data Gap
850.4250	123-1	Vegetative vigor dose-response in rice	1,3,4,7,8,11,12	Data Gap
850.4400	123-2	Aquatic vascular plant dose-response toxicity- <i>Lemna</i> sp.	1,3,4,7,8,11,12	Data Gap

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
850.5400	123-2	Acute algal dose-response toxicity- 4 species	1,3,4,7,8,11,12	Data Gap
<u>TOXICOLOGY</u>				
870.1100	81-1	Acute Oral – Rat, Mouse	1,3,4,7,8,11,12	MRID# 45738401 MRID# 93074006 MRID# 93076011 MRID# 93077008
870.1200	81-2	Acute Dermal - Rabbit	1,3,4,7,8,11,12	MRID# 93076013 MRID# 93076025
870.1300	81-3	Acute Inhalation – Rat	1,3,4,7,8,11,12	MRID# 43654101
870.2400	81-4	Acute Eye Irritation - Rabbit	1,3,4,7,8,11,12	N/A
870.2500	81-5	Acute Skin Irritation - Rabbit	1,3,4,7,8,11,12	MRID# 93076017 MRID# 93074011 MRID# 93075014 MRID# 93077009
870.2600	81-6	Dermal Sensitization	1,3,4,7,8,11,12	MRID# 41670001
870.3050		28-Day Oral Toxicity - Mouse	1,3,4,7,8,11,12	MRID# 45738402
870.3100	82-1 A	90-Day feeding-Rodent	1,3,4,7,8,11,12	MRID# 42009201
870.3150	82-1 B	90-Day feeding-Non-rodent/dog	1,3,4,7,8,11,12	No study is available. However, a chronic toxicity study is available
870.3200	82-2	21/28-Day Dermal Toxicity – Rat	1,3,4,7,8,11,12	No study is available. However, a 90-day dermal toxicity study is available.
870.3250	82-3	90 Day Dermal-Rodent	1,3,4,7,8,11,12	MRID # 43173901

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
870.3465	82-4	90-Day Inhalation – Rat	1,3,4,7,8,11,12	Study required to assess risks from formaldehyde exposure, will be assessed in the RED assessment for formaldehyde.
870.4100	83-1 A	Chronic Toxicity-Rodent	1,3,4,7,8,11,12	MRID# 43397702 MRID# 44095901
870.4100	83-1 B	Chronic Toxicity-Non-rodent/dog	1,3,4,7,8,11,12	MRID# 43553101 MRID# 43813301
870.4200	83-2 A	Oncogenicity-Rat	1,3,4,7,8,11,12	MRID# 43397702 MRID# 44095901
870.4200	83-2 B	Oncogenicity-Mouse	1,3,4,7,8,11,12	MRID# 43397701 MRID# 44063901
870.3700	83-3 A	Prenatal Developmental Toxicity -Rat	1,3,4,7,8,11,12	MRID# 42432701
870.3700	83-3 B	Prenatal Developmental Toxicity – Rabbit	1,3,4,7,8,11,12	MRID# 42413101 MRID# 42205401
870.3800	83-4	Reproduction and fertility effects - Rat	1,3,4,7,8,11,12	MRID# 42462502
870.4300	83-5	Combined Chronic toxicity/carcinogenicity	1,3,4,7,8,11,12	MRID# 43397702
870.5100	84-2 A	Bacterial Reverse Mutation Test - Ames	1,3,4,7,8,11,12	Acc# 137100 Acc#164036 MRID# 265457 TRID# 433401118
870.5300	84-2 B	Gene Mutation In vitro Mammalian Cell Assay	1,3,4,7,8,11,12	Acc# 132165 Acc# 137089 TRID# 433401121 TRID# 433401127

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
870.5375	84-2 C	In Vitro Mammalian Chromosome Aberration Test	1,3,4,7,8,11,12	Acc# 137096 Acc# 137101 Acc# 164037 Acc# 265457 MRID# 40348201 TRID# 433401119 TRID# 433401125 TRID# 470264004
870.5550	84-4	Unscheduled DNA Synthesis in Mammalian Cells in Culture	1,3,4,7,8,11,12	Acc# 132166 Acc# 137097 Acc# 164038 Acc# 265457 TRID# 433401120 TRID# 433401126 TRID# 470264005
870.7485	85-1	General Metabolism	1,3,4,7,8,11,12	MRID# 42123802 MRID# 42173901
ENVIRONMENTAL FATE				
835.2120	161-1	Hydrolysis of Parent and Degradates	1,3,4,7,8,11,12	MRID# 43281801 MRID# 42466201
835.2240	161-2	Photodegradation – Water	1,3,4,7,8,11,12	MRID# 42466202
835.4400	162-3	Anaerobic Aquatic Metabolism	1,3,4,7,8,11,12	MRID# 42738401
REENTRY PROTECTION				
875.1200 875.1600	233 236	Dermal Indoor Exposure	1,3,4,7,8,11,12	Data Gap
875.1400 875.1600	234 236	Inhalation Indoor Exposure	1,3,4,7,8,11,12	Data Gap

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DATA REQUIREMENT				CITATION(S)
New Guideline Number	Old Guideline Number	Study Title	Use Pattern	MRID Number
875.2800	133-1	Descriptions of Human Activity	1,3,4,7,8,11,12	Data Gap
<u>RESIDUE CHEMISTRY</u>				
860.1100	171-2	Chemical Identity	1,3,4,7,8,11,12	N/A
860.1200	171-3	Directions for Use	1,3,4,7,8,11,12	N/A

Appendix C. Technical Support Documents

Additional documentation in support of this RED is maintained in the OPP docket, located in Room 119, Crystal Mall #2, 1801 Bell Street, Arlington, VA. It is open Monday through Friday, excluding legal holidays, from 8:30 am to 4 pm.

OPP public docket is located **in Room S-4400, One Potomac Yard (South Building), 2777 South Crystal Drive**, Arlington, VA, 22202 and is open Monday through Friday, excluding Federal holidays, from 8:30 a.m. to 4:00 p.m.

The docket initially contained the September 10, 2004 preliminary risk assessment and the related documents. EPA then considered comments on these risk assessments (which are posted to the e-docket) and revised the risk assessments. The revised risk assessments will be posted in the docket at the same time as the RED.

All documents, in hard copy form, may be viewed in the OPP docket room or downloaded or viewed via the Internet at www.regulations.gov

These documents include:

- Halohydantoins Preliminary Risk Assessment; Notice of Availability, 9/10/04.
- Halohydantoins Case Overview Reregistration Case Number 3055, 3/17/03

Preliminary Risk Assessment and Supporting Science Documents:

- Halohydantoins: Preliminary Risk Assessment for the Reregistration Eligibility Decision, PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 12/15/03.
- Product Chemistry Science Chapter on halohydantoins. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 9/21/00, Chris Jiang.
- Environmental Modeling for Halohydantoins PDM4 Model, PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 08/05/04.
- Dihalodialkylhydantoins: Ecological Hazard and Environmental Risk Assessment, PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 09/07/04, Kathryn Montague, M.S.
- Halohydantoins Toxicology Chapter. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 10/01/02.
- Dimethylhydantoin [Acute, Probabilistic, Chronic, Cancer] Dietary Exposure Assessment[s] for the [Section (3, 18) Reregistration Eligibility Decision, etc.]. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 05/08/03, A. Najm Shamim, Ph.D.
- Dihalodialkylhydantoin Occupational Residential Exposure Assessment. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, Timothy F. McMahon, Ph.D.
- Incident Reports Associated with Halohydantoins. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division, 7/27/04.

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- Environmental Fate Assessment of hydantoins. PC Codes 006135, 006137, 028501, 128826, Case 3055, Antimicrobials Division Antimicrobials Division, 12/11/02, A. Najm Shamim, Ph.D.
- Comments from the Regional Water Quality Control Board, SF Bay Region. 9/23/04, Bill Johnson, Pesticide TMDL Coordinator.
- Comments from the Sanitation Districts of LA County. 9/24/04, James F. Stahl, Industrial Waste Section.
- Comments from the Natural Resource Defense Council (NRDC). 9/24/04, Aaron Colangelo, staff attorney NRDC
- Comments from the California Regional Water Quality Control Board, SF Bay Region. 9/28/04, Bill Johnson, Pesticide TMDL Coordinator.
- Comments from the ACC Brominated Biocides Panel. 9/29/04.
- Comments from the ACC Brominated Biocides Panel. 10/05/04.
- Comments from the California Regional Water Quality Board SF Bay Region. 10/12/04, Bill Johnson, Pesticide TMDL Coordinator.

Appendix D. Citations Considered to be Part of the Data Base Supporting the Reregistration Decision (Bibliography)

1. MRID Studies

<u>MRID #</u>	<u>Citation</u>
46053	Horne, J.D.; Groover, R.D.; Afzal, M.; et al. (1980) 96-Hour Static Bioassays Using Two Great Lakes Chemical Corporation Compounds with Three Marine and Three Freshwater Species. (Unpublished study received Aug 1, 1980 under 1729-122; prepared by NUS Corp., submitted by Tesco, Inc., Marietta, Ga.; CDL:243015-B)
132165	Kirby, P.; Pizzarello, R.; Rogers-Back, A.; et al. (1983) L5178Y TK+/- Mouse Lymphoma Mutagenesis Assay: Test Article 447:34-2: Study No. T1803.701001. (Unpublished study received May 9, 1983 under 38906-5; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL:250313-J)
132166	Thilagar, A.; Pant, K.; Kumaroo, P. (1982) Unscheduled DNA Synthesis in Primary Cultures of Rat Hepatocytes (by Autoradiography): Test Article 447:34-2: Study No. T1803.380002. (Unpublished study received May 9, 1983 under 38906-5; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL: 250313-K)
137088	Fink, R.; Beavers, J.; Joiner, G.; et al. (1981) Acute Oral LD50-- Bobwhite Quail: Dibromodimethylhydantoin: Project No. 178-106. Final rept. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Wildlife International Ltd., submitted by Glyco, Inc., Greenwich, CT; CDL:252094-B)
137089	Fink, R.; Beavers, J.; Brown, R.; et al. (1981) Eight-day Dietary LC50--Mallard Duck: Dibromodimethylhydantoin: Project No. 178- 105. Final rept. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Wildlife International Ltd., submitted by Glyco, Inc., Greenwich, CT; CDL:252094-C)
137095	Haworth, S.; Lawlor, T.; Gaudette, L.; et al. (1982) Salmonella/ Mammalian-microsome Preincubation Mutagenicity Assay (Ames Test): Study No. T1805.502. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL:252095-D)
137096	Thilagar, A.; Gaudette, L.; Kumaroo, P. (1982) Cytogenicity Study-- Chinese Hamster Ovary (CHO) Cells in vitro: Ethylmethylhydantoin: Study No.

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T1805.338. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL:252095-E)

- 137097 Thilagar, A.; Gaudette, L.; Pant, K. (1982) Unscheduled DNA Synthesis in Primary Cultures of Rat Hepatocytes (By Autoradiography): Ethylmethlhydantoin: Study No. T1805.380002. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL:252095-F)
- 137100 Haworth, S.; Gaudette, L.; Lawlor, T.; et al. (1982) Salmonella/ Mammalian-microsome Preincubation Mutagenicity Assay (Ames Test): Dimethylhydantoin: Study No. T1803.502. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL: 252095-J)
- 137101 Thilagar, A.; Gaudette, L.; Kumaroo, P.; et al. (1982) Cytogenicity Study-- Chinese Hamster Ovary (CHO) Cells in vitro: Dimethylhydantoin: Study No. T1803.338. (Unpublished study received Dec 27, 1983 under 38906-7; prepared by Microbiological Assoc., submitted by Glyco, Inc., Greenwich, CT; CDL:252095-K)
- 145356 Larkin, J. (1984) The Acute Toxicity of 1,3-Dichloro-5-ethyl-5-methylhydantoin to Bluegill Sunfish (*Lepomis macrochirus*): Project No. 84-E-042B. Unpublished study prepared by Biospherics Inc. 11 p.
- 145357 Larkin, J. (1984) The Acute Toxicity of 1,3-Dichloro-5-ethyl-5-methylhydantoin to *Daphnia magna* Straus: Project No. 84-E-042DM. Unpublished study prepared by Biospherics Inc. 11 p.
- 145358 Larkin, J. (1984) The Acute Toxicity of 1,3-Dichloro-5-ethyl-5-methylhydantoin to Rainbow Trout (*Salmo gairdneri*): Project No. 84-E-042R. Unpublished study prepared by Biospherics, Inc. 11 p.
- 147319 Beavers, J. (1985) An Acute Oral Toxicity Study in the Bobwhite with Halobrom: Final Report: Project No. 191-106. Unpublished study prepared by Wildlife International Ltd. 16 p.
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- 147322 McAllister, W.; Cohle, P. (1984) Acute Toxicity of Halobrom to Bluegill Sunfish (*Lepomis macrochirus*): Static Acute Toxicity Report 3242 Unpublished study prepared by Analytical Biochemistry Laboratories, Inc. 52 p.
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- 252719(4) Graney, R.; Spare, W.; Hutchinson, C.; et al. (1981) The Acute Toxicity of Glybrom to *Daphnia magna* straus: Final Report: Project No. 371-1. Unpublished study prepared by Biospherics Inc. 14 p.
- 253071(1) Fink, R.; Beavers, J.B.; Joiner, G.; et al. (1981) Final Report: Acute Oral LD50-- Bobwhite Quail: Project No. 178-103. (Unpublished study received Sep 24, 1981 under 38906-3; prepared by Wildlife International, Ltd., submitted by Glyco Chemicals, Inc., Greenwich, Conn.; CDL:245992-A)
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- 253071(5) Fink, R.; Beavers, J.B.; Joiner, G.; et al. (1981) Final Report: Eight-day Dietary LC150^--Mallard Duck: Project No. 178-102. (Unpublished study received Sep 24, 1981 under 38906-3; prepared by Wildlife International, Ltd. and Washington College, sub- mitted by Glyco Chemicals, Inc., Greenwich, Conn.; CDL:245996-A).
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Appendix E. Generic Data Call-In

The Agency intends to issue a Generic Data Call-In at a later date for Halohydantoins.
Case # 3055, PC code # 006315

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Appendix F. Product Specific Data Call-In

The Agency intends to issue a Product Specific Data Call-In at a later date for:

Halohydantoins Case #3055 PC Code #006315

Appendix G. Batching of Halohydanotoin Products for Meeting Acute Toxicity Data Requirements for Reregistration

In an effort to reduce the time, resources and number of animals needed to fulfill the acute toxicity data requirements for reregistration of products containing any of the halohydantoins as an active ingredient, the Agency has batched products which can be considered similar for purposes of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), type of formulation (e.g., emulsifiable concentrate, aerosol, wettable powder, granular), and labeling (e.g., signal word, use classification, precautionary labeling). Note that the Agency is not describing batched products as "substantially similar," since they may not have similar use patterns.

Using available information, batching has been accomplished by the process described in the preceding paragraph. Notwithstanding the batching process, the Agency reserves the right to require, at any time, acute toxicity data for an individual product should the need arise.

Registrants of products within a batch may choose to cooperatively generate, submit or cite a single battery of six acute toxicological studies to represent all the products within that batch. It is the registrants' option to participate in the process with all other registrants, only some of the other registrants, or only their own products within a batch, or to generate all the required acute toxicological studies for each of their own products. If a registrant chooses to generate the data for a batch, he/she must use one of the products within the batch as the test material. If a registrant chooses to rely upon previously submitted acute toxicity data, he/she may do so provided that the data base is complete and valid by today's standards (see partial list of acceptance criteria attached), the formulation tested is considered by EPA to be similar for acute toxicity, and the formulation has not been significantly altered since submission and acceptance of the acute toxicity data. The Agency must approve any new or canceled formulations (that were presented to the Agency after the completion of the RED) before data derived from them can be used to cover other products in a batch. Regardless of whether new data is generated or existing data is referenced, registrants must clearly identify the test material by EPA Registration Number. If more than one confidential statement of formula (CSF) exists for a product, the registrant must indicate the formulation actually tested by identifying the corresponding CSF.

In deciding how to meet the product specific data requirements, registrants must follow the directions given in the Data Call-In Notice and its attachments appended to the RED. The DCI Notice contains two response forms which are to be completed and submitted to the Agency within 90 days of receipt. The first form, "Data Call-In Response," asks whether the registrant will meet the data requirements for each product. The second form, "Requirements Status and Registrant's Response," lists the product specific data required for each product, including the standard six acute toxicity tests. A registrant who wishes to participate in a batch must decide whether he/she will provide the data or depend on someone else to do so. If a registrant supplies the data to support a batch of products, he/she must select one of the following options: Developing Data (Option 1), Submitting an Existing Study (Option 4), Upgrading an Existing

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Study (Option 5) or Citing an Existing Study (Option 6). If a registrant depends on another's data, he/she must choose among: Cost Sharing (Option 2), Offers to Cost Share (Option 3) or Citing an Existing Study (Option 6). If a registrant does not want to participate in a batch, the choices are Options 1, 4, 5 or 6. However, a registrant should know that choosing not to participate in a batch does not preclude other registrants in the batch from citing his/her studies and offering to cost share (Option 3) those studies.

If a registrant would like to have the batching status of a product reconsidered, he/she needs to submit detailed information on the product, including a detailed rationale for the inclusion of the product into a batch. An MSDS for each "inert" ingredient should be included where possible. However, registrants and manufacturers should realize that the more unusual their formulation is, the less likely it is to be able to batch that product.

One hundred and five (105) products were found which contain one of the halohydantoins as an active ingredient. These products have been placed into ten batches and a "No Batch" category in accordance with the active and inert ingredients and type of formulation. Any product in a batch may cite new or previously submitted acute toxicity data (if it meets current Agency standards) from any other product in the same batch, except as specified below:

- In Batches 1, 4, 5, and 7, the highest-concentration products in the batch should **not** cite data from the lowest-concentration products in the batch: Reg. No. 5185-457 in Batch 1, Reg. No. 5185-469 in Batch 4, Reg. No. 5185-487 in Batch 5, and Reg. No. 6836-120 in Batch 7.
- In the No Batch category, each product must cite its own data.

Batch 1	EPA Reg. No.	% Active Ingredient
	1448-356	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	1448-420	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	1448-428	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	3876-150	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-420	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-446	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-452	1-Bromo-3-chloro-5,5-dimethylhydantoin 99%
	5185-454	1-Bromo-3-chloro-5,5-dimethylhydantoin 97%
	5185-455	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-456	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-457	1-Bromo-3-chloro-5,5-dimethylhydantoin 94%

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Batch 1	EPA Reg. No.	% Active Ingredient
	5185-480	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-489	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5185-490	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-57	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-63	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-65	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-69	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-70	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	5785-105	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	6836-314	1-Bromo-3-chloro-5,5-dimethylhydantoin 97.41%
	6836-315	1-Bromo-3-chloro-5,5-dimethylhydantoin 97.7%
	6836-316	1-Bromo-3-chloro-5,5-dimethylhydantoin 97.7%
	6836-317	1-Bromo-3-chloro-5,5-dimethylhydantoin 97.7%
	6836-318	1-Bromo-3-chloro-5,5-dimethylhydantoin 97.7%
	8622-25	1-Bromo-3-chloro-5,5-dimethylhydantoin 98%
	8622-28	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	8622-29	1-Bromo-3-chloro-5,5-dimethylhydantoin 98%
	8622-30	1-Bromo-3-chloro-5,5-dimethylhydantoin 98%
	8622-41	1-Bromo-3-chloro-5,5-dimethylhydantoin 98%
	8622-70	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	42177-74	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	42177-75	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	53735-10	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	67262-23	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%
	69681-16	1-Bromo-3-chloro-5,5-dimethylhydantoin 96%

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Batch 2	EPA Reg. No.	% Active Ingredient
	3377-61	1,3-Dibromo-5,5-dimethylhydantoin 99.4%
	3377-62	1,3-Dibromo-5,5-dimethylhydantoin 99.4%
	3377-63	1,3-Dibromo-5,5-dimethylhydantoin 99.4%
	3377-71	1,3-Dibromo-5,5-dimethylhydantoin 96.4%
	3377-72	1,3-Dibromo-5,5-dimethylhydantoin 96.4%

Batch 3	EPA Reg. No.	% Active Ingredient
	6836-109	1,3-Dichloro-5,5-dimethylhydantoin 97%
	6836-319	1,3-Dichloro-5,5-dimethylhydantoin 97%

Batch 4	EPA Reg. No.	% Active Ingredient
	5185-421	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	5185-433	1-Bromo-3-chloro-5,5-dimethylhydantoin 93.5%
	5185-469	1-Bromo-3-chloro-5,5-dimethylhydantoin 88%
	5785-100	1-Bromo-3-chloro-5,5-dimethylhydantoin 89.5%
	5785-106	1-Bromo-3-chloro-5,5-dimethylhydantoin 93.5%
	5785-107	1-Bromo-3-chloro-5,5-dimethylhydantoin 93.5%
	5785-108	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	7124-102	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	7124-103	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	7124-104	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	8622-26	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	8622-27	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%
	57787-24	1-Bromo-3-chloro-5,5-dimethylhydantoin 92.5%

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Batch 5	EPA Reg. No.	% Active Ingredient
	5185-483	1-Bromo-3-chloro-5,5-dimethylhydantoin 40%
	5185-487	1-Bromo-3-chloro-5,5-dimethylhydantoin 35%

Batch 6	EPA Reg. No.	% Active Ingredient
	6836-110	1-Bromo-3-chloro-5,5-dimethylhydantoin 90% 1,3-Dibromo-5,5-dimethylhydantoin 9%
	6836-124	1-Bromo-3-chloro-5,5-dimethylhydantoin 88.7% 1,3-Dibromo-5,5-dimethylhydantoin 8.8%
	6836-211	1-Bromo-3-chloro-5,5-dimethylhydantoin 90% 1,3-Dibromo-5,5-dimethylhydantoin 9%
	6836-312	1-Bromo-3-chloro-5,5-dimethylhydantoin 90% 1,3-Dibromo-5,5-dimethylhydantoin 9%

Batch 7	EPA Reg. No.	% Active Ingredient
	6836-120	1-Bromo-3-chloro-5,5-dimethylhydantoin 81.9% 1,3-Dibromo-5,5-dimethylhydantoin 8.1%
	6836-121	1-Bromo-3-chloro-5,5-dimethylhydantoin 84.1% 1,3-Dibromo-5,5-dimethylhydantoin 8.4%
	6836-122	1-Bromo-3-chloro-5,5-dimethylhydantoin 85.1% 1,3-Dibromo-5,5-dimethylhydantoin 8.4%
	6836-123	1-Bromo-3-chloro-5,5-dimethylhydantoin 86.4% 1,3-Dibromo-5,5-dimethylhydantoin 8.6%
	66397-1	1-Bromo-3-chloro-5,5-dimethylhydantoin 86.4% 1,3-Dibromo-5,5-dimethylhydantoin 8.6%
	66397-2	1-Bromo-3-chloro-5,5-dimethylhydantoin 86.4% 1,3-Dibromo-5,5-dimethylhydantoin 8.6%

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Batch 8	EPA Reg. No.	% Active Ingredient
	6836-113	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-114	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-256	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-263	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-280	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-287	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-288	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-291	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-296	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%
	6836-297	1,3-Dichloro-5,5-dimethylhydantoin 81.1% 1,3-Dichloro-5-ethyl-5-methylhydantoin 16.1%

Batch 9	EPA Reg. No.	% Active Ingredient
	6836-115	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-116	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-117	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-118	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4%

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Batch 9	EPA Reg. No.	% Active Ingredient
		1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-196	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-197	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-210	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-237	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-242	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-243	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-250	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-251	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-255	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-272	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-273	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-274	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4%

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Batch 9	EPA Reg. No.	% Active Ingredient
		1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-275	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-281	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-282	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-299	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%
	6836-300	1-Bromo-3-chloro-5,5-dimethylhydantoin 60% 1,3-Dichloro-5,5-dimethylhydantoin 27.4% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.6%

Batch 10	EPA Reg. No.	% Active Ingredient
	6836-264	1-Bromo-3-chloro-5,5-dimethylhydantoin 57% 1,3-Dichloro-5,5-dimethylhydantoin 26% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.1%
	6836-265	1-Bromo-3-chloro-5,5-dimethylhydantoin 57% 1,3-Dichloro-5,5-dimethylhydantoin 26% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.1%

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No Batch	EPA Reg. No.	% Active Ingredient
Each “No Batch” product must cite its own data.	5785-62	1-Bromo-3-chloro-5,5-dimethylhydantoin 25.2%
	5813-65	1-Bromo-3-chloro-5,5-dimethylhydantoin 51% 1,3-Dichloro-5,5-dimethylhydantoin 23.3% 1,3-Dichloro-5-ethyl-5-methylhydantoin 9%
	5813-66	1-Bromo-3-chloro-5,5-dimethylhydantoin 45% 1,3-Dichloro-5,5-dimethylhydantoin 20.6% 1,3-Dichloro-5-ethyl-5-methylhydantoin 8%
	6836-279	1,3-Dichloro-5,5-dimethylhydantoin 52.7% 1,3-Dichloro-5-ethyl-5-methylhydantoin 10.5%

Halohydantoins RED

Appendix H. List of All Registrants Who Will Be Sent the Data Call-In

BUCKMAN LABORATORIES, INC.
1256 NORTH MCLEAN BLVD
MEMPHIS TN 38108
(901) 278-0330

GE BETZ, INC.
4636 SOMERTON ROAD
TREVSE, PA 190536783
(215) 953-5588

BIO –LAB, INC
PO Box 300002
LAWRENCEVILLE GA, 300491002
(678) 502- 4149

GREAT LAKES CHEM CORP
PO Box 2200
WEST LAFAYETTE, IN 479962200
(765) 497-6391

CLOROX CO., THE
PO Box 493
PLEASANTON, CA 945660803
(925) 425-6842

LONZA INC.
90 BOROLINE ROAD
ALLENDALE, NJ 07401
(201) 785-9011

ALDEN LEEDS INC.
55 JACOBUS AVE
SOUTH KEARNY, NJ 07032
(973) 589-3544

AMERIBROM, INC.
95 MACCORKLE AVENUE, SOUTHWEST
SOUTH CHARLESTON WV 253031411
(304) 746-3101

ALLIANCE TRADING, INC.
109 NORTHPARK BLVD, 4TH FLOOR
COVINGTON LA 70433

KING TECHNOLOGY INC.
530 11TH AVENUE SOUTH
HOPKINS MN 55343
(952) 933- 6118

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HAVILAND CONSUMER PRODUCTS, INC.
421 ANN STREET, NW
GRAND RAPIDS, MI 495042075
(616) 361-6691

ENVIRO TECH CHEMICAL SERVICES, INC.
500 WINMOORE WAY
MODESTO CA 95358
(209) 581-9576

MID-CONTINENT PACKAGING INC.
1200 N 54TH ST
ENID, OK 73701
(201) 589-3544

RECREATIONAL WATER PRODUCTS, INC.
PO Box 1449
BUFORD GA 305151449
(678) 502 4149

ALLCHEM PERFORMANCE PRODUCTS, LP
6010 NW FIRST PLACE
GAINESVILLE, FL 32607
(352) 333-7357

E.I. DUPONT DE NEMOURS AND COMPANY
PO Box 80402
WILMINGTON DE 198800402
(302) 695-2910

CONNECT CHEMICAL USA, LLC
107 COLONY PARK DRIVE, SUITE 100
CUMMINGS GA 30040
(678) 947-4410

SANI-CARE SALON PRODUCTS INC.
5295 WEBB PKWY
LILBURN GA 30047
(770) 279-7722

BWA WATER ADDITIVES US, LLC
1979 LAKESIDE PARKWAY, SUITE 925
TUCKER GA 30084
(678) 802-3024

ALBEMARLE
451 FLORIDA ST
BATON ROUGE LA 70801
(504) 388-7650

Attachment 8

CONSULTATIONS AND WORKSHOPS

Benefits and Risks of the Use of Chlorine-containing Disinfectants in Food Production and Food Processing

Report of a Joint FAO/WHO Expert Meeting

Ann Arbor, MI, USA, 27–30 May 2008



**Food and Agriculture
Organization of
the United Nations**



**World Health
Organization**

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EXECUTIVE SUMMARY

Background

The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) expert meeting on the use of chlorine-containing disinfectants¹ in food production and food processing was held on 27–30 May 2008 in Ann Arbor, Michigan, United States of America. The meeting was supported by NSF International, WHO Collaborating Centre for Food and Water Safety and Indoor Environment.

The meeting was organized to provide scientific advice in response to a request made by the Codex Alimentarius Commission based on proposed terms of reference prepared by the thirty-seventh session of the Codex Committee on Food Additives and Contaminants and the thirty-seventh session of the Codex Committee on Food Hygiene on the safety and benefits of the use of “active chlorine” in food processing.

The primary intended benefits of disinfection processes are the reduction of microbial foodborne disease risk and the reduction of spoilage by control of contamination by pathogenic and non-pathogenic microorganisms. Control can be through direct treatment of foods and through management of cross-contamination from processing water and food contact surfaces. Disinfection treatment may lead to residues of disinfectants and disinfection by-products, which need to be considered in a risk–benefit assessment. The control of spoilage bacteria by disinfection, which increases the shelf life and stability of foods, was not considered by the expert meeting, as it has no direct impact on health risks.

Results

The expert meeting considered all available data related to the benefits and risks for human health of the use of disinfection processes in the food production and food processing industry. Emphasis was placed on chlorine-containing compounds, but alternative substances and methods used for disinfection of food and food contact surfaces were also considered.

The main goal of the meeting was to compare the health risk of chemical residues in food products following disinfection during food production and processing (including handling) with the benefit of lowering the risk of microbial hazards. The efficacy of chlorine treatment was considered, taking into account different treatment scenarios, different chlorine-containing substances and different combinations of pathogens and food commodities. These considerations focused on the most common current practices in various food sectors, as well as taking into account certain proposed new practices. Consideration was given to the efficacy and feasibility of potential alternative treatments to replace chlorine use. Unintended consequences, such as the potential for development of tolerance to microorganisms and effects on nutritional and organoleptic qualities, were also reviewed.

The main categories considered in food production and processing (including handling) were:

- meat and poultry;

¹ Chlorine-containing disinfectants include hypochlorous acid and its conjugate base, hypochlorite ion; chlorous acid and its conjugate base, chlorite ion; chlorine gas; and chlorine dioxide. Chloramines, chloramine-T and dichloroisocyanurate were included only where of relevance to the food processing industry.

- fish and fishery products;
- fresh produce (including hydroponics and sprouts);
- food contact surfaces.

Previous work and assessments carried out on national/regional and international levels formed the primary basis for the assessment, but additional information submitted in response to an open call for information was considered, as well as publicly available scientific studies and other information.

The approach taken was to identify the most common disinfection practices for the food categories described above; identify possible chemical residues in foods resulting from these treatments; estimate dietary exposure to these residues; estimate the potential risk to health from exposure to these chemical residues in foods; evaluate the efficacy of treatment in reducing the prevalence and numbers of pathogenic microorganisms on food; and estimate the potential resulting decreased health risk. The strength of the evidence was evaluated in all cases. Potential health risk from chemical exposure was then compared with the potential benefits of decreased health risk from reduced pathogen exposure in a systematic and stepwise approach.

A number of key use scenarios for each food category were described. Sodium hypochlorite is the most widely used disinfectant, in particular in the production and processing of poultry meat, leafy greens, sprouts, hydroponics and seafood, whereas its use in red meat processing is less common. Acidified sodium chlorite solutions are commonly used as an alternative to sodium hypochlorite in specific poultry processing steps. The use of chlorine-containing compounds in the fish and fishery products industry is focused mainly on disinfection prior to distribution, and the use on edible portions of fish and shellfish is limited. Non-chlorine-based chemical alternatives included peroxyacetic acid in poultry production and organic acids in meat production. Physical treatments were not considered.

A number of chlorine-containing disinfectants and their disinfection by-products as well as disinfectant alternatives can lead to residues in foods and hence to possible health risk. The toxicology of these substances was reviewed and compared with estimated dietary intakes. The identified residues of chlorine-containing disinfectants and disinfection by-products did not raise health concerns based on estimated dietary exposures. However, the evidence for health concerns associated with hypochlorite use in poultry, fish and shellfish was weak, owing to a lack of qualitative and quantitative information on the formation and presence of trihalomethanes (which are disinfection by-products) on the food. It was noted that although generally conservative estimates were used, there was a high degree of uncertainty in the dietary exposure assessments, as data on by-products were available primarily for drinking-water, and these data would have limited applicability to food. However, chlorine-containing chemicals are unstable, and it was concluded that there is a low potential for the presence of by-products in foods as consumed.

Microbiological risk assessments were performed for the key use scenarios, based on available studies and available risk assessments. It was concluded that the antimicrobial effects of disinfectants in food production may be overestimated by a lack of industrial-scale studies and a lack of inclusion of controls for the physical effects of water alone. In contrast, the effects may be underestimated by studying processes in isolation in industries where disinfectants have already been applied in previous steps. There was evidence for a reduction of pathogens on poultry carcasses and red meats by application of acidified sodium chlorite and chlorine dioxide and in smoked fish by application of sodium hypochlorite. There was also evidence that no pathogen reduction is achieved by application of sodium hypochlorite on poultry carcasses and red meats. Limited data provided evidence for reduction of cross-contamination by the application of disinfectants (in particular, sodium hypochlorite) in wash

and flume waters. Effective disinfection of food contact surfaces is an important means of reducing human exposure to pathogens in food.

Regarding unintended consequences of disinfection practices, the changes in nutrient content are low relative to the normal dietary intake of these nutrients. There is also no evidence to indicate that the use of chlorine-containing disinfectants and their alternatives is associated with acquired antimicrobial resistance to therapeutic agents.

Risk–benefit assessment integrates the results of two separate activities, risk assessment and benefit assessment, which can be done in a qualitative or quantitative way. Owing to a lack of data that would allow a quantitative assessment, the meeting developed a stepwise approach to risk–benefit assessment of chlorine-containing disinfectants and other alternatives to allow for a systematic comparison in a qualitative manner. Where scientific data were available, an assessment of risk and/or benefit was undertaken. The meeting categorized the use scenarios per food commodity in one of the following four categories:

- 1) No health concern identified; no benefits identified.
- 2) No health concern identified; benefits identified.
- 3) Health concern identified; no benefits identified.
- 4) Health concern identified; benefits identified.

The meeting identified several disinfectant use scenarios where there were no health concerns identified but for which there was a benefit. Only use scenarios for which it was concluded that there are both health concerns and benefits were considered to need further evaluation. However, the meeting did not identify any use scenarios that were of this type (i.e. both health concerns and benefits identified). The level of evidence supporting these conclusions as well as the uncertainties are discussed in the report.

Recommendations

The meeting identified important gaps in the available data. These data gaps constrained the scope of the risk–benefit assessments. Consequently, the meeting agreed on a number of recommendations for further scientific studies and the development of standardized practices.

The meeting emphasized that disinfectant treatment of water used in food processing must not be used to mask poor hygienic practices. The meeting recommended that disinfectants be used within the framework of good hygienic practice, with a system based on hazard analysis and critical control points where applicable and with adequate process controls in place.

INTRODUCTION

The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) expert meeting on the use of chlorine-containing disinfectants¹ in food production and food processing was held on 27–30 May 2008 in Ann Arbor, Michigan, United States of America, at NSF International, WHO Collaborating Centre for Food and Water Safety and Indoor Environment.

The meeting was organized to provide scientific advice in response to a request made by the Codex Alimentarius Commission (FAO/WHO, 2006) based on proposed terms of reference prepared by the thirty-seventh session of the Codex Committee on Food Additives and Contaminants (FAO/WHO, 2005a) and the thirty-seventh session of the Codex Committee on Food Hygiene (FAO/WHO, 2005b) on the safety and benefits of the use of “active chlorine” in food processing.

The primary intended benefit of disinfection processes is the reduction of foodborne disease risk by control of contamination by pathogenic and non-pathogenic microorganisms through the direct treatment of foods and the elimination or management of cross-contamination from processing water and food contact surfaces. Such treatment may lead to residues of chemical by-products, which need to be considered in a risk–benefit assessment.

The expert meeting considered all available data related to the benefits and risks for human health associated with the use of disinfectants in the food production and food processing industry. Emphasis was placed on chlorine-containing compounds, but alternative substances and methods used for disinfection of food and food contact surfaces were also considered.

The main goal of the meeting was to compare the health risk of chemical residues in food products following the use of chlorine for disinfection purposes during food production and processing (including handling) with the benefit of lowering the risk of microbial hazards, taking into consideration the relevance and feasibility of potential alternative approaches (i.e. to replace chlorine use). The efficacy of chlorine treatment was considered, taking into account different treatment scenarios, different chlorine-containing substances and different combinations of pathogens and food commodities. These considerations were based on current practices in various food sectors, as well as taking into account certain proposed new practices. Unintended consequences, such as the potential for development of tolerance to microorganisms and effects on nutritional and organoleptic qualities, were also reviewed.

The main categories considered in food production and processing (including handling) were:

- meat and poultry;
- fish and fishery products;
- fresh produce (including hydroponics and sprouts);
- food contact surfaces.

Previous work and assessments carried out on national/regional and international levels formed the primary basis for the assessment, but additional information submitted in

¹ Chlorine-containing disinfectants include hypochlorous acid and its conjugate base, hypochlorite ion; chlorous acid and its conjugate base, chlorite ion; chlorine gas; and chlorine dioxide. Chloramines, chloramine-T and dichloroisocyanurate were included if of relevance to the food processing industry.

response to an open call for information was considered, as well as publicly available scientific studies and other information.

The experts invited to the meeting had expertise in many different disciplines essential for the complex topic of the assessment of the benefits and risks of the use of disinfectants in food production and food processing: food technology and food processing, chemistry, food microbiology, toxicology, dietary exposure assessment, epidemiology and risk–benefit assessment in the field of diet and human health. The list of invited experts is provided in Annex 1. Professor Gabriel Adegoke, Mr John Fawell, Dr Emma Hartnett, Dr Jean-Charles Leblanc, Professor Mark Nieuwenhuijsen and Mr Alan Reilly were not able to participate in the meeting.

Declaration of interests

The participating experts completed the WHO form on Declaration of Interests and a confidentiality undertaking. Mr Scott L. Burnett and Dr Michael Graz declared interests, as they are or had recently been employed by a relevant industry. The meeting considered that this could constitute a potential conflict of interest. It was decided that the expertise of Mr Burnett and Dr Graz would be very valuable for the discussion on the current uses of disinfectants, but that they could not participate in the discussion and decisions regarding conclusions and recommendations of the meeting. These participants therefore left the meeting at that point.

Preparatory work

FAO and WHO issued an open call for experts and data in March 2007. In consideration of the complexity of the request for scientific advice, it was decided to invite a core group of experts with expertise in the various areas to be covered to a meeting, held at the FAO Headquarters in Rome, Italy, on 7–9 November 2007. The invited members of the core group were Dr Bassam Annous, Dr Diane Benford, Dr Joseph Cotruvo, Dr Steve Crossley, Dr Joseph Frank, Dr Arie Havelaar, Professor Mark Nieuwenhuijsen, Mr Alan Reilly and Dr Inger-Lise Steffensen. The aim of this core group meeting was to provide input on the scope of the project, to outline and prepare the background documentation for the expert meeting and to identify potential experts for the drafting of these documents. The core group of experts also served as coordinators for the preparatory work for this expert meeting. The following outline of the background documentation was agreed to, and this outline was also followed in the report from this meeting:

- Chapter 1. Description of current processes
- Chapter 2. Chemistry of the compounds used
- Chapter 3. Chemical risk assessment
 - Toxicology and exposure assessment
 - Epidemiology
- Chapter 4. Microbiological risk assessment
- Chapter 5. Unintended consequences
- Chapter 6. Risk–benefit assessment
- Chapter 7. Conclusions and recommendations

The list of drafting experts is provided in Annex 2. FAO and WHO decided that it was not necessary to invite some of the experts drafting parts of the background document on current uses.

Definitions for the purpose of this meeting

For the purpose of this meeting, the following definitions were adopted:

- *Disinfectants*: Substances used in aqueous solutions in food production and processing to eliminate or reduce the number of microorganisms on the food in washing, chilling and other processes. In some countries, a distinction is made between disinfection and sanitization, but for the purpose of this document, no such distinction is made.
- *Disinfection by-products*: Chemical compounds formed during disinfection processes, other than the original substances introduced in the aqueous solution used for disinfection.

References

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FAO/WHO (2005b). *Report of the thirty-seventh session of the Codex Committee on Food Hygiene, Buenos Aires, 14–19 March 2005*. Rome, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Food Standards Programme, Codex Alimentarius Commission (ALINORM 05/28/13, Appendix VI; http://www.codexalimentarius.net/download/report/638/al28_13e.pdf).

FAO/WHO (2006). *Report of the twenty-ninth session of the Codex Alimentarius Commission, Geneva, 3–7 July 2006*. Rome, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Food Standards Programme, Codex Alimentarius Commission, p. 25, para. 225 (ALINORM 06/29/41; http://www.codexalimentarius.net/download/report/662/al29_41e.pdf).

1. USE OF CHLORINE-CONTAINING COMPOUNDS IN FOOD PROCESSING

1.1 Introduction

The purpose of this chapter is to describe current practices in use of chlorine-containing compounds and their alternatives in food processing. The chapter is not meant to be a complete literature review of the subject, but rather is a summary of widely used and accepted current practices. Proposed alternatives to chlorine that do not have widespread current use within the industry are not within the scope of this chapter.

Current use information is presented in tabular form according to commodity, the unit process that uses chlorine compounds and the type of chlorine chemistry employed in each unit process. The tables present a summary of information obtained from multiple industrial and government sources and reflect common usage in countries where such uses are allowed. This information was obtained from responses to a request for information by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) and through direct contact with government agencies and suppliers. Sources of the current use information include the Codex Alimentarius Commission Codes of Practice, Food Standards Australia New Zealand, United States Department of Agriculture and personal communications with industrial suppliers to the food industry. Specific sources of information for the current use tables are not further specified, as information from all sources was compiled in the summary tables. Some information on efficacy is provided in this chapter as it relates to current uses, but a more comprehensive evaluation of the beneficial effects associated with the use of chlorine-containing compounds and their alternatives in food processing is provided in chapter 4 as a basis for the risk–benefit assessment in chapter 6.

Many food processes require water to wash, cool or transport the product. Potable water must be used for these processes. This document is concerned with the addition of chlorine compounds to process water in excess of what is required to ensure potability. This excess chlorine is required because active chlorine molecules readily react with organic matter on the product surface and from product exudates, resulting in loss of antimicrobial activity. The maintenance of antimicrobial activity in process water can have multiple functions, depending on the specific process. These functions include preventing the transfer of pathogenic and spoilage microorganisms between product items within a batch, preventing the transfer of pathogenic and spoilage microorganisms between batches of product, inhibiting biofilm formation by spoilage and pathogenic microorganisms on equipment surfaces during processing, and inactivating a portion of pathogenic and spoilage microorganisms that are attached to the food tissue. If the process is adequately controlled, the net result is a safer food product with a longer shelf life.

It should be noted that chlorine-containing disinfectants or their alternatives can be used at any food processing stage. In practice, these compounds may sometimes be used sequentially in several food processing stages (e.g. pre-chill spray or dip, chiller water immersion, post-chill spray or dip). In most cases, however, the treatments described in this chapter are not normally used in sequential combinations, and it is therefore reasonable to evaluate these treatments as stand-alone processes. It should also be noted that the use of chlorine in product wash water does not disinfect product surfaces, as insufficient pathogen reductions are obtained to make a contaminated product safe to consume without additional

treatment (i.e. cooking). Currently used chlorine alternatives also do not disinfect product surfaces.

Food processors recognize the public health benefits of chlorine by including chlorination of process water as a critical control point in their hazard analysis and critical control point (HACCP) plan (Rushing, Angulo & Beuchat, 1996). As HACCP plans are developed to control specific health hazards, the purpose of the chlorine treatment is usually specified as controlling specific pathogens associated with the product. These pathogens are referred to in this chapter as the “target” microorganisms. Although use of chlorine often provides control of spoilage microorganisms, HACCP plans are not directed towards spoilage, and therefore spoilage microorganisms are not usually recognized as a target of the process. As a result, there are few data on the effectiveness of chlorine and chlorine alternatives against spoilage microorganisms. The use of chlorinated water in food processing has limitations, which include inactivation of active agents by organic matter, loss of product quality if levels are excessive, dependence on appropriate pH for activity, metal corrosion at low pH or if excessive concentrations are used, and generation of chlorine gas at low pH. Most processors have controls in place to ensure that excessive concentrations of chlorine compounds are not used and that pH levels are controlled so that product sensory quality, worker safety and equipment surfaces are not compromised. The impact of high chlorine levels on sensory properties of food is manifest as discoloration or unacceptable flavours. These adverse sensory impacts probably limit consumer exposure to chlorination by-products through accidental overuse.

The previously mentioned limitations to the effectiveness of chlorine have led to the development of alternative treatments for process water disinfection. These alternatives are process and product specific, as processes differ in the expected functionality of chlorine use. Alternatives must be adopted with caution, because all the functional aspects of chlorine use may not be adequately realized. For example, if a product must be washed to remove field dirt or extraneous matter, the water may still need to be treated with chlorine (or other antimicrobial chemical), even if a chlorine-free antimicrobial treatment of the product occurs later in the process. In addition, active chlorine compounds rapidly inactivate suspended vegetative cells, with low levels of hypochlorous acid providing 90% inactivation in less than 10 s and contact times for effectiveness anywhere from 1.5 to 100 s (Marriott, 1999). A chlorine alternative that requires a longer contact time to achieve disinfection may not be practical or may require a redesign of the process.

Because the active chlorine content of process water is considered a critical control point in many HACCP plans, the ability to monitor the process is critical for maintaining process integrity. Chlorine monitoring equipment and test kits are readily available and widely used. If process water is treated with alternative chemicals, the processor must have the ability to monitor the level of the alternative active agent. Alternative agents that are not amenable to in-process monitoring may not provide the degree of confidence in process integrity required by the food processor for adequate HACCP implementation.

The effectiveness of chlorine and non-chlorine treatments for process water is dependent on various process factors, including temperature, pH, amount of organic matter, type of organic matter, product surface topography and contact time. The need for these treatments to reduce microorganisms on product surfaces and rapidly inactivate microorganisms suspended in process water makes selection of an appropriate biocidal agent a complex process. Treatments that show promise in laboratory- or pilot-scale trials often fail in commercial situations. Therefore, this chapter addresses primarily alternative treatments that have been proven in commercial application.

1.2 Poultry processing

Modern poultry processing is a complex, highly automated process that starts with a live animal transported to a slaughter facility and ends with a fully processed eviscerated and chilled carcass. Further processing includes activities that occur after the whole carcass has been chilled. These can include, but are not limited to, carcass cut up, bone removal, skin removal, marinating, breading, battering and cooking. This section focuses on chicken processing. However, the processes discussed also apply to other poultry species.

1.2.1 Initial loads of bacteria upon entry to processing

When a broiler chicken arrives at the processing plant, it has a substantial number of bacteria associated with it. These organisms are found both on the outer surfaces of skin, feet and feathers and in the alimentary tract, including the crop, colon, caeca and cloaca (Berrang, Buhr & Cason, 2000). Although some bacteria are resident on the skin and feathers of a market-age broiler, much of the external contamination is found in faeces or results from faecal contamination during production. Regardless of the source of the bacteria, poultry processing is designed to reduce the numbers of bacteria on the outer and inner surfaces of the carcass in order to produce a high-quality, safe and wholesome product. Overall, modern broiler processing is effective at providing the consumer with a product having low levels of pathogenic and spoilage bacteria, considering the product is a raw carcass with skin (Izat et al., 1988; Waldroup et al., 1992; Berrang & Dickens, 2000).

1.2.2 Cross-contamination of carcasses during processing

During poultry processing, most procedures lower the number of bacteria found on carcasses. However, feather removal is a notable exception (Izat et al., 1988; Berrang & Dickens, 2000). Cross-contamination occurs when equipment surfaces become contaminated with bacteria of concern, such as *Salmonella* or *Campylobacter*. This concept was demonstrated by study of commercial Belgian processing plants wherein carcasses from a *Salmonella*-negative flock became contaminated with *Salmonella* that was present on slaughter line equipment (Rasschaert, Houf & DeZutter, 2006). A detailed study of the potential for cross-contamination indicated that it can occur at multiple sites throughout transport, slaughter and processing. Mead, Hudson & Hinton (1994) found that cross-contamination could be demonstrated during transport in cages, by the automatic killing knife, during feather removal, in the head puller, on the transfer belt, in the vent opener and in the water chiller. Using an antimicrobial-resistant strain of *Escherichia coli*, Mead, Hudson & Hinton (1994) demonstrated that an inoculated knife in an automatic killer spread contamination to at least 500 carcasses; using a chlorinated spray (10 mg/l) resulted in 250–400 carcasses being contaminated at levels from 0.4 to 1.3 log lower than with the unwashed knife. Similar results were seen with the head puller, which spread contamination to 500 carcasses, but a chlorinated spray (25 mg/l) stopped the spread after only 25–100 carcasses. Inclusion of chlorine in chiller water at 18–30 mg/l made no difference in the spread of the antimicrobial-resistant *E. coli* to carcasses adjacent to inoculated carcasses (Mead, Hudson & Hinton, 1994). Although use of a chlorinated water spray or inclusion of chlorine in the chiller water did not eliminate cross-contamination, it did help to reduce it at each point (Mead, Hudson & Hinton, 1994). Therefore, part of the reason that chemicals such as chlorine are used in poultry processing is to limit the likelihood of cross-contamination by sanitizing equipment and food contact surfaces. The use of chlorine during air chill may not

be as helpful; spraying carcasses with chlorine at 50 mg/l did not prevent cross-contamination during air chilling of poultry (Mead et al., 2000).

1.2.3 Control of contamination during processing

1.2.3.1 Physical

Non-chemical approaches can be applied in poultry processing to limit the effects of cross-contamination. These include, but are not limited to, scheduled or logistic slaughter, counter-current scald, counter-current immersion chill, brush washers of carcasses or equipment, and hot water spray or immersion.

1.2.3.2 Chemical

In many countries, antimicrobial chemicals are used to disinfect process water and equipment surfaces to control cross-contamination and to reduce the numbers of bacteria on carcass surfaces. Chlorine may be added to carcass washers, equipment wash water, immersion chiller water and pre-chiller water. Online reprocessing is an extra wash step that, when instituted, is applied to every carcass on the shackle line to control faecal contamination prior to the chill tank. These online reprocessing systems may incorporate a chemical treatment. Chemicals used to treat poultry throughout the process include acidified sodium chlorite (ASC), calcium hypochlorite, sodium hypochlorite, cetylpyridinium chloride (CPC), chlorine gas, chlorine dioxide, 1,3-dibromo-5,5-dimethylhydantoin, electrolytically generated hypochlorous acid, citric acid with hydrochloric acid with or without phosphoric acid, ethyl lauroyl arginine, ozone, peroxyacetic acid, octanoic acid, acetic acid, peroxyoctanoic acid, 1-hydroxyethylidene-1,1-diphosphonic acid, sodium metasilicate and trisodium phosphate (TSP) (USDA, 2007). The chemicals used most commonly or on which most research has been conducted are discussed further in the remaining chapters of this report.

1.2.4 Effectiveness of control measures

1.2.4.1 Evaluating the literature

It is difficult to evaluate published literature relative to the effectiveness of chemicals for reducing cross-contamination and reducing levels of pathogens on poultry skin. It is not always clear if test conditions and logistics provided adequate experimental design, including the use of proper controls. For example, it may be possible that a non-chlorinated wash step may be just as effective as a chlorinated wash step to lower bacterial numbers on carcasses, but these types of controls are not always available when working in poultry processing plants. Therefore, laboratory and pilot plant research can be useful, especially with the experimental nature of some chemicals studied.

However, laboratory and pilot plant studies can be problematic as well, because many of them are conducted using inoculated skin or carcasses. Under these circumstances, the inoculated bacteria may not be adapted to the chicken skin environment, which could affect attachment, survival and the likelihood of detection after treatment. Under ideal circumstances, chemical efficacy research would utilize naturally occurring bacterial populations.

Another concern is failure to inactivate an antimicrobial chemical following treatment and before bacterial culture. Some studies may overestimate the effectiveness of a chemical treatment because the activity of the chemical was not neutralized prior to bacterial

culture. This can result in the chemical continuing to kill bacteria after the treatment is over, during the time when the number of viable cells remaining is being estimated.

1.2.4.2 Chlorine-based chemicals (Tables 1.1 and 1.2)

Tables 1.1 and 1.2 present summaries of information received on the current use of chlorine-based chemicals in the poultry industry. Aerobic microbial counts recovered from broiler carcasses have been shown to be reduced by about 1 log colony-forming units (cfu) per square centimetre from the use of chlorine at 50 mg/l in the final washer compared with unchlorinated water spray controls (Sanders & Blackshear, 1971). A 1976 study (Thomson, Cox & Bailey, 1976) reported that chlorine at 50 mg/l in an immersion pre-chill treatment at 45 °C was effective at preventing cross-contamination from carcasses inoculated with *Salmonella* to uninoculated carcasses. Thomson, Cox & Bailey (1976), however, also noted that in order to lessen numbers of *Salmonella* on inoculated carcasses, the chlorinated chiller water required the addition of acid for pH adjustment. Chlorine is most effective at neutral or lower pH; therefore, effectiveness can be optimized by careful control of pH in an immersion chill or pre-chill tank. Bailey et al. (1986) found that using chlorine at 40 mg/l in wash water to combat bacteria in a chicken fat matrix on stainless steel reduced numbers of *Salmonella* by 96% compared with a 50% reduction by using an unchlorinated water spray.

Table 1.1. Summary information for chlorine-based interventions in poultry processing: raw product

Process application	Use level (mg/l)	Exposure time
Hypochlorous acid/hypochlorite, calcium hypochlorite, chlorine gas and electrically generated hypochlorous acid (target microorganisms: <i>Salmonella</i> and <i>Campylobacter</i>)		
Pre-chill carcass spray	<50 or 3–5 free chlorine	5 s
Carcass rinse	200	60 s
Reprocessing eviscerated carcasses – pre-chill	20–50	NA
Chiller water	<50	45–60 min
Immersion chill	3–5 free chlorine	10–120 min
Recycling water	5	NA
Acidified chlorite/chlorous acid (target microorganisms: <i>Salmonella</i> and <i>Campylobacter</i>)		
Pre-chill carcass spray or dip	500–1200	10–15 s
Pre-chill or chiller water	50–150	35–60 min
Post-chill spray or dip	500–1200	NA
Chlorine dioxide generated at >90% efficiency (target microorganisms: <i>Salmonella</i> , <i>Campylobacter</i> , <i>E. coli</i>)		
Pre-chill spray	1–3 residual on carcass	15–20 s
Chill or pre-chill immersion	1–3 residual on carcass	40–60 min
Post-chill spray or dip	1–3 residual	15–20 s
Chlorite/chlorous acid (III) (target microorganisms: <i>Salmonella</i> and <i>Campylobacter</i>)		
Pre-chill spray or dip	500–1200	15–20 s
Pre-chill or chill tank	50–150	60 min
Post-chill spray or dip	500–1200	1–20 s

NA, data not available

Table 1.2. Summary information for chlorine-based interventions in poultry processing: ready-to-eat product

Process application	Use level (mg/l)	Exposure time
Chlorite/chlorous acid (III) (target microorganisms: <i>Salmonella</i> and <i>Campylobacter</i>)		
Product spray	500	15 s

Waldroup et al. (1992) demonstrated the effectiveness of a combined treatment that included physical methods (counter-current scalding and chilling) with chemical methods (chlorine at 20 mg/l in bird washers in the picking room, transfer belt and final washer and chlorine at 1–5 mg/l in the immersion chiller water). In that study, *Salmonella* was significantly lessened in two of five plants by an estimated 0.5 log cfu/ml carcass rinse; *Campylobacter* was lessened in four of five plants by 0.4–0.8 log cfu/ml. Bashor et al. (2004) found that carcass washers with chlorine at 25–35 mg/l reduced the numbers of *Campylobacter* by 0.5 log, but the design did not include a wash step without chlorine for comparison.

Northcutt et al. (2005) reported that adding chlorine at 50 mg/l to the water in a broiler inside–outside bird spray wash station did not have any effect on the numbers of *E. coli*, *Salmonella* or *Campylobacter* compared with an unchlorinated control; the conclusion was that physical removal from washing may be as important as chemical inactivation for these bacteria.

Berrang et al. (2007) found that use of a chlorinated spray before evisceration did not affect post-chill numbers of *Campylobacter* in commercial processing plants; however, chlorination in the immersion chill tank did result in lower numbers of *Campylobacter* on fully processed carcasses. Stopforth et al. (2007) examined numbers of bacteria before and after various processing steps in commercial poultry plants. They found that chlorine at 20–50 mg/l in carcass wash steps was not effective at significantly lowering numbers of bacteria, although most of these washes did lessen the incidence of *Salmonella*. The opposite was true for chilling treatments. Chlorine (20–50 mg/l) with ASC (sodium chlorite at 50–150 mg/l acidified to pH 2.8–3.2 by citric acid) in the chill tank was effective for lowering numbers of total bacteria by 1.2 log and *E. coli* by 0.8 log, but not for lessening the incidence of *Salmonella*.

Chlorinated water can be made by running an electric current through pure water with sodium chloride added. The result is referred to as electrolysed oxidizing water or electrically generated hypochlorous acid (Table 1.1). Kim, Hung & Brackett (2000) found that electrolysed oxidizing water was effective against various pathogens associated with meat and poultry foods. When applied in a poultry washing system, electrolysed oxidizing water at 50 mg/l resulted in a 1.7–1.9 log decrease in inoculated *Campylobacter* compared with water-sprayed controls (Park, Hung & Brackett, 2002).

ASC (Table 1.1) can be used as a carcass treatment during online reprocessing or carcass chilling. Addition of ASC to an online reprocessing system to remove faecal contamination reduced the numbers of *Campylobacter* by 99.2%, which represented a significant improvement over the 84.5% seen in the plant's standard online reprocessing system (Kemp & Schneider, 2002). This difference, however, was no longer evident after carcasses proceeded through an immersion chill tank. Addition of ASC to carcass washers was found to increase the effectiveness above that seen with chlorine at 25–35 mg/l by an additional 1.26 log decrease in numbers of *Campylobacter* (Bashor et al., 2004). Application of ASC after the chilling process may hold promise. A decrease of 0.9–1.2 log was noted when whole carcasses were dipped in ASC immediately following immersion chill (Oyarzabal et al., 2004).

1.2.4.3 Non-chlorine-based alternatives (Tables 1.3 and 1.4)

There are various alternatives to chlorine-based chemicals for reducing pathogen levels on poultry carcasses. Many alternatives that have been approved for use or made available have not been widely studied or evaluated in peer-reviewed research. The current use of alternatives to chlorine-based chemicals is presented in Tables 1.3 and 1.4.

Table 1.3. Summary information for non-chlorine-based alternative interventions in poultry processing: raw product

Process application	Use level (mg/l) ^a	Exposure time
Peroxyacetic acid/hydrogen peroxide (POA), hydrogen peroxide (HP), 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP), sodium metasilicate (SM), ethyl lauroyl arginate (LAE), 1,3-dibromo-5,5-dimethylhydantoin (DBDMH), ozone, cetylpyridinium chloride (CPC), trisodium phosphate (TSP) (target microorganisms: <i>Salmonella</i> and <i>Campylobacter</i>)		
Spray or dip carcasses, parts, trim and organs	220–230 POA, 110–165 HP, 13–14 HEDP	NA
Scald tank dip	230 POA, 165 HP, 14 HEDP	30–120 s
Carcass chill tank	230 POA, 165 HP, 14 HEDP, <50 POA	60 min
Inside–outside bird washer	<80 POA	5 s
Online reprocessing	<200	15 s
Marinades	<2% SM by weight	NA
Inside–outside bird washer	1.1–6% SM	15 s
Carcass spray, pre-chill, fresh cut pieces	<200 (LAE)	5 s
Carcass spray, pre-chill	<200 DBDMH	5 s
Fresh cut raw or ready to eat	<200 DBDMH	NA
Chill tank immersion	100 DBDMH	60 min
Chiller water (ozone)	NA	NA
Raw whole carcass spray prior to chill	0.7 g CPC/kg product	NA
Raw whole carcass spray post-chill	0.7 g CPC/kg product	NA
Raw whole carcass spray or dip pre- or post-chill	8–12% TSP in water with chlorine at 20 mg/l	30 s

NA, data not available

^a Unless otherwise specified.

Table 1.4. Summary information for non-chlorine-based alternative interventions in poultry processing: ready-to-eat product

Process application	Use level (mg/l) ^a	Exposure time
Ozone, octanoic acid, citric acid, ethyl lauroyl arginate (LAE), lactic acid (target microorganism: <i>Listeria monocytogenes</i>)		
Product spray	2–3 ozone	30 s
Product spray	<400 octanoic acid	5 s
Product in casing prior to slicing (bologna)	10% citric acid	5 s
Product in casing prior to casing removal	3% citric acid	5 s
Product prior to casing removal	200 LAE	5 s
Prior to final packing	85 000–95 000 lactic acid	20–30 s

^a Unless otherwise specified.

CPC is considered an alternative to chlorine-based chemicals, as the chloride portion of the molecule is non-functional. CPC and TSP (Table 1.3) have been thoroughly evaluated for use in poultry processing. In a study of inoculated skin samples, 0.1% CPC applied as a 15 °C spray was effective at lowering numbers of *Salmonella* by 0.9–1.7 log compared with a water spray control. The decrease was larger when the CPC was sprayed at an elevated temperature (Kim & Slavik, 1996). Other studies conducted with 0.1% CPC resulted in a 1.6 log reduction in inoculated *Salmonella* on pre-chill chicken carcasses (Li et al., 1997) and up to a 1 log decrease in *Salmonella* numbers on chicken skin compared with a water control (Wang et al., 1997). Xiong et al. (1998) found that CPC applied as a spray at 0.1% and 0.5% lowered numbers of *Salmonella* by 0.5 and 0.9 log cfu/ml, respectively, compared with water-washed controls.

TSP can be applied to the carcass as a dip or a spray. The pH of TSP is very high (11–12); such alkaline conditions are by nature antibacterial. In much of the published literature evaluating the use of TSP to lower bacteria associated with poultry, it is unclear if the high pH was neutralized prior to bacterial culture, which could cause an inflated sense of efficacy. In addition, this high pH can cause waste disposal problems.

When broiler carcasses were dipped for 15 s in 10% TSP at pH 12, Whyte et al. (2001) were unable to detect *Salmonella* from the neck skin of TSP-treated carcasses compared with 1.04 log cfu/g detected on water control samples. Furthermore, they found a 1.1 log reduction in the numbers of *Campylobacter*. Application of 10% TSP as a spray has been tested under experimental conditions as well. Wang et al. (1997) found that, compared with water controls, TSP under these conditions resulted in up to a 1 log decrease in *Salmonella* inoculated on chicken skin. Compared with unsprayed controls, Xiong et al. (1998) found that 10% TSP resulted in a decrease of 0.9 log in numbers of inoculated *Salmonella* compared with water spray controls. Addition of TSP to a carcass washer in a processing plant increased the effectiveness by reducing numbers of *Campylobacter* an additional 1.0 log beyond that achieved using chlorine at 25–35 mg/l (Bashor et al., 2004).

An interesting series of studies conducted by Bourassa et al. (2004, 2005) evaluated the use of TSP to lower the recovery of *Salmonella* from broiler carcasses. In the first study (Bourassa et al., 2004), a 5 s dip in 10% TSP prior to chill significantly lowered the recovery of *Salmonella* from individually chilled carcasses (46% for controls, 26% for treated carcasses). This difference was maintained through 7 days of storage at 4 °C; 20% of control carcasses were positive for *Salmonella*, whereas only 4% of treated carcasses were positive. However, the authors noted that the TSP treatment resulted in significantly higher pH of the carcass rinses. In the later study (Bourassa et al., 2005), the authors adjusted the pH of the culture medium and found no difference in *Salmonella* prevalence between control and TSP-treated carcasses. This suggests that TSP may serve to wash some bacteria off and prevent outgrowth in culture media, but may not kill the pathogens of interest outright.

1.2.5 Conclusions

Chlorine-containing compounds are useful and effective in poultry processing for controlling cross-contamination and limiting the presence and numbers of pathogenic and spoilage bacteria on the product. Non-chlorine-containing alternatives have been developed for reducing pathogen levels on poultry carcasses, and their efficacy has been determined at laboratory or pilot scale. Little information is available on the ability of alternatives to chlorine-based chemicals to prevent cross-contamination or reduce biofilm formation on equipment surfaces. Some data on alternative chemicals may be misleading because of a lack of chemical inactivation before bacterial culture. This has been particularly evident in some of the TSP studies, where the efficacy of TSP to actually lower numbers of bacteria by killing

is questionable. At this point, chlorine-containing compounds remain the most common and effective choice for controlling bacterial contamination during poultry processing.

1.3 Red meat processing

The red meat processing industry can be divided into primary and secondary (further) processing. These are in most cases independent of each other and often conducted by separate companies. This is unlike the case in the poultry industry, where these processes are often conducted contiguously by the same company. Primary processing entails the slaughter of animals and all processes up to the dispatch of whole animal parts, trim and by-products. Further processing entails the conversion of a variety of cuts of meat into products, such as sausages and sliced meat products, through various processing steps, including grinding, curing, cooking and slicing. In most cases, further processing also involves the addition and use of other ingredients, such as spices, brines and binders. The degree of automation varies substantially between primary and secondary processing; the former is a labour-intensive process, whereas the later is often highly automated. As a result of differences between primary and further processing, the microbiological issues also differ, resulting in concomitant differences in the use of chlorine-containing compounds. The primary and further red meat processing sectors are therefore considered separately in this section.

1.3.1 Primary red meat processing

Whereas the muscle tissues of healthy animals are considered sterile before slaughter, the hide, gastrointestinal tract and lymph nodes are sources of a diversity of microbiological contaminants. Specifically, contact of hides with the carcasses during hide removal and the puncturing of the gastrointestinal tract and the spilling of its contents onto carcasses result in the majority of visible and microbiological contamination and cross-contamination during primary meat processing. Contamination of carcasses with microorganisms originating in the processing environment is possible, but of lesser importance (Sofos, 1994).

The main microorganisms of concern with respect to primary meat processing are *E. coli*, as an indicator of hygiene, and pathogenic *E. coli*, especially the O157 serotype. A number of outbreaks of disease associated with *E. coli* O157 and other pathogenic Shiga toxin-producing strains have been reported (Erickson & Doyle, 2007). These pathogens contaminate the meat directly from either the hides or the gastrointestinal passage of incoming animals. Cross-contamination from individual animals shedding high numbers of *E. coli* O157 is substantial as a result of the high throughput and degree of manual handling in processing facilities (Fegan et al., 2005a). *Salmonella* is another pathogen of concern during primary meat processing, and its presence is also linked to cross-contamination from individual animals, although patterns of transmission may differ from that of *E. coli* (Fegan et al., 2005b). The microorganisms of concern and issues related to processing for different animal species are similar, with some minor variations. In all cases, however, microbial contamination of carcasses with pathogens can occur to some degree, and intervention strategies to control contamination are useful for mitigating this risk.

The meat processing industry puts substantial effort into controlling microbial contamination of carcasses. The control measures applied are largely physical or process control in nature and may entail pre-slaughter animal washes, dehairing and mechanical methods to prevent rupture of the gastrointestinal tract (Sofos & Smith, 1998). Many of these methods are effective at removing visible contamination, but ineffective or only marginally effective at removing microbiological contamination (Gill, 2004). For these reasons, carcass

washing with online sprays or other interventions (e.g. steam) are widely used to control microbiological contamination. In many countries, including the United States of America (USA), additives to the water used in these washes are permitted and even required. In other countries, regulations on the use of additives are stricter and currently prevent the use of many additives in these washes.

1.3.1.1 Effectiveness of chlorine-based control measures (Tables 1.5 and 1.6)

Information on the use of chlorine compounds in red meat processing is presented in Tables 1.5 and 1.6. Chlorine was one of the first chemical treatments to be used for microbial control in the red meat industry. Significant reductions in microbial counts on carcasses have been achieved, although inconsistently, using water chlorinated at 200–500 mg/l. For example, water chlorinated to 200 mg/l gave 1.5–2.3 log cfu/cm² reductions in total aerobic bacteria on beef carcasses, depending on temperature and pH (Kotula et al., 1974). Similarly, Emswiler, Pierson & Kotula (1976) reported that chlorine in water at levels from 100 to 400 mg/l resulted in reductions of 1.4–1.8 log cfu/cm² in total aerobic bacteria on beef. By contrast, Stevenson, Merkel & Lee (1978) reported no reduction in coliforms and total aerobic bacteria on beef carcasses after treatment with chlorine at 200 mg/l. More recently, sprays containing chlorine at 50, 100, 250, 500 and 900 mg/l were found to be only marginally (<1 log/cm²) effective in reducing numbers of two strains of *E. coli* O157 that had attached to the surface of beef carcasses and lean fat. Delmore et al. (2000) and Kalchayanand et al. (2008) found that chlorine was largely ineffective at reducing levels of *E. coli* and total aerobic bacteria on various meat types. Reasons for these discrepancies may be related to pH effects and levels of contamination on carcasses. The degree of efficacy of chlorine treatments is often less for naturally contaminated carcasses or meat than it is for inoculated carcasses or meat.

Table 1.5. Summary information for chlorine-based interventions in red meat processing: raw product

Process application	Use level (mg/l)	Exposure time (s)
Hypochlorous acid/hypochlorite, calcium hypochlorite, chlorine gas and electrically generated hypochlorous acid (target microorganisms: <i>E. coli</i> O157:H7 and <i>Salmonella</i>)		
Carcass spray	50	3–5
Primal cut spray	20–50	3–5
Pre-hide removal spray	50	3–5

Chlorine dioxide has been considered as an alternative to traditional chlorine, as it has a pH-independent activity. Cutter & Dorsa (1995) observed that the use of chlorine dioxide at 20 mg/l resulted in little or no difference in numbers of total aerobic bacteria on beef compared with using potable water.

ASC has been applied as a microbial control treatment in the primary processing of meat. Harris et al. (2006) demonstrated that ASC at 1200 mg/l resulted in a reduction of 1.5–2.5 log cfu/g for *Salmonella* Typhimurium and *E. coli* O157:H7 on beef trim and ground beef. Castillo et al. (1999), in contrast, showed that phosphoric acid- and citric acid-activated ASC showed a reduction of *E. coli* O157:H7 and *Salmonella* Typhimurium of up to 4.6 log cfu/cm² on inoculated beef carcasses. ASC at 1600 mg/l sprayed onto naturally contaminated chilled beef carcasses was found to be ineffective in reducing aerobes, coliforms and *E. coli* in some cases (Gill & Badoni, 2004). In other cases, ASC was less effective than acetic acid in reducing numbers of these pathogens.

Table 1.6. Summary information for chlorine-based interventions in red meat processing: raw product and further processed meat

Process application	Use level (mg/l)	Exposure time (s)
Acidified chlorite/chlorous acid (target microorganisms: <i>E. coli</i> O157:H7 and <i>Salmonella</i> for raw product, <i>Listeria monocytogenes</i> for further processed product)		
Carcass and part spray	500–1200	15–20
Carcass and part immersion	500–1200	15–30
Trim decontamination	500–1200	15–30
Further processed meat	500–1200	15
Chlorine dioxide generated at >90% efficiency (target microorganisms: <i>E. coli</i> O157:H7 and <i>Salmonella</i> for raw product, <i>Listeria monocytogenes</i> for further processed product)		
Carcass and part spray	<3 residual	10–20
Trim decontamination	<3 residual	10–20

1.3.1.2 Effectiveness of non-chlorine-based alternatives (Table 1.7)

Non-chlorine-based alternatives for decontamination of meat during primary processing are widely used, probably more frequently than chlorine-based products (Table 1.7). Most typically, these are organic acid-based products, although ozone, peroxyacetic acid, 0.5% CPC and TSP, among others, have also been evaluated and may be used. Many of the recent studies previously discussed make direct comparisons of the efficacy of chlorine-based and non-chlorine-based compounds.

Table 1.7. Summary information for non-chlorine-based alternative interventions in red meat processing: raw product

Process application	Use level	Exposure time (s)
Hydrogen peroxide/ peroxyacetic acid mixture (POA), ozone, lactic acid (target microorganisms: <i>E. coli</i> O157:H7 and <i>Salmonella</i>)		
Carcass and part spray	POA at 220 mg/l	15–25
Trim decontamination	POA at 220 mg/l	15–25
Carcass and part spray	Ozone at 2–3 mg/l	15–30
Carcass and part spray	5% lactic acid	1–3
Subprimal and trim	2–5% lactic acid	1–3

Lactic acid is the most widely used compound in washes for primary processing of red meat. In the study by Harris et al. (2006), for example, the use of 2% acetic acid and the use of 4% lactic acid were compared with the use of ASC at 1200 mg/l, and no differences were found in the ability of any of the methods to reduce *Salmonella* Typhimurium and *E. coli* O157:H7 on trim and ground beef. Delmore et al. (2000), in contrast, demonstrated that 2% acetic acid and 2% lactic acid were more effective than chlorine-based compounds at reducing levels of *E. coli* and total aerobic bacteria on beef carcasses.

Peroxyacetic acid at 180 mg/l reduced *E. coli* O157:H7 inoculated onto carcass surfaces of beef and veal by 3.6 log cfu/cm² (Penney et al., 2007). Using ozone at 95 mg/l in water, the reduction of *E. coli* O157:H7 and *Salmonella* Typhimurium was similar to that of water alone (Castillo et al., 2003). CPC at a concentration of 0.5% resulted in a 2.50 log cfu/cm² reduction in *E. coli* O157 on fresh beef. Cutter & Rivera-Betancourt (2000) observed reductions of *E. coli* O157:H7 and *Salmonella* Typhimurium of >3 log cfu/cm² by treating beef carcasses with TSP; however, they did not counter the effects of the TSP by neutralizing the growth medium.

1.3.2 Further red meat processing

1.3.2.1 Sources, types and control of contamination

Survival of bacteria associated with further processed meats may occur if process control is lost, but the risk is low if adequate cooking and/or curing steps are followed (Doyle et al., 2001). Products may be contaminated throughout post-lethality processing before final packaging (Farber & Peterkin, 1991).

Listeria monocytogenes is the pathogen of greatest concern with respect to ready-to-eat cooked meat and meat products, such as pâté, sausages, hotdogs, bologna, ham and luncheon meats. These products often have high water activities and pH values that are favourable to the growth of this pathogen (Farber & Peterkin, 1991). Furthermore, they are frequently stored under refrigerated conditions that inhibit the growth of many competing spoilage bacteria, but allow the growth of *L. monocytogenes*, often to high numbers (Dykes, 2003). In the case of fermented meat products, such as salami, the survival and subsequent growth of pathogens such as *E. coli* O157 in products produced under conditions that are not strictly controlled are of substantial public health concern, and a number of outbreaks of disease have been associated with these products (Tilden et al., 1996). In general, all the above bacteria contaminate further processed meat at low initial levels and subsequently become a problem after growth on the product (Doyle et al., 2001).

Control of pathogens and spoilage microorganisms in further processing largely entails the application of hygiene and the HACCP system during processing. As contamination can occur during slicing and other equipment contact, effective cleaning of surfaces is critical (Farber & Peterkin, 1991). Whereas these processes may be effective in reducing numbers, they are not capable of eliminating pathogens on further processed meats. The inclusion of preservatives in processed meats to prevent the growth of pathogens is widely applied throughout the industry. Although chlorine-based compounds are often used on processing surfaces during further processing of red meat, these compounds do not usually have direct product application (with the exception of ASC). Therefore, issues related to chlorine use are not as prevalent in further red meat processing as in primary processing.

1.3.2.2 Effectiveness of chlorine-based control measures

One of the few reported studies of the use of chlorine compounds in further processing of meats demonstrated that solutions of ASC at 250, 500, 750 and 1000 mg/l sprayed onto cooked roast beef resulted in up to a 2.5 log cfu/g reduction of *L. monocytogenes* on this product (Beverly, Janes & Oliver, 2006). ASC is used for this purpose in some countries (see Table 1.6).

1.3.2.3 Effectiveness of non-chlorine-based alternatives

Non-chlorine-based chemical compounds as well as physical preservative methods such as in-pack pasteurization are widely used to control *L. monocytogenes* on further processed meats. The compounds listed in Table 1.4 for poultry products are also used for further processed red meat products. Additional alternatives are presented in Table 1.7.

As with primary processed meats, many of the control methods used for further processed products are based on organic acids. A study that investigated the combined effects of antimicrobials on frankfurters and hotdogs (Samelis et al., 2002) concluded that post-processing contamination by *L. monocytogenes* on these cured meats may be controlled by 1.8% sodium lactate (which is lower than the 3% permitted by the USA) in combination with

permissible levels (0.25%) of sodium acetate, sodium diacetate or glucono-delta-lactone in the formulation. Islam et al. (2002) also found that higher concentrations of generally recognized as safe (GRAS) chemicals were required if the product was sprayed than if it was immersed in the preservative. Schlyter et al. (1993) found that antilisterial activity was enhanced in treatments containing sodium lactate (2.5%) and sodium diacetate (0.1%) compared with similar treatments containing sodium diacetate or sodium lactate alone. Bacteriocins (which are antibacterial toxins produced by bacteria) have also been applied as antimicrobials during red meat processing. The data indicate that bacteriocins reduce but often do not stop growth or prevent survival of *L. monocytogenes* on food (Katla et al., 2001). Furthermore, the initial reduction in viable numbers is often followed by regrowth of the microorganism, probably due to the presence of a subpopulation of bacteriocin-resistant cells (Gravesen et al., 2002). Although data on chlorine-based compounds are limited, it seems clear that options for control of bacteria on further processed meats using non-chlorine-based compounds are substantial.

1.3.3 Conclusions

Overall, the use of chlorine-based compounds in the red meat industry is less than that in many other food industries, such as poultry and fresh produce processing. An issue that casts some doubt on their usefulness and requires further consideration is the apparent lower efficacy of chlorine-based compounds against natural compared with inoculated contamination. In addition, there are a substantial number of other compounds available for most processing applications that appear to be at least as effective as, or often more effective than, the chlorine-based ones. However, chlorine-based compounds are still used for controlling microbial contamination, particularly during primary processing of carcasses.

1.4 Fish and fishery product processing

Fish and fishery products cover a variety of products derived from finfish, which are any of the cold-blooded aquatic vertebrates, and shellfish, which are those species of aquatic molluscs and crustaceans that are commonly used for food that may be processed for fresh or frozen distribution. The source of the products can be either from the capture of wild stock or from aquaculture and can be either marine or freshwater in nature.

Freshly harvested finfish contain a diverse natural microflora, whose levels may range from 2 to 7 log cfu/cm² (Liston, 1980). Furthermore, the presence of large amounts of non-protein nitrogen in fish tissue and the near-neutral pH (>6.0) make fish tissue an ideal medium for growth of bacteria (Gram & Huss, 1996). Shellfish contain similar groups of microorganisms but may also contain the microbial pathogens in the waters in which they grow, as molluscs are filter feeders and concentrate these within themselves. Therefore, processing needs to include steps to reduce the microbial load on the surface of the fish and keep the surfaces that come in contact with fish clean to prevent cross-contamination. Successful use of chlorine in water disinfection for over a century has provided the background for use of chlorinated water in washing fish and cleaning processing surfaces and containers, among others.

The fishing industry includes a large number of small and medium-sized industries that are mechanized to varying degrees, from artisanal to fully automated processes. Furthermore, an important feature of the fish processing industry is the diversity of fish species handled (several hundred different species in the European Union alone), each with different intrinsic characteristics with respect to microbial load and microbial hazards; and

the large diversity in the products, ranging from raw whole fish to ready-to-eat products with widely ranging quality and safety requirements.

As indicated previously, the source of fish and fishery products is divided between wild-caught and aquaculture. In the wild-caught industry, the pre-harvest microbial hazards include organisms naturally occurring in the aquatic environment (e.g. *Vibrio parahaemolyticus*, *V. vulnificus*, *V. cholerae*), whereas post-harvest, they include those present in the general environment (e.g. *Listeria monocytogenes*) and those introduced as contaminants during handling (e.g. *Salmonella*) (Huss, Ababouch & Gram, 2003). In the aquaculture industry, especially in non-maricultural systems, owing to the high densities of biomass of fish in a limited area and the level of human intervention, pathogens such as *Salmonella* and *L. monocytogenes* could be associated with the fish and fishery products pre-harvest (Angulo, 1999). In both cases, this does not include any microorganisms that may contaminate the product through cross-contamination.

1.4.1 Types of chlorine compounds used in fish processing

Many countries provided data on the use of chlorine in the fish processing sector at the national level (Reilly, 2000). Examples of industry practices in the whitefish industry from South Africa are shown in Table 1.8. Although practices differ, most countries follow the WHO drinking-water guidelines (WHO, 2008) for potable water used in processing and the Codex Alimentarius Commission Code of Practice for Fish and Fishery Products for the level of chlorine in water that comes in contact with fish and fishery products (FAO/WHO, 2008c). Uses of chlorine in the fish and fishery product industry are summarized in Table 1.9.

The most commonly used forms of chlorine in the fish processing industry are calcium hypochlorite (granular or powdered form) and sodium hypochlorite (liquid form). The most common procedure is to utilize tanks to produce a solution from calcium hypochlorite salt or from concentrated sodium hypochlorite solutions; this solution is then pumped and mixed with a large tank containing the final chlorinated water. Alternatively, constant input of a high-concentration solution of hypochlorite is provided in the incoming water flow through automatic and semiautomatic devices like a flow metering pump. In most simple systems, the input of the solution is adjusted to the water input flow. However, in the more sophisticated control systems, the free chlorine content is adjusted automatically, through continuous amperometric analysers.

Chlorine dioxide has been shown to be effective in eliminating large populations of microorganisms and to extend the storage time of many foods, including fishery products (Richardson et al., 1998). Some of the reported advantages of chlorine dioxide over aqueous chlorine as a disinfection agent are that it is 7 times more potent than hypochlorite in killing bacteria, the bactericidal activity of chlorine dioxide is not affected by alkaline conditions and/or the presence of high levels of organic matter (Lin et al., 1996) and chlorine dioxide treatment produces very little or no trihalomethanes (THMs) in treated water (Kim et al., 1999). The use of chlorine dioxide resulted in up to 4.8 log reductions in the pathogenic population on fish (Kim et al., 1999; Andrews et al., 2002; Shin, Chang & Kang, 2004). Chlorine dioxide has also been used for treatment of seawater and ice-water slurry for storage of fish during the sorting process (Table 1.8).

Chlorine dioxide gas is unstable, and the hazards involved in handling and transportation are factors contributing to its limited application. Industrially, it could be prepared via the reduction of sodium chlorate by sulfur dioxide in aqueous solution.

Table 1.8. Application of chlorine-based sanitizers in the whitefish industry^a

Chemical	Medium	Application	Concentration used (mg/l)	Temperature (°C)	pH	Time	Where applied
Sodium hypochlorite	Liquid	End-point sanitizing of food contact surfaces with post-sanitization rinse	25	Ambient	5.5–7	15 min	Land based and on fishing vessels
		End-point sanitizing and cleaning of non-food contact surfaces	50–100	8–22			
Calcium hypochlorite	Powder	End-point sanitizing and cleaning of non-food contact surfaces, both smooth and rough	50–100	Ambient		10–15 min	Land based for drains and floors and on fishing vessels
		End-point sanitizing of food contact and non-food contact areas after potential contamination of surfaces with post-sanitization rinse	200	8–22			Land based and on fishing vessels
Chlorine dioxide	Gas dissolved in water	Treatment of raw water	5	4–22		Up to 6 h	Land-based treatment of seawater (where used)
		General processing	2.5	0–4		Up to 30 min ^b	Storage of fish during sorting process prior to draining of water from ice-water slurry
Chlorine gas	Gas	Treatment of raw water	50–100	8–12			Land-based treatment of seawater (where used)

^a From Graz (2008).^b Time depends on the period taken to sort fish into specific weight ranges using an automated grader. After 30 min, a tub is replaced. Water containing chlorine dioxide is drained 10 min after completion of the grading, and the fish is left on ice.

Table 1.9. Summary information for chlorine-based interventions in fish and fishery product processing

Process application	Use level (mg/l)	Exposure time
Sodium/calcium hypochlorite (target microorganisms: <i>Vibrio</i> , <i>Salmonella</i> for raw product and <i>Listeria monocytogenes</i> for further processed and ready-to-eat product)		
Post-harvest rinse of whole or headed and gutted finfish	10	NA
Washing of slaughtered fish pre-processing (salmon)	200	Up to 8 h if transport
Immersion of headless shell on shrimp	50	NA
Treatment of water for depuration of shellfish	5	NA
Chlorine dioxide generated at >90% efficiency (target microorganisms: <i>Vibrio</i> , <i>Salmonella</i> for raw product and <i>Listeria monocytogenes</i> for further processed and ready-to-eat product)		
Ice to cool fish	100	NA
Dipping of fillets	5	NA
Acidified sodium chlorite (target microorganisms: <i>Vibrio</i> , <i>Salmonella</i> for raw product and <i>Listeria monocytogenes</i> for further processed and ready-to-eat product)		
Washing of salmon	50	1 min
Storage of salmon fillets on ice	50	7 days

NA, data not available

1.4.2 Industry practices

Fish and fishery products can be exposed to chlorine-containing compounds by dipping in baths, either in batches or in continuous processing, or by sprays (with or without pressure). In some cases, washings can be conducted in association with other operations, such as de-scaling inside rotating horizontal washers. Washing in batches usually takes a longer time than the other types of processes and could be associated with other operations, such as thawing or incorporation of additives (e.g. polyphosphates or sulfites). Washing by immersion in belts or by spray usually takes a few minutes (an exception could be fish thawing), and speed can usually be adjusted by adjusting belt speed or rotating speed and lean angle, in the case of rotating washers.

By far the largest exposure of fish could be to free chlorine in the water from melting ice. Time on ice since capture or harvest (from aquaculture) depends on the shelf life of the specific fish (e.g. for a fish with a 12- to 14-day maximum shelf life in ice, 7–9 days could be the maximum storage period on board before landing). There are two possible scenarios with respect to melting ice. First, chlorine dioxide may be added to the ice during the ice-making process, notwithstanding the potential corrosive effect on the ice bunker. This would suggest that the fish may be exposed to an excess of chlorine. This practice, however, affects the natural microflora on the surface of the fish, which, if present, reduce the attachment of cross-contaminating organisms by competitive exclusion and may, if not properly controlled, lead to the creation of an environment conducive to the contamination of the fish. Second, ice is produced with potable water having low free chlorine (sometimes water is dechlorinated to produce ice by filtering through charcoal), to avoid corrosion problems in ice machines. Therefore, the practical challenge in icing fish could be the lack of chlorine rather than an excess.

The number of times that fish and fishery products are exposed to chlorine between landing/harvest and the plant could vary according to distribution and marketing chains; in many cases, there is a washing/de-icing step followed by a re-icing after weighing at the time of the first sale or delivery to a proprietary processing plant. Fresh water is normally utilized

for this step, but in some locations, treated seawater is utilized. Free chlorine levels in the fresh water at this point are low, usually corresponding to the normal concentrations in public drinking-water. Free chlorine in the treated seawater may be elevated if chlorine is used as the disinfectant to treat the seawater. In the salmon industry, the use of solutions of free chlorine at 200 mg/l has been described for rinsing/washing steps of the whole slaughtered fish prior to processing or for transport of slaughtered fish from the growing centres to the processing plants.

The number of exposures to chlorine throughout the process depends on the conditions of the raw material, the type of final product to be processed and the type of technology utilized in the plant. At reception, there could be a de-icing step, which includes a rinse by immersion, followed by icing for storage before processing (and after weighing and coding). There could be a de-icing step as described previously before the fish enter the processing lines. The current practice of rapid processing to produce frozen fillets and fillet derivatives from whole fish may include 2–4 immersions in water, which may be chlorinated. The three initial washing/rinsing steps are after the heading and gutting (which may also be performed on the vessels at sea, depending on the process used by the capturing vessel), between the “dirty” and “clean” zones in a plant, and potentially after filleting, skinning and trimming. Further rinses could be used, but this is process dependent (e.g. addition of polyphosphates). If the time between the initial de-heading process and freezing is too long, there could be intermediate immersions in chlorine-containing ice-water slurries in the so-called “chillers”, aimed at reducing the temperature of fillets or intermediate products (the cooling effect can be achieved by icing the intermediate product, but in this case, a bath to de-ice would be necessary). The current tendency is towards “cleaner production”, which includes the reduction of the amount of water utilized in food and fish processing, thereby reducing the number of multiple immersions to reduce fish temperature.

There may be specific requirements in certain industries to reduce the load of high-risk pathogens. Overchlorinated water with chlorine levels of 200 mg/l has been used to control raw materials contaminated with pathogenic bacteria. It must, however, be noted that at free chlorine levels above 200 mg/l, sensory changes are induced in fish fillets (Castell, 1947). The most discussed situation is the handling of raw fish intended for raw consumption or the preparation of ready-to-eat products, in particular, cold-smoked salmon. In this specific case, the hazard is *Listeria monocytogenes*, and usual handling practices, including potable water wash and icing, do not reduce the pathogen load (Huss, Jorgensen & Vogel, 2000; Gram, 2001). Bremer & Osborne (1998) reported that wash regimes with water containing chlorine at 200 mg/l could eliminate over 99% of *L. monocytogenes* artificially inoculated on the surface of gilled and gutted king salmon (*Oncorhynchus tshawytscha*), but could not ensure a *Listeria*-free product. The current practice in the smoked salmon industry is to use free chlorine at 50–200 mg/l to dip fillets. This process has also been encountered in the processing of fresh whitefish fillets prior to air transport. A similar practice has been reported for control of *L. monocytogenes* in shrimp, probably intended for the sushi and sashimi market (FAO/WHO, 2008a,b). Although the previously described process has been criticized on different grounds, attempts to solve the problem of *L. monocytogenes* contamination using chlorinated water have continued. It is recognized that for the cold-smoked fish industry, it is vital that there be a control step to eliminate possible *Listeria* contamination on the external surface of fish prior to filleting and skinning (Bremer, Fletcher & Osborne, 2003).

Dinesh (1991) noted about 2 log reductions in counts of pathogens such as *Vibrio cholerae*, *V. parahaemolyticus*, *V. vulnificus* and *Salmonella* in laboratory-contaminated shrimp following washing with water containing chlorine at 10 mg/l or iodophor at 1 mg/l. Thampuran, Sreeranga & Surendran (2006) reported that chlorine at 4 mg/l could completely eliminate 10^3 *V. cholerae*/g in shrimp meat in 10 min, whereas in headless shell-on shrimp,

7 mg/l was required to achieve this reduction. Ice containing chlorine dioxide at 100 mg/l caused 4.8, 2.6 and 3.3 log reductions in numbers of *Escherichia coli* O157:H7, *S. Typhimurium* and *L. monocytogenes* on fish (mackerel) skin (Shin, Chang & Kang, 2004). Reduction in microbial levels up to 3 log units in shrimp and 1 log unit in crawfish was obtained after pressure washing with chlorine dioxide at ≥ 30 mg/l (Andrews et al., 2002). The dipping/washing of shrimp in solutions of hypochlorite at 50 mg/l has also been described, both in practice as well as in laboratory studies (FAO/WHO, 2008a,b; see Table 1.9). ASC wash of salmon fillets resulted in a 0.5 log unit reduction of *L. monocytogenes*, and the antimicrobial activity of ASC was enhanced when salmon was washed in ASC and stored in ASC ice (Su & Morrissey, 2003).

Bivalve molluscs from waters subject to microbiological contamination can be made safer by relaying in a suitable area or by using a depuration process, which may be done in water chlorinated to 5 mg/l as free chlorine to reduce the level of pathogenic bacteria in the water. This latter step can be performed only with low concentrations of chlorine, as higher concentrations would be toxic to the bivalves.

Norovirus infections must be considered an emerging infectious disease, with contaminated bivalve molluscs playing a major role in foodborne transmission. Other viral infections with regard to bivalve molluscs, particularly hepatitis A, must also be considered. Noroviruses serve as a model for other enteric viruses, such as hepatitis A virus, hepatitis E virus and the enteroviruses (FAO/WHO, 2006).

No evidence has been found that chlorine-based compounds are applied directly to fish and fishery products for the specific reduction of viruses.

1.4.2.1 Chlorine-based solutions for non-product contact situations

Chlorinated water not in contact with fish and fish products is utilized in the fish industry for different purposes, such as to clean facilities and equipment, to clean utensils (e.g. knives, cutting boards), to clean garments (boots, gloves, aprons), to wash empty packages (if necessary), for hand sanitation after hand washing and to cool sterilized products (e.g. cans, jars and pouches taken out from retorting).

In the case of cleaning of facilities and equipment, chlorinated waters are utilized in the rinsing and disinfection steps. Rinsing is usually performed with low chlorine concentration water (e.g. normal tap water); disinfection is performed with high chlorine concentrations (see Table 1.8). Whereas products other than chlorine have been suggested for disinfection and are utilized, chlorinated water (with and without the addition of acids or other disinfecting substances) is widely utilized in the fish industry, in both developed and developing countries. In a recent study on the general microbial ecology of fish processing plants, Bagge-Ravn et al. (2003) observed that in four different fish industries (two of cold-smoked salmon, semipreserved herring and caviar), disinfection was carried out with hypochlorite in three of them (alone or in association with other products); only in one was the disinfecting agent peroxyacetic acid.

Cleaning is usually performed by hand and/or utilizing some movable equipment, such as low-pressure foam cleaners. In more advanced and mechanized fish processing plants, a part of the line could be covered by the clean-in-place procedure.

The number of cleaning steps is variable, but in general they encompass the following: 1) cleaning of the fish processing plant for the removal of debris (by brush or scraping); 2) washing with clean water and appropriate detergents; 3) intermediate rinsing to eliminate remaining detergent; 4) disinfection (e.g. with chlorinated water); 5) rinsing to eliminate the excess of disinfecting agent; and 6) draining and drying with filtered hot air

(drying without rinsing is not recommended because of the possible production of chlorine gas).

Drying with hot air to obtain a clean, dry plant is a tendency in modern food and fish processing; however, it is not a step followed in all the fish industry around the world yet. Formerly, it was recommended that the disinfecting solution be left overnight and that rinsing be performed before restarting production the following day (Clucas & Ward, 1996). Today, however, it is preferred to dry the plant after disinfection, because chlorine-depleted water could become a vector for cross-contamination.

The disinfection of garments (e.g. gloves before entering the processing room) and plastic and rubber items such as boots and aprons is performed with a chlorine solution of 50 mg/l. Cleaning procedures for crates, boxes and plastic containers usually include a disinfection step with 50 mg/l. These are then rinsed in normal tap water (up to 5 mg/l as free chlorine).

Water for cooling canned products just after retorting is chlorinated, because at that stage, the sealing compound in the double seams is still molten; therefore, the vacuum forming in the headspace could pull micro-drops and bacteria through the double seams. Common chlorination levels taken at the drain point are usually in the order of 5–20 mg/l as residual chlorine (Clucas & Ward, 1996). This is because cans are usually somewhat contaminated on their exterior with organic material, such as oil, sauce and fish debris, all of which will consume chlorine, depleting the cooling solution and therefore increasing the risk of cross-contamination.

1.4.2.2 Non-chlorine-based alternatives

There are very few studies on alternatives to chlorine in fish processing. Whereas Rice, Graham & Lowe (2002) reported ozone as a microbiocidal agent reducing bacterial numbers in various types of foods, including fish, Vaz-Velho et al. (2006) noted that ozone treatment had no significant effect on *Listeria* counts in salmon-trout. The ineffectiveness of ozone treatment in reducing bacterial numbers in fish has been reported by several investigators (Haragushi, Simudu & Aiso, 1969; Ravesi, Licciardello & Racicot, 1987; Da Silva, Gibbs & Kirby, 1998). However, Gelman et al. (2005) noted that ozone pretreatment of tilapia extended the storage life when stored at 5 °C. Similarly, Campos et al. (2006) reported an extension of shelf life of farmed turbot in ozone-slurry ice. Thus, the results are not consistent, and it should be pointed out that ozone treatment is much more expensive than chlorine treatment.

Other alternatives to chlorine in fish processing that have been applied or trialled in the industry include quaternary ammonium compounds (QACs), which have been successfully used for the sanitation of hard surfaces (especially in areas sensitive to corrosion). Peroxyacetic acid and phosphoric acid have been trialled successfully for end-point disinfection (South African Deep Sea Trawling Industry Association Whitefish Technical Committee, personal communication, 2007) and in the wash steps prior to processing, but have not been implemented.

1.4.3 Summary

The use of chlorine-based compounds in the fish and fishery product industry is mainly focused on the end-point disinfection of product contact and non-product contact surfaces. Chlorine-based products, especially hypochlorites, are used because of their high antimicrobial efficacy and their relatively low cost, notwithstanding the corrosive nature of the products.

The application of chlorine-based compounds directly to the edible portions of fish and shellfish is limited to wash or rinse steps on whole fish and the dipping of fillets for pathogen reduction. Chlorine may also be used to treat water for depuration of bivalve molluscs.

Whereas chlorine is effective against the viruses associated with foodborne disease in, especially, shellfish, the application of chlorine directly to the product to reduce virus levels has not been reported to date.

1.5 Fresh fruits and vegetables

1.5.1 Leafy greens

Fresh fruits and vegetables are often washed to cool the product and remove field dirt before distribution. Water used to wash fresh produce is often treated with chemical disinfectants to prevent cross-contamination and reduce microbial growth on equipment surfaces. The washing process may also reduce microbial populations on produce surfaces. Leafy greens are discussed in this section as a representative of fresh fruits and vegetables. Leafy greens present a large surface to volume ratio, thereby incurring a greater exposure of edible tissue to the disinfectant compared with other fresh produce. In addition, the washing of leafy greens in water disinfected with chlorine is widely practised in countries where it is allowed.

The processing of fresh leafy greens has changed dramatically during the past 20 years. Products such as head lettuce are washed and bagged in the field. The production of bagged salad mixes is highly mechanized. Produce harvested into bins at the field is placed into refrigerated trucks. The leafy greens are moved to a refrigerated warehouse/processing facility and subsequently blended by being dumped onto a conveyor, which may carry the greens through a shaker to remove foreign material; the greens are then washed and sanitized in a water flume and centrifuged to remove excess water. The greens are then ready to be packaged.

1.5.1.1 Initial load of bacteria upon entry to processing

Leafy greens are a raw agricultural commodity and, as such, carry a robust bacterial load prior to entering the processing facility. The total aerobic bacterial levels can range from 5 to 6 log cfu/g on leafy greens (Johnston et al., 2006). These organisms may come from the soil, irrigation water, fertilizers, pesticides or human contact. Although coliforms may be present in substantial numbers, reaching 5 log cfu/g, they are generally not a human health concern. Pathogenic microbes are rarely found in association with field-harvested leafy greens; when they are present, levels are generally extremely low. The leafy green processing practices are designed to prevent cross-contamination, reduce the levels of microbes on the surface of the product and minimize any increase in microbial population associated with processing (Parish et al., 2003). The use of novel technology and maintenance of a cold chain from field to retail has been effective in limiting the growth of microorganisms with fresh and minimally processed leafy greens. The processing environment and particularly equipment (conveyor belts, bins and centrifuge) may have substantial microbial loads depending on the microbial load of the commodity handled and the cleaning and sanitizing programme in place (see section 1.6). Pathogens of concern, including *Escherichia coli* O157:H7, *Salmonella* and *Listeria monocytogenes*, and the predominant spoilage contaminant, *Pseudomonas* spp., can survive for extended periods on food contact surfaces (Wilks, Michels & Keevil, 2006).

1.5.1.2 Control of contamination during processing

Chemical control

Microorganisms associated with produce processing facilities and leafy greens are typically controlled through the use of disinfectants. Chlorine is perhaps the most universal disinfecting agent used. Chlorine is used to sanitize equipment and to control microbial populations in wash waters and on commodities. Disinfectants used to treat water for washing leafy greens include chlorine gas, ASC, calcium and sodium hypochlorite, chlorine dioxide, hydrogen peroxide, iodine, ozone, peroxyacetic acid and TSP. Information on the use of these disinfectants is presented in Tables 1.10 and 1.11.

Table 1.10. Summary information for chlorine-based interventions in uncut leafy green processing

Process application	Use level (mg/l)	Exposure time
Hypochlorous acid/hypochlorite (target microorganisms: enteric pathogenic bacteria and viruses and spoilage microorganisms)		
Whole product spray, at harvest, pre-cooling	50–200	2–10 s
Whole product dip or spray, post-harvest	25	2 min
Flume water for transport of leafy greens	10–50	30 s – 5 min
Flume water for whole fruits and vegetables prior to final wash	3	15 min
Pre-package spray or dip	200	5–10 s
Chlorite/chlorous acid (target microorganisms: enteric pathogenic bacteria and viruses and spoilage microorganisms)		
Processing water leafy greens	500–1200	15 s – 2 min
Generated chlorine dioxide (target microorganisms: enteric pathogenic bacteria and viruses and spoilage microorganisms)		
Flume water	3	NA
Whole fruits/vegetables	3	NA
Lettuce wash with spray	3	30 s – 5 min

NA, data not available. See text for activity under non-commercial conditions.

Table 1.11. Summary information for non-chlorine-based alternative interventions in uncut leafy green processing

Process application	Use level (mg/l)	Exposure time
Ozone (target microorganisms: enteric pathogenic bacteria and viruses and spoilage microorganisms)		
Flume water	2–3	30 s
Peroxyacetic acid (target microorganisms: enteric pathogenic bacteria and viruses and spoilage microorganisms)		
Flume water	20–30	1 min

Non-chemical control

The types of non-chemical methods that can be used to control microorganisms on leafy greens are few and include irradiation and ultraviolet (UV) light. The advantage of irradiation is that post-package (bagged) leafy greens can be treated, basically eliminating the potential for cross-contamination. Research suggests that human enteric pathogens may become internalized into leaf tissue (Solomon, Potenski & Matthews, 2002; Solomon, Yaron & Matthews, 2002; USFDA, 2009). Levels of internalized *Escherichia coli* O157:H7

associated with lettuce and spinach were reduced by 4 and 3 log, respectively, following irradiation by 1.0 kGy (Niemira, 2007). The D_{10} value (the radiation dose needed to inactivate 1 log of a target microorganism) obtained for *E. coli* O157:H7 in the study was 0.39 kGy, which is approximately 3- to 4-fold higher than that obtained for surface-inoculated *E. coli* on various types of leaf lettuce (Niemira, Somers & Fan, 2002). The United States Food and Drug Administration (USFDA) is reviewing the use of irradiation for prepackaged fresh produce, including leafy greens (USFDA, 2006). In 2008, the USFDA approved the use of irradiation for packaged iceberg lettuce and spinach. However, products to be treated by irradiation may still need to be washed to cool or remove field dirt. This wash water may require the addition of a chemical disinfectant.

1.5.1.3 Effectiveness of control measures

The efficacy of various disinfectants for the control of foodborne pathogens associated with leafy greens has been extensively studied under laboratory and pilot plant conditions. These conditions may not be accurate representations of commercial production. This research provides guidance with respect to the efficacy of washing treatments against a range of pathogenic and non-pathogenic microorganisms that could not be evaluated under commercial conditions.

When evaluating research presented in these papers, inoculation methods, sample size, sample processing and statistical analysis must all be considered. Many studies include conditions that would not be used or acceptable under commercial production practices. For example, commodity exposure times beyond 2 min or use of flume water temperatures above 4 °C are practices not currently used and would be difficult to implement, especially with respect to elevated flume water temperatures.

Chlorine-based interventions (Table 1.10)

The forms of chlorine commonly used to disinfect water used in the processing of leafy greens include chlorine gas, sodium hypochlorite and calcium hypochlorite (Table 1.10). The efficacy of chlorine in preventing cross-contamination and reducing the microbial load by dipping or spraying the commodity depends on the amount of free available chlorine in the solution, the pH and the amount of organic matter. There are many benefits to the use of chlorine, including cost and ease of implementation, and numerous studies demonstrate a 1–2 log reduction in microbial populations on the product as a result of washing in disinfected water (García, Mount & Davidson, 2003; Kim, Ryu & Beuchat, 2006). High loads of organic matter in the wash water likely play a significant role in limiting the effectiveness of chlorine. Most studies investigating the efficacy of chlorine compounds in reducing the microbial load on lettuce have used lettuce pieces. The action of cutting the lettuce tissue releases exudates that can significantly reduce chlorine availability. This can also lead to reduced effectiveness of the disinfectant in eliminating cross-contamination.

Bacteria adhere to a greater extent to cut than to uncut fresh lettuce, resulting in significant differences in the effectiveness of wash treatments. Seymour et al. (2002) showed approximately a 1 log greater reduction in *Salmonella* Typhimurium on uncut lettuce compared with cut lettuce following washing in potable water. The researchers achieved a 0.72 log reduction in *Salmonella* on cut lettuce following exposure to a solution of free chlorine at 100 mg/l (pH 7.0) for 10 min. Washing in potable water resulted in a 0.38 log reduction of *Salmonella*. Other studies using fresh-cut lettuce have shown no significant decrease in *E. coli* O157:H7 levels following treatment with chlorine at 20 mg/l (Li et al., 2001).

The use of chlorine dioxide in reducing levels of microorganisms on fresh vegetables has received considerable attention, as the activity of this compound is not substantially diminished in the presence of organic matter, and it does not react with ammonia to form chloramines (Huang et al., 2006; Mahmoud & Linton, 2008). Populations of *E. coli* O157:H7 and *Salmonella enterica* on lettuce leaves were reduced more than 5 log following exposure to chlorine gas at 5 mg/l for 14.5 and 19.0 min, respectively. However, the processing conditions had a negative impact on the visual quality of the product. Exposure of lettuce leaves for 30 min to chlorine dioxide at 4.3 mg/l decreased the levels of *E. coli* O157:H7, *Listeria monocytogenes* and *Salmonella* Typhimurium by 3.4, 5.0 and 4.3 log units, respectively (Lee, Costello & Kang, 2004).

Non-chlorine-based alternatives (Table 1.11)

Ozone and peroxyacetic acid are the main alternatives to chlorine for disinfection of water used in processing of leafy greens (see Table 1.11). Bacteria are killed very quickly in ozonated water; however, the efficacy of ozone gas in the inactivation of microorganisms associated with fresh uncut leafy greens is variable. The efficacy of ozone is influenced by the surface properties of the commodity, concentration, exposure time, relative humidity and microbial load. Again, studies reported in the literature have been conducted using fresh lettuce leaves cut into smaller sections. Ozone reduced the aerobic plate count of iceberg lettuce by about 1.0 log when it was treated with ozone at 7.5 mg/l for 10 min (García, Mount & Davidson, 2003). The reduction was comparable to treatment with chlorine at 200 mg/l. Similarly, exposure of lettuce to ozone at 5 mg/l for 5 min at ambient temperature resulted in a 1.4 log cfu/g reduction in aerobic plate count (Koseki & Isobe, 2006). Peroxyacetic acid in wash water reduced the level of *Listeria monocytogenes* on cut pieces of iceberg lettuce by 1.7 log units, which was significantly greater than the 1.0 log reduction achieved by using chlorine rinse (Hellstrom et al., 2006). Beuchat, Adler & Lang (2004) observed similar reductions in *L. monocytogenes* for these treatments when using iceberg lettuce pieces, but reductions were less for shredded lettuce and romaine lettuce pieces.

1.5.1.4 Summary

Chlorine-containing compounds are widely used throughout the fresh produce industry. Depending on the operation, whole intact leafy greens may be sprayed with or immersed into water containing elevated levels of chlorine. Chlorine is effective at reducing cross-contamination due to wash water, but minimal reduction in microbial load of the commodity is reported. Non-chlorine-based alternatives added to wash water have been evaluated for reducing pathogenic microorganisms on uncut leafy greens. The efficacy of these treatments is generally similar to that of chlorine.

1.5.2 Hydroponic fresh produce

The principal fresh fruits and vegetables produced hydroponically are sweet peppers, tomatoes, cucumbers, eggplants and lettuce. As hydroponic production generally requires a high initial financial investment, advanced technology and large material input, most hydroponic production is in developed countries, such as the Netherlands, Spain and France in Europe, Canada and the USA in North America, and Japan and the Republic of Korea in Asia. Because of stringent environmental policies and water shortages, increasing numbers of hydroponic greenhouse operations have started recycling their irrigation water. For example, a survey conducted by Richard, Zheng & Dixon (2006) reported that 58% of the hydroponic vegetable greenhouse area in Ontario, which has the most acreage of hydroponic production

in Canada, recycles its nutrient solutions. One of the biggest risks of recycling nutrient solution in hydroponic systems is the spread of plant diseases. To prevent disease spread in hydroponic systems, an array of water treatment technologies are being utilized. The most common technologies are heat treatment (pasteurization), UV radiation, ozonation and slow sand filtration. Although not common, chlorination as well as copper ionization (Zheng, Wang & Dixon, 2005), hydrogen peroxide treatment, ultrafiltration and iodine treatment are also used in some hydroponic systems for irrigation solution treatment.

The major target microorganisms for hydroponic water disinfection treatment include waterborne fungal pathogens (e.g. *Pythium*, *Phytophthora*, *Verticillium* and *Fusarium* spp.), bacterial pathogens (e.g. *Erwinia*, *Xanthomonas*, *Pseudomonas* spp.) and viral pathogens (e.g. cucumber green mottle mosaic virus, tomato mosaic virus). The most commonly used chlorine compounds are sodium hypochlorite, calcium hypochlorite and chlorine gas. For water disinfection, chlorine compounds are either injected into irrigation lines or injected/dissolved (for calcium hypochlorite) into water holding tanks. In most cases, water temperature is maintained around 20 °C; however, it often ranges from 15 °C to 30 °C. The recommended pH of the nutrient solution for hydroponic vegetable production ranges from 5.2 to 6.5. However, the pH during disinfection can range from 5.0 to 7.5, depending on individual situations.

There is little published information on the effectiveness of using chlorination in disinfecting the irrigation water or nutrient solution in commercial hydroponic systems. The information on the effectiveness of chlorination is mostly generated from small-scale research settings. For example, research conducted in a small-scale hydroponic tomato production system showed that free chlorine at 3 mg/l was as effective as a UV treatment and reduced the total counts of bacteria by 80% (Ewart & Chrimes, 1980). Hong et al. (2003) and Hong & Richardson (2004) reported that free chlorine at 2 mg/l at pH 6 provided complete control of zoospores of 15 isolates of *Pythium* and 8 isolates (7 species) of *Phytophthora* and concluded that free chlorine at 2 mg/l at discharge points (e.g. sprinklers) could effectively control zoospores of *Pythium* and *Phytophthora* species in irrigation water. Cayan et al. (2009a) reported that free chlorine at 0.3–1 mg/l could kill zoospores or sporangia of two *Phytophthora* species with a 3 to 6 min contact time; free chlorine at 2 mg/l could kill zoospores of *Pythium aphanidermatum* with a contact time of 3 min; however, chlorine concentrations of 14 and 12 mg/l were required to control *Fusarium oxysporum* conidia and *Rhizoctonia solani* mycelia with a 10 or 6 min contact time, respectively. These experiments were conducted at room temperature with a nutrient solution of pH 6.5–7.0. Cayan et al. (2009b) also found that free chlorine at 2.4 mg/l with a contact time of 5 min killed *Fusarium* sp., *Phytophthora* sp., *Pythium* sp. and *Verticillium dahliae* that were present in the irrigation water at a southern Canadian commercial nursery operation. Most of the aforementioned research used sodium hypochlorite.

Regardless of which chlorine compound is used, the main limitation is the risk of phytotoxicity due to high concentration of the free chlorine. Ewart & Chrimes (1980) reported damage in roots of hydroponic tomatoes when a free chlorine concentration of 3 mg/l was used in the hydroponic system. Cayan et al. (2009b) reported that 8 out of 22 plant species investigated showed negative chlorine effects when overhead irrigation solution contained free chlorine at 2.4 mg/l. Use of each chlorine compound has its advantages and disadvantages. Whereas chlorine gas is easily injected into an irrigation solution and without any adverse effects on the hydroponic system, the initial investment is very expensive. Also, safety and security are major issues, whereby users are required to build special facilities to secure chlorine gas. Although sodium hypochlorite is readily soluble, cheap and easy to use and the initial investment in equipment is more economical than that of chlorine gas, the potential for having high concentrations of sodium ion in the hydroponic system is not

desirable. Calcium hypochlorite is much safer to handle compared with both chlorine gas and sodium hypochlorite; however, calcium deposition may cause clogging of the irrigation lines.

1.5.3 *Sprouts and sprouting seeds*

1.5.3.1 Chlorine-based interventions

The use of chlorine to minimize microbial risks associated with sprout production varies considerably, depending on regulatory policies related to chlorine use in different countries, whether particular types of sprouts are traditionally consumed raw or cooked, and other factors.

Because of the microbial risks involved, sprout production is generally defined as a food process. As such, it may involve the use of chlorine or other sanitizers in ways similar to what could be expected in a wide range of food processing environments—that is, for food contact surfaces and, in some instances, at low concentrations as a final product rinse. Seed disinfection treatments using strong calcium hypochlorite solutions (e.g. 20 000 mg/l) are used by some sprout producers in order to be in compliance with the USFDA's guidance recommendations for minimizing microbial risks associated with sprouts (USFDA, 1999a,b).

The rationale for strong seed disinfection interventions is that seed has been determined to be a likely vehicle by which microbial contamination can get into sprouts (USFDA, 1999a,b). However, the research evidence in support of the use of such high levels of chlorine for seed sanitization has shown inconsistent results. Published reports on the efficacy of the use of 20 000 mg/l chlorine seed soaks mention pathogen reductions ranging from <1 to 8 log units (Montville & Schaffner, 2004, 2005). Possible factors for such a wide range of results include different properties of different seed types and individual seed lots (Charkowski, Sarreal & Mandrell, 2001), the use of inoculated samples rather than naturally contaminated seeds (Stewart et al., 2001), the “tailing effect” (Periago et al., 2002) and the lack of a standard protocol for carrying out seed sanitization studies (Beuchat et al., 2001).

1.5.3.2 Non-chlorine-based alternatives

There have been many investigations into alternatives to chlorine-based chemicals as a disinfection treatment in the production of sprouts (Beuchat, 1997; Beuchat & Taormina, 1999; Fett & Rajkowski, 2005). Several have shown effectiveness comparable to, or possibly greater than, that of chlorine seed treatments (Hu, Churey & Worobo, 2004; Fett & Rajkowski, 2005; Kumar et al., 2006; Bari et al., 2008).

Rapid immersion in hot water is used effectively for disinfecting mung beans (Bari et al., 2008), and dry heat over periods of several days or longer has also shown promising results with mung bean seed (Hu, Churey & Worobo, 2004). However, the variety of seed types (and sizes) being used for sprouts, plus variations in the condition of the seed coat, may require trial and error adjustments in heat settings and duration for each seed type, and possibly even for different seed lots within a given type.

Gamma irradiation (Thayer et al., 2003) and electron beam irradiation of seed have also been investigated. With both, there is some loss of yield with doses adequate for disinfection. With electron beam irradiation of alfalfa seed, some stunting of growth and curling of the sprouts were observed that might negatively affect value and customer acceptance (R. Sanderson, personal communication, 2008).

Regarding other possibly effective treatment options that may exist, as of May 2008, no alternatives to the 20 000 mg/l chlorine seed treatment have been acknowledged as being acceptable by the USFDA, and so many producers in the USA are reluctant to use them.

The use of a sanitization step, such as chlorine or any alternative, as a seed treatment is somewhat problematic, in that it is done at the start of the sprouting process and is therefore followed by 2–6 or more days of sprout growth in warm, moist conditions in a nutrient-rich environment, allowing for the possible recovery and proliferation of any treatment survivors (USFDA, 1999a,b). For this reason, it may make sense to consider treatment options other than the usual kill-step approach (Montville & Schaffner, 2004).

Research into the use of competitive exclusion as a pathogen control method in sprout production has shown promise (Matos & Garland, 2005; Fett, 2006). Further research is needed to determine whether a single organism or combination of organisms would be most effective in inhibiting or eliminating organisms of concern. One attractive aspect of the competitive exclusion approach is that the establishment and maintenance of benign microbial populations may inhibit growth of organisms inaccessible to treatment, as well as lessen vulnerability to cross-contamination that can result from a disinfection step, where commensal flora are reduced or eliminated.

1.6 Food contact surfaces

1.6.1 Disinfection of food contact surfaces using chlorine-based compounds

1.6.1.1 Function and target microorganisms

The function of the application of chlorine-containing compounds onto hard non-porous food contact surfaces prior to the beginning of a food processing shift is to reduce populations of disease- and spoilage-causing microorganisms that may be present on equipment or utensils after cleaning. The cleaning and disinfecting programmes associated with food production processes include multiple steps, generally beginning with a pre-rinse with potable water to remove large food soils and debris. This is followed by the application of a cleaner, which is selected by considering the nature of the soil to be removed, the characteristics of the water in the food processing facility, the material composition of the surface being cleaned, the method of application and the environmental impact that the chemistry may play in the waste stream. A post-rinse step typically follows cleaning to remove residual cleaning chemicals. Next, a disinfectant is applied and, in some cases, is followed again by a potable water rinse. The use of chemical disinfectants in food processing facilities is generally regulated by governmental bodies throughout the world. Routine application of disinfectants at concentrations of active biocide resulting in the reduction of populations of vegetative bacterial pathogens is in some countries referred to as “sanitization” and is not followed by a water rinse. This application is hereby referred to as “no-rinse disinfection”. In some instances, disinfectants are applied at relatively higher active biocide concentrations, which are followed by a water rinse. In the European Union and other parts of the world, the application of a disinfectant at any level to a food contact surface is required to be followed by a potable water rinse to remove residual chemicals.

Biocides are also used during operation to control the accumulation of microbial populations on the food contact surfaces associated with conveyor belts and slicers. The majority of these applications are located in fresh and ready-to-eat meat and poultry processing facilities. Conveyor belts are used to transfer product through processing and ultimately to packaging. Over the course of production, fat and protein soils accumulate on belt and slicer surfaces along with a population of microorganisms originating predominantly from the product being conveyed or processed in a slicer. Cross-contamination between the food contact surfaces and food product is therefore a concern to processors. Control of

pathogenic bacteria such as *Salmonella*, *Listeria monocytogenes*, *Escherichia coli* O157:H7, *Campylobacter* and spoilage-causing bacteria is critical.

1.6.1.2 Active chlorine compounds used

There are six primary forms of chlorine-containing compounds used in food production and processing for the disinfection of food contact surfaces. The hypochlorites are most commonly used. ASC and chlorine dioxide are used primarily to disinfect process water; their use to disinfect surfaces is a secondary benefit in the process application. Working solutions with an operational pH of 2.3–3.2 exhibit a chemistry that is principally that of chlorous acid, which forms on acidification of chlorite (Rao, 2007).

To a lesser extent than the inorganic forms, organic chlorine compounds are used, particularly chloramine-T and dichloroisocyanurate. Chloramine-T contains approximately 25% available chlorine, whereas the sodium and potassium salt forms of dichloroisocyanurate contain 60% and 59% available chlorine, respectively (Dychdala, 2001).

1.6.1.3 Treatment conditions

Conditions for the treatment of food contact surfaces with chlorine-containing biocides are presented in Table 1.12. In practice, disinfectant solutions are applied to surfaces in a number of different ways. They can be sprayed or circulated through equipment, referred to commonly as “flooding the surface”. They may also be atomized or fogged into the air to help reduce airborne contamination. Key to their effectiveness is intimate contact of a proper disinfectant concentration with the target microbial cell. Therefore, adequate coverage and exposure time over a precleaned surface are required.

Table 1.12. Treatment conditions for chlorine-containing compounds applied to food contact surfaces prior to operation

Compound	Application	Exposure time (min)	Concentration (mg/kg) ^a	pH	Temperature (°C)
Hypochlorite/ hypochlorous acid (I)	No-rinse disinfection ^b	1	Up to 200	6–8	12–21
	Disinfection	10	600–1200	6–8	12–21
Chlorite/chlorous acid (III)	No-rinse disinfection	1	Up to 335	2–3	12–21
Mixed oxychlorine species (III/IV)	No-rinse disinfection	1	Up to 200 (chlorine dioxide)	2–7	12–21
Chlorine dioxide (IV)	No-rinse disinfection	1	Up to 200	5–7	12–21
Chloramine-T	No-rinse disinfection	1	Up to 200 (available chlorine)	8.5	12–21
	Disinfection	5	0.3–0.5% solution	8.5	12–21
Dichloroisocyanurate	No-rinse disinfection	1	Up to 200 (available chlorine)	5–7	12–21

^a Unless otherwise specified.

^b Limited to the application of United States Environmental Protection Agency–registered sanitizers for food contact surfaces.

In clean-in-place programmes, the disinfectant is applied as a separate step in the cleaning programme. Disinfectants may also be applied via a central disinfection system,

which consists of a centralized preparation and distribution system to carry the use solution to the point of use. The disinfectant is distributed via piping and drop hoses to the locations where it will be used. This significantly increases ease of use and helps to ensure that the disinfectant will be used.

The minimal time of exposure depends on regional governmental requirements as well as the surface and related food processing-specific conditions. In the USA, chlorine use solution concentrations of generally up to 200 mg/kg as free chlorine are not required to be rinsed off food contact surfaces prior to operation. After the no-rinse disinfectant is applied, it must be allowed to adequately drain from surfaces before contact with food. In other regions throughout the world, a potable water rinse is required.

To disinfect belts during processing operations, use solutions are generally sprayed onto the surface continuously throughout production. A spray nozzle manifold is fitted over the return side of the conveyor belt, and nozzles are configured on both sides of the belt to ensure adequate coverage. The use solution is sprayed over the surface via a low-flow, low-pressure application to minimize the potential for aerosolization of soils and microorganisms. The application is generally not followed by a potable water rinse. Sanitizer is allowed to drain from food contact surfaces as the belt travels through the return side, underneath the conveyor.

Disinfectants applied to slicers are generally applied intermittently (i.e. when food product is not actively being sliced or processed), and the application is typically not followed by a potable water rinse.

1.6.1.4 Effectiveness of the process

When used appropriately and in accordance with manufacturer recommendations, chlorine-containing biocides for food contact surfaces are generally effective in reducing populations of microorganisms in the food plant environment. In the USA, the United States Environmental Protection Agency (USEPA) requires no-rinse disinfectants for food contact surfaces to achieve a 5 log reduction in populations of suspended *Escherichia coli* and *Staphylococcus aureus* in 30 s at an exposure temperature of 25 °C. The antimicrobial activity of chlorine is dependent on environmental factors during exposure of microorganisms to the biocide. Factors such as pH, temperature, organic load and water hardness can all play significant roles in antimicrobial efficacy.

The influence of chlorine use solution pH on antimicrobial efficacy has been well characterized. Dychdala (2001) reviewed much of the early research in this area. Most commercial hypochlorite solutions produce a slightly alkaline pH at their use dilution. The antimicrobial properties of chlorine are not as favourable under slightly alkaline conditions; however, the stability of the solution is much improved. Other commercial products, however, are formulated to ensure a buffered pH of 6–7.5 to maximize efficacy (Stopforth et al., 2002). Chlorine is not affected by hard water salts unless they cause an upward drift in pH of the working use solution.

The effect of organic matter on the bactericidal efficacy of chlorine compounds is well documented (Kotula et al., 1997; Dychdala, 2001). The type of organic soil and the amount of this material present influence the extent to which efficacy is depressed (Hekmati & Bradley, 1979). Differences between soil types may contribute to the binding of free chlorine by amino groups in the proteinaceous lean versus lipid- or carbohydrate-based materials (Cords et al., 2005). The tenacity of bacterial cells within biofilms to resist inactivation or death by exposure to chlorine compounds has been repeatedly demonstrated (Joseph et al., 2001; Stopforth et al., 2002; Cords et al., 2005). Resistance is likely the result of impedance by the biofilm extracellular matrix of chlorine penetration by a reaction-

diffusion interaction (Chen & Stewart, 1996). Ronner & Wong (1993) demonstrated that recoverable cells within biofilm communities associated with rubber gasket material were reduced by less than 1–2 log following treatment with free chlorine at 100 mg/l. Their planktonic counterparts were completely killed following similar treatment in suspension.

The fungicidal activity of chlorine has not been as extensively reported as its bactericidal activity. Cheng & Levin (1970) studied the inactivation of *Aspergillus niger* conidiospores upon exposure to free chlorine at 1–20 mg/l. A comparison of their findings with those of other authors (Hays, Elliker & Sandine, 1967; Ito & Seeger, 1980) indicates that fungal spores are more resistant than vegetative bacteria. Ver Kuilen & Marth (1980) investigated the sporicidal effect of hypochlorite on *A. parasiticus*. Following treatment with chlorine at 3 mg/l for 15 min, the number of recovered conidia fell by 3.5 log units.

Factors affecting the efficacy of chlorine may not necessarily apply to chlorine dioxide, which does not form hypochlorous acid when dissolved in water, like other chlorine sources. For example, chlorine dioxide is more tolerant of organic material than chlorine.

Few published data are available regarding the effectiveness of hypochlorite or ASC in controlling the growth and/or accumulation of bacteria on belt and slicer surfaces during processing operations. Effectiveness can be inferred through studies evaluating the impact of organic material on chlorine efficacy.

1.6.1.5 Limitations of the process

The significant contributors to the limitation of effectiveness of the use of chlorine compounds on food contact surfaces are inadequate cleaning and preparation of surfaces prior to disinfection, improper concentration of free chlorine or active species in the use solution, inadequate exposure time and lack of complete coverage or accessibility to target microorganisms. The latter may be due to improper design of processing equipment or equipment that has not been suitably maintained, allowing for the harborage of microbial niches. The effectiveness of chlorine compounds during processing operations is limited by the accumulation of organic matter, although some treatment systems strive to reduce the presence of soil prior to the disinfection step through the use of scrapers or brushes. Disinfectants more tolerant of organic matter are clearly better suited for most in-process applications.

Also critical is the quality of the water in a food processing facility used to dilute concentrated chlorine chemicals to working use solutions. Although not directly affected by hard water salts, upward drifts in pH may limit the efficacy of free chlorine. Alternatively, reductions in pH levels below 4 may result in the generation of chlorine gas and/or cause corrosion of stainless steel surfaces. Stainless steel corrosion is of particular concern to food manufacturers processing acidic foods, such as tomato products. Residual food soils, if left on food contact surfaces, may combine with chlorine solutions, resulting in pitting of stainless steel. Pitting can present harborage sites for accumulation of food soils and microorganisms.

Use of chlorine dioxide to disinfect food contact surfaces is limited by the innate instability of the chemistry, the need to generate the active chemical on site and the safety risks that chlorine dioxide gas poses to workers if ventilation systems are inadequately designed or maintained. The high initial capital cost of a chlorine dioxide generator is another factor limiting its use.

1.6.2 Disinfection of food contact surfaces using non-chlorine-based alternative compounds

Several non-chlorine-based alternative biocidal compounds are utilized to disinfect hard non-porous food contact surfaces. They have functions and target microorganisms similar to those of chlorine-based compounds.

1.6.2.1 Alternative compounds used

The most widely used inorganic peroxide on food contact surfaces is hydrogen peroxide. Organic peroxygen compounds used for the sanitization of food contact surfaces include peroxyacetic acid, peroxyoctanoic acid and mixtures of the two. Hydrogen peroxide is widely used for sterilization of equipment and containers in aseptic packaging for foods and drinks. In the USA, it is approved by the USFDA for this application (USFDA, 1990). Peroxyacetic and peroxyoctanoic acids are widely used to disinfect food contact surfaces. Peroxyacetic acid has application as well for use as a commercial sterilant in aseptic packaging operations.

Iodophors, which are mixtures of iodine and surface-active agents that act as carriers and solubilizers for the iodine, are commonly used on food contact surfaces in the beverage industry.

Also commonly used on food contact surfaces are QACs. QACs approved as no-rinse disinfectants for food contact surfaces include the “second generation” QAC, *n*-alkyldimethylbenzylammonium chloride; the “third generation” dual QACs, *n*-alkyldimethylbenzylammonium chloride and *n*-alkyldimethylethylbenzylammonium chloride; the “fourth generation” twin or dual chain QACs, didecyldimethylammonium chloride and dioctyldimethylammonium chloride; and “fifth generation” mixtures of fourth-generation and second-generation QACs.

Ozone is a powerful and naturally unstable oxidizing gas that, when dissolved in water, is used for the sanitization of food contact surfaces. Because of its instability, it must be produced on site at the food processing facility.

Peroxyacetic and/or peroxyoctanoic acids, QACs and ozonated water may be applied to conveyor belts and slicers during processing.

1.6.2.2 Treatment conditions

Treatment conditions for the application of non-chlorine-based alternatives to food contact surfaces are presented in Table 1.13. Generally, environmental, application and regulatory conditions are similar to those applicable to the use of chlorine-based compounds on food contact surfaces, described above.

1.6.2.3 Effectiveness of alternative compounds

As with the chlorine compounds, these alternative compounds are generally effective if food contact surfaces are sufficiently prepared (i.e. cleaned and rinsed) prior to the application of the biocide. Appropriate design and maintenance of processing equipment are also essential to ensure contact between the active chemical and the target microorganisms.

Table 1.13. Treatment conditions for alternative compounds applied to food contact surfaces prior to operation

Compound	Application	Exposure time	Concentration (mg/kg) ^a	pH	Temperature (°C)
Peroxyacetic acid	No-rinse disinfection ^b	1 min	Up to 315	3–4.5	12–21
	Disinfection	10 min	Up to 2320	3–4.5	12–21
	Commercial sterilization	Up to 20 s		3–4.5	40–60
Peroxyoctanoic acid	No-rinse disinfection	1 min	Up to 122	1.5–2	12–21
	Disinfection	10 min	Up to 547	1.5–2	12–21
Hydrogen peroxide	Commercial sterilization	3–7 s	35%	2–3.5	21
Iodophor	No-rinse disinfection	1 min	Up to 25	2–5	12–21
	Disinfection	10 min	Up to 75	2–5	12–21
QACs	No-rinse disinfection	1 min	Up to 200 (1st–4th generation); up to 400 (5th generation)	7–8	12–21
	Disinfection	10 min	800–1200	7–8	12–21
Ozonated water	No-rinse disinfection	1 min	1.5–4	6–8.5	12–21

^a Unless otherwise specified.

^b Limited to the application of USEPA-registered sanitizers for food contact surfaces.

The effectiveness of peroxyacetic and peroxyoctanoic acids has been reviewed (Block, 2001; Cords et al., 2005). Their efficacy is influenced by numerous factors, including concentration, contact time, temperature and pH of the use solution. Other factors include the presence of organic material and, to a lesser extent, the impact of hard water salts. Organic peroxygen compounds achieve a broad spectrum of activity over a broader pH range than hypochlorous-generating chlorine compounds. Antimicrobial activity has been observed to diminish above pH 7 (Cords et al., 2005). The effect of pH may be a result of the shifting of the equilibrium action of the peroxygenated compounds in a use solution. Peroxyacetic and peroxyoctanoic acids exhibit significant bactericidal activity at low temperatures, a characteristic that lends itself to wide use in food and beverage processing environments, including broad applications in clean-in-place systems. The presence of organic material has less impact on the efficacy of these organic peroxygen compounds compared with chlorine (Block, 2001). Holah et al. (1990) evaluated 12 commonly used surface disinfectants using bacterial biofilms developed on stainless steel. The authors concluded that peroxyacetic acid was the most effective of the compounds tested. Similar results were observed in studies reported by Stopforth et al. (2002), Krysinski, Brown & Marchisello (1991) and Carpentier & Cerf (1993), in which peroxyacetic acid was compared with other biocides. Fatemi & Frank (1999) presented similar results using organic challenges.

Iodine, unlike chlorine, is bactericidal over a fairly broad pH range against a wide spectrum of microorganisms, including yeasts and moulds. Iodophors may also provide a weak acid rinse for mineral buildup control and are less irritating to the skin than chlorine (Cords et al., 2005). In many cases, iodophors are effective at much lower concentrations than chlorine (Gershenfeld & Witlin, 1955; Trueman, 1971). Lindsay & von Holy (1999) investigated the effectiveness of an iodophoric preparation at 35 mg/l as iodine to reduce

populations of planktonic and sessile *Bacillus subtilis* and *Pseudomonas fluorescens*. The iodophor performed as well as the peroxyacetic acid-based and chlorhexidine-based sanitizers also analysed. Iodophors do not lose antimicrobial efficacy as rapidly as chlorine in the presence of organic material (Cords et al., 2005). This is especially true at low pH (Davis, 1962). At higher pH, an organic matter effect becomes apparent. Generally, iodophors are more adversely affected by hard water salts than chlorine, and the degree of influence depends on the specific type of iodophor being evaluated.

Because of the diversity of QACs commercially available, general statements regarding the effectiveness of QACs and the environmental conditions that influence them are difficult. The pH, temperature, organic matter and water hardness may all influence activity. Much of the early research that examined the effect of hydrogen ion concentrations on the antimicrobial activity of QACs suggests that maximum efficacy is exhibited in the alkaline pH range (Soike, Miller & Elliker, 1952). However, further work has indicated that the effect of pH may vary with bacterial species, with Gram negatives being more susceptible to QACs in the acid pH range and Gram positives in the alkaline pH range (Cords et al., 2005). QACs are generally not as effective as chlorine, iodophors or peroxyacids at cold temperatures. The activity of various QAC formulations against bacterial biofilms was studied by Kryszinski, Brown & Marchisello (1991). The residual activity of QACs has been noted (Cords et al., 2005) and is an attribute often sought after by food processors.

Ozone is a powerful broad-spectrum biocide. Reviews of the applicability of ozonated water in food processing suggest the range of ozone concentrations needed to achieve effective sanitization of a food contact surface is 1.5–4 mg/kg (Kim, Yousef & Dave, 1999; Weavers & Wickramanayake, 2001). Ozone is quite unstable and has limited solubility in water at high temperature and pH.

1.6.2.4 Limitations of alternative compounds

The general limitations of the alternative compounds in terms of their ability to effectively sanitize or disinfect food contact surfaces are similar to those described above. Additionally, each alternative biocide may be associated with limitations specific to its chemical nature.

Peroxyacetic and peroxyoctanoic acids are sensitive to metal ions, so the quality of water used in the preparation of working solutions is critical. These biocides are also corrosive to soft metals, such as brass, copper, mild steel and galvanized steel. Corrosivity is accelerated by the presence of high concentrations of chloride in the water (>75 mg/kg). High temperatures will also exacerbate the corrosion rate. Concentrated peroxyacetic acid has a strong, pungent odour.

QACs, when used in mechanical operations, can foam and therefore are not recommended for use in clean-in-place systems. They are also not effective at low temperatures (Cords et al., 2005) and have little tolerance of hard water salts.

A large capital investment is required of food processors implementing the use of ozone for disinfection of their facility. Ozone must be generated and monitored on site. Additionally, many applications require adequate ventilation systems to operate within established exposure limits (e.g. <0.1 mg/l continuous 8 h exposure). Validation that the process is achieving required thresholds of disinfection effectiveness is required.

1.6.2.5 Summary

Active chlorine compounds are broadly used in food processing facilities to disinfect food contact surfaces prior to the beginning of operation. Of the active chlorine compounds,

sodium hypochlorite is the most commonly used. The process is generally effective if surfaces are properly cleaned and prepared before the application of the biocide. Several non-chlorine-based alternative compounds are utilized as well, including peroxyacids, iodophors, QACs and ozonated water.

Additionally, biocides are used to mitigate the accumulation of bacterial populations on food contact surfaces during production. Hypochlorite, ASC, peroxyacids, QACs and ozonated water may be used for this application.

Requirements related to completing the cleaning and disinfection cycle with a potable water rinse vary globally from region to region and from country to country. The final step of the cycle in food processing facilities within the USA is the application of a USEPA-registered no-rinse food contact disinfectant. The practice mandates that treated surfaces be adequately drained prior to production, but it is expected that chemical residues contact food. Potable water rinsing is generally not practised in those applications in which biocides are applied to food contact surfaces (e.g. conveyor belts and slicers) during production. Because this application is practised in close proximity to the contact of the treated surface with food, one can expect chemical residues to come into contact with the food as well. There is, however, little information available regarding the quantification of such residuals on foods.

1.7 References

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2. CHEMISTRY OF DISINFECTANTS AND FORMATION OF DISINFECTION BY-PRODUCTS IN FOOD AND WATER

2.1 Introduction

This chapter describes the most common disinfectants/sanitizers used in food processing and summarizes information on their chemistry and the by-products that may be produced during their interactions with foods during processing. These disinfectants include chlorine-based disinfectants, such as acidified sodium chlorite (ASC), *N*-chloramines (especially monochloramine), chloramine-T, chlorine dioxide, hypochlorite-related compounds and sodium dichloroisocyanurate, as well as non-chlorine-based alternative disinfectants, including 1,3-dibromo-5,5-dimethylhydantoin, hydrogen peroxide, ozone, peroxyacids, quaternary ammonium salts, such as cetylpyridinium chloride (CPC), iodophors, sodium metasilicate and trisodium phosphate (TSP).

The common disinfectants are oxidants and chemically reactive and differ in their disinfection efficacy. They also vary in their oxidation capability and other chemical activity (Table 2.1). The ideal disinfectant would have high broad-spectrum efficacy against microorganisms and low by-product formation potential.

Table 2.1. Relative characteristics of oxidants/disinfectants^a

Oxidant	Disinfecting efficiency	Oxidizing efficiency	Halogenation capability
Chlorine	High	High	High
Chlorine dioxide	High	High	Low
Monochloramine	Low	Low	Low
Ozone	High	High	None (no bromide)
Hydrogen peroxide	Low	Moderate	None
Bromine	High	Moderate	High
Iodine	High	Low	Low

^a From Rice & Gomez-Taylor (1986).

The chemistry of disinfection by-products (DBPs) that may be formed in water and on foods—bromate, chloral hydrate, chlorate, chlorite, dimethylhydantoin, haloacetic acids (HAAs), haloacetonitriles (HANs), halofuranones (MX and MX analogues), *N*-nitrosamines and trihalomethanes (THMs)—is also addressed in this chapter, in connection with the respective treatments that may generate the by-products.

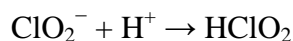
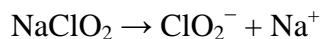
Other disinfectants may have some applications in food and/or water processing, but they were beyond the scope of this assessment. Among these are ionizing radiation (e.g. gamma), ultraviolet (UV) light, electron beam radiation and copper ionization.

2.2 Acidified sodium chlorite

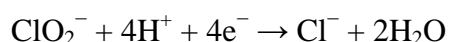
2.2.1 Chemistry

ASC (NaClO_2) is a combination of sodium chlorite (25%) and a food-grade acid (50%). It is clear and colourless. The chemical name is sodium chlorite (chlorous acid,

sodium salt; Chemical Abstracts Service [CAS] registry number 7758-19-2). Sodium chlorite is activated with any food-grade acid at levels sufficient to reach pH values in the range 2.3–2.9 for spray and dip solutions. The active components are chlorous acid, which is a strong oxidizing agent, and chlorine dioxide. The addition of acid to sodium chlorite generates chlorous acid:



The oxidation/reduction of chlorous acid and chlorite ion (ClO_2^-) may also generate chloride ion via the following reactions:



2.2.2 Application and fate in foods

ASC is used as a broad-spectrum disinfectant in poultry chiller water as well as in processing of meats, poultry, seafoods, fruits and vegetables. Its antimicrobial action is derived from chlorous acid and chlorine dioxide, the concentrations of which are dependent on the pH of the solution (USDA, 2002). ASC is approved under several national regulations for application onto the surface of different types of fresh and processed foods at a sodium chlorite concentration range of 50–1200 mg/l (e.g. FSANZ, 2006; USFDA, 2006). The sodium chlorite concentrations used are within the range 500–1200 mg/l for spray and dip solutions (pH 2.3–2.9) and 50–150 mg/l for chiller water (pH 2.8–3.2). Fresh and processed fruits and vegetables are subjected to a water rinse after ASC application followed by a 24 h withholding time (for cut produce only). Treatment of whole or parts of poultry carcasses, sausages or delicatessen meats (cold cuts) is carried out by spraying or dipping prior to or after chilling. ASC is also used to treat pre-chilling and chilling water at relatively low levels (i.e. 50–150 mg/l as sodium chlorite) into which poultry carcasses are submerged. Poultry and meat products are not rinsed subsequent to treatment.

Chlorine dioxide, chlorite ion and chlorate ion (ClO_3^-) are generated as reaction products; chloride is the final reduction product. The respective concentrations will vary depending on the pH of the mixture. The dissociation of chlorite to chlorous acid is about 31% at pH 2.3, 10% at pH 2.9 and 6% at pH 3.2, and the amount of chlorine dioxide does not exceed 1–3 mg/l (USDA, 2002). Thus, a 1200 mg/l solution of ASC is expected to convert to chlorous acid at 376 mg/l at pH 2.3 or 123 mg/l at pH 2.9; a 50 mg/l solution of ASC is expected to convert to chlorous acid at 16 mg/l at pH 2.3 or 3 mg/l at pH 3.2 (FAO, 2007).

The residual concentrations of chlorite and chlorate as reported in the data submitted to the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) (WHO, 2008a) for raw products of three food categories that had been treated with ASC solution were as follows: meat and meat products, including poultry, 0.1 mg/kg for both chlorite and chlorate; fish and fish products, 0.01 mg/kg for chlorite and 0.1 mg/kg for chlorate; and fruits and vegetables, 0.01 mg/kg for chlorite for all fruits and vegetables, except for leafy vegetables (0.23 mg/kg), and 0.01 mg/kg for chlorate. The treatment was at the proposed sodium chlorite use level of 1200 mg/l and under optimum conditions to fulfil the technological purpose (with sufficient time of spray or immersion and drip with water wash and holding time). The results showed

that residues of chlorite and chlorate in most foods treated with ASC declined to levels below the limits of detection with time (after treatment, rinsing and a holding period).

Residues of chlorite and chlorate were reported by SCVPH (2003) for poultry carcasses immersed in a 150 mg/l ASC solution at pH 2.8 and 5 °C for 1 h, then drained for 5 min and rinsed for 5 min in clean water. The residue levels were lower than the detection limit (chlorate <19 µg/kg) or became so after 2 h (chlorite <16 µg/kg). Furthermore, cooking of foods treated with chlorite solutions may either drive off chlorite and chlorate residues or reduce them to chloride (USFDA, 1995). Therefore, the concentrations of chlorite and chlorate in poultry and seafood after cooking would be negligible. In treatments with ASC at 500, 850 and 1200 mg/l for 5 s and dip in rinse water, both raw and cooked meat samples were below the estimated detection limit (0.03 µg/cm² of meat surface) for chlorite and chlorate (USFDA, 1997). However, residues would remain in seafood consumed raw. One industry sponsor estimated that 1 mg/kg as chlorite and 9 mg/kg as chlorate could remain in raw seafood (USFDA, 1998a).

A manufacturer provided analyses of different fish and seafood (salmon, snapper, catfish, scallops and shrimp) treated by immersion for 30 s in ASC at 1200 mg/l at pH 2.3 and allowed to drip for 30 s. The chlorate and chlorite residues were analysed without a potable water rinse post-treatment after 0, 24 and 48 h post-treatment. No chlorate was detected (limit of detection [LOD] 0.1 mg/kg) at any point, and chlorite was not detected (LOD 0.01 mg/kg) after 24 h. When a post-treatment potable water rinse was performed, no chlorite residues were detected in salmon, scallops and shrimp at any time; chlorite was detected in grouper and catfish samples at 0 h, but the concentration was below the LOD after 24 h (USFDA, 2004a). No total organic halide residues were detected (LOD 0.01 mg/kg) in any control or treated seafood samples (USFDA, 2004a).

Residue levels were measured in several fruits and vegetables after treatment with ASC at 1200 mg/l for 5 or 10 s and then either not rinsed and air-dried or rinsed with water. Primary results were given as residue weight per item, not in units of concentration. The concentrations were then calculated using average weights for each fruit or vegetable (USFDA, 1998b), as shown in Table 2.2 for the air-dried samples (not rinsed).

Table 2.2. Chlorite and chlorate residue levels after treatment with ASC solution

Fruit/vegetable	Chlorite concentration (mg/kg)	Chlorate concentration (mg/kg)
Apple (medium)	0.29	<0.07
Orange (Florida)	0.30	<0.06
Carrot (19.1 cm)	2.29	<0.14
Cantaloupe quarter (medium)	32.83	<0.07
Potato (medium)	0.34	<0.08
Lettuce (one leaf)	8.80	495

A potable water rinse following ASC treatment would probably reduce the levels of residual chlorite and chlorate. This was observed in a later study (USFDA, 2001) in which fruits (melons, apples, oranges, strawberries) and vegetables (carrots, lettuce, onions and french fries) were treated with ASC at 1200 mg/l at pH 2.5 and analysed for chlorite and chlorate after dwell times of 1, 2, 6, 24 and 48 h. The protocols were as follows:

- 1) 30 s ASC dip followed by 5 s post-treatment deionized water rinse;
- 2) 30 s ASC dip with no post-treatment water rinse;
- 3) 30 s ASC spray followed by 5 s post-treatment deionized water rinse;
- 4) 30 s ASC spray with no post-treatment water rinse.

The analysis revealed that the chlorate concentration was below the LOD (0.1 mg/kg) for any of the tested samples and conditions used. In the case of chlorite, the values were below 0.1 mg/kg for all the tested foods except for the following: carrots with 1.49 mg/kg in protocol 2 and 0.89 mg/kg in protocol 4; melons with 1.04 mg/kg in protocol 2 and 1.1 mg/kg in protocol 4; lettuce with 0.23 mg/kg in protocol 1, 15.3 mg/kg in protocol 2, 0.56 mg/kg in protocol 3 and 2.98 mg/kg in protocol 4; oranges with 0.23 mg/kg in protocol 2; and onions with 16.82 mg/kg in protocol 4. In the case of lettuce, the residues of chlorite were very high, and the manufacturer proposed a water rinse followed by a dip or spray treatment for 30 s with ASC at 1200 mg/l and a post-treatment rinse with deionized water with 0, 1, 2, 4, 6, 24 and 48 h dwell times. The chlorite concentration was reduced to <0.01 mg/kg after a 24 h dwell time for the dip and a 6 h or 48 h dwell time for the spray treatment, even though 0.99 mg/kg was still detected at 24 h.

2.2.3 Reactions of acidified sodium chlorite with food components

ASC may interact with either organic matter in solution or proteins, fats or other compounds in the foods with the potential for the formation of different reaction products. The potential reactions are described below.

A treatment of poultry carcasses under exaggerated conditions (immersion in ASC at 2525 mg/l, pH 2.78, for 5 min) was performed by a manufacturer to check the effect on amino acids in comparison with controls. In both cases, proteins were hydrolysed, and the distribution of amino acids in the disinfected carcasses was identical to that in the controls. This also includes amino acids such as cysteine, tyrosine, threonine and tryptophan, which may be prone to oxidation due to easily oxidizable functional groups. Other reaction products that could be potentially generated were not analysed (EFSA, 2005).

The potential formation of chlorinated organic compounds after ASC treatment of poultry carcasses under different conditions was tested as follows (EFSA, 2005):

- 1) Poultry carcasses were immersed in ASC at 2525 mg/l, pH 2.78, for 5 min, rinsed with distilled water, then blotted dry and soaked in hexane overnight for the extraction of lipid residues. The analysis of the samples by gas chromatography did not detect any chlorinated organic compounds. The LOD was about 0.05 mg/kg.
- 2) Poultry carcasses were sprayed with ASC at 1200 mg/l, pH 2.5, for 15 s, then air chilled for 2 h. The analysis did not reveal increases of organically bound chlorine (LOD 0.05 mg/kg).

The poultry carcasses were also screened to detect oxidation or changes in the fatty acid profiles under different treatment conditions:

- 1) immersion of the poultry carcasses in ASC at 1200 mg/l for 5 s, then 5 min dripping and 1 h immersion in water (pre-chill study);
- 2) immersion of the carcasses in ASC at 150 mg/l for 1 h and then 5 min dripping (chiller study);
- 3) dipping the carcasses in ASC at 1200 mg/l for 15 or 30 s with no rinsing and dwell times of 1, 2, 4 and 8 h (post-chill study);
- 4) dipping the carcasses in ASC at 1200 mg/l for 15 or 30 s, followed by 5 s water rinsing and 30 s dwell time (post-chill study);
- 5) dipping the carcasses in ASC at 1200 mg/l for 15 or 30 s with no rinsing and 30 s dwell time (post-chill study).

The analysis did not reveal any chlorinated organics (LOD 0.05 mg/kg). In all cases, samples and controls were cooked.

The results of the analysis of fatty acids in the lipid fractions of the carcasses after all ASC treatments were found to be similar to the controls. Similar results were reported for red meat treated with ASC at 500, 850 and 1200 mg/l for 5 s and dipped in rinse water (USFDA, 1997) and for seafoods treated with ASC at 1200 mg/l at pH 2.3 (USFDA, 2004a). The 2-thiobarbituric acid reactive substances (TBARS) analysis was also performed to detect any oxidation of fatty acids. TBARS values were higher in the skin after the treatments but not in the muscle, which remained unaffected regardless of the treatment. A study of the skin treated with ASC at 150 mg/l at pH 3.05 and 5 °C for 45 min (chiller treatment) gave TBARS increases equivalent to 2.8 times the control (USFDA, 1995). The chiller treatment gave higher TBARS values in the skin than did the use of ASC in spray. However, cooking gave much higher TBARS values, even in the controls. In the case of red meat treated as described above, the TBARS values were 0.29–0.36 mg/kg for treated samples in comparison with 0.26 mg/kg for the controls. The TBARS values for cooked samples were 5–6 times those of the raw samples, probably due to oxidation of fatty acids by heating (USFDA, 1997). In the case of seafood, no significant increase of TBARS values was reported after immersion for 30 s in ASC at 1200 mg/l at pH 2.3 (USFDA, 2004a).

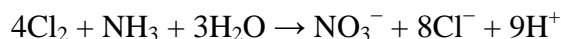
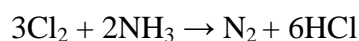
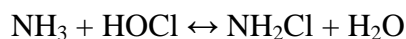
2.2.4 Summary

Based upon the available data, chlorate and chlorate are the main by-products that may remain as residues on food.

2.3 N-Chloramines

2.3.1 N-Chloramine chemistry

N-Chloramines are produced from the chemical reactions between ammonia or organic amines and chlorine. The most common form used as a disinfectant is monochloramine (NH₂Cl; CAS No. 10599-90-3). Chloramines may be deliberately produced by combining the ammonia or amines with chlorine prior to contact with the medium to be disinfected (food or water), or they may be spontaneously formed whenever chlorine is used if ammonia or amines are present in the medium:

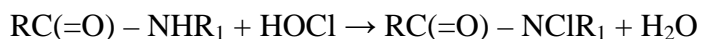


The two final common products of ammonia oxidation with excess chlorine are nitrogen and nitrate (Montgomery, 1985), and this is called breakpoint chlorination. The process is a function of chlorine to ammonia ratio, temperature, and pH and alkalinity of the solution. The goal for disinfection is to maximize monochloramine formation and minimize dichloramine and trichloramine formation. This is achieved by maintaining the pH between 6.5 and 8.5 with a chlorine to ammonia ratio of approximately 4:1 (Zentox, 2007). In addition

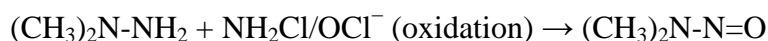
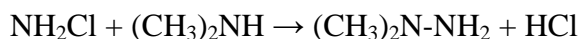
to inorganic *N*-chloramine, there are analogous organic *N*-chloramines. *N*-Chlorodimethylamine is an example of an organic amine formed from dimethylamine. *N*-Chloramines are labile, so they will exchange halogens as well as transfer halogens to other amine or amide compounds with which they are in proximity.

Because of its low oxidizing efficiency and low halogenation capability in water, monochloramine has a lesser tendency to produce halogenated DBPs and oxidation products, but it also has much lower disinfection potency than free chlorine under most conditions. However, some of its DBPs are of greater concern than many of the chlorination products.

Related chemicals are *N*-chloroamides that could be formed by reactions of chlorine with amides such as protein peptides:



Monochloramine can react in water with secondary amines such as dimethylamine to produce dimethylhydrazine, which can be oxidized in the presence of the monochloramine to *N*-nitrosodimethylamine (NDMA; CAS No. 62-75-9) (Choi & Valentine, 2002; Mitch & Sedlak, 2002a):



The ability of chloramines to form nitrosamines with diverse secondary amine precursors has been demonstrated in laboratory studies (Mitch & Sedlak, 2002b). The most efficient formation of a nitrosamine appears to result when chloramine forms a hydrazine intermediate, which reacts with a secondary amine to form the nitrosamine (Choi & Valentine, 2002; Mitch & Sedlak, 2002a).

NDMA formation has been extensively documented (Valentine et al., 2005). The typical ranges produced in drinking-water are shown in Table 2.3. Recent measurements have shown that NDMA is generally present at low concentrations (2–180 ng/l) in chloraminated/chlorinated drinking-water (WHO, 2006). However, these values apply predominantly to water supplies that use monochloramine and whose source waters are significantly impacted by upstream wastewater discharges. A survey of wastewater plants revealed nanogram per litre concentrations, and one plant produced NDMA at concentrations as high as 960 ng/l (Valentine et al., 2005). However, many drinking-water plants produce no NDMA, demonstrating the requirement for the presence of dimethylamine or a precursor of this secondary amine with respect to this formation mechanism. Certain ion exchange resins or polymers used as flocculants have been shown to be precursors of NDMA. The occurrence of *N*-nitrosomorpholine (CAS No. 59-89-2), *N*-nitrosodiethylamine (CAS No. 55-18-5) and *N*-nitrosopyrrolidine (CAS No. 930-55-2) has been observed in some drinking-waters resulting from disinfection when the corresponding secondary amines are also present (Charrois et al., 2004).

2.3.2 Application and fate in foods

Monochloramine is proposed for use as an antimicrobial agent in poultry process chiller water at levels up to 50 mg/l (Russell & Axtell, 2005; USFDA, 2008a).¹

¹ Note that the petition (USFDA, 2008a) was being held in abeyance by the United States Food and Drug Administration (USFDA) as of 1 June 2009 (<http://www.fda.gov/Food/FoodIngredientsPackaging/FoodAdditives/ucm082418.htm>). Note also that the Food Safety and Inspection Service (FSIS) of the United

Chloraminated drinking-water is regulated so as not to exceed 4 mg/l as chlorine (Cl₂) in the United States of America (USA) (USEPA, 2009); the WHO *Guidelines on Drinking-water Quality* guideline value is 3 mg/l as monochloramine (WHO, 2008b).

Table 2.3. NDMA occurrence in drinking-waters disinfected with chlorine or monochloramine^a

Site	Total number of samples	Number of samples with NDMA detected	Percentage of total	NDMA concentrations (ng/l)
Drinking-water plant influents	81	6	7.4	0.6–1.8
Drinking-water plant effluents	81	28	35	0.6–30
Distribution samples	79	49	62	0.6–24

^a From Valentine et al. (2005).

Organic *N*-chloramines have long been known to form in drinking-water treated with chlorine or monochloramine. They are largely regarded as a nuisance, as they reduce the disinfectant activity by decreasing the available free chlorine. There has been little systematic work to characterize the forms of organic *N*-chloramine that are present in water beyond the formation of the *N*-chloramines of α -amino acids. Organic *N*-chloramines produced from α -amino acids present in many foods are generally more readily formed and degrade more readily than compounds either that have no carboxyl group or whose carboxyl group is further removed from the amine group. While slower in formation, dichloramines are more readily formed with non-amino acid nitrogens at physiological pH and probably in drinking-water (Nightingale et al., 2000). At the macromolecular level, exocyclic nitrogens of purine and pyrimidine bases react more readily to form *N*-chloramines; over time, however, the chlorine is transferred to cyclic nitrogen-containing moieties.

In a comparison of total chlorine levels in poultry carcasses immersion-chilled with tap water (presumably chlorinated) or water containing monochloramine at 50 mg/l, the skin and fat levels ranged between 0.3 and 0.7 mg/kg, and the concentrations in the tap water-chilled products were higher than those in the monochloramine-chilled products (Axtell, Russell & Berman, 2006). Levels of lipid peroxidation products as measured by TBARS in roasted chicken tissues were in a small range: in breast meat, from 3.86 mg/kg (tap water) to 2.73 mg/kg (monochloramine roasted and stored); in thigh meat, from 3.62 mg/kg (monochloramine fresh roasted) to 3.39 mg/kg (monochloramine stored and roasted); and in skin and fat, from 2.96 mg/kg (monochloramine stored and roasted) to 2.96 mg/kg (monochloramine fresh roasted). Fatty acid profiles in the various tissues prepared with tap water (presumably chlorinated) versus water with monochloramine at 50 mg/l and roasted showed similar distributions of oleic (33.9–45.2 mg/kg), linoleic (16–18.9 mg/kg), linolenic (0.15–0.39 mg/kg) and arachidonic acids (0.10–1.00 mg/kg).

2.3.3 Nitrosamine residues in foods

There are extensive published data on the presence of nitrosamine residues in numerous types of foods. Their formation is attributable to several mechanisms, of which interaction with active chlorine compounds is a minor contributor. Nitrosamines may be formed by nitrosation of secondary amines by nitrite/nitrous acid, reactions of *N*-chloramines

States Department of Agriculture (USDA) lists the monochloramine poultry chiller antimicrobial treatment system on its February 2006 list of new technologies that it has reviewed and has no objection to their use in FSIS establishments (USDA, 2006).

with secondary amines, thermal/cooking processes and undoubtedly others, including biological processes. Detected nitrosamines have included NDMA, *N*-nitrosoproline (CAS No. 7519-39-0), *N*-nitrosopyrrolidine and *N*-nitrosopiperidine (CAS No. 100-75-4). Concentrations of nitrosamines in foods are summarized in Appendix A at the end of the chapter (Jakszyn et al., 2004a).

In a study of potential in situ nitrosamine formation in three sets of poultry carcasses that were chilled in 1) iced distilled water containing monochloramine at 50 mg/l, 2) iced distilled water containing sodium hypochlorite at 50 mg/l and 3) iced distilled water only, the carcasses were in contact for 6 h versus the usual ~1 h contact. The chickens were then roasted at 160 °C for 45 min (Zentox, 2007). *N*-Nitrosomorpholine, *N*-nitrosodiethylamine, NDMA, *N*-nitrosodibutylamine and *N*-nitrosopiperidine were not detected in any of the samples, with a detection limit of 1 µg/kg. However, *N*-nitrosopyrrolidine was detected in all three treatment conditions at 3.53 µg/kg (monochloramine), 2.92 µg/kg (sodium hypochlorite) and 2.74 µg/kg (distilled water). It initially appeared that the monochloramine-treated roasted chickens showed a slightly increased production of *N*-nitrosopyrrolidine. In a retest in which the cooking time was determined by reaching an internal temperature of 80 °C, the extent of *N*-nitrosopyrrolidine formation was proportional to the cooking time (Zentox, 2007) and independent of chiller treatment water disinfectant. Thus, its formation was not related to the disinfection system.

2.4 Chloramine-T

The chemical name of chloramine-T (CAS No. 127-65-1) is *N*-chloro-4-methylbenzenesulfonamide trihydrate, sodium salt. The molecular formula is $C_7H_7ClNOS^- \cdot Na^+ (3H_2O)$. The trihydrate form of chloramine-T ($C_7H_8ClNO_2SNa \cdot 3H_2O$) is CAS No. 7080-50-4. Other names for chloramine-T are sodium *p*-toluene sulfonchormide, *N*-chloro-*p*-toluenesulfonylamide, sodium chloro[(4-methyl phenyl)sulfonyl]azanide and *N*-chlorotosylamide, sodium salt (Figure 2.1). Chloramine-T is a white crystalline powder that decomposes at 130 °C and is highly soluble in water (~15% at 25 °C; IPCS, 2004). It is used as a biocide and mild disinfectant. The commercial product chloramine-T is synthesized through the chlorination of benzene sulfonamide or *p*-toluene sulfonamide (Haneke, 2002).

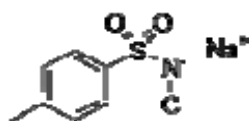


Figure 2.1. Chemical structure of chloramine-T

As an *N*-chloro-compound, chloramine-T contains electrophilic chlorine and can be compared with the *O*-chlorinated sodium hypochlorite or *N*-chloramines. Chloramine-T is nearly neutral (pH typically 8.5). In water, it hydrolyses to hypochlorite (OCl^-). After chlorine is released into solution, the stable residue would be *p*-toluenesulfonamide ($C_7H_9NO_2S$; CAS No. 70-55-3). Chloramine-T is used for disinfection and as an algicide, bactericide and germicide, for parasite control and for drinking-water and food application disinfection. The molecular structure of toluenesulfonylamide is similar to that of *p*-aminobenzoic acid, an intermediate in bacterial metabolism that can be disrupted by this sulfonamide. Therefore, chloramine-T is capable of inhibiting bacterial growth by two mechanisms, with both the phenylsulfonamide moiety and the electrophilic chlorine. It is a

method for delivering stabilized chlorine. Chloramine-T is used to disinfect food contact surfaces and equipment that are then specified to be rinsed with water prior to use. Solution concentrations are 0.3–0.5%. As the surfaces are specified to be rinsed with clean water prior to use, the amounts of either chloramine-T or *p*-toluenesulfonamide that could be transferred to food would be very small (Axcentive, 2008).

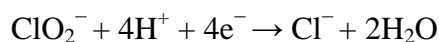
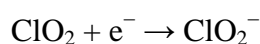
2.5 Chlorine dioxide

Chlorine dioxide (ClO₂; CAS No. 10049-04-4) is an antimicrobial agent recognized for its disinfectant properties since the early 1900s. The mechanism of action by which chlorine dioxide inactivates microorganisms is not entirely understood. However, it is known that chlorine dioxide kills microorganisms by either altering or disrupting transport of nutrients across the cell wall and also penetrating into the cell and disrupting protein synthesis (Young & Setlow, 2003; EFSA, 2005).

2.5.1 Chemistry

Chlorine dioxide is a greenish-yellow gas at room temperature that is very soluble in water (EFSA, 2005). It may be produced by 1) mixing a solution of chlorine with a solution of sodium chlorite, 2) acidification of chlorates with hydrochloric or sulfuric acid, 3) reduction of chlorates in acid medium, 4) reacting acids with chlorites and 5) electrolysis, using sodium chloride, sodium chlorite and water (Dychdala, 2001).

The chemistry of chlorine dioxide differs from that of other chlorine compounds, in that hypochlorous acid is not formed from reduction of chlorine dioxide. Chlorine dioxide is reduced in water, generating the chlorite ion, which is then reduced to chloride ion:



In the absence of oxidizable substances and in the presence of alkali in water, chlorine dioxide is reduced, generating chlorite and chlorate ions:

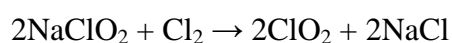


The chlorite ion is further reduced to the chloride ion, as shown above.

Chlorine dioxide has a relative molecular mass of 67.45, a melting point of –59 °C, a boiling point of 11 °C and a solubility of 3.01 g/l at 25 °C and 4.6 kPa.

2.5.2 On-site generation of chlorine dioxide

Because chlorine dioxide is unstable as a gas, it is almost always used as a dissolved gas in water at a concentration of 0.5–10 g/l, and it must be generated on site at the point of use:



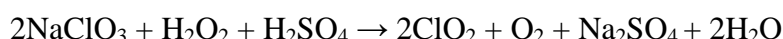
Whereas either the oxidation or acidification of sodium chlorite solution will generate chlorine dioxide, the oxidative method gives much better yields. Most commercial generators

use sodium chlorite as the common precursor chemical to generate chlorine dioxide for drinking-water application (USEPA, 1999). Chlorine dioxide is 10 times more soluble than chlorine gas in water, depending upon the pH, and does not hydrolyse in solution. It remains as a “true” dissolved gas that retains its biocidal properties throughout the entire pH 2–10 range (SCVPH, 2003).

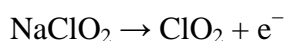
A combination of sodium hypochlorite (NaOCl) and hydrochloric acid (HCl) solutions is also used when chlorine gas, the most common oxidizing agent, is not desired:



Chlorine dioxide can also be generated from the reaction of aqueous solution of sodium chlorate with hydrogen peroxide and sulfuric acid:



or from electrolysis of an aqueous solution of sodium chlorite:



Conversion of sodium chlorite to chlorine dioxide by chemical oxidation can exceed 95%. The USFDA (2005) requires that the generator effluent contain at least a weight fraction of 90% of chlorine dioxide with respect to all chlorine species, as determined by Method 4500 ClO_2 -E of *Standard Methods for the Examination of Water and Wastewater* (APHA, AWWA & WEF, 1998).

2.5.3 Application and fate in foods

Chlorine dioxide gas and liquid formulations have many commercial food uses: 1) washing fruit and vegetables, 2) disinfecting meat and poultry, 3) disinfecting fish and seafood, 4) disinfecting food processing equipment and 5) sanitizing water. In the USA, chlorine dioxide is currently regulated for use as an antimicrobial agent in water used for poultry processing and in water used to wash fruit and vegetables that are not raw agricultural commodities (when followed by a potable water rinse), in an amount not to exceed 3 mg/kg as residual chlorine dioxide (USFDA, 2005). Once applied, chlorine dioxide quickly breaks down into chlorite, chlorate and chloride ions.

2.5.3.1 Fresh produce

Chlorine dioxide is efficacious on a variety of vegetables and fruits largely because its efficacy is little affected by pH and organic matter and it does not react with ammonia to form chloramines, as is the case with sodium hypochlorite and hypochlorous acid. Traditionally, aqueous chlorine dioxide at concentrations of 50–200 mg/kg is widely used to wash fruits and vegetables; however, its effectiveness is limited to a reduction of 1–2 log colony-forming units (cfu) for pathogenic and spoilage bacteria (Brackett, 1992).

Washing produce with an aqueous chlorine dioxide solution has limited efficacy due to the hydrophobic nature of the produce and organic matter on its surface. However, as a gas has greater surface penetration than a liquid, chlorine dioxide gas may be more effective for surface sanitation than aqueous chlorine dioxide (Han et al., 2001). Treatment of cut and peeled fruits and vegetables with dilute chlorine dioxide solution (approximately 10 mg/kg) did not result in the detection of any halocarbons (USFDA, 1994).

2.5.3.2 Poultry and red meat

Poultry chiller water typically initially contains chlorine dioxide at 20–50 mg/l, which rapidly decomposes to chlorite and chlorate in a ratio of 7:3, leaving generally approximately 5% of the initial chlorine dioxide concentration. Thus, the resulting concentrations in poultry chiller water are approximately 2.5 mg/l as chlorine dioxide, 33 mg/l as chlorite and 14 mg/l as chlorate (SCVPH, 2003). Chlorite itself is an oxidant and can be ultimately reduced to chloride (reduction potential: +0.76 V). The poultry carcasses would absorb chlorite and chlorate, which may react with components of poultry tissues during processing and storage or be further reduced during the poultry chilling process. Hence, a decontamination process of 1 h applying chlorine dioxide would result in maximum residue levels of 0.13 mg/kg carcass for chlorite and 0.06 mg/kg carcass for chlorate (SCVPH, 2003). The poultry will be cooked prior to consumption, so chlorine-containing residues would be volatilized or react to form more innocuous species (e.g. chloride), which would reduce the level of any residues of chlorine dioxide and its by-products (chlorite and chlorate) on poultry as consumed.

Chlorine dioxide is expected to react with poultry components (i.e. biomolecules such as lipids, vitamins, proteins, etc.) as well as organic materials present in chiller water. Studies of TBARS values for malonaldehyde, a secondary lipid oxidation product, and fatty acid profiles have suggested that the potential lipid oxidation in poultry (USFDA, 1993) and ground beef (Jiménez-Villarreal et al., 2003) is not significant. The use of a chlorine dioxide solution (approximately 3 mg/kg) on poultry did not appreciably affect TBARS values of chilled poultry (USFDA, 1993). Furthermore, there is no consistent pattern in fatty acid levels that would suggest more pronounced oxidation and loss of unsaturated fatty acids from chlorine dioxide-treated poultry compared with untreated poultry. TBARS analyses have also indicated that chlorine dioxide-treated (200 mg/l) beef trimmings and untreated ground beef patties showed little differences in lipid oxidation (Jiménez-Villarreal et al., 2003).

2.5.3.3 Fish and other seafood

Chlorine dioxide is employed as a disinfectant in water and ice used to rinse, wash, thaw, transport or store seafood. No chlorine residuals were present following chlorine dioxide treatment (10–40 mg/l). Also, total organic halogen analysis of shrimp and crawfish indicated that no chlorine by-products were produced from sanitizing treatment with chlorine dioxide (Kim et al., 1999).

2.5.4 *Reactions with food components*

Chlorine dioxide in water and DBP chemistry have been described by Rice & Cotruvo (1978). Aqueous chlorine dioxide can react with carbohydrates, lipids, amino acids, peptides and proteins (Fukayama et al., 1986; Rice & Gomez-Taylor, 1986). Chlorine dioxide, which also contains a mixture of chlorite and chlorate in water, acts primarily as an oxidant rather than as a chlorinating agent, and its redox potential in aqueous solution ($\text{ClO}_2 + \text{e}^- = \text{ClO}_2^-$, 1.15 V) is less than that of hypochlorous acid ($\text{HClO} + \text{H}^+ + 2\text{e}^- = \text{Cl}^- + \text{H}_2\text{O}$, 1.49 V). Therefore, chlorine dioxide is likely to be less reactive and produce fewer by-products than chlorine in the reaction during food processing, such as in poultry chiller water (Tsai, Higby & Schade, 1995). Chlorine dioxide is a comparatively weak oxidizing agent and has a lower oxidation potential than ozone, chlorine or hypochlorous acid. Because chlorine dioxide has lower oxidation strength, it is more selective in its reactions. Typically, chlorine dioxide will react with compounds that have activated carbon bonds, such as phenols, or with other active

compounds, such as sulfides, cyanides and reduced iron and manganese compounds (Fukayama et al., 1986; SCVPH, 2003). Most importantly, chlorine dioxide is very specific in its reactivity and enters into only a few side reactions compared with chlorine. Further, if chlorine dioxide is pure, it does not chlorinate organic material and therefore does not form THMs and other chlorinated DBPs.

Chlorine dioxide can oxidize simple carbohydrates (e.g. glucose) to form carbonyl derivatives that are subsequently oxidized to carboxylic acids. Polysaccharides (e.g. cellulose) are also susceptible to oxidation and may produce gluconic acid. However, some of these reactions require elevated temperatures ($>80^{\circ}\text{C}$) and are not likely to occur in foods treated with aqueous chlorine dioxide unless processed under elevated temperatures. Further, meat, poultry and fish do not contain carbohydrates in appreciable amounts.

Proteins are subject to oxidation, substitution and addition reactions following treatment with aqueous chlorine dioxide. However, no significant effects on the protein content of salmon and red grouper fillets were reported after treatment with chlorine dioxide (20–200 mg/l in brine solution for 5 min). Also, there was no obvious change in the lipid content or fatty acid composition in both salmon and red grouper fillets after treatment (Kim et al., 1998). Therefore, there are no specific data available on chlorine dioxide by-product formation from fish proteins or lipids. Furthermore, no effects on the vitamin content or on proximate composition of fish have been reported, with the exception of significant reductions in thiamine (salmon and red grouper) and riboflavin (red grouper) levels after treatment (Kim et al., 1998).

Unsaturated fatty acids in lipids can react with chlorine dioxide and produce a variety of compounds, such as unsaturated ketones, chloroketones, chlorohydrins, dichloro-addition products and epoxides (Rice & Cotruvo, 1978; Rice & Gomez-Taylor, 1986). Saturated aliphatic hydrocarbons are neither oxidized nor chlorinated by chlorine dioxide or chlorine. In commercial poultry chiller water in the presence of chlorine, saturated and unsaturated aliphatic aldehydes (pentanal, hexanal, heptanal, octanal, *trans*-2-octenal, nonanal, *trans*-2-nonenal, decanal, 2,2-nonadienal, *trans*-2-decenal, 2,4-decadienal and *trans*-2-undecenal) were detected by gas chromatographic/mass spectrometric (GC/MS) analysis, and hexanal and nonanal were the two major aldehydes detected (Tsai, Mapes & Huxsoll, 1987). The presence of aldehydes is indicative of autoxidation in the poultry chiller water.

Chlorine dioxide is relatively inert towards individual amino acids, and reactions are pH dependent (Tan et al., 1987). Chlorine dioxide oxidizes tryptophan to form indoxyl, isatine and indigo red (Fukayama et al., 1986). Tyrosine formed dopaquinone upon oxidation by chlorine dioxide. Sulfur-containing amino acids (cystine and methionine) are oxidized to bisulfoxide and sulfonic acid derivatives (Rice & Gomez-Taylor, 1986). The reaction of aqueous chlorine dioxide with peptides and proteins is considered to be mainly due to interaction with individual amino acid moieties in the peptides.

Chlorine dioxide, unlike chlorine, does not react with ammonia or water (Rice & Gomez-Taylor, 1986). Additionally, the reaction of the bromide ion (Br^-) with chlorine dioxide is thermodynamically unfavourable. However, with intense sunlight and high concentrations of chlorine dioxide, chlorine dioxide does oxidize the bromide ion to hypobromite (BrO^-) and bromate (BrO_3^-) (Rice & Gomez-Taylor, 1986).

Phenols and hydroquinones can be oxidized in reactions with chlorine dioxide; *p*-benzoquinone and aromatic carboxylic acids are produced when chlorine dioxide is present in excess (Wajon, Rosenblatt & Burrows, 1982). Chlorine dioxide does not produce THMs from reactions with humic acid and other natural materials in raw water when pure, but it is reported to produce oxidation products (i.e. benzenepolycarboxylic acids, aliphatic dibasic acids, carboxyphenylglyoxylic acids and aliphatic monobasic acids). Several derivatives of

furan and dioxane were also identified in the reaction with humic acid and other natural materials (Rice & Gomez-Taylor, 1986).

A trace amount of chloroform ($<2\text{--}30\text{ }\mu\text{g/kg}$) was reported to be formed when poultry carcasses were exposed to water containing chlorine dioxide (Robinson, Mead & Barnes, 1981). However, this volatile compound was considered to be an artefact of the GC/MS analytical method, formed as a result of the reaction between chlorine dioxide and 2,6-diphenyl-*p*-phenylene oxide that was used in the sample concentrator, and was not formed by the reaction of chlorine dioxide (USFDA, 1993). Also, the above discussion on the lack of volatile halocarbons (i.e. chloroform) being formed in the treatment of fresh produce with chlorine dioxide also supports the absence of chlorination reactions.

More than 40 DBPs were detected in finished drinking-water from a water plant using chlorine dioxide (Richardson et al., 1994). Multispectral identification techniques were employed, but the products were not quantified. The predominant identified products were organic esters, acids and olefins, and only two aldehydes (benzaldehyde and ethylbenzaldehyde) were detected. A few halogenated compounds were detected, probably from some chlorine in the treatment process. Numerous aliphatic carboxylic acids were detected, including maleic acid/anhydride. It is possible that other aldehydes were formed and oxidized during treatment or processing, and also that some of the products were formed from precursors that were not ordinarily part of the natural organic matter (NOM) in the water.

2.5.5 Summary

Chlorine dioxide may induce chemical changes in food. The residues or transformation products that could possibly result from food processing with chlorine dioxide are inorganic oxychlorine anions (i.e. chlorite, chlorate), chloroorganics (i.e. chlorinated lipids, chlorinated proteins) and oxidized organics (i.e. oxidized lipids, oxidized amino acids).

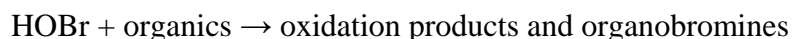
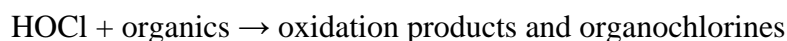
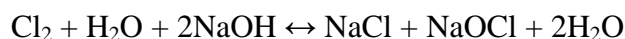
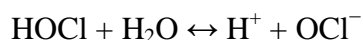
2.6 Hypochlorite-related compounds (chlorine gas, sodium hypochlorite, calcium hypochlorite, hypochlorous acid, hypochlorite ion)

2.6.1 Chemistry

Chlorine, whether in the form of chlorine gas (Cl_2 ; CAS No. 7782-50-5) or as the solids sodium hypochlorite (NaOCl ; CAS No. 7681-52-9) or calcium hypochlorite (Ca(OCl)_2 ; CAS No. 7778-54-3), dissolves in water to form hypochlorous acid (HOCl ; CAS No. 7790-92-3) and hypochlorite ion (OCl^-). Chlorine is the most common form of active chlorine used in food sanitation; it is certainly the most common disinfectant used in drinking-water and wastewater treatment. It was introduced into drinking-water treatment in the first decade of the 20th century and resulted in immediate reductions in the risk of transmission of waterborne diseases. Drinking-water treatment and chemistry are of interest in this food context, because chlorinated drinking-water or more highly chlorinated water is frequently used as the vehicle for food contact sanitation, and some of the chemical products in the water may be accumulated to some degree in the food product, in addition to whatever products form from the contact of the food with the disinfectant.

Chlorine is produced from electrolysis of sodium chloride and is provided commercially as chlorine gas or in various concentrations in basic solution as the hypochlorite (e.g. common bleach), partly due to handling and storage difficulties associated with gaseous chlorine (Montgomery, 1985). Electrolysis of sodium chloride salt that contains some

bromide will also produce hypobromous acid (HOBr) and bromate as by-products, which will be carried forward in the chlorine product:



A chlorine solution at about pH 7.4 is approximately 50% hypochlorite and 50% hypochlorous acid (Asano et al., 2007); at pH 10, it is approximately 100% hypochlorite. It should not be used below pH 5 due to the excessive presence of gaseous chlorine in the equilibrium mixture. The biocidal effectiveness is greatest in the acid form as hypochlorous acid, but hypochlorite is also an effective, but slower-acting, biocide.

Hypochlorites are available as powders or liquids, depending on the type of salt used. Calcium hypochlorite comprises the majority of the powdered offerings, whereas sodium hypochlorite and potassium hypochlorite are generally available as liquid solutions (Dychdala, 2001). Commercial solutions of sodium hypochlorite usually contain 12.5–17% available chlorine (household bleach may be approximately 5–10% sodium hypochlorite), but the composition will change upon storage, particularly under the influence of light and heat; chlorate (not a disinfectant) and chlorite are major products of this decomposition (disproportionation). For example, a 16.7% solution stored at 26.7 °C will lose 10% of its available chlorine in 10 days, 20% in 25 days and 30% in 43 days (Asano et al., 2007), so it should be stored in a cool place and used relatively quickly. For that reason, disinfectant solutions are made to approximate concentrations, and then concentrations are specifically determined by measurement of active chlorine residuals.

Chlorine as hypochlorous acid or hypochlorite is a very reactive chemical, and it can engage in numerous chemical processes under mild environmental conditions, including in iced water. It can function as both an oxidizing agent and a halogenating agent (Rice & Gomez-Taylor, 1986). Oxidation is probably the predominant chemical process occurring in chlorine's water and food contact applications, but the halogenated by-products have received the most attention. Chlorine will oxidize bromide to hypobromous acid, which is an active brominating agent. The chemistry and distribution of by-products produced differ somewhat with the pH of the solution as well as the composition of the precursor chemicals that are available for reaction. For example, in chlorination of bromide-containing fresh waters or seawater, which contains bromide at about 60–80 mg/l, organobromine DBPs will predominate over organochlorine DBPs (Huang, Chen & Peng, 2004; Westerhoff, Chao & Mash, 2004; Cotruvo et al., in press). Although chlorine produces DBPs, its high efficacy, ease of use and low cost make it the disinfectant of choice in many applications.

There are numerous detailed assessments and reviews of the chemistry and toxicology of chlorine and by-products in water (IPCS, 2000; Woo et al., 2002; Bull et al., 2006; USEPA, 2006; WHO, 2008b), and some in foods (FAO/WHO, 2000). Several of those DBPs formed between chlorine and organic substances have been regulated (Appendix B), either

for their own sake or as THMs and HAAs, principally as indirect indicators of the presence of other non-quantified or unidentified by-products (Cotruvo, 1981, 1982).

2.6.1.1 Chemistry of chlorine interactions with organic matter

The chemistry of and by-product formation from chlorine interactions with foods is much less studied than that of interactions with organic matter in drinking-water. This is partly because the chemistry of food contact is much more complex than drinking-water chemistry; thus, direct comparisons are difficult to make in the absence of adequate information on chlorine chemistry in food contact. Analyses are much more difficult because of the medium and contact conditions. In drinking-water, many of the halogenated DBPs are small molecules, hydrophobic and volatile; some have higher molecular weights. Contact times between disinfectant and precursor chemicals may be several days during water storage and distribution to consumers, and the formation chemistry will continue as long as disinfectant and precursors are present. Heating the water for beverage use will drive reactions to completion, consume the residual disinfectant and deplete volatile organics and DBPs, but less volatile substances will remain.

With food contact, precursor chemicals that can react with the disinfectant could include the complex natural organics in the water and fats/lipids, proteins, carbohydrates and numerous other chemical products in the food. For example, it has been demonstrated under *in vitro* conditions that hypochlorous acid is reactive with both free and peptide-bound tyrosine, *N*-acetyltyrosine and bovine serum albumin, and it can generate chlorotyrosine, 3,5-dichlorotyrosine and chlorinated aldehydes (Fu et al., 2000). However, food contact conditions are much different from *in vitro* conditions, and they differ among meats in cold water chillers and sprays, iced seafood and sprayed fresh fruits and vegetables. As foods are sprayed or immersed in water containing disinfectants, water may be absorbed into the food product and carry with it DBPs that were present in the water. This would add to the potential exposure from the food. On the other hand, storage and/or cooking of the foods probably result in losses of DBPs from volatilization and degradation.

2.6.2 Disinfection by-products in drinking-water

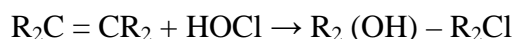
Chlorinated/brominated by-products from chlorination are the most extensively studied chemicals produced from disinfectants in contact with water and food. One reason is that, compared with non-halogenated compounds, they are more readily separated from water solutions for analysis because of their hydrophobicity. In the 1970s, when standard gas chromatographic analytical procedures were first used to analyse drinking-water, it was discovered that THMs were being formed in microgram per litre concentrations from reactions of chlorine/hypochlorite with the NOM commonly present in water sources, particularly in surface water sources.

The chemistry of chlorine interacting with organic precursors in drinking-water is highly complex, and most of the specific precursors and mechanisms are not known in detail. There may be a limited relationship to DBPs from chlorine and food contact. The complexity is probably best illustrated by the numerous categories of halogenated by-products that have been detected in one or more studies (see Tables 2.4 and 2.5 below). Naturally occurring polyphenolic compounds are some of the most likely precursors for many of the products. THMs are halogen-substituted single-carbon compounds with the general formula CHX_3 , where X may be fluorine, chlorine, bromine or iodine, or a combination thereof. The THMs of principal interest are chloroform (CHCl_3 ; CAS No. 67-66-3), bromodichloromethane (BDCM) (CHBrCl_2 ; CAS No. 75-27-4), dibromochloromethane (DBCM) (CHBr_2Cl ; CAS

No. 124-48-1) and bromoform (CHBr_3 ; CAS No. 75-25-2); several other THMs have been detected more rarely and at lower concentrations. Since the initial analyses from the 1970s, numerous families and hundreds of individual halogenated DBPs have been identified and quantified in chlorinated drinking-water. Among these are HAAs, HANs, haloketones, halopicrins, halophenols and halofuranones, in addition to non-halogenated oxidized products such as acids, aldehydes and ketones. The THMs and HAAs usually account for the largest portion of the identifiable DBPs in chlorinated drinking-water (up to 50%). Another chemical group of compounds that has been detected at nanogram per litre levels in chlorinated drinking-water is the MX-related chemicals. MX is the common name applied to one member (3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone) of a group of halomethylhydroxy-furanones formed from oxidation, halogenation and ring cleavage of phenolic-type natural organics in the water. They are cyclic lactones or open chain carboxyl compounds and would not be highly volatile. Levels of MX up to 310 ng/l have been detected in drinking-water (Weinberg et al., 2002).

In an attempt to identify substances of interest for further studies, structure–activity techniques and genotoxicity data were applied as a method for pre-screening of 209 DBPs in order to rank them with respect to carcinogenic potential from long-term exposure (Woo et al., 2002). In a study on structure–activity relationships of novel by-product formation from substructures of haloquinones identified in NOM, quantitative structure–activity relationships and analogies with related compounds were used to identify other by-products that could be of interest (Bull et al., 2006). Chemicals identified in this study included those identified by Woo et al. (2002), but the study also provided an additional list of probable by-products. Those considered to be of most concern were a number of halogenated quinones, halogenated cyclopentenoic acid derivatives, halonitriles and various *N*-chloramines. The formation of the major by-products goes through a series of intermediates with various phenolic (Figure 2.2) and other unidentified precursors that naturally occur in surface waters, but may not occur in many foods. Changing from processes that utilize free chlorine to the use of monochloramine has a high likelihood of preserving some of the intermediate species. Figure 2.2 illustrates the changes in products that would be expected by reactions with phenol treated with monochloramine in place of free chlorine. A variety of quinone structures have been shown to occur with monochloramine that will be destroyed by ring cleavage with free chlorine (Heasley et al., 2004). It has long been known that various phenolic precursors are intermediates in the formation of most of the THMs and HAAs. Excess chlorine results in cleavage of the phenolic ring to give rise to haloacids and THMs. If monochloramine is utilized in place of free chlorine to reduce THMs and HAAs, it is likely that higher concentrations of halogenated quinones will be encountered (Heasley et al., 2004; Bull et al., 2006).

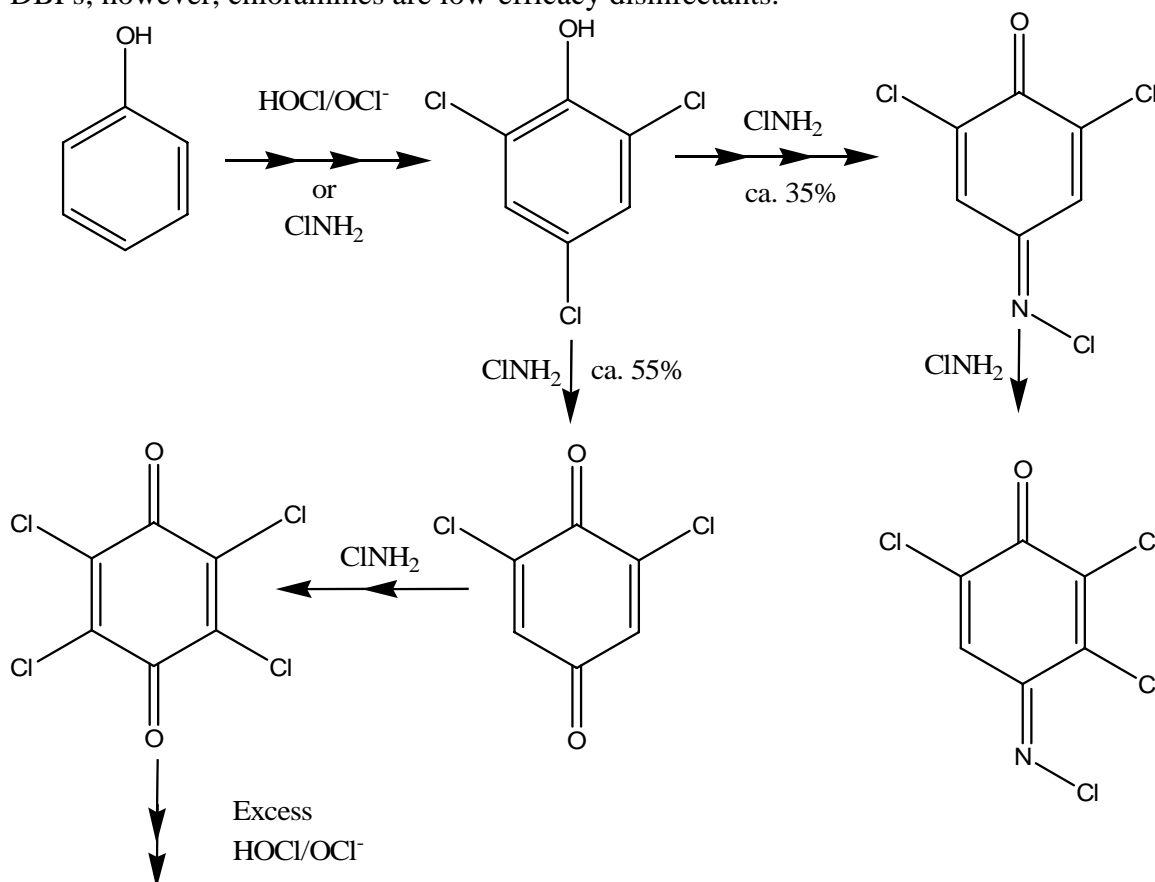
Other basic chemical oxidation processes that can occur include oxidation of alcohols to aldehydes, ketones and carboxylic acids as well as formation of chlorohydrins:



Chlorine will oxidize bromide in water to HOBr , which is a more active halogenating agent than HOCl ; thus, in the presence of bromide, the analogous brominated and mixed halogenated by-products will be formed.

The aggregated total concentration of halogenated organic products in drinking-water may range from a few micrograms per litre in very low organic carbon groundwater or membrane-treated water to perhaps a milligram per litre or more in some waters with high levels of NOM precursors, depending upon the chlorine dosage, quantity of NOM precursors, pH, temperature and contact time. In the presence of ammonia and organic amines,

chloramines will rapidly form. They are poor halogenating and oxidizing agents, so the presence of ammonia will suppress the formation of most of the halogenated and oxidized DBPs; however, chloramines are low-efficacy disinfectants.



Haloacids and aliphatic products

Figure 2.2. Formation of haloquinones

Although many DBPs have been identified, there are good comprehensive quantitative data available for only a few dozen in water supplies. Data from a recent study of 12 utilities in the USA and Canada by the United States Environmental Protection Agency (USEPA) (Weinberg et al., 2002) are provided in Tables 2.4 and 2.5, which are not comprehensive, but are probably indicative of many water supplies. The disinfectants used varied among these utilities, with ozone (one utility) and chlorine dioxide (four utilities) employed in some utilities, but all systems employed chlorine or chloramines at some stage in the treatment. These data may differ slightly from those reported, because the means represent the average of utility means, rather than an overall mean of all samples. There are earlier data sets that are available (e.g. USEPA/AMWA, 1989), but those surveys included fewer by-products. As the USEPA-funded survey included only 12 utilities and mixed disinfectants, it probably does not reflect extreme occurrences of DBPs. Nevertheless, the variation of DBP concentrations among the 12 utilities ranges up to 2 orders of magnitude. It should not be assumed that the concentrations co-vary with one another in dependable patterns among water utilities or even within the same system in different seasons of the year (Wright et al., 2002; Bull et al., 2009).

2.6.3 Disinfection by-products in foods

Chlorine and hypochlorite are commonly used in chillers and sprays for sanitization of food products. Poultry, meats, fish, fruits and vegetables, and other foods (e.g. milk, cheese) are exposed for various periods of time, ranging from seconds to hours (Fukayama et al., 1986). A summary of these treatments is provided in chapter 1. Chlorine and chlorine-containing compounds and by-products present in water used in food processing may penetrate into the surface biofilms to some degree. Quinone derivatives are less likely to be formed in the produce per se but may be formed in processing water and taken up because of their relatively non-polar character. Their stability upon heating is not known.

Table 2.4. Disinfection by-products in 12 drinking-water utilities in the USA and Canada^a

DBP	Number of utilities	Concentration (µg/l) ^b		
		Mean	Median	Range
Chloroform	12	16	12	0.5–47
BDCM	12	10	12	2.2–19
DBCM	12	6.5	4.7	0.1–20.5
Bromoform	12	2.1	0.7	nd–6.4
Dichloriodomethane	12	1.1	0.45	0.08–1.5
Bromochloriodomethane	12	0.4	0.3	nd–2.5
Dibromiodomethane	10	0.29	nd	nd–2.5
Chlorodiodomethane	12	0.11	nd	nd–1.1
Bromodiodomethane	12	0.03	nd	nd–0.4
Iodoform	12	0.04	nd	nd–0.4
Monochloroacetic acid	12	1.6	nd	nd–3.9
Monobromoacetic acid	12	0.3	0.27	nd–1.0
Dichloroacetic acid	12	14	15	1.4–22
Bromochloroacetic acid	12	5.9	4.4	1.7–11
Dibromoacetic acid	12	3.4	1.2	nd–12
Trichloroacetic acid	12	9.4	6.1	0.5–35
Bromodichloroacetic acid	12	4.6	5.5	nd–9.4
Dibromochloroacetic acid	12	2.2	1.5	nd–5.9
Tribromoacetic acid	12	0.12	nd	nd–0.9
Chloroacetonitrile	12	0.07	0.055	nd–0.26
Bromoacetonitrile	12	0.005	nd	nd–0.04
Dichloroacetonitrile	12	1.4	1.2	0.1–4.1
Bromochloroacetonitrile	11	0.8	0.6	nd–2.6
Dibromoacetonitrile	12	0.6	0.3	nd–2.3
Trichloroacetonitrile	12	0.02	nd	nd–0.15
Bromodichloroacetonitrile	12	nd	nd	nd–0.4
Dibromochloroacetonitrile	12	0.01	nd	nd–0.15
Tribromoacetonitrile	12	nd	nd	nd
Dichloroacetaldehyde	12	2.2	1.7	0.4–11.1
Bromochloroacetaldehyde	12	0.5	0.32	nd–1.3
Chloral hydrate	12	2.2	1.8	0.2–5.9
Tribromoacetaldehyde	12	0.19	0.04	nd–0.93
Chloropropanone	12	0.22	0.11	nd–1.1

Use of Chlorine-containing Disinfectants in Food Production and Food Processing

DBP	Number of utilities	Concentration ($\mu\text{g/l}$) ^b		
		Mean	Median	Range
1,1-Dichloropropanone	12	0.61	0.58	0.12–1.3
1,3-Dichloropropanone	12	nd	nd	nd
1,1-Dibromopropanone	12	0.032	nd	nd–0.12
1,1,1-Trichloropropanone	12	1.3	1.4	0.03–3.6
1,1,3-Trichloropropanone	12	0.02	0.02	nd–0.13
1-Bromo-1,1-dichloropropanone	12	0.24	0.2	nd–0.95
1,1,1-Tribromopropanone	12	nd	nd	nd
1,1,3-Tribromopropanone	12	0.005	nd	nd–0.033
1,1,3,3-Tetrachloropropanone	12	0.05	nd	nd–0.26
1,1,1,3-Tetrachloropropanone	12	0.08	0.07	nd–0.13
1,1,3,3-Tetrabromopropanone	12	0.05	nd	nd–0.025
Chloronitromethane	12	0.04	nd	nd–0.16
Bromonitromethane	12	0.02	nd	nd–0.08
Dichloronitromethane	12	0.12	0.24	nd–0.38
Bromodichloronitromethane	12	0.11	nd	nd–0.42
Dibromonitromethane	12	0.07	nd	nd–0.19
Chloropicrin	12	0.26	0.16	0.04–0.92
Bromodichloronitromethane	12	0.32	0.24	nd–1.0
Dibromochloronitromethane	12	0.30	0.18	nd–0.44
Bromopicrin	12	0.35	nd	nd–0.63

^a Adapted from Weinberg et al. (2002).

^b The concentrations reported as “nd” were not detected. The LODs for the various substances were between 0.02 and 3 $\mu\text{g/l}$, but these LODs varied slightly between sampling occasions and analytical methods used.

Table 2.5. Additional analyses of disinfection by-products and total organic halogen in a survey of 12 utilities in the USA and Canada^a

DBP	Number of utilities	Concentration ($\mu\text{g/l}$) ^b		
		Mean	Median	Range
Monochloroacetaldehyde	12	0.42	0.22	nd–1.3
Dichloroacetaldehyde	12	3.4	2.7	0.5–9.5
Bromochloroacetaldehyde	11	1.2	1.1	0.1–3.5
3,3-Dichloropropenoic acid	12	0.43	0.14	nd–2.7
Bromochloromethylacetate	12	0.036	nd	nd–0.4
Monochloroacetamide	8	0.14	nd	nd–0.5
Monobromoacetamide	8	0.24	nd	nd–1.1
2,2-Dichloroacetamide	12	1.5	1.7	nd–3.8
Dibromoacetamide	8	0.87	0.25	nd–2.8
Trichloroacetamide	8	0.51	0.30	nd–1.1
BMX-1	10	0.034	nd	nd–0.13
BEMX-1	10	0.10	nd	nd–0.72
BMX-2	10	0.028	nd	nd–0.15
BEMX-2	10	0.12	nd	nd–0.81

DBP	Number of utilities	Concentration ($\mu\text{g/l}$) ^b		
		Mean	Median	Range
BMX-3	10	0.004	nd	nd–0.04
BEMX-3	10	0.097	nd	nd–0.41
MX	12	0.11	0.020	nd–0.18
Red-MX	2	0.033	nd	nd–0.29
EMX	12	0.013	nd	nd–0.10
ZMX	10	0.011	nd	nd–0.12
Ox-MX	10	nd	nd	nd
Mucochloric acid (ring)	12	0.085	0.01	nd–0.71
Mucochloric acid (open)	12	0.081	0.09	nd–0.19
TOX	12	169	182	65–236

BEMX-1, BEMX-2, BEMX-3: corresponding brominated analogues of EMX; BMX-1: 3-chloro-4-(bromochloromethyl)-5-hydroxy-2(5H)-furanone; BMX-2: 3-chloro-4-(dibromomethyl)-5-hydroxy-2H(5H)-furanone; BMX-3: 3-bromo-4-(dibromomethyl)-5-hydroxy-2H(5H)-furanone; EMX: (*E*)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid; MX: 3-chloro-4-(dichloromethyl)-5-hydroxy-2H(5H)-furanone; Ox-MX: oxidized MX, (*Z*)-2-chloro-3-(dichloromethyl)butenedioic acid; Red-MX: reduced MX, 3-chloro-4-(dichloromethyl)-2(5H)-furanone; TOX: total organic halides; ZMX: (*Z*)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid

^a Adapted from Weinberg et al. (2002).

^b The concentrations reported as “nd” were not detected. The LODs for the various substances were between 0.1 and 3 $\mu\text{g/l}$, but these LODs varied slightly between sampling occasions and analytical methods used.

For example:

- *Carrots*: Cut carrots were washed with chlorinated water at 4 °C, then with warm tap water at 50 °C, and it was reported that by-product formation due to chlorination was negligible (Klaiber et al., 2005).
- *Cheese*: Chloroform was reported at concentrations ranging from 2.4 to 17 $\mu\text{g/kg}$ in cheese (Entz, Thomas & Diachenko, 1982).
- *Butter*: Chloroform was reported at 56 $\mu\text{g/kg}$ and BDCM at 7 $\mu\text{g/kg}$ (Entz, Thomas & Diachenko, 1982).
- *Shrimp*: Following immersion in a 150 mg/l solution of hypochlorous acid, 2% of the chlorine was incorporated into shrimps, with 75% in the edible portion; 73% of the 2% taken up was as chloride ion (Cunningham & Lawrence, 1977).
- *Poultry*: Chloroform (447 $\mu\text{g/kg}$) was found in fresh uncooked poultry after immersion in 50 mg/l aqueous chlorine. However, it was not determined whether the chloroform came from the water or from reactions with the tissues. The highest levels were in depot fat (Robinson, Mead & Barnes, 1981).
- *Poultry*: Chloroform levels were reported in tissues from chickens that had been immersed in chiller water, then stored or roasted immediately; a control used tap water (presumably chlorinated) instead of chiller water (Axtell, Russell & Berman, 2006). The concentrations of chloroform did not vary greatly in all of the tested products and were in the range of 0.27–0.3 mg/kg. The skin and fat chloroform concentrations were very similar for all three conditions and ranged between 0.18 and 0.22 mg/kg.
- *Poultry patties*: No significant differences in triglycerols, phospholipids or fatty acid compositions were found between stored hypochlorous acid and non-chlorinated treated chicken patties (Erickson, 1999).

Semicarbazide ($\text{NH}_2\text{NHCONH}_2$; CAS No. 79-17-4) was shown to be formed in foods under usually extreme conditions of contact and room temperature incubation with hypochlorite solutions at concentrations ranging from 0.015% to 12%. Concentrations of semicarbazide in the range of 1–20 mg/kg were detected only at chlorine concentrations of about 1% and higher. Hypochlorite reactions forming semicarbazide occurred in vitro with arginine, creatine, creatinine and urea, but not with histidine and citrulline, at a hypochlorite concentration of 0.015% (Hoenicke et al., 2004). Under usual food processing conditions, it is unlikely that semicarbazide is formed.

2.6.4 Other reactions with foods

Chlorinated poultry chiller water was analysed by GC/MS for the presence of saturated and unsaturated aliphatic aldehydes (Tsai, Mapes & Huxsoll, 1987). These aldehydes were pentanal, hexanal, heptanal, octanal, *trans*-2-octenal, nonanal, *trans*-2-nonenal, decanal, 2,2-nonadienal, *trans*-2-decenal, 2,4-decadienal and *trans*-2-undecenal. Their presence is indicative of autoxidation occurring in the chiller water, which may also involve the presence of oxidizer sanitizers. There is buildup of filterable and non-filterable solids in chiller water to a variable degree, depending on chiller design, production rate, cleanliness, fat content on the carcass surface and other factors. The solids content tends to reach a steady state from incoming carcasses and overflow as processing continues. The fatty acid and lipid content in the chicken skin and flesh are a function of feed type. The aldehydes identified are predictably formed by autoxidation of fatty acids. From the presence of those acids and esters in chlorinated chiller water, it would be expected that secondary organic chlorine-containing compounds may be formed in the presence of oxygen (Fukayama et al., 1986), but none were detected in the study (Tsai, Mapes & Huxsoll, 1987).

2.7 Sodium dichloroisocyanurate

2.7.1 Chemistry

Sodium dichloroisocyanurate (NaDCC; 1,3-dichloro-1,3,5-triazinane-2,4,6-trione; $\text{NaC}_3\text{N}_3\text{O}_3\text{Cl}_2$) is the sodium salt of a chlorinated hydroxytriazine. It is a form of stabilized chlorine, which provides a convenient way to handle chlorine. The product contains 55–62% available chlorine; it is very soluble in water. When dissolved in water, it undergoes equilibrium-controlled dissociation into chlorine and several isocyanurate chemicals and ultimately isocyanuric acid as the stable end product (FAO, 2003). It is marketed in an anhydrous, >97% pure form (CAS No. 28933-78-9) and as a dihydrate, >99% pure form ($\text{NaC}_3\text{N}_3\text{O}_3\text{Cl}_2 \cdot 2\text{H}_2\text{O}$; CAS No. 51580-86-0). The principal impurity in NaDCC is sodium chloride.

2.7.2 Application and fate in foods

NaDCC is used like chlorine, especially for outdoor swimming pool disinfection, because it reduces the solar decomposition of hypochlorite, as an emergency drinking-water disinfectant for short-term use and in food sanitation applications. In its applications, it can be treated as though it were chlorine, although because of its control of chlorine release and concentration in solution, it should produce smaller amounts of DBPs. In addition, a residue of stable cyanuric acid will remain in solution (e.g. 1 mg of anhydrous NaDCC corresponds to 0.59 mg of cyanuric acid).

An example of a food sanitizing application includes treatment of salad vegetables. NaDCC was used in a solution of 100 mg/l available chlorine, and the pH was adjusted to 5 with hydrochloric acid (Nicholl, McInerney & Prendergast, 2004). Salad greens and cabbage were soaked and drained. The maximum free available chlorine on the vegetables was 0.8 mg/l, and cyanuric acid residues were not detected.

2.8 1,3-Dibromo-5,5-dimethylhydantoin (active bromine)

DBDMH (CAS No. 77-48-5) is used as an alternative to active chlorine in the disinfection of water.

2.8.1 Chemistry

DBDMH is a stable, white crystalline solid. Dissolution of DBDMH in water quantitatively produces two molecules of hypobromous acid and one molecule of dimethylhydantoin (DMH) (Figure 2.3), which are in equilibrium until the hypobromous acid is consumed in other reactions. However, atomic bromine may be postulated as a transfer intermediate that could convert to hypobromous acid. Hypobromous acid, like hypochlorous acid, is an excellent oxidizing agent and has found use as a disinfectant to treat water for drinking, recreational waters (e.g. swimming pools, spas and hot tubs) (Seidel, 2004) and water used in food processing.

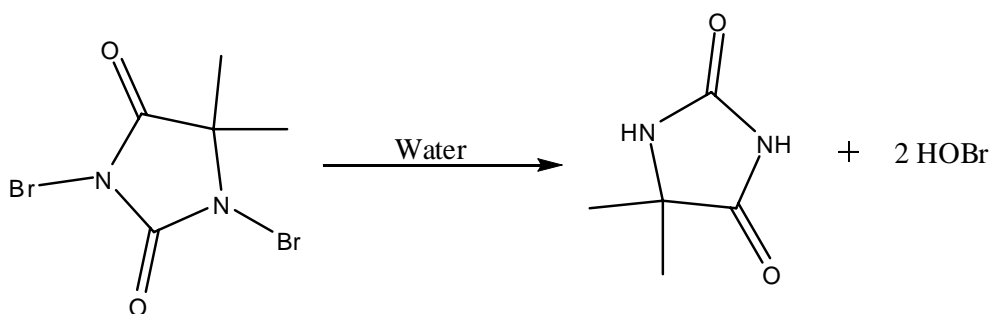


Figure 2.3. Hydrolysis of DBDMH

2.8.2 Application and fate in foods

DBDMH is authorized in the USA for use as a disinfectant in water and ice used in the processing of poultry and as a disinfectant in water used to process beef hides, carcasses, heads, trim, parts and organs. The use level of DBDMH in poultry process water and ice is limited to 100 mg/kg as available bromine, which is equivalent to 90 mg/kg as DBDMH. The use level of DBDMH in process water used to treat beef carcasses is limited to 300 mg/kg as available bromine, or 270 mg/kg as DBDMH. As DBDMH decomposes in water and with heat, it is not expected to be present on food at the time of consumption. However, its breakdown product, DMH, would be an expected residue on foods that are not washed or further processed before consumption. In addition, other DBPs, such as organobromine DBPs, bromide and bromate, would also be potential residues on food treated with aqueous solutions of DBDMH.

2.8.2.1 DMH

The amount of DMH that remains on poultry carcasses after processing was estimated using 1) the maximum use level of DBDMH in poultry chiller water (90 mg/kg), 2) the water uptake by poultry carcasses (8% by weight), 3) the assumption that DMH and other breakdown products will be absorbed by the carcass in an amount proportional to the amount of water taken up by the carcass while it is in the chiller tank and 4) the amount of chiller water allowed to be recirculated (50% in the USA). The concentration of DMH on raw poultry is estimated to be 0.005 mg/g. The concentration of DMH in the chiller tank at any given time would be no greater than 60 mg/kg (USFDA, 2003). Therefore, the concentration of DMH in poultry would not be greater than 0.005 mg/g chicken, or 5 mg/kg chicken.

The maximum use level of DBDMH in water used to process beef is limited to 300 mg/kg as active bromine, which is equivalent to 270 mg/kg as DBDMH. The amount of DMH that remains on beef carcasses after processing can be estimated using 1) the maximum use level of DBDMH in water applied to beef as a spray (270 mg/kg), 2) the assumption that the amount of DMH absorbed by the carcass is proportional to the amount of water taken up by the carcass while it is treated with the disinfectant spray (1%) (USFDA, 2008b) and 3) the molecular weights of DBDMH (285 g/mol) and DMH (128 g/mol). The concentration of DMH on raw beef would be approximately 0.001 mg/g.

2.8.2.2 Bromide

The quantity of residual bromide on a poultry carcass treated with a solution of DBDMH can be estimated using assumptions 2, 3 and 4 from section 2.8.2.1 above and the worst-case assumption that 100% of the bromine liberated from DBDMH is converted to bromide; however, organobromine products actually account for a portion of the initial bromine. Therefore, a worst-case estimate for residual bromide is 6 mg/kg in raw chicken (USFDA, 2003). Using a conservative estimate of residual bromide on beef, assuming 100% conversion of the active bromine to bromide, the concentration of bromide on beef would be approximately 0.002 mg/g.

2.8.2.3 Trihalomethanes

Chloroform is not expected to be present in the poultry or poultry processing water or ice beyond what is normally observed in potable water produced using accepted disinfection processes. However, the USFDA (2003) estimated a bromoform concentration of approximately 0.005 µg/g raw chicken and DBCM or BDCM concentrations of less than 0.0004 µg/g raw chicken. The residue values for DBCM and BDCM are data from the USFDA (2003) indicating that DBCM and BDCM were not detected in the poultry process water above the LOD of 5 µg/l.

Chloroform is not expected to be present in the beef or beef processing water beyond what is normally observed in potable water produced using accepted disinfection processes. However, the average concentration of bromoform found in the spray used to treat beef was 5.5 µg/kg. The above assumptions give a residual bromoform level of 0.000 06 µg/g beef (USFDA, 2008b). The presence of DBCM and BDCM on beef is related to the method used to generate the potable water used in the beef processing water and to the use of DBDMH. Data from the USFDA (2008b) indicate that these compounds were not detected in the process water above the LOD of 5 µg/kg. Using the assumptions above and the LOD, the concentration of either DBCM or BDCM would be less than 0.000 05 µg/g raw beef.

2.8.2.4 Bromate

Although bromate may potentially be generated in small amounts during the use of DBDMH and may migrate to poultry during processing, bromate is a strong oxidant (Seidel, 2004) and is expected to be reduced to bromide during cooking (USFDA, 2003). Therefore, bromate is not expected to be present on food at the time of consumption.

2.8.2.5 Brominated and iodinated compounds

The type of water used in food processing and the disinfectants added may have an influence on the formation of brominated and iodinated compounds. The use of seawater to process seafood will be associated with higher concentrations of bromide and some iodide. These salts will then be converted to hypobromous or hypoiodous acids in the presence of chlorine and some other disinfectants and result in the production of brominated and iodinated by-products in addition to chlorinated by-products. Organobromine by-products will also be produced when fresh waters containing bromide are chlorinated. Reactions with proteins or lipids in the foods may be possible; however, there is no reported evidence for the formation of brominated organic species in food under conditions approved in, for example, the USA (USFDA, 2003, 2008b).

2.8.3 Summary

Considering the available data on treatment of poultry and beef with DBDMH, it is unlikely that significant amounts of DBPs would be formed and would remain as residues. Chemical residues could include DMH, bromide, DBCM, BDCM and bromoform.

2.9 Ethyl lauroyl arginate

Ethyl lauroyl arginate (synonyms: lauramide arginine ethyl ester, LAE) is synthesized by esterifying L-arginine with ethanol to obtain ethyl arginate hydrochloride (HCl), which is then reacted with lauroyl chloride to form the active ingredient ethyl-*N*^α-lauroyl-L-arginate hydrochloride (C₂₀H₄₁N₄O₃Cl; CAS No. 60372-77-2). It is a cationic surfactant that has a wide spectrum of activity against bacteria, yeasts and moulds. *N*^α-Lauroyl-L-arginine is a principal by-product in the manufacture of ethyl-*N*^α-lauroyl-L-arginate HCl and is also formed by enzymatic action in fresh food. In the USA, ethyl lauroyl arginate is generally recognized as safe for use on meat and poultry products and other food products, including flavoured drinks, fish, dried legumes and prepared salads, at levels up to 200 mg/kg (FAO, 2008).

The extent of hydrolysis of ethyl lauroyl arginate under various conditions was determined by measurement of the percentage of ethyl-*N*^α-lauroyl-L-arginate HCl recovered in each sample. In 24 out of 33 samples, no hydrolysis process took place. Only 9 samples showed interaction with the components of the sample. In 4 of these 9 samples, ethyl lauroyl arginate was hydrolysed to *N*^α-lauroyl-L-arginine, which is the main metabolite. In the remainder of the samples, in which it was combined with nitrite, meat or soya proteins or ovo-albumin or lacto-albumin, more extensive hydrolysis occurred. In spite of this, no formation of nitrosamines was observed (FAO, 2008).

The stability of ethyl-*N*^α-lauroyl-L-arginate HCl was evaluated in eight different food matrices. Five of these matrices were examples of processed foods, and the rest were examples of fresh foods. It was found to be stable throughout the duration of the study in all processed food matrices; only in the fresh food matrices was a decrease in concentration observed (FAO, 2008).

2.10 Ozone (active oxygen)

Ozone (triatomic oxygen, O₃; CAS No. 10028-15-6), either in the gaseous phase or in an aqueous solution, is used as a disinfectant in the processing, treatment and storage of foods, including fresh produce, meat and poultry. Ozone treatment is approved for such uses in the USA (USFDA, 2003) and Australia (FSANZ, 2006). There are currently no restrictions on its use, save that Good Manufacturing Practice must be followed.

2.10.1 Chemistry and preparation

Ozone is unstable and must be generated at the point of application using one of three major methods: 1) irradiation of air using high-intensity UV lamps (185 nm), 2) corona discharge (used to produce large volumes of ozone) and 3) passage of dry air or oxygen across a high-voltage discharge gap (Kirk-Othmer, 2004). Additional methods of generation of ozone have been described (Kim, Yousef & Dave, 1999). In the gas phase, the decomposition of ozone is catalysed by light, trace organic matter, nitrogen oxides, peroxides, metals and metal oxides. The mechanisms of decomposition are outlined in Figures 2.4 and 2.5, where M represents any species present in the gas phase (Kirk-Othmer, 2004).

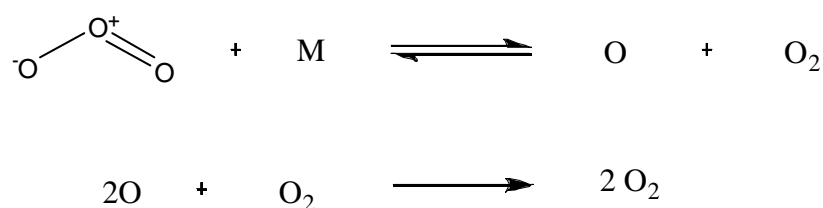


Figure 2.4. Decomposition of ozone

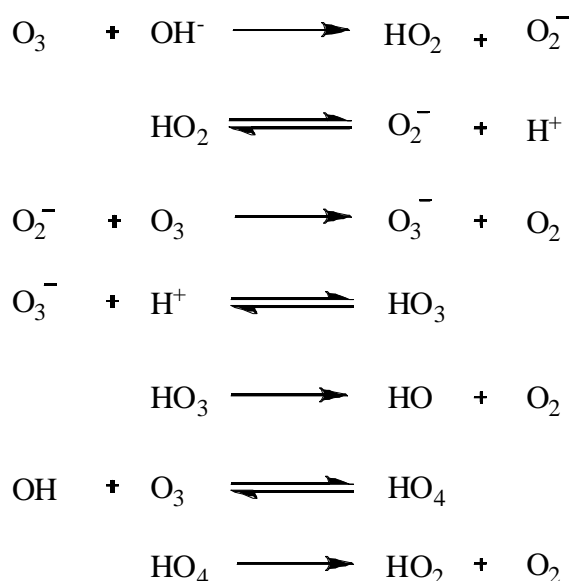


Figure 2.5. Decomposition of ozone in water

Although the decomposition of gaseous ozone is relatively simple and produces only oxygen as a by-product, the decomposition of ozone in the aqueous phase is far more

complex, generating a large number of reactive species that can participate further in numerous side reactions or hasten its decomposition. In pure water, ozone decomposes by a radical chain reaction initiated by hydroxide and propagated by superoxide and hydroxyl radicals (Kirk-Othmer, 2004).

Ozone in water and its reaction product and by-product chemistry have been described in an early review (Rice & Cotruvo, 1978). Owing to its high oxidation potential ($E^0 = 2.07$ V), ozone reacts with a large number of compounds. For example, halogens, with the exception of fluorine, form hypohalite ions that, in the presence of excess ozone, are oxidized to halites (Rice & Cotruvo, 1978; Rice & Gomez-Taylor, 1986; Kirk-Othmer, 2004). Metal ions such as Fe^{2+} and Mn^{2+} are converted to hydroxides ($\text{Fe}(\text{OH})_3$) or metal oxides (MnO_2) (Kirk-Othmer, 2004). In addition, ozone reacts with most organic substrates, including, but not limited to, olefins, acetylenes, aromatics, and C–H, C=N, N=N, Si–H and Si–C bonds (Kirk-Othmer, 2004). Under extended reaction times and high concentrations of ozone, hydrocarbons can be broken down into carbon dioxide and water (Rice & Gomez-Taylor, 1986). The most common transformation induced by ozone is the cleavage of olefin double bonds, forming, depending on the location and substitution of the double bond, ketones or aldehydes (Figure 2.6).

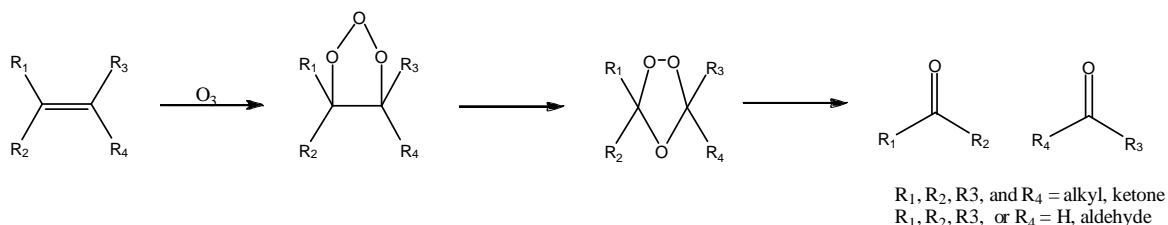


Figure 2.6. Ozonation of olefins

The reactivity of ozone in solution depends greatly on the conditions employed during ozonation. For example, at pHs below 6 and at or below room temperature, ozone reacts directly with organic molecules. Above pH 8, ozone decomposes to highly energetic hydroxyl radicals that react non-selectively with materials via electron transfer, hydrogen abstraction, addition reaction, etc. Between pH 6 and 8, ozone can react by both pathways (Rice & Gomez-Taylor, 1986). Therefore, the conditions under which ozone is used as a disinfectant must be closely monitored and controlled to give the desired result.

2.10.2 Application and fate in foods

Ozone is used to disinfect water and ice used in the processing of foods, including seafood and fish, and there is the potential for reaction of ozone with components of water, such as bromide and chloride. Reaction of ozone with halides can produce oxyhalides, such as hypochlorous acid or hypobromous acid. The hypohalous acids would react with organic matter in the water, and chlorate and bromate could be formed in reaction with additional ozone (IPCS, 2000). Bromate formed through reactions with molecular ozone may contribute in the range of 30–80% to the overall bromate ion formation in waters containing NOM. The presence of bromide ion in the aqueous solution treated with ozone may lead to formation of additional by-products, such as bromoform and other brominated THMs, dibromoacetonitrile and dibromoacetone. Also, aldehydes, ketones, ketoacids and carboxylic acids may be formed by ozonation, with aldehydes, such as formaldehyde, being dominant.

Ozone is extremely reactive and would be expected to react with most components of food (e.g. proteins, fatty acids, vitamins, etc.) that contained unsaturation or were oxidizable. There are reports that, under laboratory conditions, hypobromous acid reacts with proteins, peptides and amino acids, producing brominated tyrosine and short-lived *N*-brominated species, such as bromamines and bromamides. Hawkins & Davies (2005) reported that greater than 40% of hypobromous acid generated in the presence of bovine serum albumin is converted to short-lived bromamides and bromamines. Above 4 °C, these protein-derived *N*-bromo compounds decompose rapidly (either directly or through the formation of free radicals) by a number of pathways, including oxidation of tyrosine, formation of carbonyl moieties in proteins, and rearrangement and fragmentation of proteins. Although bovine serum albumin and fish muscle proteins are not identical, they contain tyrosine. There would, however, be variation in the quantities of the reaction products owing to the macromolecular configuration of the individual proteins. Given the reactive nature of hypobromous acid and the *N*-bromo compounds and the variation of the chemical composition of protein chains and their macromolecular configuration, small quantities of numerous compounds would be expected. However, specific compounds or classes of compounds have not been identified. Although brominated tyrosine is expected to be stable under these conditions, the data by Hawkins & Davies (2005) indicate that the concentration of these brominated compounds in fish and seafood would be insignificant.

2.10.3 Summary

Ozone and its rapid decomposition limit its reactivity to the surface of foods. The quantities of oxidation products resulting from the treatment of seafood and fish would be small compared with those resulting from oxidation due to the cooking of food; however, brominated DBPs could be formed with available bromide.

2.11 Peroxyacids and peroxides

A number of oxygen-based alternatives to chlorine-containing disinfectants are currently being used in the processing of fresh meat, poultry, fish and fresh and processed fruits and vegetables. They include hydrogen peroxide and peroxyacids, as well as ozone (see section 2.10). Peroxy compounds are a group of peroxide compounds containing at least one pair of oxygen atoms (-O-O-) bonded by a single covalent bond. Peroxides may be divided into two groups: inorganic and organic peroxy compounds.

2.11.1 Chemistry of peroxyacids and hydrogen peroxide

JECFA recently evaluated peroxyacid-based antimicrobials containing 1-hydroxy-ethylidene-1,1-diphosphonic acid (HEDP) (C₂H₈O₇P₂; CAS No. 2809-21-4) as a stabilizer (FAO, 2004; FAO/WHO, 2005). The following is a summary of the chemistry of the peroxyacid antimicrobial washes from these reports. Peroxyacid antimicrobial solutions are typically prepared by mixing aqueous hydrogen peroxide (4–12%) (CAS No. 7722-84-1) and aqueous acetic acid (40–50%) (CAS No. 64-19-7), which results in an equilibrium mixture of acetic acid, peroxyacetic acid (CAS No. 79-21-0), hydrogen peroxide and water (Figure 2.7).

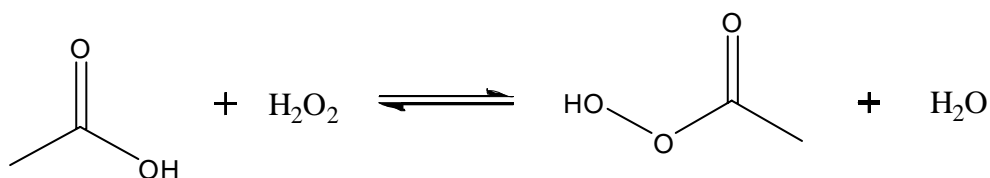


Figure 2.7. Peroxyacid formation from hydrogen peroxide

These antimicrobial washes may sometimes contain 3–10% octanoic acid (CAS No. 124-07-2), which, when treated with hydrogen peroxide, produces an equilibrium mixture of octanoic acid and peroxyoctanoic acid (CAS No. 33734-57-5). The peroxyacid solutions are typically sold as concentrates and are diluted with water to a total peroxyacid concentration of 80–200 mg/kg.

Peroxyacids are inherently unstable and decompose into non-toxic chemicals in the presence of heat, acids and certain transition metal ions (e.g. copper). Two mechanisms for the decomposition are 1) hydrolysis to their corresponding organic acid and hydrogen peroxide and 2) decomposition to their corresponding organic acid and oxygen (Figure 2.8) (FAO, 2004). The hydrogen peroxide in these solutions decomposes into water and oxygen. To counteract the deleterious effects of metal ions, manufacturers incorporate <1% HEDP as a chelating agent. Unlike hydrogen peroxide and the peroxyacids, HEDP is stable and is expected to remain in the antimicrobial wash and on food after treatment.

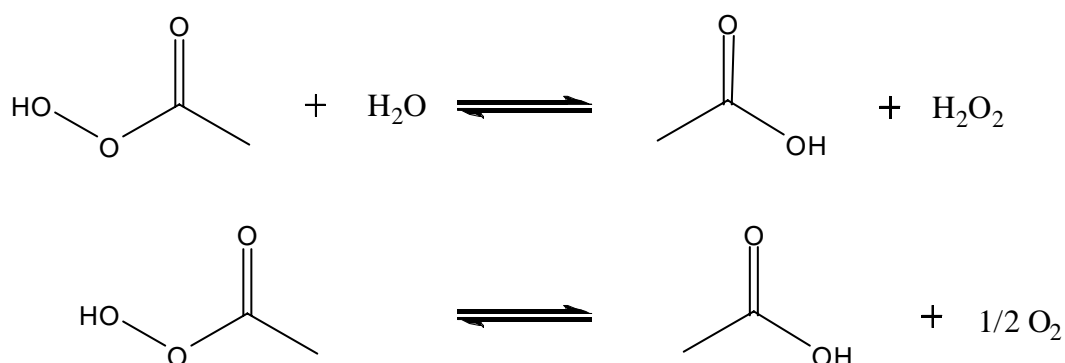


Figure 2.8. Decomposition equilibria of peroxy compounds

2.11.2 Application and fate in foods

Given the highly reactive nature of the peroxyacids and hydrogen peroxide, these compounds are not expected to be present on foods at the time of consumption. However, their breakdown products (e.g. acetic acid or octanoic acid) and residual HEDP would be expected residues on foods that are not washed, peeled or further processed before consumption. HEDP residues will remain on foods that are not washed or further processed. Being less reactive than hypochlorite, peroxyacids may survive longer in contact with organic matter and may penetrate biofilms more effectively; however, they are also lesser biocides than hypochlorite.

The peroxyacids would be expected to react with components of food (e.g. proteins, fatty acids, vitamins). However, the data available to JECFA on the TBARS values (as a measure of the oxidation of fatty acids) and fatty acid profiles of raw and cooked poultry and beef indicated that there were no significant differences between treated and control samples.

In the USA, the use of peroxyacid disinfectants on poultry carcasses and red meat is currently authorized; the maximum concentration of peroxyacids is 220 mg/kg as peroxyacetic acid, the maximum concentration of hydrogen peroxide is 85 mg/kg and the maximum concentration of HEDP is 11 mg/kg (USFDA, 2009). The use of peroxyacid disinfectants in wash water and chilling water for fruits and vegetables is authorized in the USA, with a limit of HEDP of 9.6 mg/kg. The worst-case scenario that was estimated for leafy greens was 0.53 mg/kg as HEDP (USFDA, 2007a). The use of peroxyacid disinfectants in water and ice used to commercially process fish and seafood is also authorized in the USA, with a limit of HEDP of 10 mg/kg in the wash water and ice. Given that 1 kg of fish retains approximately 9 g of water, the residue level of HEDP on fish would be around 90 µg/kg fish (USFDA, 2007b).

2.11.3 Summary

The only chemical residue in food resulting from the use of peroxyacid disinfectants in food processing is HEDP.

2.12 Quaternary ammonium compounds (including cetylpyridinium chloride)

Quaternary ammonium compounds, commonly referred to as QACs or Quats, are widely used as surface sanitizers in hospital settings, nurseries (Rutala, 2005) and food processing facilities. QACs are organically substituted ammonium compounds in which the nitrogen atom has a valency of five. They have the general structure $R_4N^+X^-$, where the Rs can be numerous alkyl or alkylbenzyl moieties, including several different groups in the same molecule, and the X is a halide ion, often chloride. They are ionic and water soluble. However, their solubility can be affected by water quality factors (e.g. hard water) and pH. They are commonly used on food contact surfaces, and several are registered as “no-rinse sanitizers” (Cords et al., 2005), which would be indicative of a regulator’s conclusions of their low toxicity under those conditions of use and residue transport. No-rinse sanitizers for food contact surfaces include the “second-generation” QAC, *n*-alkyldimethylbenzylammonium chloride; the “third-generation” dual QACs, *n*-alkyldimethylbenzylammonium chloride and *n*-alkyldimethylethylbenzylammonium chloride; the “fourth-generation” twin or dual-chain QACs, didecyldimethylammonium chloride and dioctyldimethylammonium chloride; and “fifth-generation” mixtures of fourth-generation and second-generation QACs. They are also common components of antiseptic hand soaps (Sattar, 2004).

2.12.1 Cetylpyridinium chloride

CPC is a QAC found in an anhydrous form ($C_{21}H_{38}NCl$; CAS No. 123-03-5) or as cetylpyridinium chloride monohydrate ($C_{21}H_{38}NCl \cdot H_2O$; CAS No. 6004-24-6). CPC has been approved for food contact use in the USA (USFDA, 2004b) as an antimicrobial agent to treat the surface of raw poultry carcasses only in systems that collect and recycle solution that is not carried out of the system with the treated poultry carcasses. CPC should be applied at a maximum level of 0.66 g/kg of raw poultry carcass as a fine mist spray of an ambient-temperature aqueous solution to raw poultry carcasses prior to immersion in a chiller. The aqueous solution should also contain propylene glycol at a concentration 1.5 times that of the CPC. The requirement for collection of the solution is due to the fact that water from poultry processing may be recycled into animal feed. Water retention in poultry carcasses may be

initially up to 12% by weight (Zentox, 2007), so the maximum would be a function of the concentration in the chiller water and the amount of retained chiller water.

The safety analysis connected with the promulgation of the regulation in the USA (USFDA, 2004b) contained information related to residual CPC on poultry carcasses following treatment using a number of different protocols. The carcasses were treated and cooked in a manner to simulate consumer practices. In five different studies involving more than 400 carcasses, it was noted that the residue of CPC on the carcass was directly proportional to the level in the wash and that use of a potable water wash following treatment did not result in significantly lower residues of CPC on the carcass than allowing the carcass to drip dry following treatment. The average residual level of CPC on carcasses ranged from 4.4 mg/kg for a 0.05% solution wash to 20 mg/kg for a 2.0% solution wash. The concentration of CPC in treatment solutions used in the USA is limited to no more than 0.8% CPC.

2.13 Iodophors

Iodophors are widely used as surface sanitizers in hospital settings, nurseries (Rutala, 2005) and food processing facilities. They are also common components of antiseptic hand soaps (Sattar, 2004). Iodophors are mixtures of iodine (I_2 ; CAS No. 7553-56-2) and surface-active agents such as alcohols and polyethoxyls that act as carriers and solubilizers for the iodine. Iodine has low solubility in water, so the solubilizers help to keep it in suspension as well as act as a dispensing medium to control the continuous release of iodine into the water and stabilize the concentration of iodine in the water (Gottardi, 2001). The result is a water-soluble material that releases free iodine (12.5–25 mg/l) in solution.

Iodophors are primarily produced from polyethoxylated nonylphenol or polyol, which is a block copolymer of propylene and ethylene oxide. Polyethoxyphenols, including nonylphenolethoxylates, which are commonly used surfactants, have been suspected of being weak endocrine-active agents in water. Various other surfactants, including anionics, cationics, amphoterics and other nonionics, have also been used (Batey, 1976). The nature of the interaction between the iodine and the surfactant has not been clearly defined. It is known, however, that the iodine is bound in micellar aggregates in the carrier and that, on dilution, the micelles are dispersed and the linkage of the iodine is progressively reduced (Twomey, 1968, 1969).

Iodine easily undergoes oxidation and reduction to iodide and iodate, and it can react with organic thiols, such as cysteine, as well as amines and peptides. After ingestion, it is assumed that iodide and/or iodate are available for bioconversion to forms that are part of the iodine pool.

2.14 Sodium metasilicate

Sodium metasilicate (waterglass) is commercially available in three forms: anhydrous (Na_2SiO_3 ; CAS No. 6834-92-0), pentahydrate ($Na_2SiO_3 \cdot 5H_2O$; CAS No. 10213-79-3) and nonahydrate ($Na_2SiO_3 \cdot 9H_2O$; CAS No. 13517-24-3) (IPCS, 1997). Sodium metasilicate is used in solution as a detergent-type cleaning and degreasing agent for surfaces of poultry, beef and pork in slaughtering process operations. It is used in concentrations of about 1.1–1.6% in both pre-chiller and post-chiller topical applications to sanitize the carcasses. Sodium metasilicate seems to function as a bactericide principally due to the high pH of the working solutions, which ranges from about 12.6 to 13.3, and it is used at higher temperatures (30–

40 °C) and lower temperatures (7–13 °C). Residues on treated poultry carcasses were reported to be a maximum 171 mg/kg.

2.15 Trisodium phosphate

TSP (Na_3PO_4 ; CAS No. 7601-54-9) can be obtained in anhydrous or hydrated form and is also referred to as trisodium monophosphate or trisodium orthophosphate. It has a variety of uses in manufacturing of detergents (as builders, i.e. substances added to soaps or detergents to increase their cleansing action) due to the ability to sequester cations and because of the fairly high pH of solutions with TSP. Its use has declined, as phosphate discharges in wastewaters can contribute to environmental effects. The pH of a 1% solution is 11.5–12.5. The distribution of phosphate forms in solution is a function of solution pH.

TSP is used in aqueous solution typically at 8–12%, in which it is ionized to sodium (Na^+) and phosphate ions (PO_4^{3-}). These ions can be absorbed into food, but further reactions are considered unlikely (EFSA, 2005). Poultry treated with a 12% TSP solution for 15 min at 3 °C and pH 13.03, drained and then stored at 3 °C had a longer shelf life and lower bacterial populations. The pH of the treated poultry decreased to approximately 8 at day 0, then declined to about 6.2 after 5 days of storage (Del Río et al., 2007). Phosphate residue levels were not reported.

2.16 Other considerations

2.16.1 Vaporization and loss of residue chemicals

Many of the halogenated DBPs are non-polar/non-ionic organic chemicals and therefore have sufficient vapour pressures to result in spontaneous losses from foods during storage, processing and cooking, thus reducing residue levels. The Henry's Law constant is an indication of the volatility of a chemical. It characterizes the equilibrium distribution of dilute concentrations of volatile soluble chemicals between gas and liquid (USEPA, 2007). The Henry's Law constant will be temperature dependent and also subject to numerous physical factors of the medium. It can be presented on a concentration basis (1-Pa/mol), but also as a dimensionless value for relative comparisons. Table 2.6 illustrates the dimensionless Henry's Law constants for the principal THMs and 2-chlorophenol at 25 °C and 50 °C as an indication of relative loss potential during processing.

Table 2.6 Dimensionless relative Henry's Law constants

Chemical	Henry's Law constants	
	25 °C	50 °C
Chloroform	0.147–0.150	0.351–0.412
BDCM	0.0654–0.0832	~0.179
DBCM	0.0320–0.0431	~0.0707
Bromoform	0.0198–0.0218	0.0728–0.0821
2-Chlorophenol	0.0159	0.0655

In Table 2.6, the series from chloroform to bromoform is a set of somewhat polarized neutral compounds with increasing molecular weights and concurrent reducing volatility, and the values of the constants decline concurrently. The values increase at the higher listed

temperature (50 °C), which is well below cooking temperatures. Although the molecular weight of 2-chlorophenol is similar to that of chloroform, its constant is considerably lower than that for bromoform, because it has more ionic character, and therefore its volatility is lower. Residue data and before and after cooking data were not available for most of the DBPs that are usually produced at much lower concentrations than THMs, but Henry's Law constants can give an approximate indication of their loss propensity relative to THMs.

2.16.2 Opportunities for further studies

Most of the data available on DBPs in the environment have been obtained from studies of drinking-water disinfection. Existing qualitative and quantitative residue studies of DBPs in food products have tended to focus on THM (including chloroform) measurements in processed and cooked foods, particularly poultry. This is probably due to the fact that THMs were the first DBPs regulated in drinking-water and because of the relative ease of analysis. It might not have been understood that the THMs were regulated primarily as indicators or surrogates for the unquantified mix of other DBPs that are generated during water treatment processes from the precursors present in natural source waters.

Very limited information is available on actual DBP residues in food products. Extrapolations from DBPs in drinking-water to DBPs in food are difficult to make because the conditions of the chemical interactions, dosages, temperatures, contact times and especially the precursors are very different. In addition, the consequences of cooking may reduce the presence of volatile compounds (e.g. chloroform), but also form additional compounds (e.g. in the case of nitrosamines). As a particular point, under some oxidation conditions, bromide can be converted to hypobromous acid, which would shift the composition of by-products to organobromine compounds.

Additional, more detailed studies of the formation and composition of DBPs in foods are needed to improve the ability to determine whether any significant risks may be associated with the use of disinfectant treatments in food production and food processing, and in particular how cooking and other types of food preparation may alter the composition of DBPs in foods.

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Appendix A: Data on nitrosamines in foods

Food type	Concentrations of nitrosamines (one or more, combined; µg/100 g)
Potato	0.015–1.44
Cabbage	0.014–0.19
Corn	0.002–0.83
Tomato	0.187–0.27
Fermented vegetables	nd–0.50
Cheese	0.02–9.75
Milk	0.03–3.70
Milk (sour)	0.08–11.9
Flour	0.02–1.44
Bacon	nd–6.50
Beef	Up to 788
Frankfurters	Up to 27
Ham	0.1–79
Salami	Up to 131
Sausage	nd–0.42
Fish	nd–140
Fish (processed)	nd–3.9
Seafood/shrimp	nd–13.1
Oil	nd–0.38
Beer	Up to 6.8
Tea	0.2–1.5
Coffee	Up to 0.5

nd, not detected

Appendix B: Drinking-water guidelines and regulations

The THMs were originally regulated in 1978 in the USA at 0.100 mg/l as indicator chemicals for the unidentified DBPs that are produced during the chlorination process. HAAs were regulated later as individual contaminants as well as general indicators. In the WHO *Guidelines for drinking-water quality* (GDWQ) (WHO, 2008b) and the USEPA (2009) regulations, guideline values (GVs) and maximum contaminant levels (MCLs), respectively, have been set for many of the THMs and several other DBPs.

Table 2B.1 provides WHO guidelines and USEPA and European Union (EU) regulations for selected disinfectants and DBPs.

Table 2B.1. WHO guidelines and USEPA and EU regulations^a

Disinfectant/DBP	GDWQ GV (mg/l)	USEPA MCL (mg/l)	EU standard (mg/l)
Chloroform	0.3	0.08	—
Bromoform	0.1	0.08	—
BDCM	0.06	0.08	—
DBCM	0.1	0.08	—
Total THMs	—	0.08	0.1 ^b
Trichloroacetaldehyde (chloral hydrate)	— ^c	—	—
Cyanogen chloride	— ^d	—	—
Chloroacetic acid	0.02	0.06	—
Bromoacetic acid	—	0.06	—
Dibromoacetic acid	—	0.06	—
Dichloroacetic acid	0.05 (P)	0.06	—
Trichloroacetic acid	0.2	0.06	—
Total of 5 HAAs	—	0.06	—
Dibromoacetonitrile	0.07	—	—
Dichloroacetonitrile	0.02 (P)	—	—
Bromate	0.01 (P)	0.010	0.01
Chlorate	0.7 (P)	—	—
Chlorite	0.7 (P)	1	—
Chlorine	5 ^e	4 ^b	—
Monochloramine	3 ^e	4 ^b (as chlorine)	—
NDMA	0.0001	—	—

P, provisional guideline value

^a After EU (1998); WHO (2008b); USEPA (2009).

^b Maximum allowed value. The other values are normally average values of multiple samples over a specified time period.

^c A health-based value of 0.1 mg/l can be calculated for chloral hydrate. However, because chloral hydrate usually occurs in drinking-water at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a formal guideline value.

^d Although a GV of 0.07 mg/l was included in the third edition of the GDWQ, it has been proposed that the GV be withdrawn in the fourth edition, because cyanogen chloride is unlikely to be present at concentrations of toxicological concern. As it is not considered necessary to derive a formal guideline value, a health-based value of 0.3 mg/l as cyanide is proposed (M. Sheffer, personal communication, 2009).

^e Partly for organoleptic aspects.

3. CHEMICAL RISK ASSESSMENT

3.1 Toxicology and exposure assessment

3.1.1 *Introduction*

3.1.1.1 Chemical risk assessment

The chemical risk assessments are mostly based on existing authoritative assessments that were available at the international or national level, rather than re-evaluating original publications and undertaking risk characterization de novo. However, original studies used for risk characterization are cited.

In reality, the direct exposure by ingestion to many of the chemically reactive disinfectants and some of their inorganic halogenated by-products will most likely be less than calculated here, as they will be partially or completely degraded in saliva or stomach juice after ingestion. However, at this time, these effects were not included because of the lack of quantitative data.

3.1.1.2 Dietary exposure assessment for foods (other than drinking-water)

Dietary exposure assessments were drafted for all chlorine-based disinfectants, alternative disinfectants and disinfection by-products (DBPs) that were relevant to the processes described in chapter 1 and the chemistry in chapter 2. These assessments drew primarily on existing authoritative assessments that were available at the national or international level, rather than re-evaluating occurrence data and undertaking an exposure assessment de novo.

The occurrence (i.e. concentration in food) data available for this assessment and supporting other authoritative assessments were relatively limited. There is therefore a relatively high level of uncertainty associated with the dietary exposure assessments. In some cases, very conservative assumptions were applied to compensate for this uncertainty. The degree of uncertainty and conservatism is articulated for each of the chemicals for which an exposure assessment is undertaken. The level of uncertainty and conservatism needs to be taken into consideration in the risk–benefit assessments (see chapter 6). For some of the by-products, no occurrence data were available for food, other than drinking-water.

3.1.1.3 Dietary exposure assessment for drinking-water

An exposure assessment for drinking-water was conducted for each of the DBPs for which occurrence data were available. The World Health Organization (WHO) uses a default consumption value of 2 litres for drinking-water and a typical body weight of 60 kg to estimate the WHO drinking-water guideline values (WHO, 2008d). This usually represents a conservative value for water consumption. However, the default assumption of 2 litres/day is not always appropriate or conservative for some populations and climates. Reference hydration value intakes could differ, for example, under average conditions: 2.2 litres for adult women, 2.9 litres for adult men and 1 litre for children. For physically active persons and increased temperatures, the reference values could be 4.5 litres for men, women and children; 4.8 litres for pregnant women; and 3.8 litres for lactating women (WHO, 2003a). In Australia, the mean consumption of water in food (all respondents), based on a 1995 national

nutrition survey, was reported as 969 g/day, equivalent to 0.969 litre/day. The average body weight associated with the survey was 68 kg, with respondents being 2 years of age and older (FSANZ, 2008).

In the United States of America (USA), analysis of data from the 1994–1996 and 1998 Continuing Survey of Food Intakes by Individuals (CSFII), which includes children, indicated that average estimated daily per capita ingestion of community water and all water sources was 0.926 litre/day and 1.233 litres/day, respectively. This represented 75% from community water, 13% from bottled water, 10% from other sources (well, spring, cistern, etc.) and 2% from non-identifiable sources. The consumption values did not include water found naturally in foods (biological water) and water added by commercial food and beverage manufacturers (commercial water). The average self-reported body weight associated with the same survey was 65 kg (USEPA, 2004). The community water consumption value is considered the most representative of water to which chlorine-containing disinfectants may have been applied.

For Europe, data for “tap water” from the Concise European Food Consumption Database were available for Belgium, the Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, the Netherlands, Norway, Slovakia, Sweden and the United Kingdom. These data were for adults and generally related to the age group 16–64 years (EFSA, 2008).

A summary of the food consumption and body weight values used in the dietary exposure assessments for drinking-water is presented in Table 3.1.

3.1.1.4 Other information

Concentrations of chemicals are given in SI units (Système international d’unités) (e.g. mg/kg, mg/l), in keeping with Food and Agriculture Organization of the United Nations (FAO)/WHO policy.

The expressions “acceptable daily intake” (ADI) and “tolerable daily intake” (TDI) are used as stated in the original publications and may therefore not be used consistently throughout the document (e.g. TDI is usually used for substances that are contaminants). This may be the case also for the expressions no-observed-(adverse-)effect level (NO(A)EL) and lowest-observed-(adverse-)effect level (LO(A)EL).

3.1.2 Chlorine-containing disinfectants

3.1.2.1 Acidified sodium chlorite

Introduction

Acidified sodium chlorite (ASC), which is produced by combining sodium chlorite with a food-grade acid, is used as a broad-spectrum disinfectant. The active ingredient is chlorous acid, and its reaction products are chlorine dioxide, chlorite and chlorate.

ASC was evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 2007 (WHO, 2008a). JECFA noted that residual chlorine dioxide is lost by evaporation; hence, chlorite, chlorate and chloride are the principal residues expected. The chloride generated as a result of treatment with ASC is negligible compared with the chloride already present in food. As chlorine dioxide acts as an oxidizing agent, it does not form trihalomethanes (THMs) or by-products other than chlorite and chlorate ions. The residues of the food-grade acids (e.g. phosphate, citrate, malate, sulfate) are commonly present in food and have previously established ADIs. Therefore, JECFA focused its toxicological evaluation

on ASC, chlorite and chlorate. The review of the chemistry of ASC in section 2.2 confirms that this approach is justified.

Table 3.1. Summary of the drinking-water consumption and body weight data used for the drinking-water exposure assessments

Country	Approximate number of respondents	Mean body weight of all respondents (kg)	Mean consumption of drinking-water for all respondents ^a (litre/day)
Australia	13 800	68	0.969
Belgium	1 720	71	0.100
Czech Republic	1 750	75	0.288
Denmark	3 150	74	0.840
Finland	2 010	77	0.886
France	2 000	66	0.283
Germany	3 550	77	0.071
Hungary	930	73	0.001
Iceland	1 080	76	0.670
Ireland	1 370	75	0.284
Italy	1 540	66	0.206
Netherlands	4 290	75	0.209
Norway	2 310	73	0.312
Slovakia	2 210	75	0.224
Sweden	1 090	73	0.480
United Kingdom	1 720	76	0.205
USA	25 000	65	0.926
WHO	–	60	2 ^b

^a For the European countries, data for “tap water” were used (EFSA, 2008). The consumption of tap water in Hungary was reported as being only 1 ml/day (mean consumption for all respondents).

^b The WHO consumption value is for the model drinking-water diet used in the WHO drinking-water guidelines (WHO, 2008d).

In order to assess the safety of ASC, JECFA set ADIs for sodium chlorite (0.03 mg/kg body weight [bw] per day, expressed as chlorite [ClO_2^-]) and sodium chlorate (0.01 mg/kg bw per day, expressed as chlorate [ClO_3^-]) (WHO, 2008a).

The European Food Safety Authority (EFSA) has also reviewed ASC for treatment of poultry carcasses, confirming the JECFA evaluation, as no further data had been made available (EFSA, 2005). EFSA (2005) concluded that the exposure to chlorite residues arising from treated poultry carcasses would be of no safety concern.

Toxicological data

JECFA concluded that the available toxicological data were sufficient to assess the safety of ASC by setting ADIs for chlorite and chlorate (WHO, 2008a). The available studies on ASC related to a germicidal product, and some of these involved parenteral administration. These studies were not directly relevant to oral exposure but provided useful supplementary information that did not raise concern about the use of acidified chlorite as a processing aid.

The toxicological information relating to chlorate and chlorite is considered in sections 3.1.4.3 and 3.1.4.4, respectively.

Dietary exposure

There is no direct dietary exposure to ASC. The dietary exposure to residues resulting from use of ASC is considered in sections 3.1.4.3 and 3.1.4.4.

Risk characterization

As there is no direct dietary exposure to ASC, it is not a risk to consumers. The toxicologically relevant residues (i.e. chlorate and chlorite) are considered in sections 3.1.4.3 and 3.1.4.4.

3.1.2.2 Chloramine (monochloramine)

Introduction

The toxicology of monochloramine was evaluated and described in Environmental Health Criteria 216 (IPCS, 2000). The WHO *Guidelines for drinking-water quality* (WHO, 2006a) as well as original publications have also been used as sources of information on monochloramine. A TDI of 94 µg/kg bw per day for monochloramine was derived in the WHO *Guidelines for drinking-water quality* (WHO, 1993). This was confirmed in subsequent evaluations (IPCS, 2000; WHO, 2004a, 2006a).

Toxicological data

The NOAEL after chronic oral exposure, used for establishing the TDI, was identified from a study by the United States National Toxicology Program (NTP, 1992). Monochloramine was administered for 2 years to male and female F344/N rats and B6C3F1 mice at 0, 50, 100 or 200 mg/l in the drinking-water. These solutions were prepared from gaseous chlorine and neutralized to pH 9 by the addition of sodium hydroxide. At this pH, almost all chlorine will be available as hypochlorite. Monochloramine was generated by adding the buffered sodium hypochlorite solution to a dilute ammonium hydroxide solution. Stability studies indicated that 92% of the initial target concentration remained after 2 days of preparation. The buffered hypochlorite stock solutions were prepared once weekly, and solutions for drinking were prepared 4 times weekly.

The monochloramine concentrations corresponded to average doses of 0, 2.9, 5.2 and 9.4 mg/kg bw per day in male F344/N rats and 0, 3.1, 5.7 and 10.2 mg/kg bw per day in female rats. There were no clinical findings or alterations in haematological parameters considered to be attributable to the consumption of chloraminated water. There were no biologically significant differences in survival or in absolute or relative organ weights between dosed and control groups. Mean body weights of rats given the highest dose were 5–10% lower than those of their respective control groups throughout the study. Based on these considerations, the authors considered the NOAELs for this study to be 5.2 and 5.7 mg/kg bw per day for male and female rats, respectively. Feed consumption by dosed animals was similar to controls. However, it is probable that the observed weight decreases were a direct result of the unpalatability of the drinking-water, as a dose-related decrease in water consumption was seen in both sexes from the first week and throughout the study. The water consumption during the second year of the study by high-dose rats was 34% lower than controls for males and 31% lower for females. No treatment-related non-neoplastic lesions were observed in either male or female rats (NTP, 1992). There was no evidence of carcinogenic activity in the male rats. In the female rats, there was equivocal evidence of carcinogenic activity based on a significant increase in the incidence of mononuclear cell leukaemia above the concurrent and historical controls. The incidences were 8/50 for controls, 11/50 for the low dose, 15/50 for the intermediate dose and 16/40 for the high dose. The following factors did not support an association between the occurrence of mononuclear

cell leukaemia and the consumption of chloraminated drinking-water: the increases in leukaemia incidence in dosed female rats were small and not clearly dose related, there was no decrease in tumour latency in the dosed groups, the effect was not observed in male rats or in female and male mice (see below), and the incidence in concurrent controls was less than the mean incidence in historical controls.

B6C3F1 mice were exposed for 2 years to average doses of monochloramine in their drinking-water of 0, 5.4, 9.8 and 17.0 mg/kg bw per day for males and 0, 5.8, 10.6 and 19.0 mg/kg bw per day for females. The authors reported that there were no clinical findings or alterations in haematological parameters attributable to the consumption of chloraminated water. There were no biologically significant differences in survival or in absolute or relative organ weights between dosed and control groups. As was observed in rats, there were dose-related decreases in water consumption—in high-dose mice, 42% lower than controls in males and 40% lower in females. Feed consumption by dosed male mice was similar to that of controls throughout the study. In females, mean feed consumption was similar in all treatment groups except the high-dose group, in which it was slightly lower than in the other groups. There was a dose-related decrease in mean body weights of both sexes of dosed mice compared with controls throughout most of the study. No treatment-related non-neoplastic lesions were observed in either male or female mice. There was no evidence of carcinogenic activity in male or female B6C3F1 mice (NTP, 1992; WHO, 2004a).

Although monochloramine has been shown to be mutagenic in some *in vitro* studies, it did not induce micronucleus formation, chromosomal aberrations or aneuploidy in the bone marrow of CD-1 mice or sperm abnormalities in B6C3F1 mice (IARC, 2004). Monochloramine induced the formation of micronuclei in erythrocytes of newt larvae *in vivo* (IARC, 2004). The International Agency for Research on Cancer (IARC) evaluated monochloramine as not classifiable as to its carcinogenicity to humans (Group 3) (IARC, 2004), because there was inadequate evidence in humans and experimental animals.

WHO (1993) derived a TDI of 94 µg/kg bw per day by applying an uncertainty factor of 100 (for intraspecies and interspecies variation) to the dose of approximately 9.4 mg/kg bw per day, which was the highest dose administered in the 2-year NTP rat drinking-water study. This was considered to be a NOAEL rather than a LOAEL because of the probability that the small reduction in body weight at this dose was caused by the unpalatability of the drinking-water (NTP, 1992).

Dietary exposure

In the USA, monochloramine has been proposed for use for poultry chiller water disinfection at levels up to 50 mg/l (USFDA, 2008), whereas the maximum residual level for drinking-water in the USA is 4 mg/l as chlorine (USEPA, 2009). Dietary exposure to monochloramine (as chlorine) from the consumption of drinking-water could be 8 mg/day (0.13 mg/kg bw per day for a 60-kg person), assuming that one consumes 2 litres of water per day. Dietary exposure from the consumption of meat would be lower, as per the analyses below.

Zentox (2007) developed a conservative hypothetical estimation of dietary exposure to monochloramine following the chiller treatment of poultry in water. Assumptions included a 12% uptake (by weight) of chiller water containing monochloramine at 50 mg/l; therefore, a carcass that weighed 1 kg would contain 6 mg of monochloramine.

Table 3.2 shows the consumption of meat in three European countries, estimated from the Concise European Food Consumption Database by EFSA (2005). Combining these meat consumption figures with the potential residual levels in meat gives a dietary exposure of up to 2 mg/person per day, or 0.04 mg/kg bw per day for a 60-kg person consuming meat at the 99th percentile.

Table 3.2. Consumption of meat and meat products (including offal) in the adult population of France, Italy and Sweden

Country	Number of subjects	Number of consumers	Average daily consumption in consumers only (g/day)						
			Mean	SD	50th	90th	95th	97.5th	99th
France	1875	1861	120	66	110	206	243	274	321
Italy	1425	1419	137	67	127	224	264	292	351
Sweden	1214	1204	151	68	141	233	263	297	346

SD, standard deviation

At the international level, the use of the Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme (GEMS/Food) consumption cluster diets (WHO, 2007b) allows the preparation of another conservative estimate of dietary exposure to monochloramine. Cluster K shows the highest consumption of poultry products at 145.9 g/day, with cluster M having the highest total meat consumption at 279.3 g/day. Using these food consumption figures yields dietary exposure estimates up to 0.9 mg/person per day (poultry), again assuming that no monochloramine is lost upon treatment and that there is a 12% uptake of water into the meat product. The dietary exposure assessments for each of the GEMS/Food consumption cluster diets are presented, on a kilogram body weight basis, in Table 3.3.

Table 3.3. Estimates of per capita dietary exposure to monochloramine, using a hypothetical residue concentration, following the dipping of chicken in chlorine, based on the 13 GEMS/Food consumption cluster diets

	Per capita dietary exposure (µg/kg bw per day) ^{a,b,c}												
	A	B	C	D	E	F	G	H	I	J	K	L	M
Chicken meat	0.55	4.31	2.86	2.21	3.86	2.63	1.2	4.34	1.5	0.44	6.4	2.68	9.67
Poultry ^d	0.71	5.85	3.19	2.4	6.1	2.73	1.76	13.13	2.51	0.47	14.59	2.77	11.51

^a Assuming a 60-kg average body weight.^b WHO consumption cluster diets based on food balance sheet data; August 2006 version used (<http://www.who.int/entity/foodsafety/chem/ClusterDietsAug06.xls>).^c Hypothetical concentration of 6 mg/kg in chicken and other poultry was used for the exposure assessment.^d The poultry exposure assessment has been presented on the assumption that the dipping use of chlorine is also applied to other poultry.

The estimates of dietary exposure presented herein are highly conservative. Although monochloramine is known to be less reactive than chlorine and other alternative chlorine antimicrobials, it does decompose when in contact with organic materials. Studies with poultry have shown, however, that levels of haloforms and total chlorine-containing material are higher in cooked poultry that had been immersed in control (non-sanitized) water compared with monochloramine-treated water. Additionally, there is no measurable difference in fatty acid profiles of poultry treated with monochloramine compared with control water-treated poultry after cooking. Treatment of poultry with monochloramine followed by roasting resulted in no greater formation of *N*-nitrosopyrrolidine than in the controls.

The dietary exposure to monochloramine can be expected to be negligible in comparison with that from treated water. For consumers not exposed to monochloramine-treated waters, a conservative estimate of dietary exposure would be 2 mg/person per day (0.04 mg/kg bw per day).

Risk characterization

The estimated dietary exposure of 40 µg/kg bw per day is well below the TDI of 94 µg/kg bw per day. Exposure to monochloramine in drinking-water has the potential to exceed the TDI and to be up to about 4 times the exposure from monochloramine-treated food. Therefore, no health concern was identified with use of monochloramine in poultry chiller water.

3.1.2.3 Chloramine-T

Introduction

Chloramine-T has been evaluated by the European Medicines Agency (EMA) as a disinfectant used as treatment for bacterial gill disease in cultured fish (EMA, 1999), for teat and udder disinfection in lactating cows (EMA, 2001) and for treatment of skin disease in horses (EMA, 2005). In addition, information was found in a document submitted by industry (Axcentive SARL, 2008) and in a literature review prepared for the United States National Institute of Environmental Health Sciences (Haneke, 2002b).

p-Toluenesulfonamide (PTSA) is the primary reaction product and marker metabolite of chloramine-T (EMA, 2005). *o*-Toluenesulfonamide is not formed in aqueous solutions of chloramine-T and is therefore not relevant for the safety evaluation of chloramine-T (EMA, 1999). Chloramine-T is also converted very quickly in the stomach/gastrointestinal system into PTSA (Axcentive SARL, 2008).

No ADI or TDI has been identified for chloramine-T or for PTSA.

Toxicological data

EMA evaluated the available toxicity studies on chloramine-T and PTSA in 1999. No chronic studies were found in rats or mice, and a TDI could not be established. However, the highest dose of chloramine-T tested without any effect (NOAEL) was approximately 15 mg/kg bw per day, from 300 mg/kg in the feed, in a 90-day study in rats (EMA, 1999, 2001). In this study, Wistar rats (10 per sex per group) were exposed to diets containing chloramine-T at 0, 100, 300, 1000 or 3000 mg/kg feed, equivalent to approximately 0, 5, 15, 50 or 150 mg/kg bw per day. A slight reduction of weight gain and food efficiency was observed in females at 3000 mg/kg feed. Relative kidney weight was significantly increased in both sexes at doses equal to or higher than 1000 mg/kg feed. In females at 1000 and 3000 mg/kg feed, increased severity and frequency of calcareous deposits in kidneys were observed. The NOAEL was 300 mg/kg feed, equivalent to approximately 15 mg/kg bw per day. The rest of the toxicity studies evaluated by EMA in 1999 were for an exposure duration shorter than 90 days, were performed in dogs, gave no effects or were performed or reported in such a way that a NOAEL could not be identified.

Axcentive SARL (2008) reported a subchronic 90-day dietary study in rats (conducted according to Organisation for Economic Co-operation and Development [OECD] Test Guideline 408) with PTSA given at 1000, 3000 and 10 000 mg/kg in feed. A decreased body weight gain in animals at the highest dose, up to 21% in males and up to 11% in females, was observed. Also, a minimal degree of hyperplasia of the urothelium of the urinary bladder was observed in two males. These effects were observed only at the highest level of 10 000 mg/kg feed, which was equal to PTSA doses of 738 mg/kg bw per day in males and 795 mg/kg bw per day in females; converted to chloramine-T, the doses were 1210 mg/kg bw per day for males and 1303 mg/kg bw per day for females. At the other dose levels, no effects were observed. Based on these results, the NOEL was 3000 mg/kg feed—that is, 214 mg/kg bw per day as PTSA, corresponding to 351 mg/kg bw per day as chloramine-T. The LOAEL was the highest dose tested, equivalent to 1210 mg/kg bw per day

as chloramine-T, according to Axcentive SARL (2008). No raw data or details other than those reported above were provided; therefore, the validity of the NOEL and LOAEL values cannot be evaluated.

Decreased body weight in rats exposed to 351 mg/kg bw per day (3000 mg/kg feed) in the 90-day subchronic dietary study was regarded as the critical effect of chloramine-T (Axcentive SARL, 2008). As the pharmacokinetic studies indicated no potential for bioaccumulation, Axcentive SARL (2008) proposed that the default safety factor of 100 could be used to derive a TDI of 3.51 mg/kg bw per day for chloramine-T. However, this proposal has not been supported by an independent expert body.

In a two-generation study in rats (conducted according to OECD Test Guideline 416), with PTSA given at concentrations of 1000, 3000 and 10 000 mg/kg in feed, dose-related decreased body weight gain and changes in absolute and relative organ weights were observed at 3000 and 10 000 mg/kg feed in the parent and F₁ groups (Axcentive SARL, 2008). The NOAEL for parent and F₁ animals in this experiment was 1000 mg/kg feed—that is, 52–78 mg/kg bw per day as PTSA for males and 75–161 mg/kg bw per day as PTSA for females, corresponding to 85–128 mg/kg bw per day as chloramine-T for males and 123–264 mg/kg bw per day as chloramine-T for females.

The genotoxicity of chloramine-T has been assayed in the following tests: a non-Good Laboratory Practice (GLP) *Salmonella* microsomal test (*S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation); a non-GLP deoxyribonucleic acid (DNA) repair test on *Escherichia coli*, with and without activation; a GLP-compliant gene mutation assay in mouse lymphoma L5178Y cells, with and without activation; and a GLP-compliant micronucleus assay in mice treated by gavage with 300, 600 and 1200 mg/kg bw per day for 2 days. All these tests gave negative results (EMA, 1999).

In a non-GLP *Salmonella* microsomal test, PTSA was evaluated in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation, with negative results. Based on these available data, neither chloramine-T nor PTSA is genotoxic (EMA, 1999). One bacterial reverse mutation test and one gene mutation test in mouse lymphoma cells in vitro and one in vivo micronucleus test were also reported by industry as negative (no data provided) (Axcentive SARL, 2008). No carcinogenicity studies have been found for either chloramine-T or PTSA.

None of the available studies involved chronic exposure, nor were the available results reported in sufficient detail to be properly evaluated. The expert meeting did not establish a TDI for chloramine-T.

Dietary exposure

The United States Food and Drug Administration (USFDA) models the situation in which sanitizing solutions are not washed off prior to the use of the preparation surface, and all food consumed in a day would be in contact with this surface (USFDA, 1993). This approach leads to a very conservative estimate that the expert meeting considered not relevant in this context.

The expert meeting calculated a more refined dietary exposure estimate in which it was assumed that *one* meal per day was prepared on the treated, unwashed surface. Parameters are used from the USFDA model (USFDA, 1993), assuming that treatment results in chloramine-T residues of 4.6 µg/cm² surface. It is then assumed that the food would contact 4000 cm² of this treated surface, resulting in a dietary exposure to chloramine-T of 6 mg/day, equivalent to 0.1 mg/kg bw per day for a 60-kg individual. This model still represents a conservative estimate of dietary exposure, given the assumption relating to the amount of chloramine-T residues, lack of rinsing after disinfection and daily consumption of such prepared food.

There are no data on chloramine-T-treated water, either consumed as such or used on food, to allow an estimate of exposure from this route. However, chloramine-T decomposes rapidly in cooking, and human exposure would probably be intermittent and at much lower levels than estimated by this model.

Risk characterization

No TDI could be established for chloramine-T due to the lack of long-term toxicity data and limited detail on the available studies. The dietary intake of 0.1 mg/kg bw per day has been estimated, which is a margin of 150 times lower than the NOAEL of 15 mg/kg bw per day for effects on the kidney in a 90-day rat study. Taking into account that actual exposure is likely to be much lower and intermittent, the margin is expected to be much larger, and no health concern was identified.

3.1.2.4 Chlorine dioxide

Introduction

Chlorine dioxide is an unstable gas that has to be generated at the point of use as an antimicrobial agent. It is produced by oxidation or acidification of sodium chlorite, by combination of sodium hypochlorite and hydrochloric acid or by reaction of sodium chlorate with hydrogen peroxide and sulfuric acid.

In its review of ASC, JECFA noted that residual chlorine dioxide is lost by evaporation; hence, chlorite, chlorate and chloride are the principal residues expected. As chlorine dioxide acts as an oxidizing agent, it does not form THMs or by-products other than chlorite and chlorate ions. The review of the chemistry in chapter 2 confirms that chlorite and chlorate are the main residues in food expected to result from use of chlorine dioxide as a disinfectant.

Chlorine dioxide was most recently evaluated by EFSA (2005), which referred to the TDI of 0.03 mg/kg bw per day for chlorite set by WHO (IPCS, 2000) and confirmed by JECFA (WHO, 2008a).

Toxicological data

The toxicological information relating to chlorate and chlorite is considered in sections 3.1.4.3 and 3.1.4.4, respectively.

Dietary exposure

There is no direct dietary exposure to chlorine dioxide. The dietary exposure to residues resulting from use of chlorine dioxide is considered in sections 3.1.4.3 and 3.1.4.4.

Risk characterization

As there is no direct dietary exposure to chlorine dioxide, it is not a risk to consumers. The toxicologically relevant residues are considered in sections 3.1.4.3 and 3.1.4.4.

3.1.2.5 Hypochlorite-related compounds (chlorine gas, sodium hypochlorite, calcium hypochlorite, hypochlorous acid, hypochlorite ion)

Introduction

Chlorine, whether in the form of chlorine gas from a cylinder or as the solids sodium hypochlorite or calcium hypochlorite, dissolves in water to form hypochlorous acid and hypochlorite ion (WHO, 2006a). Therefore, based on considerations of the chemistry of either chlorine gas or hypochlorites used in aqueous solutions as disinfectants in the food

industry, the main components expected to be of toxicological relevance are hypochlorite ion and, possibly, hypochlorous acid. Chlorine gas, hypochlorous acid and hypochlorite ion are in equilibrium with each other, their concentrations depending on the pH of the solution. At pH 7, the chlorine solution is approximately 50% hypochlorite and 50% hypochlorous acid. Its biocidal effectiveness is greatest when it is in the acid form as hypochlorous acid and is a function of the concentration of the residual active chlorine, temperature and pH of the solution, and contact time.

The mechanisms of the toxicity of aqueous chlorine (i.e. chlorine gas, hypochlorous acid and hypochlorite) are basically similar (ATSDR, 2007).

The toxicology of hypochlorite-related substances has been described in Environmental Health Criteria 216 (IPCS, 2000). The Agency for Toxic Substances and Disease Registry's draft *Toxicological profile for chlorine* (ATSDR, 2007) and the WHO *Guidelines for drinking-water quality* (WHO, 2006a), as well as some original publications, have also been used as sources of information on hypochlorite-related compounds.

A TDI of 150 µg/kg bw per day for free chlorine was established in the WHO *Guidelines for drinking-water quality* (WHO, 1993). IPCS (2000) indicated that there were no new data to suggest that this TDI should be changed.

Toxicological data

The NOAEL used for establishing the TDI was obtained from a 2-year NTP bioassay (NTP, 1992). Chlorine was administered to F344/N rats and B6C3F1 mice (70 per sex per group) at 0, 70, 140 or 275 mg/l (expressed as elemental chlorine, Cl) in drinking-water. Groups of 10 rats or mice of each sex were predesignated for evaluation at 14 or 15 weeks and 66 weeks. The solutions were prepared from gaseous chlorine and neutralized to pH 9 by the addition of sodium hydroxide. At this pH, almost all chlorine will be available as hypochlorite. Stability studies indicated that 85% of the initial target concentration remained after 3 days of preparation. Stock solutions were prepared once weekly, and solutions for drinking were prepared 4 times weekly. Based on body weight and water consumption, the doses were approximately 0, 4, 7 and 14 mg/kg bw per day for male rats; 0, 4, 8 and 14 mg/kg bw per day for female rats; 0, 7, 14 and 24 mg/kg bw per day for male mice; and 0, 8, 14 and 24 mg/kg bw per day for female mice. A dose-related decrease in water consumption was observed throughout the study in the treated groups from both sexes in both rats and mice. Water consumption by high-dose rats during the second year of the study was 21% lower than controls for males and 23% lower than controls for females. Water consumption by high-dose mice was 31% lower than controls for males and 26% lower than controls for females. Mean body weights and food consumption were comparable between treated and control groups. There were no clinical findings attributable to treatment, no alterations in haematological parameters and no biologically significant differences in survival rates or absolute or relative organ weights between treated and control groups. No treatment-related non-neoplastic lesions were observed in either rats or mice. There was no evidence of carcinogenic activity in male F344/N rats receiving 70, 140 or 275 mg/l as atomic chlorine. There was equivocal evidence of carcinogenic activity of chlorinated water in female F344/N rats, based on a significant increase in the incidence of mononuclear cell leukaemia in mid-dose, but not high-dose, female rats receiving chlorinated water compared with controls ($P = 0.014$ by the life table test) (controls, 8/50; low dose, 7/50; intermediate dose, 19/51; high dose, 16/50). The factors not supporting this association include the following: the increase in leukaemia in dosed female rats was slight and not clearly dose related, there was no decrease in tumour latency, the incidence in concurrent controls was less than in historical controls and there was no supporting evidence of this effect in male

rats. There was no evidence of carcinogenic activity of chlorinated water in male or female B6C3F1 mice receiving 70, 140 or 275 mg/l as atomic chlorine.

The lowest NOAEL from this study was 14 mg/kg bw per day as chlorine for female rats, based on absence of findings in histopathology of tissues and organs and haematological parameters. The lowest NOAEL for B6C3F1 mice in the same study was 24 mg/kg bw per day as chlorine in females, based on absence of findings in histopathology of tissues and organs and haematological parameters.

Based on the lowest NOAEL value of 14 mg/kg bw per day as chlorine (rounded to 15 mg/kg bw per day as chlorine) and using an uncertainty factor of 100 (10 each for intraspecies and interspecies variation), WHO (1993) established a TDI of 150 µg/kg bw per day for free chlorine (WHO, 1993), which was confirmed by IPCS (2000).

Although sodium hypochlorite has been shown to be mutagenic in some in vitro studies, it did not induce micronucleus formation or chromosomal aberrations in the bone marrow of mice in vivo (ATSDR, 2007). Sodium hypochlorite induced the formation of micronuclei in erythrocytes of newt larvae in vivo (ATSDR, 2007). Hypochlorite salts were assigned to Group 3: the compounds are not classifiable as to their carcinogenicity to humans by IARC (1991), based on inadequate evidence for the carcinogenicity in experimental animals and no available data from studies in humans.

Dietary exposure

Chlorine gas is approved for use in red meat and poultry processing in the USA (USDA, 2007). No dietary exposure to chlorine gas following such use is expected. Chlorine in the form of hypochlorous acid and hypochlorite ion is highly reactive and is expected to result in the formation of DBPs when it comes into contact with food. Nitrosamines, chloroform and chloramines can be produced from the chemical reactions between ammonium or amines present in food and free active chlorine. The dietary exposure to hypochlorous acid and hypochlorite ion per se will therefore be minimal. The dietary exposures to the DBPs that are formed are considered elsewhere within this chapter.

Risk characterization

Chlorine in the form of hypochlorous acid and hypochlorite ion is expected to react on contact with food to form DBPs. There is no direct dietary exposure to chlorine, and therefore it is not a risk to consumers. The toxicologically relevant DBPs are considered under the respective headings in this chapter.

3.1.2.6 Dichloroisocyanurate

Introduction

Sodium dichloroisocyanurate (NaDCC) is used as a source of free available chlorine (in the form of hypochlorous acid) (WHO, 2004b, 2007a).

The description of the toxicology of dichloroisocyanurate is based mainly on WHO Food Additives Series, No. 52 (WHO, 2004b). However, a background document for the WHO *Guidelines for drinking-water quality* (WHO, 2007a) and some original publications have also been used as sources of information on NaDCC.

JECFA (WHO, 2004b) concluded that studies of the toxicity of sodium cyanurate were appropriate for assessing the safety of NaDCC, because any residues of intact NaDCC in drinking-water would be rapidly converted to cyanuric acid on contact with saliva. JECFA established a TDI for anhydrous NaDCC of 0–2.0 mg/kg bw per day for intake from drinking-water treated with NaDCC for the purpose of disinfection.

Toxicological data

In a 2-year study, groups of 80 male and 80 female Charles River CD-1 rats were given drinking-water containing sodium cyanurate at a concentration of 0, 400, 1200, 2400 or 5375 mg/l, corresponding to estimated doses of 0, 26, 77, 154 or 371 mg/kg bw per day, with control groups receiving drinking-water containing an equivalent amount of sodium hippurate or untreated drinking-water (IRDC, 1985). Survival was slightly lower in the group receiving the highest dose compared with the control group receiving untreated drinking-water, but not compared with the control group receiving sodium hippurate. There was no substance-related increase in tumour incidence. Multiple lesions of the urinary tract (calculi and hyperplasia, bleeding and inflammation of the bladder epithelium, dilated and inflamed ureters and renal tubular nephrosis) and cardiac lesions (acute myocarditis, necrosis and vascular mineralization) were reported in males that died during the first year of the study and that were receiving a dose of 371 mg/kg bw per day. No toxicologically significant treatment-related effects were observed at 154 mg/kg bw per day, which was considered to be the NOAEL in this study. In a similar 2-year study in which B6C3F1 mice received a dose of sodium cyanurate equivalent to 0, 30, 110, 340 or 1523 mg/kg bw per day in drinking-water (from concentrations of 0, 100, 400, 1200 and 5375 mg/l), survival was similar in all groups, and there were no treatment-related changes in the incidence of tumours or other histopathological lesions (Serota et al., 1986).

Sodium cyanurate was not mutagenic in in vitro *Salmonella typhimurium* mutagenicity tests, with or without activation, in mouse lymphoma cells or in a test of sister chromatid exchanges in Chinese hamster ovary (CHO) cells. No effects were observed for cytogenetic alterations in bone marrow of rats in vivo at a dose of 5000 mg/kg bw (WHO, 2004b).

The NOAEL for sodium cyanurate derived from the 2-year study in rats was 154 mg/kg bw per day, equivalent to 220 mg/kg bw per day as anhydrous NaDCC. With the application of an uncertainty factor of 100, a TDI for anhydrous NaDCC of 0–2.0 mg/kg bw per day was established for intake from drinking-water treated with NaDCC for the purpose of disinfection (WHO, 2004b).

Dietary exposure

NaDCC decomposes in water to release free chlorine, which is then available for the disinfection of drinking-water. Consequently, there is no direct human dietary exposure to NaDCC. Conventional chlorination of drinking-water with elemental chlorine gives rise to a number of by-products as a result of the reaction of free available chlorine with natural organic matter (NOM). The safety of these by-products has been addressed by WHO, with the development of guidelines for drinking-water quality. The use of NaDCC as a source of free available chlorine is not expected to lead to greater production of such by-products than does the use of elemental chlorine. The sixty-first meeting of JECFA (FAO/WHO, 2004) concluded that the continued reaction of NaDCC-released free chlorine with organics in water would eventually result in residues of cyanuric acid in water; hence, this was the only organic by-product for which human exposure was estimated.

Human exposure to cyanuric acid was evaluated by assuming that 1 mol of NaDCC results ultimately in 1 mol of cyanuric acid in treated water. The daily intake of cyanuric acid from the consumption of water by adults, assuming a maximum application of NaDCC of 3.2 mg/l (equivalent to 2 mg/l as free chlorine) and consumption of 2 litres of water per day, would be equivalent to 6.4 mg/person per day, expressed as NaDCC (equivalent to 0.03 mg/kg bw per day for a 60-kg person), or 4.2 mg/day as cyanuric acid.

Risk characterization

The estimated dietary exposure of 0.03 mg/kg bw per day for a 60-kg person is well below the upper end of the TDI range of 0–2.0 mg/kg bw per day, expressed as NaDCC. Therefore, no health concern was identified.

*3.1.3 Alternative disinfectants**3.1.3.1 1,3-Dibromo-5,5-dimethylhydantoin**Introduction*

No comprehensive toxicological evaluations of 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) were found.

Toxicological data

No data were found for DBDMH on the end-points chronic toxicity, mutagenicity, carcinogenicity, or developmental or reproductive toxicology. No data were available with which to establish a TDI for DBDMH.

Dietary exposure

Currently in the USA, DBDMH is authorized for use as a disinfectant in water and ice used in the processing of poultry and as a disinfectant in water used to process beef hides, carcasses, heads, trim, parts and organs. Given that DBDMH rapidly decomposes in water to hypobromous acid and dimethylhydantoin (DMH), it is not expected to be present on food at the time of consumption. Therefore, there is no direct dietary exposure to DBDMH. Exposures to DMH (see section 3.1.4.5) and potential DBPs, such as bromate (see section 3.1.4.1), dibromochloromethane (DBCM) (see section 3.1.4.10), bromodichloromethane (BDCM) (see section 3.1.4.10) and bromoform (see section 3.1.4.10), are considered separately.

Risk characterization

As there is no direct dietary exposure to DBDMH, no health concern was identified.

*3.1.3.2 Ethyl lauroyl arginate**Introduction*

Ethyl lauroyl arginate is a cationic surfactant that has a wide spectrum of activity against bacteria, yeasts and moulds. *N*^α-Lauroyl-L-arginine is a principal by-product in the manufacture of the active ingredient ethyl-*N*^α-lauroyl-L-arginate hydrochloride and is also formed by enzymatic action in fresh food.

Ethyl lauroyl arginate was evaluated by JECFA in 2008 (WHO, 2009) and was previously evaluated by EFSA (2007). The toxicological data are not available in the public domain but are described in the JECFA monograph (WHO, 2009) and in the EFSA opinion (EFSA, 2007).

JECFA established an ADI of 0–4 mg/kg bw for ethyl lauroyl arginate, expressed as ethyl-*N*^α-lauroyl-L-arginate hydrochloride (WHO, 2009).

Toxicological data

Ethyl lauroyl arginate is well absorbed and rapidly metabolized by hydrolysis of the ethyl ester and lauroyl amide, via *N*^α-lauroyl-L-arginine and, to a lesser extent, L-arginine ethyl ester, to arginine, lauric acid and ethanol. Arginine subsequently undergoes normal

amino acid catabolism via the urea and citric acid cycles, with ultimate elimination as carbon dioxide in the expired air and urea in the urine. Lauric acid enters normal fatty acid metabolism, and ethanol is converted to acetate, which enters normal biochemical pathways. Both lauric acid and ethanol are also present naturally in foods. Given the rapid degradation of ethyl lauroyl arginate, exposure to this compound and *N*^α-lauroyl-L-arginine in vivo is likely to be short.

Ethyl lauroyl arginate is of low acute toxicity. In feeding studies in rats at high dietary concentrations, the major observations were forestomach changes. JECFA concluded that these changes represented local irritation in the forestomach caused by storage of ingested diet and thus were not indicative of systemic toxicity. A reduction in the concentration of leukocytes in the peripheral blood was also reported at some doses and time points. These differences were due to lower concentrations of neutrophils or lymphocytes with occasional effects on monocytes and large unstained cells, with no consistent pattern of changes in leukocytes. In addition, evidence of neurobehavioural effects (higher low- and high-beam motor activity) was seen in the male rats at 18 000 mg/kg feed. In the absence of other evidence for an effect on the nervous system, this higher level of exploratory behaviour was considered of doubtful association with treatment and not indicative of neurotoxicity. JECFA noted that the observed effects on leukocytes were inconsistent within and between studies and were not likely to be biologically significant. Furthermore, the changes were not accompanied by histopathological changes in the progenitor cell populations of the bone marrow or lymphoid tissue, which would be expected if the effect were due to systemic toxicity. Therefore, JECFA concluded that the highest dietary concentration tested, 18 000 mg/kg (equal to average doses of ethyl lauroyl arginate of approximately 900 mg/kg bw per day in male rats and 1100 mg/kg bw per day in female rats) was the NOAEL for systemic toxicity. Long-term studies of carcinogenicity were not available.

A range of studies in vitro (bacterial mutation, cytogenetics and gene mutation in mouse lymphoma cells) with ethyl lauroyl arginate and *N*^α-lauroyl-L-arginine did not provide evidence of genotoxicity. The absence of pre-neoplastic lesions in the 52-week study and the absence of genotoxic activity do not suggest that ethyl lauroyl arginate has carcinogenic potential.

In two studies of reproductive toxicity in rats, ethyl lauroyl arginate at a dietary concentration of 15 000 mg/kg delayed vaginal opening by 4 days in the female offspring. Although this effect was not accompanied by functional changes, JECFA considered this effect to be potentially adverse and concluded that the NOAEL for the dams was a dietary concentration of 6000 mg/kg, corresponding to 502 mg/kg bw per day expressed as ethyl lauroyl arginate or 442 mg/kg bw per day expressed as the active component, ethyl-*N*^α-lauroyl-L-arginate hydrochloride.

JECFA established an ADI of 0–4 mg/kg bw for ethyl lauroyl arginate, expressed as ethyl-*N*^α-lauroyl-L-arginate hydrochloride, based on the NOAEL of 442 mg/kg bw per day identified in studies of reproductive toxicity and a safety factor of 100.

Dietary exposure

The dietary exposure to ethyl lauroyl arginate was estimated by combining food consumption data for beef and poultry with the maximum use level of 200 mg/kg in the USA. This mean dietary exposure was 2.5 mg/kg bw per day, and the dietary exposure was 4.7 mg/kg bw per day for someone consuming these foods at the 90th percentile.

EFSA has also prepared an estimate of dietary exposure to ethyl lauroyl arginate as part of its overall safety evaluation of the preservative. The potential dietary exposure to ethyl lauroyl arginate was estimated based on United Kingdom food consumption data and on the assumption that it would be present in all food categories for which use levels are proposed.

The mean potential exposure to ethyl lauroyl arginate in consumers only ranged from 0.11 mg/kg bw per day in the elderly to 0.83 mg/kg bw per day in children aged 1.5–4.5, whereas high potential exposure (97.5th percentile in consumers only) ranged from 0.37 mg/kg bw per day in the elderly to 2.89 mg/kg bw per day in children aged 1.5–4.5. EFSA concluded that, based on the data available, the average dietary exposure to ethyl lauroyl arginate across Europe would be unlikely to exceed 1 mg/kg bw per day, and high-level exposure (at the 97.5th percentile) would be unlikely to exceed 3 mg/kg bw per day.

Risk characterization

JECFA concluded that some estimates of high-percentile dietary exposure to ethyl lauroyl arginate exceed the ADI of 0–4 mg/kg bw, but recognized that these estimates were highly conservative and that actual intakes were likely to be within the ADI. Therefore, no health concerns were identified.

3.1.3.3 Ozonated water

Introduction

Because of its reactivity, the toxicity of ozone is mostly related to its reaction products, especially after oral exposure. The presence of bromide ion in the aqueous solution treated with ozone may lead to the formation of, for example, hypobromite ion, bromate ion, bromoform and other brominated THMs, dibromoacetonitrile (DBAN) and dibromoacetone (IPCS, 2000). Aldehydes, ketones, ketoacids and carboxylic acids may also be formed by ozonation.

The use of ozone in disinfection of drinking-water is described in IPCS (2000) and WHO (2006a), but no toxicity or risk characterization of ozone itself is given in these documents. Therefore, no evaluations of the toxicity of ozone from oral exposure have been found.

A review of available chemical data supports the hypothesis that rapid decomposition of ozone and its breakdown products limits their reactivity to the surface of food, and residues often will be removed by washing or peeling before eating or volatilized and decomposed during cooking.

Toxicological data

No evaluations of the toxicity of ozone from oral exposure have been found (see section 3.1.4.1 for bromate).

Dietary exposure

No dietary exposure to ozone is expected (see section 3.1.4.1 for information on exposure to bromate).

Risk characterization

As there is no direct dietary exposure to ozone, no health concerns were identified.

3.1.3.4 Peroxyacids and peroxides

Introduction

Peroxyacid antimicrobial solutions are typically prepared by mixing hydrogen peroxide and acetic acid in aqueous solution, which results in an equilibrium mixture of acetic acid, peroxyacetic acid, hydrogen peroxide and water. Preparations may also contain octanoic acid, which, when treated with hydrogen peroxide, produces an equilibrium mixture

of octanoic acid and peroxyoctanoic acid. As described in chapter 2, peroxyacids decompose to their corresponding organic acid and hydrogen peroxide or oxygen. The hydrogen peroxide in these solutions decomposes into water and oxygen. Preparations may contain 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP), which is stable and is expected to remain in the antimicrobial wash and on food after treatment.

Peroxyacid solutions were most recently evaluated by JECFA in 2005 (WHO, 2006c). JECFA considered that, owing to the high reactivity of peroxyacids and hydrogen peroxide towards organic matter, they would break down into acetic acid, octanoic acid and water, respectively, and therefore be of no safety concern (WHO, 2006c). This is the most recent international evaluation of peroxyacids.

EFSA has also reviewed peroxyacids for treatment of poultry carcasses and concluded that the estimated intakes of residues of peroxyacetic acid, hydrogen peroxide, acetic acid, octanoic acid and HEDP arising from the treatment of poultry carcasses would be of no safety concern (EFSA, 2005).

Toxicological data

In 2005, JECFA considered the safety of antimicrobial solutions using HEDP as a sequesterant or stabilizer and containing three or more of the following components: acetic acid, hydrogen peroxide, octanoic acid and peroxyacetic acid (WHO, 2006c). These solutions are intended to be diluted before use to achieve peroxyacid concentrations in the range 80–220 mg/kg. JECFA concluded that the peroxy compounds in these solutions would break down into acetic acid and octanoic acid and that small residual quantities of these acids on foods at the time of consumption would not pose a safety concern; JECFA therefore focused its evaluation on the residues of HEDP that are anticipated to remain on foods (WHO, 2006c).

JECFA noted that absorption of HEDP from the gastrointestinal tract is very limited and that its metabolism is negligible. HEDP did not show evidence of mutagenic activity. In 90-day toxicity studies in dogs and rats, the NOELs were 250 mg/kg bw per day and 500 mg/kg bw per day, respectively (WHO, 2006c). In reproductive toxicity studies, a NOEL of 50 mg/kg bw per day was identified for both rats and rabbits. HEDP has not shown any evidence of mutagenic activity. Based on the available toxicity data, together with a margin of exposure of >1000 when comparing the highest estimate of intake of HEDP with the starting oral dose of 5 mg/kg bw per day used in clinical treatment of patients with Paget disease, JECFA concluded that HEDP does not pose a safety concern at the concentrations of residue that are expected to remain on foods (WHO, 2006c).

JECFA evaluated acetic acid in 1974, allocating an ADI “not limited”¹ (FAO/WHO, 1974a). This ADI was retained at a subsequent evaluation in 1997 (FAO/WHO, 1999). In evaluating the acceptance of acetic acid, emphasis was placed on its established metabolic pathways (metabolized to carbon dioxide) and its consumption by humans as a normal constituent of the diet. Also in 1997, JECFA concluded that use of octanoic acid as a flavouring agent posed no safety concerns at intakes of up to 63 µg/kg bw per day (FAO/WHO, 1999). JECFA evaluated hydrogen peroxide in 1966 as a preservative and sterilizing agent for use in milk, concluding that it was not possible to set an ADI for humans because of the instability of hydrogen peroxide in contact with food (FAO/WHO, 1966). However, it was noted that hydrogen peroxide may be used only in circumstances where more acceptable methods of milk preservation are not available (FAO/WHO, 1966). This was confirmed in a subsequent evaluation in 1974 (FAO/WHO, 1974b).

¹ This is a term no longer used by JECFA that has the same meaning as ADI “not specified” (see Annex 4).

Dietary exposure

Human exposure to components of antimicrobial peroxyacid solutions was evaluated by the sixty-third meeting of JECFA (FAO/WHO, 2005). Additionally, an EFSA evaluation was published in 2005. Consistent with what is known about the chemistry of peroxy compounds, no residues of hydrogen peroxide, peroxyacetic acid or peroxyoctanoic acid are anticipated to be present on foods that have been washed in, sprayed with or otherwise treated using peroxyacid solutions derived from acetic or octanoic acid and subsequently cooked. Regardless, the EFSA evaluation included a highly conservative estimate of 1.46 µg/kg bw per day for possible residual peroxyacids and hydrogen peroxide (at the 99th percentile). This estimate was based on a detection limit of 1 mg/l, assuming that peroxide concentrations no higher than 0.25 mg/kg carcass would be present 2 min after treatment.

Acetic and octanoic acids present at equilibrium in the solutions and as by-products from the corresponding peroxyacids would be expected to remain on any treated foods that are not washed or further processed after treatment. JECFA reported that the mean intake of octanoic acid from foods consumed as part of the diet in the USA had been estimated to be approximately 200 mg/day. A highly conservative estimate of exposure to octanoic acid resulting from the use of the antimicrobial solutions of 1.9 mg/day was noted (WHO, 2006c). The intake of acetic acid was not explicitly analysed for JECFA, but its use in and on foods (as vinegar) would result in a greater exposure than that from the use of peroxyacid antimicrobial solutions. There would be no need to further consider exposure to these common food acids. The EFSA evaluation did not consider exposure to the fatty acid by-products.

HEDP is expected to remain on foods that are treated with antimicrobial solutions and that are not further washed, processed or cooked. JECFA reported that, on the international level, the highest estimate of intake of HEDP, prepared using GEMS/Food diets, was that for the European diet: 3.6 µg/kg bw per day, for the upper-bound estimate using a model for vegetables with a high surface area. JECFA also considered national estimates of intake from the Czech Republic, the USA and the United Kingdom. The upper-bound estimate of exposure was 2.2 µg/kg bw per day for the Czech Republic. The mean and 90th-percentile upper-bound estimates of intake for the USA were 2.2 and 4.7 µg/kg bw per day, respectively. The mean and 90th-percentile upper-bound estimates of intake for the United Kingdom were 1.8 and 3.3 µg/kg bw per day, respectively. The EFSA estimate of dietary exposure to HEDP was 1 µg/kg bw per day at the 99th percentile. EFSA noted that its estimates did not consider washing or food preparation and that actual dietary consumption is likely to be lower.

JECFA was aware of non-food uses of HEDP. HEDP is used as an anti-scalant for water treatment and in boilers worldwide (the regulatory limit for this use is 25 µg/l in the USA). HEDP is also used as a drug to treat Paget disease and in some over-the-counter cosmetic and pharmaceutical formulations. The USEPA (1998) estimated that exposure to HEDP from all these uses was not more than 6 µg/kg bw per day, including 0.04 µg/kg bw per day from its use on food. JECFA noted that this estimate of exposure resulting from food uses of HEDP was much less conservative than that used in the present evaluation.

Overall, a conservative estimate of the chronic dietary exposure to HEDP would be 5 µg/kg per day, based on the 90th-percentile national estimate from the USA.

Risk characterization

As JECFA concluded that HEDP does not pose a safety concern at the concentrations of residue that are expected to remain on foods, no health concerns were identified.

3.1.3.5 Quaternary ammonium compounds (cetylpyridinium chloride)

Introduction

Quaternary ammonium compounds (QACs) are organically substituted ammonium compounds that are commonly used as surface sanitizers in processing facilities. Cetylpyridinium chloride (CPC) is a QAC found in an anhydrous form or as the monohydrate.

The toxicity data used in this document are from reports provided to the USFDA in connection with a toxicological evaluation of the use of CPC as an antimicrobial agent on the surface of raw poultry carcasses (secondary direct food additive) (USFDA, 2007a,b). The USFDA established an ADI for CPC of 8 µg/kg bw per day (USFDA, 2007a).

Toxicological data

No chronic (2-year) or carcinogenicity studies of CPC were found. CPC was reported to be not mutagenic in *Salmonella typhimurium* strains TA97a, TA98, TA100 and TA1535 and *Escherichia coli* WP2 *uvrA* (pkM101), with or without activation, and it was not clastogenic in the in vitro chromosomal aberration assay with CHO cells, with and without activation (USFDA, 2007a).

Twenty male and 20 female Sprague-Dawley rats per treatment were fed CPC-containing diet at a dose level of 0, 125, 250, 500 or 1000 mg/kg for 90 days, equivalent to 0, 8.97, 17.94, 35.36 or 70.23 mg/kg bw per day in males and 0, 10.85, 22.30, 42.40 or 82.66 mg/kg bw per day in females (USFDA, 2007a). Feed consumption, clinical observations, body weights and absolute and relative organ weights were recorded, and haematology, serum chemistry, urinalysis, ophthalmic and neurological examinations, gross examination and histopathology were performed. The study conclusions were that 1000 mg/kg feed was the LOAEL in rats based on decreased body weights and body weight gain in both sexes and reduced heart weight in females. The NOEL was 500 mg/kg feed, equivalent to 35.36 and 42.40 mg/kg bw per day, respectively, for male and female rats.

Male and female purebred Beagle dogs, four animals per sex per dose, were fed diets containing CPC at 0, 250, 375, 500 or 1000/500 mg/kg feed for 90 days. The test compound was withheld from animals in the 1000 mg/kg group from study day 29 until day 42/41 (males/females) because of significant weight loss in this dose group. The CPC treatment was then resumed, but at 500 mg/kg feed for the duration of the study. Corresponding time-weighted average doses of CPC were 0, 7.82, 11.76, 14.15 and 16.65 mg/kg bw per day in males and 0, 8.01, 10.79, 17.29 and 17.14 mg/kg bw per day in females, respectively. Feed consumption, clinical observations, body weights, and absolute and relative organ weights were recorded, and haematology, serum chemistry, urinalysis, ophthalmic and neurological examinations, gross examination and histopathology were done. The study conclusions were that, based on the reduction in body weight gain seen in both sexes in the CPC-treated dogs and decreased red blood cell parameters (i.e. red blood cell count, haemoglobin level and haematocrit), the LOAEL was 375 mg/kg feed. A NOEL of 250 mg/kg feed, equivalent to 8 mg/kg bw per day (7.82 and 8.01 mg/kg bw per day for males and females, respectively), was established.

Because the NOEL in the 90-day dog study was lower than the NOEL in the 90-day rat study, to be conservative, the NOEL from the dog study was used to calculate the ADI for CPC. Using the NOEL of 8 mg/kg bw per day from the dog study and applying a safety factor of 1000, the USFDA established an ADI for CPC of 8 µg/kg bw per day, or 0.48 mg/day for a person with a body weight of 60 kg (USFDA, 2007a).

Dietary exposure

Consumption data for chicken taken from a survey in the USA were used to calculate exposure to CPC. As it was shown in the residue studies that the CPC exposure was almost exclusively due to consumption of skin, only data for skin-on poultry were used (with 8.8% of poultry weight being skin). Poultry consumption of 22 g/day was combined with the CPC residual data taken from the studies using 0.8% solutions (mimicking the United States regulation; see section 2.12.1) to give a CPC exposure of 26 µg/person per day.

Dietary exposure to CPC from consumption of treated poultry can be generalized using the GEMS/Food database for consumption data. The highest consumption of poultry meat is for cluster K, 146 g/person per day. Using this figure (assuming that the skin is consumed with the poultry at 8.8%, as above) with the maximum mean residual level of 20 mg/kg (from use of a 2.0% solution of CPC; see section 2.12.1) gives an exposure to CPC of 260 µg/person per day, equal to 4.3 µg/kg bw per day for a 60-kg person.

It is noted that CPC also has potential uses in dentifrices at 0.005–2% of product, from which some ingestion can occur during tooth brushing (USP, 1991).

Risk characterization

The estimated dietary exposure of 4.3 µg/kg bw per day is below the ADI for CPC of 8 µg/kg bw per day established by the USFDA. Therefore, no health concern was identified with use of CPC on food contact surfaces.

3.1.3.6 Iodophors

Introduction

Iodophors are mixtures of iodine and surface-active agents that act as carriers and solubilizers for the iodine. The result is a water-soluble material that releases free iodine (12.5–25 mg/l) in solution. The information used here is from the background document on iodine for development of the WHO *Guidelines for drinking-water quality* (WHO, 2003b).

Toxicological data

Iodine is an essential element in the synthesis of the thyroid hormones thyroxine (T₄) and triiodothyronine (T₃) through the precursor protein thyroglobulin and the action of the enzyme thyroid peroxidase. The estimated dietary iodine requirement for adults ranges from 80 to 150 µg/day (WHO, 2003b). Chronic consumption of iodinated drinking-water has not been shown to cause adverse health effects in humans, although some changes in thyroid status have been observed (WHO, 2003b).

In 1988, JECFA set a provisional maximum tolerable daily intake (PMTDI) for iodine of 1 mg/day (17 µg/kg bw per day) from all sources, based mainly on data on the effects of iodide (WHO, 1989). However, recent data from studies in rats indicate that the effects of iodine in drinking-water on thyroid hormone concentrations in the blood differ from those of iodide (WHO, 2003b). Available data therefore suggest that derivation of a guideline value for iodine on the basis of information on the effects of iodide is inappropriate, and there are few relevant data on the effects of iodine. Because iodine is not recommended for long-term disinfection, only for emergency disinfection of drinking-water in the field, lifetime exposure to iodine from water disinfection is unlikely. For these reasons, a guideline value for iodine has not been established (WHO, 2003b).

Dietary exposure

Currently in the USA, iodophores are regulated for use as sanitizers on hard surfaces that may contact food; they are not used directly on food. However, because sanitizers used

in the USA are not washed from food contact surfaces before the surfaces are used to process food, there may be some carryover from the surface to the food. The USFDA (1993) models this situation as follows. It is assumed that 1 mg of end user solution (maximum allowable iodine concentration in the USA is 25 mg/l) resides on each square centimetre of treated surface. For iodophores, this results in a residual iodine level of $0.03 \mu\text{g}/\text{cm}^2$ surface. It is then assumed that all food consumed in a day would contact 4000 cm^2 of this treated surface. This highly conservative model derives a dietary exposure to iodophores of 0.1 mg/person per day (about $2 \mu\text{g}/\text{kg}$ bw per day for a 60-kg individual).

WHO (2003b) estimated that the main natural sources of dietary iodide are seafood (200–1000 $\mu\text{g}/\text{kg}$) and seaweed (1000–2000 mg/kg). Iodide is also found in cow's milk (20–70 $\mu\text{g}/\text{l}$) and may be added to table salt (100 μg of potassium iodide per gram of sodium chloride) to ensure an adequate intake of iodine. Exposure to iodine may occur through drinking-water, pharmaceuticals and food. At a concentration of 4 $\mu\text{g}/\text{l}$ in drinking-water, adult human daily intake will be 8 μg iodine, on the assumption that 2 litres of drinking-water are consumed per day.

The WHO dietary exposure assessment did not take into account emergency disinfection of drinking-water in the field. However, lifetime exposure to iodine from water disinfection is unlikely.

Risk characterization

The highly conservative estimate of dietary exposure to iodine from use of iodophores ($2 \mu\text{g}/\text{kg}$ bw per day) is well below the PMTDI of $17 \mu\text{g}/\text{kg}$ bw per day. There are other sources of iodine in the food. If these result in total dietary exposure approaching or exceeding the PMTDI, the contribution from iodophores would be minimal. Therefore, no health concerns were identified.

3.1.3.7 Sodium metasilicate

Introduction

Sodium metasilicate (waterglass) is commercially available in three forms: anhydrous (Na_2SiO_3 ; CAS No. 6834-92-0), pentahydrate ($\text{Na}_2\text{SiO}_3 \cdot 5\text{H}_2\text{O}$; CAS No. 10213-79-3) and nonahydrate ($\text{Na}_2\text{SiO}_3 \cdot 9\text{H}_2\text{O}$; CAS No. 13517-24-3) (IPCS, 1997).

Sodium metasilicate is not included in WHO's *Guidelines for drinking-water quality* (WHO, 2006a). It is described in an IPCS (1997) document and has been evaluated by the USEPA (2006), by the OECD (2004) in a Screening Information Dataset document on soluble silicates, including sodium metasilicate, and in a document prepared for the United States National Institute of Environmental Health Sciences (Haneke, 2002a). In addition, a document was submitted by industry on products containing either anhydrous or pentahydrate forms of sodium metasilicate (DANISCO, 2007). These reports have been used as sources of information in this section.

In 1973, JECFA allocated an ADI "not limited" for silicon dioxide and certain silicates except magnesium silicate and talc (FAO/WHO, 1974b). This was on the basis of the biological inertness of these compounds.

Toxicological data

No lifetime (2-year) studies were found on sodium metasilicate. In a 2-year study reported in USEPA (2006), rats and mice were fed silicon dioxide (SiO_2 , a degradation product of sodium metasilicate pentahydrate) at dietary levels of up to 50 000 mg/kg (5% of the diet), giving doses of approximately 2500 and 7500 mg/kg bw per day for rats and mice, respectively. The only effect noted was a significant reduction in body weight at the highest

dose at the 10-week point in mice, which continued throughout the rest of the study. This was likely attributable to a nutritional imbalance rather than a toxic effect of the high percentage of silica in the daily diet of the mice. No adverse effects were observed in rats. (The lower doses were not stated, and the reference to the study was not given.)

In a 90-day study in rats, anhydrous sodium metasilicate was administered in drinking-water at concentrations of 200, 600 and 1800 mg/l, corresponding to approximately 26.4, 76.2 and 227.1 mg/kg bw per day for males and approximately 32.1, 97.6 and 237.2 mg/kg bw per day for females. No clearly treatment-related effects were found; therefore, the NOAEL was 227–237 mg/kg bw per day (the highest dose tested) in the rats (OECD, 2004).

In a 90-day study in mice, anhydrous sodium metasilicate was administered in drinking-water at concentrations of 300, 900 and 2700 mg/l to males and 333, 1000 and 3000 mg/l to females, corresponding to approximately 96–100, 264–280 and 776–832 mg/kg bw per day in males and approximately 88–104, 260–284 and 716–892 mg/kg bw per day in females (OECD, 2004). Body weight, urinalysis, clinical chemistry, haematology, organ weights and histopathology were examined. No fatalities occurred. In females, a significant decrease in pituitary gland weight was observed in the high-dose group. Other effects occasionally observed were single incidences and not dose related. The NOAELs were therefore 776–832 mg/kg bw per day in males (highest dose tested) and 260–284 mg/kg bw per day in females. The LOAEL was 716–892 mg/kg bw per day in female mice.

The chemical structure of sodium metasilicate does not contain elements that raise concern for genotoxicity (OECD, 2004). None of the substances sodium metasilicate, silicic acid and silicon dioxide showed point mutation activity in three bacterial test species (USEPA, 2006). Anhydrous sodium metasilicate at concentrations of 0.005–0.5 mol/l (<6.2%) was not genotoxic in DNA damage and repair assays conducted on *Bacillus subtilis* recombination repair-deficient and wild-type strains without metabolic activation (OECD, 2004; DANISCO, 2007). Anhydrous sodium metasilicate was negative in the Ames test with *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, with and without metabolic activation, at concentrations of 0.1–10 mg/plate and in the mouse bone marrow chromosomal aberration test in vivo after single oral doses of 740–1340 mg/kg bw (OECD, 2004).

There are no Codex Alimentarius Commission maximum residue levels established for residues of sodium metasilicate (USEPA, 2006).

Dietary exposure

Sodium metasilicate is widely used in cosmetics, hair and skin products, detergents and a variety of cleaning products and as an active ingredient in insecticides, fungicides and antimicrobial pesticides at concentrations up to 4% (USEPA, 2006). There are therefore several potential sources of exposure to sodium metasilicate.

Silica and silicates are permitted for use as direct food additives, primarily as flow agents in powdered foods or to absorb water (Haneke, 2002a; EFSA, 2004; USEPA, 2006). The sodium metasilicate pentahydrate is also classified by the USFDA as “generally recognized as safe” (GRAS) as an indirect food additive for use in washing mixtures of fruits and vegetables, in sanitizing solutions on food contact surfaces, in boiler water and for other uses (Haneke, 2002a; USEPA, 2006). Residues of the pentahydrate, when used in fruit and vegetable washes, are expected to be orders of magnitude less than the estimated daily dietary consumption of 20–30 mg silica (silicon dioxide, silicon) from natural sources and drinking-water (USEPA, 2006). EFSA (2004) referenced earlier work where the daily intake from the British diet had been estimated to be 20–50 mg (Pennington, 1991; Bellia, Birchall & Roberts, 1994). The relative contributions were 55% from water, coffee and beer, 14% from grain products and 8% from vegetables. The dietary silicon exposure estimated from the

British diet was 20–50 mg/day, corresponding to 0.3–0.8 mg/kg bw per day for a 60-kg person, and EFSA considered that these intakes were unlikely to cause adverse effects.

The EFSA (2004) opinion also referred to silicon, in the form of silica, being found in supplements. According to the doses recommended by the manufacturers, the supplements (e.g. products on the Norwegian market, according to the Norwegian Institute of Public Health) provide 1–75 mg/day as silicon, corresponding to 0.017–1.25 mg/kg bw per day for a 60-kg adult. Silicon in the form of amorphous silica, silicates and dimethylpolysiloxane is added to food as an anti-caking and anti-foaming agent. Dimethylpolysiloxane is used for the treatment of infant colic.

The OECD (2004) also estimated the summed systemic exposure of consumers to soluble silicates through oral, dermal and inhalation contact with detergents and cleaners to be 12.3 µg/kg bw per day, which is about 1–2 orders of magnitude lower than the estimated daily silica intake through ubiquitous natural occurrence in the diet (soluble silicates include sodium metasilicate, sodium silicate [CAS No. 1344-09-8] and potassium silicate [CAS No. 1312-76-1]). This study also reported that another important route of exposure is through the addition of sodium silicate to drinking-water as a corrosion inhibitor and sequestering agent.

Risk characterization

Dietary exposure resulting from use of metasilicate as a disinfectant is insignificant in comparison with other dietary sources of silicates, and no health concerns were identified.

3.1.3.8 Trisodium phosphate

Introduction

Trisodium phosphate (TSP) was most recently evaluated by EFSA (2005), which cited the maximum tolerable daily intake (MTDI) of 70 mg/kg bw established by JECFA in 1982 for the group of phosphoric acid and phosphate salts (WHO, 1982). The European Scientific Committee for Food (SCF, 1991) also endorsed the MTDI.

Toxicological data

JECFA evaluated TSP in 1982 as part of the group of phosphoric acid and phosphate salts (WHO, 1982). JECFA noted that the toxicological end-point of most concern was ion imbalance in the diet, with high phosphate intakes leading to calcification of soft tissues, especially the kidneys, and loss of bone density. In a series of experiments, Sherman diets containing 1%, 2.5% and 5% sodium diphosphate were fed for 16 weeks to groups of 20 male and female rats weighing between 90 and 115 g; a similar group received a diet containing 5% sodium monophosphate. In the sodium phosphate groups, growth was normal up to the 2.5% level; kidney weight was increased at the 2.5% level (females) and above; and kidney function (concentration test) was decreased at the 2.5% level (males) and above. Kidney damage (calcification, degeneration and necrosis) was observed in a greater percentage of rats in the 1% group than in the controls. At the higher concentration of sodium diphosphate, more severe kidney damage occurred; in addition, some of the animals had hypertrophy and haemorrhages of the stomach. The latter abnormality was not found in the 5% sodium monophosphate group. Other studies found no effects on the kidney at higher doses. JECFA considered the rat to be exquisitely sensitive to calcification and hydronephrosis upon exposure to acids forming calcium chelates or complexes and identified 1% as the lowest level of dietary phosphorus that might conceivably lead to nephrocalcinosis in rats. This was extrapolated to humans using the equivalent daily caloric intake to derive a phosphorus dose of 6600 mg/day. JECFA noted that “the usual calculation for provision of a margin of safety is probably not suitable for food additives that are also nutrients” and established an MTDI of

70 mg/kg bw, expressed as phosphorus, for the sum of phosphates naturally present in food and derived from additives.

The SCF (1991) noted that phosphate salts are not mutagenic in a number of test systems.

Dietary exposure

TSP is approved for use in raw unchilled poultry carcasses and giblets in the USA (USDA, 2007). TSP is also used as a food additive, and in these uses all sodium phosphates may be referred to collectively as sodium phosphate or by International Numbering System No. 339. TSP was most recently evaluated by EFSA (2005). Another report, prepared for the government in the USA (USDA, 2002), considered the efficacy and safety of TSP use in poultry processing. The report considered oral exposure, although no dietary exposure assessment was undertaken.

The EFSA (2005) assessment includes an exposure assessment estimated using the Concise European Food Consumption Database. Exposure assessment using mean and high percentiles of consumption was conducted for three European countries. Mean and high consumptions of meat and meat products (including offal) by adults were extracted from the three national food consumption surveys—namely, France (Volatier, 2000), Italy (Turrini et al., 2001) and Sweden (Becker & Pearson, 2002)—which are based on 7-day records for individuals. Average mean daily consumption of meat (edible portion) is given in Table 3.2 in section 3.1.2.2. Potential dietary exposure to all substances was estimated based on the conservative hypothesis that the concentration in the edible part of the meat is identical to the concentration in the carcass.

Previous calculations by the Scientific Committee on Veterinary Measures relating to Public Health (SCVPH, 2003) indicated that the treatment of poultry carcasses with TSP would incorporate TSP at a concentration of 480 mg/kg carcass. Using these calculations and the meat consumption data for European adults, as reported above, EFSA (2005) estimated that the potential daily exposure to TSP for a 60-kg individual would be up to 1.21 mg/kg bw at the mean meat consumption and up to 2.08 and 2.80 mg/kg bw at the 95th and 99th percentiles of meat consumption, respectively.

Risk characterization

The dietary exposure estimated to result from the use of TSP in treatment of poultry carcasses is considerably lower than the MTDI of 70 mg/kg bw, expressed as phosphorus, for the total sum of phosphates. Therefore, no health concerns were identified.

3.1.4 Disinfection by-products

3.1.4.1 Bromate

Introduction

Bromate is not normally found in water, but may be formed in water during ozonation when the bromide ion is present (WHO, 2005a). Bromate may also be present in hypochlorite solutions used to disinfect drinking-water, as a result of the presence of bromide in the raw materials (chlorine and sodium hydroxide) used in the manufacture of sodium hypochlorite and the high pH of the concentrated solution (WHO, 2005a). The toxicology and mechanisms of in vivo bromate carcinogenicity have been examined in detail (Bull & Cotruvo, 2006).

The toxicology of bromate is evaluated and described in Environmental Health Criteria 216 (IPCS, 2000), in the WHO *Guidelines for drinking-water quality* (WHO, 2006a) and in the bromate background document for development of these guidelines (WHO,

2005a). In addition, IARC monographs (IARC, 1986, 1987, 1999b) and a USEPA toxicological review of bromate (USEPA, 2001), as well as some original publications of pivotal studies, have been used as sources of information in this section.

Both a carcinogenicity assessment based on the linearized multistage model and a TDI of 1 µg/kg bw based on a non-linear approach for the carcinogenicity of bromate have been developed (IPCS, 2000).

Toxicological data

The systemic toxicity of bromate (administered as the potassium salt) has been reported from long-term studies designed to evaluate the carcinogenicity of bromate in F344 rats and B6C3F1 mice (Kurokawa et al., 1983, 1986a,b; DeAngelo et al., 1998). The data show that the kidney is the major target organ of bromate-associated toxicity and that rats are more sensitive than mice to bromate exposure (WHO, 2005a). A NOAEL could not be determined from the studies of Kurokawa et al. (1983, 1986a,b). A NOAEL for bromate of 1.1 mg/kg bw per day was identified in male F344 rats based on kidney effects (i.e. renal pelvis urothelial hyperplasia), and a NOAEL of 59.6 mg/kg bw per day was identified in male B6C3F1 mice based on studies in which no effects on survival, body weight, organ weight, serum chemistry or incidence of non-neoplastic lesions were observed (DeAngelo et al., 1998).

A physiologically based toxicokinetic model for bromate metabolism and detoxification is in the later stages of development, based upon *in vivo* studies in the rat (J.A. Cotruvo, personal communication, 2008). The liver is not a target organ, and it has been shown that the liver is significantly less susceptible than the kidney for cytotoxicity or DNA damage. Even at fairly high doses, the half-life in the rat is in minutes. Indications are that environmentally relevant bromate doses are rapidly metabolized in the liver and blood, thus significantly reducing or virtually eliminating doses to target organs. Thus, previous risk models most likely significantly overestimated the low-dose risks from bromate ingestion (J.A. Cotruvo, personal communication, 2008).

The weight of evidence demonstrated that bromate is clearly mutagenic *in vitro* and *in vivo* (IPCS, 2000; WHO, 2005a). The clearest evidence of bromate-induced cancer comes from the studies of F344 rats. In summary (WHO, 2005a), bromate produced tumours at multiple sites in male rats, including the kidney (adenomas and carcinomas), the thyroid gland (follicular cell adenomas and carcinomas) and the peritoneum (mesotheliomas) (Kurokawa et al., 1983, 1986a,b, 1987; DeAngelo et al., 1998). In the female rat, only kidney tumours were observed (Kurokawa et al., 1983, 1986b). Further, a clear dose–response relationship exists with tumour incidence and the severity/progression of tumours. The weight of evidence from the rat bioassays clearly indicates that bromate has the potential to be a human carcinogen at high doses. Bromate also caused a treatment-related, but not dose-related, increase in the incidence of renal tumours in male B6C3F1 mice (DeAngelo et al., 1998).

WHO (IPCS, 2000; WHO, 2005a) noted that there were insufficient data to conclude on the mode of carcinogenic action of bromate, whether it is cytotoxicity and reparative hyperplasia, oxidative stress, such as lipid peroxidation and free radical production, and/or DNA reactivity (genotoxicity), and stated that the mechanisms may also differ for tumours at various sites. Thiol-dependent oxidative damage to the guanine base in DNA was considered a plausible mode of action for bromate-induced cancer (Bull & Cotruvo, 2006).

The kidney is the major target organ of bromate-associated carcinogenicity, and male rats are significantly more sensitive than female rats, mice or hamsters to bromate exposure (Gold, 2005).

IARC (1986, 1987, 1999b) evaluated the carcinogenicity of potassium bromate and concluded that it is possibly carcinogenic to humans (Group 2B). There was inadequate evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of potassium bromate (IARC, 1999b). The USEPA (2001) has also classified bromate in Group B2 as a probable (likely) human carcinogen by the oral route of exposure on the basis of no evidence in humans and adequate evidence of carcinogenicity in male and female rats.

Because of insufficient information on the mode of carcinogenic action of bromate, both a carcinogenicity assessment based on the linearized multistage model as well as a TDI based on a non-linear approach for the carcinogenicity of bromate were developed (WHO, 2005a). A TDI of 1 µg/kg bw was calculated based on a no-effect level for the formation of renal cell tumours in rats at 1.3 mg/kg bw per day in the study of Kurokawa et al. (1986a) and the use of an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for possible carcinogenicity). The calculated upper 95% confidence limit of 0.1 µg/kg bw per day for a 10^{-5} excess lifetime cancer risk (WHO, 2005a) was based on an increased incidence of renal tumours in male rats given potassium bromate in drinking-water for 2 years using the same study (Kurokawa et al., 1986a).

The more recent study by DeAngelo et al. (1998) was selected for the derivation of a guideline value for drinking-water (WHO, 2005a, 2006a), because this study used lower doses and more animals per group and the tumour findings were similar to those observed in the earlier study. To estimate cancer risks based on low-dose linear extrapolation, a one-stage Weibull time-to-tumour model was applied to the incidence of each tumour type (mesotheliomas, renal tubule tumours and thyroid follicular tumours) in male rats given potassium bromate in drinking-water, using the 12-, 26-, 52- and 77-week interim kill data (DeAngelo et al., 1998). Individual cancer potency estimates were summed using Monte Carlo analysis (USEPA, 2001). The upper-bound estimate of the cancer potency for bromate was $0.19 \text{ (mg/kg bw per day)}^{-1}$. The concentrations in drinking-water associated with upper-bound excess lifetime cancer risks of 10^{-4} , 10^{-5} and 10^{-6} were 20, 2 and 0.2 µg/l, respectively.

Dietary exposure

As discussed above, bromate may be formed in water during ozonation when the bromide ion is present. Bromate may also be generated during the use of DBDMH as an antimicrobial on beef and poultry. However, bromate is a strong oxidant (Seidel, 2004) and is expected to be reduced to bromide during cooking (USFDA, 2003). Therefore, bromate is not expected to be present on beef or poultry at the time of consumption.

WHO has reported that for most people, exposure to bromate is unlikely to be significant (IPCS, 2000).

Risk characterization

Because bromate is not expected to be present on meat at the time of consumption, no health concerns were identified.

3.1.4.2 Chloral hydrate (2,2,2-trichloroethane-1,1-diol)

Introduction

Chloral hydrate ($\text{Cl}_3\text{CCH}(\text{OH})_2$; CAS No. 302-17-0) may be formed in reactions between NOM and hypochlorous acid or hypobromous acid (IPCS, 2000).

The information in this section is based mostly on IPCS (2000). In addition, IARC (1995) and some original publications have been used. A TDI of 16 µg/kg bw per day has been derived for chloral hydrate (IPCS, 2000).

Toxicological data

In a 2-year study, chloral hydrate at 1 g/l of drinking-water (166 mg/kg bw per day) induced liver tumours in male B6C3F1 mice (Daniel et al., 1992a). Lower doses were not evaluated. It is probable that the liver tumours induced by chloral hydrate involve its metabolism to trichloroacetic acid (TCA) and/or dichloroacetic acid (DCA), which are considered to act as tumour promoters (IPCS, 2000). Chloral hydrate has been shown to induce chromosomal anomalies in several in vitro tests, but it has been largely negative when evaluated in vivo (IARC, 1995). IARC (1995) has classified chloral hydrate in Group 3 (not classifiable as to its carcinogenicity to humans).

Chloral hydrate administered to Sprague-Dawley rats for 90 days in drinking-water induced hepatocellular necrosis at concentrations of 1200 mg/l and above, with no effect being observed at 600 mg/l (approximately 60 mg/kg bw per day) (Daniel et al., 1992b). Hepatomegaly was observed in male CD-1 mice at doses of 144 mg/kg bw per day administered by gavage for 14 days, whereas no effects were seen at 14.4 mg/kg bw per day for 14 days (Sanders et al., 1982). Mild hepatomegaly was observed in male CD-1 mice when chloral hydrate was administered in drinking-water at 70 mg/l (16 mg/kg bw per day) in a 90-day follow-up study (Sanders et al., 1982).

Based on the mild hepatomegaly observed when chloral hydrate was administered in drinking-water at 16 mg/kg bw per day to male CD-1 mice in the 90-day follow-up study (Sanders et al., 1982) and applying an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for the use of a LOAEL instead of a NOAEL), a TDI of 16 µg/kg bw per day was derived (IPCS, 2000).

Dietary exposure

No occurrence data on the levels of chloral hydrate in food, other than drinking-water, were identified. Occurrence data relating to the concentration of chloral hydrate in drinking-water in North America are summarized in Table 2.4 in chapter 2.

An estimate of mean dietary exposure arising from the consumption of drinking-water has been calculated and is presented in Table 3.4. Dietary exposure resulting from the consumption of drinking-water was within the range 0.000–0.073 µg/kg bw per day.

Table 3.4. Mean dietary exposure to chloral hydrate from the consumption of drinking-water^a

Exposure		Exposure	
Country	(µg/kg bw per day)	Country	(µg/kg bw per day)
Australia	0.031	Ireland	0.008
Belgium	0.003	Italy	0.007
Czech Republic	0.008	Netherlands	0.006
Denmark	0.025	Norway	0.009
Finland	0.025	Slovakia	0.007
France	0.009	Sweden	0.014
Germany	0.002	United Kingdom	0.006
Hungary	0.000	USA	0.031
Iceland	0.019	WHO	0.073

^a The mean concentration of chloral hydrate from 12 drinking-water utilities in the USA and Canada was used in the estimate of dietary exposure.

Risk characterization

No data have been identified in relation to residues of chloral hydrate in food resulting from use of chlorine-based disinfectants. Therefore, no health concern was identified, but residue data are needed.

3.1.4.3 Chlorate

Introduction

Chlorate is generated as a reaction by-product from the use of ASC or chlorine dioxide. It is also a decomposition product of stored sodium hypochlorite and can be present in treated food.

JECFA evaluated chlorate as part of its evaluation of ASC in 2007 and set an ADI for chlorate of 0.01 mg/kg bw per day (WHO, 2008a). This is the most recent evaluation of chlorate.

In reviewing ASC, EFSA (2005) noted the dietary exposure to chlorate residues, but did not specifically comment on the health implications.

Toxicological data

Chlorate is rapidly absorbed and distributed throughout the body. It is excreted primarily in the urine in the form of chloride, with lesser amounts of chlorite and chlorate.

In common with sodium chlorite, sodium chlorate has been reported to have effects on erythrocytes, but JECFA concluded that the most sensitive effects were changes to the thyroid gland of male rats in a 2-year carcinogenicity study (NTP, 2005). Groups of 50 male and 50 female F344/N rats were exposed to sodium chlorate in the drinking-water for 2 years at doses equivalent to approximately 5, 35 and 75 mg/kg bw per day for males and 5, 45 and 95 mg/kg bw per day for females. There were positive trends in the incidence of thyroid gland follicular cell carcinoma in male rats and thyroid gland follicular cell adenoma and carcinoma (combined) in male and female rats. The incidence of thyroid gland follicular cell hypertrophy was significantly increased in all exposed male groups and in the mid- and high-dose groups of females. Thyroid gland focal follicle mineralization occurred in most females in the mid- and high-dose groups. The incidences of haematopoietic cell proliferation in the spleen of high-dose males and bone marrow hyperplasia in the mid- and high-dose male groups were significantly greater than controls. Because a NOAEL was not identified in this study, JECFA decided to apply a benchmark dose (BMD) approach to derive a point of departure on the dose–response curve. Rats are considered to be highly sensitive to the effects of agents that disrupt thyroid hormone homeostasis. JECFA considered that humans are likely to be less sensitive than rats to these effects and that a safety factor for interspecies variation was not required. The rat thyroid gland follicular cell hypertrophy data were modelled in order to derive the BMD for a 10% increase in follicular cell hypertrophy (BMD₁₀) and the corresponding 95% lower confidence limit (BMDL₁₀). The BMDL₁₀ values for chlorate ranged from 1.1 to 4.4 mg/kg bw per day, with the lowest value representing the best fit.

Some positive results have been found in bacterial mutation assays in vitro using chlorate, but no positive results have been observed in in vivo genotoxicity assays. Based on the negative in vivo genotoxicity data and the nature of the histopathological observations, JECFA concluded that a non-genotoxic mode of action was likely for the induction of thyroid tumours by sodium chlorate. This mode of action is likely to be mediated via decreased serum thyroid hormones, leading to increased release of thyroid stimulating hormone (TSH) and consequent stimulation of thyroid cell proliferation and thyroid gland growth, which can lead to thyroid tumours in rodents (WHO, 2008a).

JECFA established an ADI of 0–0.01 mg/kg bw for chlorate on the basis of the BMDL₁₀ of 1.1 mg/kg bw per day, applying a safety factor of 10 to allow for intraspecies variability and an additional factor of 10 to allow for deficiencies in the database, particularly with respect to investigation of possible neurodevelopmental effects.

Dietary exposure

Dietary exposure to chlorate was considered by JECFA (WHO, 2008a) in the context of the use of ASC as a spray or dipping solution for poultry, meats, vegetables, fruits and seafoods and in poultry chilling water. JECFA stated that residual chlorine dioxide is lost by evaporation, and chloride is considered to be negligible compared with the chloride already present in food; hence, chlorite and chlorate are the principal by-product residues expected.

Potential dietary exposures were estimated by JECFA on the basis of the residual concentrations of chlorate as reported in the submitted data for raw products of three food categories (see section 2.2.2) using the 13 GEMS/Food consumption cluster diets (WHO, 2007b) and individual food consumption data from European countries for the general population using the Concise European Food Consumption Database (EFSA, 2005). International mean dietary exposures were estimated to be 0.1–0.6 µg/kg bw per day for chlorate for the 13 GEMS/Food consumption cluster diets, assuming a body weight of 60 kg. National estimates for European countries of mean to 95th-percentile daily dietary exposures in the general population were 0.3–0.6 µg/kg bw for chlorate.

The expert meeting noted that these estimates were highly conservative, as it was assumed that all the treated foods would be consumed daily over a lifetime and that all treated foods consumed contained the maximum residual level of chlorate reported in experimentation on raw products.

Risk characterization

The estimated high-end dietary exposure to chlorate of 0.6 µg/kg bw per day is well below the ADI of 0–10 µg/kg bw. Therefore, no health concerns were identified.

3.1.4.4 Chlorite

Introduction

Chlorite is generated as a reaction by-product from the use of ASC or chlorine dioxide. It is also a decomposition product of stored sodium hypochlorite and can be present in food with any of these agents.

JECFA evaluated chlorite as part of its evaluation of ASC in 2007 and set an ADI of 0–0.03 mg/kg bw per day (WHO, 2008a). This is the most recent evaluation of chlorite. EFSA (2005) also reviewed ASC for treatment of poultry carcasses and concluded that the exposure to chlorite residues arising from treated poultry carcasses would be of no safety concern.

The ADI set by JECFA, and the basis of its derivation, is the same as the TDI set by IPCS (2000).

Toxicological data

Chlorite is rapidly absorbed and distributed throughout the body. It is excreted primarily in the urine in the form of chloride, with lesser amounts of chlorite and chlorate. Toxicological studies conducted with sodium chlorite in a number of species demonstrated that the most consistent finding is oxidative stress associated with changes in erythrocytes.

Sodium chlorite has given positive results in some, but not all, in vitro genotoxicity assays and in one of the two available in vivo mouse micronucleus assays involving

intraperitoneal administration. Negative results were obtained in several *in vivo* assays involving oral administration of sodium chlorite to mice. Sodium chlorite was not carcinogenic following a number of long-term studies, although these were not conducted to current standards (WHO, 2008a).

In a two-generation reproductive study (Gill et al., 2000), Sprague-Dawley rats (30 per sex per dose) received drinking-water containing sodium chlorite at 0, 35, 70 or 300 mg/l for 10 weeks and were then paired for mating. Males were exposed through mating, then sacrificed. Exposure for the females continued through mating, pregnancy, lactation and until necropsy following weaning of their litters. Dosing continued through two generations with chlorite doses for the F₀ animals of 0, 3.0, 5.6 or 20.0 mg/kg bw per day for males and 0, 3.8, 7.5 or 28.6 mg/kg bw per day for females. For the F₁ animals, chlorite doses were 0, 2.9, 5.9 or 22.7 mg/kg bw per day for males and 0, 3.8, 7.9 or 28.6 mg/kg bw per day for females. There were reductions in water consumption, food consumption and body weight gain in both sexes in all generations at various times throughout the experiment, primarily in the 70 and 300 mg/l groups; these were attributed to a lack of palatability of the water. At 300 mg/l, reduced pup survival, reduced body weight at birth and throughout lactation in the F₁ and F₂ generations, lower thymus and spleen weights in both generations, lowered incidence of pups exhibiting a normal righting reflex, delays in sexual development in males and females in the F₁ and F₂ generations and lower red blood cell parameters in the F₁ generation were noted. Significant reductions in absolute and relative liver weights in F₀ females and F₁ males and females, reduced absolute brain weights in F₁ and F₂ animals and a decrease in the maximum response to an auditory startle stimulus on postnatal day 24 but not at postnatal day 60 were noted in the 300 and 70 mg/l groups. Minor changes in red blood cell parameters in the F₁ generation were seen at 35 and 70 mg/l, but these appear to be within normal ranges based on historical data. The NOEL in this study was 35 mg/l (2.9 mg/kg bw per day), based on lower auditory startle amplitude, decreased absolute brain weight in the F₁ and F₂ generations and altered liver weights in the two generations.

JECFA applied an uncertainty factor of 100 to the NOEL to allow for interspecies and intraspecies variability, resulting in an ADI of 0–0.03 mg/kg bw per day, expressed as the chlorite ion. This ADI was supported by the results of studies in human volunteers showing no adverse effects at this intake.

Dietary exposure

Dietary exposure to chlorite was considered by JECFA (WHO, 2008a) in the context of the use of ASC as a spray or dipping solution for poultry, meats, vegetables, fruits and seafoods and in poultry chilling water. JECFA stated that residual chlorine dioxide is lost by evaporation, and chloride is considered to be negligible compared with the chloride already present in food; hence, chlorite and chlorate are the principal by-product residues expected.

Potential dietary exposures were estimated by JECFA on the basis of the residual concentrations of chlorite as reported in the submitted data for raw products of three food categories (see section 2.2.2) using the 13 GEMS/Food consumption cluster diets (WHO, 2007b) and individual food consumption data from European countries for the general population using the Concise European Food Consumption Database (EFSA, 2005). International mean dietary exposures were estimated to be 0.2–0.7 µg/kg bw per day for chlorite for the 13 GEMS/Food consumption cluster diets, assuming a body weight of 60 kg. National estimates for European countries of mean to 95th-percentile daily dietary exposures in the general population were 0.9–3 µg/kg bw for chlorite.

The expert meeting noted that these estimates were highly conservative, as it was assumed that all the treated foods would be consumed daily over a lifetime and that all treated

foods consumed contained the maximum residual level of chlorite reported in experimentation on raw products.

Risk characterization

The estimated high-end dietary exposure to chlorite of 3 µg/kg bw per day is well below the ADI of 0–30 µg/kg bw. Therefore, no health concerns were identified.

3.1.4.5 Dimethylhydantoin

Introduction

DMH (CAS No. 77-71-4) is generated from the decomposition of DBDMH upon dissolution in water. DMH is stable and, unless washed from raw poultry or beef prior to cooking, is expected to be present on cooked poultry and beef during consumption.

No comprehensive toxicological evaluations of DMH were found. The toxicity experiments described for DMH were found at TOXNET (2008). No ADI or TDI values have been identified for DMH.

Toxicological data

DMH is listed as a suspected central nervous system depressant in humans (TOXNET, 2008).

When DMH was tested in two studies in rats (at doses of 0, 100, 320 or 1000 mg/kg bw per day and 0, 100, 300 or 1000 mg/kg bw per day, respectively) and in two studies in mice (doses as for rats) for 1.5–2 years, the chronic NOELs were 100 and 300 mg/kg bw per day in rats and 300 and 320 mg/kg bw per day in mice (TOXNET, 2008). In the first study in rats, the NOEL of 100 mg/kg bw per day was set on the basis of increased incidence of wet and dried yellow matting in the urogenital area, primarily in males at or above 320 mg/kg bw per day. There were no treatment-related effects on haematology, clinical chemistry, urinalysis, ophthalmology or histopathology. In the second study in rats, the NOEL of 300 mg/kg bw per day was based on a decreased survival time relative to controls in both sexes at 1000 mg/kg bw per day; however, it was statistically significantly decreased only in males. Body weights were statistically significantly lower (9–14%) in females at 1000 mg/kg bw per day later in the study. Body weight gains were significantly decreased in males compared with controls at 1000 mg/kg bw per day. No effects were observed in relation to haematology, clinical chemistry, urinalysis, ophthalmology, organ weights or pathology.

In the first study in mice, the NOEL of 300 mg/kg bw per day was based on decreased body weights in males and increased amyloidosis in females at 1000 mg/kg bw per day. In the second study, the NOEL of 320 mg/kg bw per day was based on slightly decreased body weights (5%) in males and increased food consumption, primarily during weeks 58–69 in both sexes, at 1000 mg/kg bw per day.

DMH was negative for carcinogenicity when tested in these studies in mice and rats for 1.5–2 years. The NOELs for carcinogenicity were >1000 mg/kg bw per day in all four studies; in other words, no treatment-related effects were observed at any of the tested doses (TOXNET, 2008).

DMH was negative when tested in various in vitro tests for mutagenicity/genotoxicity (bacterial reverse mutation assay, unscheduled DNA synthesis in rat primary hepatocytes, forward mutations in TK locus in L5178Y mouse lymphoma cells, mammalian cell transformation assay and mammalian chromosomal aberrations) (TOXNET, 2008). It was also negative when tested in vivo in a bone marrow chromosomal aberration study in rats given single doses up to 2000 mg/kg bw (TOXNET, 2008).

A number of one-generation reproductive/developmental toxicity studies of DMH, three in rabbits and four in rats, were reported in TOXNET (2008). The reported NOELs/NOAELs for maternal toxicity were 500, 1000 and 1050 mg/kg bw per day for rabbits and 500, 1000, 1000 and 1000 mg/kg bw per day for rats in the various studies. The reported NOELs/NOAELs for developmental toxicity were 100, 1000 and 1050 mg/kg bw per day for rabbits and 1000, 1000, 1000 and 2000 mg/kg bw per day for rats. In one rabbit study, no developmental effects were observed at 100 mg/kg bw per day, whereas the percentages of fetuses with 27 presacral vertebrae was numerically increased at the higher dose levels of 500 and 1000 mg/kg bw per day, and adactyly and brachydactyly of the number 1 digit on both forepaws were noted in four fetuses in the same litter at the highest dose. In addition, a two-generation reproductive/developmental toxicity study in rats using doses of 0, 250, 500 and 1000 mg/kg bw per day found NOELs for systemic toxicity in both male parents and pups of 250 mg/kg bw per day, for systemic toxicity in female parents of 1000 mg/kg bw per day and for reproductive toxicity of 1000 mg/kg bw per day. No developmental toxicity was reported in this study. Slightly (<10%) decreased mean body weights in F₁ weanling males at or above 500 mg/kg bw per day and increased absolute and relative kidney (F₀) and pituitary (F₁) weights in males at 1000 mg/kg bw per day were observed. Significantly decreased body weights were observed in F₁ pups at or above 500 mg/kg bw per day and in F₂ pups at 1000 mg/kg bw per day. F₂ mean live litter size was significantly decreased at 1000 mg/kg bw per day prior to culling.

Dietary exposure

Dietary exposure to DMH from the consumption of beef and poultry treated with DBDMH can be estimated using the United States CSFII 1994–1996, 1998. The consumption of beef and poultry at the 90% percentile (94% eaters) is 150 g/person per day. Using this value and assuming that the DMH residue level of 0.005 mg/g meat (see section 2.8.2.1) represents a worst-case value for DMH residue on beef and poultry gives an exposure to DMH of 0.8 mg/person per day, or 0.013 mg/kg bw per day for a 60-kg adult.

Risk characterization

No ADI or TDI values have been identified for DMH. The margin of exposure between the lowest NOAEL of 100 mg/kg bw per day in a number of toxicity studies and the estimated dietary exposure to DMH of 0.013 mg/kg bw per day is approximately 8000. As the available information suggests that DMH is not genotoxic or carcinogenic and the database includes studies of carcinogenicity and reproductive effects, this large margin of exposure does not raise concerns for the health of consumers.

3.1.4.6 Haloacetic acids (HAAs)

Introduction

Haloacetic acids (HAAs) produced in the chlorination of drinking-water consist of a series of chlorinated and brominated forms. The chlorinated HAAs have been more thoroughly characterized toxicologically than their brominated analogues (IPCS, 2000). Dihaloacetates and trihaloacetates occur in significantly higher concentrations than the monohaloacetates (IPCS, 2000). The HAAs described in this section are the dominant forms found in drinking-water and the ones for which extensive toxicological data have been developed.

The description of the toxicology of HAAs in this section is based mainly on Environmental Health Criteria 216 (IPCS, 2000) and references therein.

Trichloroacetic acid/trichloroacetate (TCA)*Toxicological data*

TCA (Cl_3CCOOH ; CAS No. 76-03-9) is one of the weakest activators of the peroxisome proliferator-activated receptor known (Issemann & Green, 1990). It appears to be only marginally active as a peroxisome proliferator, even in rats (DeAngelo et al., 1989). Furthermore, treatment of rats with high levels of TCA in drinking-water does not induce liver tumours (DeAngelo et al., 1997). These data strongly suggest that TCA presents little, if any, carcinogenic hazard to humans at the low concentrations found in drinking-water.

From a long-term study of TCA given in drinking-water for 576 days to female B6C3F1 mice 7–8 weeks of age, a NOAEL of 40 mg/kg bw per day was estimated for absence of hepatic toxicity (Pereira, 1996). Application of an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for possible carcinogenicity) gave a TDI of 40 $\mu\text{g/kg}$ bw per day (IPCS, 2000). IARC (1995) has classified TCA in Group 3 (not classifiable as to its carcinogenicity to humans).

Dietary exposure

No occurrence data on the levels of HAAs in foods, other than drinking-water, were identified by the expert meeting. Occurrence data relating to the concentration of TCA, DCA and dibromoacetic acid (DBA) in drinking-water in North America are summarized in Table 2.4 in chapter 2.

An estimate of mean dietary exposure to TCA, DCA and DBA arising from the consumption of drinking-water is presented in Table 3.5.

Table 3.5. Mean dietary exposure to HAAs from the consumption of drinking-water^a

Country	Exposure ($\mu\text{g/kg}$ bw per day)		
	TCA	DCA	DBA
Australia	0.134	0.200	0.048
Belgium	0.013	0.020	0.005
Czech Republic	0.036	0.054	0.013
Denmark	0.107	0.159	0.039
Finland	0.108	0.161	0.039
France	0.040	0.060	0.015
Germany	0.009	0.013	0.003
Hungary	0.000	0.000	0.000
Iceland	0.083	0.123	0.030
Ireland	0.036	0.053	0.013
Italy	0.029	0.044	0.011
Netherlands	0.026	0.039	0.009
Norway	0.040	0.060	0.015
Slovakia	0.028	0.042	0.010
Sweden	0.062	0.092	0.022
United Kingdom	0.025	0.038	0.009
USA	0.134	0.199	0.048
WHO	0.313	0.467	0.113

^a The mean concentrations of the DBPs from the 12 drinking-water utilities in the USA and Canada were used in the estimate of dietary exposure.

Risk characterization

No data have been identified in relation to residues of TCA in food resulting from use of chlorine-based disinfectants. Therefore, no health concern was identified, but residue data are needed.

Dichloroacetic acid/dichloroacetate (DCA)

Toxicological data

The induction of mutations by DCA (Cl_2CHCOOH ; CAS No. 79-43-6) is very improbable at the low doses that would be encountered in chlorinated drinking-water (IPCS, 2000). The available data indicate that DCA differentially affects the replication rates of normal hepatocytes and hepatocytes that have been initiated (Pereira & Phelps, 1996). Based upon the above considerations, it was suggested that cancer risk estimates for DCA should be modified by incorporation of newly developing information on its comparative metabolism and modes of action to formulate a biologically based dose–response model, when such data become available (IPCS, 2000).

The effects of DCA appear to be closely associated with doses that induce hepatomegaly and glycogen accumulation in mice (IPCS, 2000). The NOAEL for these effects was approximately 40 mg/kg bw per day in an 8-week study in male B6C3F1 mice treated with DCA doses of approximately 20–600 mg/kg bw per day in drinking-water (Kato-Weinstein et al., 1998). By applying an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for the short duration of the study and possible carcinogenicity), a TDI of 40 $\mu\text{g/kg}$ bw per day was calculated (IPCS, 2000).

IARC (1995) has classified DCA in Group 3 (not classifiable as to its carcinogenicity to humans).

Dietary exposure

For details of dietary exposure to DCA, see the dietary exposure section for TCA above.

Risk characterization

No data have been identified in relation to residues of DCA in food resulting from use of chlorine-based disinfectants. Therefore, no health concern was identified, but residue data are needed.

Dibromoacetic acid/dibromoacetate (DBA)

Brominated acetic acids are formed in water that contains bromide, which strong oxidizers such as chlorine and ozone are capable of oxidizing to hypobromous acid. There are very few data available on the toxicity of these chemicals.

Toxicological data

Data on the carcinogenicity of brominated acetic acids are too preliminary to be useful in risk characterization (IPCS, 2000). However, there are data on the effects of DBA (Br_2CHCOOH ; CAS No. 631-64-1) on male reproduction.

No effects were observed on male reproduction in rats at daily doses of 2 mg/kg bw per day by gavage for 79 days, whereas higher doses, from 10 mg/kg bw per day, led to progressively more severe effects (increased retention of step 19 spermatids, marked atrophy of the seminiferous tubules) (Linder et al., 1997). From this NOAEL of 2 mg/kg bw per day, using an uncertainty factor of 100 (10 each for interspecies and intraspecies variation), a TDI of 20 $\mu\text{g/kg}$ bw per day was derived (IPCS, 2000).

Dietary exposure

For details of dietary exposure to DBA, see the dietary exposure section for TCA above.

Risk characterization

No data have been identified in relation to residues of DBA in food resulting from use of chlorine-based and ozone disinfectants. Therefore, no health concern was identified, but residue data are needed.

3.1.4.7 Haloacetonitriles (HANs)

Introduction

Toxicological data are quite limited on haloacetonitriles (HANs). Dichloroacetonitrile (DCAN) (CHCl_2CN ; CAS No. 3018-12-0), bromochloroacetonitrile (BCAN) (CHBrClCN ; CAS No. 83463-62-1) and dibromoacetonitrile (DBAN) (CHBr_2CN ; CAS No. 3252-43-5) are the most important in terms of concentrations found in drinking-water (IPCS, 2000). Without appropriate human data or an animal study that involves a substantial portion of an experimental animal's lifetime, there is no generally accepted basis for estimating carcinogenic risk from the HANs (IPCS, 2000).

The description of the toxicology of HANs in this section is based mainly on Environmental Health Criteria 216 (IPCS, 2000) and references therein.

Dichloroacetonitrile (DCAN)

Toxicological data

There are some data on the reproductive toxicity of DCAN. A NOAEL of 15 mg/kg bw per day was determined for DCAN in a reproductive toxicity study in Long-Evans rats in which DCAN was given at doses of 0, 5, 15, 25 or 45 mg/kg bw per day from days 6 to 18 of gestation (Smith et al., 1989). By applying an uncertainty factor of 1000 (10 each for intraspecies and interspecies variation and 10 for severity of effects), a TDI of 15 $\mu\text{g/kg}$ bw per day was derived (WHO, 1993).

Dietary exposure

No occurrence data relating to HANs in food, other than drinking-water, were identified by the expert meeting. Occurrence data relating to the concentration of the HANs in drinking-water in North America are summarized in Table 2.4 in chapter 2.

An estimate of mean dietary exposure arising from the consumption of drinking-water containing those HANs for which toxicological information was available has been calculated and is presented in Table 3.6.

Risk characterization

No data have been identified in relation to residues of DCAN in food resulting from use of chlorine-based disinfectants. Therefore, no health concern was identified, but residue data are needed.

Dibromoacetonitrile (DBAN)

Toxicological data

Reproductive and developmental effects were observed for DBAN only at doses that exceeded those established for general toxicity (about 45 mg/kg bw per day) (Smith et al., 1987).

Table 3.6. Mean dietary exposure to HANs from the consumption of drinking-water^a

Country	Exposure (µg/kg bw per day)		
	DCAN	DBAN	TCAN
Australia	0.020	0.009	0.000
Belgium	0.002	0.001	0.000
Czech Republic	0.005	0.002	0.000
Denmark	0.016	0.007	0.000
Finland	0.016	0.007	0.000
France	0.006	0.003	0.000
Germany	0.001	0.001	0.000
Hungary	0.000	0.000	0.000
Iceland	0.012	0.005	0.000
Ireland	0.005	0.002	0.000
Italy	0.004	0.002	0.000
Netherlands	0.004	0.002	0.000
Norway	0.006	0.003	0.000
Slovakia	0.004	0.002	0.000
Sweden	0.009	0.004	0.000
United Kingdom	0.004	0.002	0.000
USA	0.020	0.009	0.000
WHO	0.047	0.020	0.001

^a The mean concentrations of the DBPs from the 12 drinking-water utilities in the USA and Canada were used in the estimate of dietary exposure.

A NOAEL of 23 mg/kg bw per day was determined for DBAN given at doses of 6, 23 or 45 mg/kg bw per day dissolved in corn oil in a 90-day toxicity study in CD rats (Hayes, Condie & Borzelleca, 1986). By applying an uncertainty factor of 1000 (10 each for intraspecies and interspecies variation and 10 for the short duration of the study), a TDI of 23 µg/kg bw per day was derived (WHO, 1993; IPCS, 2000).

Dietary exposure

For dietary exposure to DBAN, see the dietary exposure section for DCAN above.

Risk characterization

No data have been identified in relation to residues of DBAN in food resulting from use of chlorine-based and ozone disinfectants. Therefore, no health concern was identified, but residue data are needed.

Trichloroacetonitrile (TCAN)

Toxicological data

LOAELs for TCAN (CCl₃CN; CAS No. 545-06-2) were identified as 7.5 mg/kg bw per day for embryotoxicity and 15 mg/kg bw per day for developmental effects in rats (Smith et al., 1988). However, later studies suggest that these responses were dependent upon the vehicle used (Christ et al., 1996).

No TDI could be established for TCAN (IPCS, 2000).

Dietary exposure

For dietary exposure to TCAN, see the dietary exposure section for DCAN above.

Risk characterization

No data have been identified in relation to residues of TCAN in food resulting from use of chlorine-based and ozone disinfectants. Therefore, no health concern was identified, but residue data are needed.

3.1.4.8 Halofuranones (MX and MX analogues)

Introduction

3-Chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX) ($C_5H_3Cl_3O_3$; CAS No. 77439-76-0) is formed by the reaction of chlorine with complex organic matter in drinking-water or aqueous solutions after chlorination or chloramination. Brominated analogues are formed when bromide is present in addition to organic material. MX is the member of the hydroxyfuranone class that has been most extensively studied; much less is known about the other chlorinated and brominated halofuranones.

The MX-related halofuranones were ranked by expert structure–activity relationship judgement with emphasis on genotoxic cancer potential (Woo et al., 2002). Of 10 MX-related halofuranones, 3 analogues—3-chloro-4-(bromochloromethyl)-5-hydroxy-2(5H)-furanone (BMX-1), 3-chloro-4-(dibromomethyl)-5-hydroxy-2(5H)-furanone (BMX-2; CAS No. 132059-52-0) and 3-bromo-4-(dibromomethyl)-5-hydroxy-2(5H)-furanone (BMX-3)—were considered to be of moderate to high concern because of their structural analogy to MX, which has been shown to be a multitarget carcinogen in the rat (see below), and their positive mutagenicity data in the Ames test with potencies comparable to those of MX. One analogue, 2,3-dichloro-4-oxobutenoic acid (3,4-dichloro-5-hydroxy-2(5H)-furanone, mucochloric acid; CAS No. 87-56-9), was of moderate concern, because of structural analogy to MX and positive genotoxicity data (Ames test, *Escherichia coli*, sister chromatid exchange in CHO cells), but less active than MX. Four MX analogues were considered to be of low to moderate concern: (*E*)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (EMX), 3-chloro-4-(dichloromethyl)-2(5H)-furanone (red-MX; CAS No. 122551-89-7), dihydro-4,5-dichloro-2(3H)-furanone and 5-hydroxy-5-trichloromethyl-2-furanone, with more or less structural analogy to MX, but less potency. Two analogues were of marginal concern: 2-chloro-3-(dichloromethyl)-butenedioic acid (ox-MX) and (*E*)-2-chloro-3-(dichloromethyl)-butenedioic acid (ox-EMX, in later papers called ox-MX; Krasner et al., 2006). As the data available so far indicate that none of these analogues has higher carcinogenic potential than MX itself, the toxicity of MX is used to represent the “worst-case” toxicity to halofuranones. Non-cancer effects, as well as CAS numbers, are not known for most of these substances. Other brominated EMX analogues are reported more recently: (*E*)-2-chloro-3-(bromochloromethyl)-4-oxobutenoic acid (BEMX-1), (*E*)-2-chloro-3-(dibromomethyl)-4-oxobutenoic acid (BEMX-2) and (*E*)-2-bromo-3-(dibromomethyl)-4-oxobutenoic acid (BEMX-3), and an isomer of EMX, (*Z*)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (ZMX) (Krasner et al., 2006; Richardson et al., 2007).

The toxicology of MX is evaluated and described in Environmental Health Criteria 216 (IPCS, 2000). In addition, IARC (2004), the WHO *Guidelines for drinking-water quality* (WHO, 2006a) and some original publications have been used as sources of information in this section.

Toxicological data

The critical effects of MX appear to be its mutagenicity and carcinogenicity, and this section therefore has focused on the carcinogenicity.

MX was administered to Wistar rats (50 per sex per group) in drinking-water for 104 weeks at 0, 0.4, 1.3 or 5.0 mg/kg bw per day for males and 0, 0.6, 1.9 or 6.6 mg/kg bw per day for females (Komulainen et al., 1997). Dose-dependent increases in the incidence of several tumours were observed in the rats, whereas the same MX doses had no obvious toxic effects on the animals. Increases in tumours of the lung, mammary gland, haematopoietic system, liver, pancreas, adrenal gland and thyroid were observed, but few showed a clear dose-response (IPCS, 2000). In IPCS (2000), it was noted that the data from this experiment indicate that MX induces thyroid and bile duct tumours. An increased incidence of thyroid tumours was seen at the lowest dose of MX administered (0.4 mg/kg bw per day in males and 0.6 mg/kg bw per day in females). The induction of thyroid tumours with high-dose chemicals has long been associated with halogenated compounds. The induction of thyroid follicular tumours could involve modifications in thyroid function or a mutagenic mode of action. Mean plasma levels of thyroid hormones (T_4 , T_3 and TSH) at the end of the study were not significantly different between MX-treated rats and controls, suggesting that the thyroid tumours were not caused indirectly by excess hormonal stimulation. A dose-related increase in the incidence of cholangiomas and cholangiocarcinomas was also observed, beginning at the low dose in female rats, with a more modest response in males. The increase in cholangiomas and cholangiocarcinomas in female rats was used to derive a slope factor for cancer. The 95% upper confidence limit for a 10^{-5} lifetime cancer risk based on the linearized multistage model was calculated to be 0.06 $\mu\text{g/kg bw per day}$ (IPCS, 2000).

McDonald & Komulainen (2005) calculated cancer potency for MX from the carcinogenicity experiment of Komulainen et al. (1997), using either a linearized multistage model or a BMD model and Monte Carlo analysis. They obtained similar results by both methods: a mean cancer potency of $2.3 (\text{mg/kg per day})^{-1}$ and an upper 95th-percentile estimate of $4.5 (\text{mg/kg per day})^{-1}$. Using the upper 95th-percentile estimate of cancer potency of $4.5 (\text{mg/kg per day})^{-1}$, an intake of 2 litres/day and a 70-kg body weight resulted in an estimated concentration of 7.8 ng/l corresponding to a 10^{-6} lifetime cancer risk for MX.

There were no studies of toxicity or metabolism of MX or related compounds reported in humans (IPCS, 2000). There are data to suggest that MX or a mutagenically active metabolite reaches the systemic circulation in experimental animals (IPCS, 2000). Mutagenic activity has been detected in various organs and tissues using doses as low as 4.3 mg/kg bw. The available data are too limited to provide much more than very general guidance as to whether MX or a metabolite reaches critical target organs in humans also (IPCS, 2000).

MX is a potent, direct-acting mutagen that induces primarily GC \rightarrow TA transversions in both bacterial and mammalian cells (IARC, 2004). It induces DNA damage in bacterial and mammalian cells, as well as in rodents in vivo. MX is a chromosomal mutagen in mammalian cells and in rats, and it induces mammalian cell transformation in vitro. The MX-associated thyroid gland tumors in rats described above are caused by mechanisms other than TSH-mediated hormonal promotion. An overall evaluation of all the mutagenicity and genotoxicity data shows that MX is mutagenic and genotoxic both in vitro and in vivo. There is inadequate evidence in humans and limited evidence in experimental animals for the carcinogenicity of MX. IARC (2004) has classified MX in Group 2B: possibly carcinogenic to humans on the basis of rat tumorigenicity and its strong mutagenicity.

Dietary exposure

No occurrence data for halofuranones in food, other than drinking-water, were identified. Occurrence data relating to the concentration of the halofuranones in drinking-water in North America are summarized in Table 2.5 in chapter 2.

An estimate of mean dietary exposure arising from the consumption of drinking-water has been calculated and is presented in Table 3.7. Occurrence data were also available for ox-MX, with the concentrations being reported as “0” (i.e. not detected), although the limit of detection (LOD) was not available to the reviewer.

Table 3.7. Mean dietary exposure to halofuranones (MX and MX analogues) from the consumption of drinking-water^a

Country	Exposure (µg/kg bw per day)									
	BMX-1	BEMX-1	BMX-2	BEMX-2	BMX-3	BEMX-3	MX	Red-MX	EMX	ZMX
Australia	0.0005	0.0014	0.0004	0.0017	0.0001	0.0014	0.0016	0.0005	0.0002	0.0002
Belgium	0.0000	0.0001	0.0000	0.0002	0.0000	0.0001	0.0002	0.0000	0.0000	0.0000
Czech Republic	0.0001	0.0004	0.0001	0.0005	0.0000	0.0004	0.0004	0.0001	0.0000	0.0000
Denmark	0.0004	0.0011	0.0003	0.0014	0.0000	0.0011	0.0012	0.0004	0.0001	0.0001
Finland	0.0004	0.0012	0.0003	0.0014	0.0000	0.0011	0.0013	0.0004	0.0001	0.0001
France	0.0001	0.0004	0.0001	0.0005	0.0000	0.0004	0.0005	0.0001	0.0001	0.0000
Germany	0.0000	0.0001	0.0000	0.0001	0.0000	0.0001	0.0001	0.0000	0.0000	0.0000
Hungary	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Iceland	0.0003	0.0009	0.0002	0.0011	0.0000	0.0009	0.0010	0.0003	0.0001	0.0001
Ireland	0.0001	0.0004	0.0001	0.0005	0.0000	0.0004	0.0004	0.0001	0.0000	0.0000
Italy	0.0001	0.0003	0.0001	0.0004	0.0000	0.0003	0.0003	0.0001	0.0000	0.0000
Netherlands	0.0001	0.0003	0.0001	0.0003	0.0000	0.0003	0.0003	0.0001	0.0000	0.0000
Norway	0.0001	0.0004	0.0001	0.0005	0.0000	0.0004	0.0005	0.0001	0.0001	0.0000
Slovakia	0.0001	0.0003	0.0001	0.0004	0.0000	0.0003	0.0003	0.0001	0.0000	0.0000
Sweden	0.0002	0.0007	0.0002	0.0008	0.0000	0.0006	0.0007	0.0002	0.0001	0.0001
United Kingdom	0.0001	0.0003	0.0001	0.0003	0.0000	0.0003	0.0003	0.0001	0.0000	0.0000
USA	0.0005	0.0014	0.0004	0.0017	0.0001	0.0014	0.0016	0.0005	0.0002	0.0002
WHO	0.0011	0.0033	0.0009	0.0040	0.0001	0.0032	0.0037	0.0011	0.0004	0.0004

^a The mean concentration of the DBPs from the 12 drinking-water utilities in the USA and Canada were used in the estimate of dietary exposure.

Risk characterization

No data have been identified in relation to residues of halofuranones in food resulting from use of chlorine-based and ozone disinfectants. Therefore, no health concern was identified, but residue data are needed.

3.1.4.9 N-Nitrosamines

Introduction

N-Nitrosamines are well-known environmental chemicals that can be metabolized into potent genotoxic agents. N-Nitrosodimethylamine (NDMA) is a model compound for this class of substances. Currently, five N-nitrosamines have been defined as DBPs in

drinking-water, and they are found to increase in concentration in the distribution system: NDMA, *N*-nitrosopyrrolidine (NPYR), *N*-nitrosomorpholine (NMOR), *N*-nitrosodiphenylamine (NDPA; CAS No. 86-30-6) and *N*-nitrosopiperidine (NPIP) (Richardson et al., 2007). Nitrosamines detected in food are NDMA, *N*-nitrosoproline (NPRO), NPYR and NPIP (Jakszyn et al., 2004a).

N-Nitrosamines were not included in Environmental Health Criteria 216. The information in this document has been taken from the WHO *Guidelines for drinking-water quality* (WHO, 2008b,c), IARC (1978, 1982, 1987), a Concise International Chemical Assessment Document (IPCS, 2002), the toxicology database Integrated Risk Information System, or IRIS (USEPA, 2008), as well as some original publications.

Toxicological data

As NDMA and the *N*-nitrosamines as a group are potent genotoxic and carcinogenic substances, cancer is the critical end-point for risk characterization. In addition to being the best-characterized end-point, in general, tumours occur at the lowest concentration compared with those typically reported to induce non-cancer effects (IPCS, 2002). In this section, the emphasis has therefore been put on cancer as the end-point of chronic toxicity. However, effects of NDMA on the liver and kidney in repeated-dose toxicity studies (>0.2 mg/kg bw per day), embryo toxicity and embryo lethality in single-dose developmental studies (20–30 mg/kg bw) and a range of immunological effects, such as suppression of humoral and cell-mediated immunity, reversible at lowest concentrations (5 mg/l), have been reported (IPCS, 2002). In case reports, liver failure, brain haemorrhage and death have been attributed to the ingestion of NDMA by humans (doses not stated) (IPCS, 2002).

N-Nitrosamines can be metabolized into potent genotoxic agents. The genotoxicity of NDMA, the model compound for this class, is well studied. The results show that NDMA is mutagenic and clastogenic in a wide array of test systems in vitro in the presence or absence of metabolic activation in bacterial and mammalian cells (human and rodents) (IARC, 1978; Liteplo & Meek, 2001). Clear evidence of genotoxicity in many organs is also observed in various test systems in vivo. NDMA is activated to a mutagen mainly by cytochrome P450 2E1, whereas other *N*-nitrosamines were activated by various other P450 enzymes in strains of *Salmonella* containing human P450 genes (Fujita & Kamataki, 2001). The mutagenic and genotoxic potency varies between the *N*-nitrosamines. NDPA, unlike most of the other nitrosamines, is not clearly mutagenic and genotoxic in bacterial or mammalian cells in vitro or in vivo, as most studies were negative or gave conflicting results (McGregor, 1994). There were also fewer studies available showing carcinogenicity of NDPA in experimental animals.

Many nitrosamines have been tested extensively for carcinogenicity, and nearly all have shown carcinogenic effects in a variety of species exposed through various routes (IARC, 1978, 1982, 1987). The primary sites of tumour formation for the nitrosamines are the oesophagus and liver. However, other organs, including the urinary bladder, brain and lungs, are also target organs. A mixture of three *N*-nitrosamines in low doses—NPYR (0.4 mg/kg bw per day), *N*-nitrosodiethylamine (NDEA) (0.1 mg/kg bw per day) and *N*-nitrosodiethanolamine (NDELA) (CAS No. 1116-54-7; 2.0 mg/kg bw per day)—given in drinking-water to rats for their lifetime showed additivity for liver tumours (Berger, Schmähl & Zerban, 1987). A study evaluated liver and oesophageal tumours induced by NDEA or NDMA in 4080 rats at 15 doses given in drinking-water during the lifetime of the rats (Peto et al., 1991a,b). The results from this study showed that exposures to concentrations of NDEA or NDMA as low as 1 mg/l in the drinking-water resulted in 25% of the animals developing liver tumours, a dose of 0.1 mg/l caused about 2.5% and a dose of 0.01 mg/l caused about 0.25%. etc., with no indication of a threshold effect (Peto et al., 1991a). The liver tumour risk from 2 years of chronic exposure of rats to very low doses of NDMA would

be in the order of 0.03% (males) and 0.04% (females) per microgram per kilogram body weight per day, and for NDEA, in the order of 0.06% (males) and 0.1% (females) (Peto et al., 1991b).

Although no epidemiological data were available at the time, IARC (1978) found sufficient evidence in animals for the carcinogenicity of several *N*-nitrosamines and noted that these compounds should be regarded as if they were carcinogenic to humans. IARC (1987) has classified two *N*-nitrosamines in Group 2A: probably carcinogenic to humans: NDMA and NDEA, based on no adequate data in humans and sufficient evidence of carcinogenicity in experimental animals. Several other *N*-nitrosamines are classified by IARC (1987) in Group 2B: possibly carcinogenic to humans, including NPYR, NMOR, NPIP and NDELA, based on no adequate data in humans and sufficient evidence of carcinogenicity in experimental animals. Other *N*-nitrosamines are classified by IARC (1987) in Group 3: not classifiable as to their carcinogenicity to humans, including NDPA and NPRO, based on no adequate data in humans and limited or inadequate evidence of carcinogenicity in experimental animals. IRIS (USEPA, 2008) identifies the following nitrosamines as B2, probable human carcinogens: NDMA, NDEA, NDELA, NPYR and NDPA.

The WHO *Guidelines for drinking-water quality* (WHO, 2008c) indicate that for NDMA, a concentration of 100 ng/l in drinking-water is associated with an upper-bound excess lifetime cancer risk of 1 in 100 000. The USEPA (2008) provided values of 2, 100, 200 and 70 000 ng/l for NDEA, NDELA, NPYR and NDPA, respectively, as representing the 95% lower bound on the estimated concentration of the chemical in drinking-water associated with a cancer risk of 1 in 100 000.

Dietary exposure

Water treatment plants incorporating a chlorination process (e.g. sodium hypochlorite and/or chloramine) produce nitrosamines, including NDMA, as DBPs (Richardson, 2003). In assessing the dietary exposure to nitrosamines formed as a result of the use of chlorine-containing disinfectants, it is important to consider their other environmental sources. WHO (2006b) reported a number of different routes by which NDMA enters the environment and drinking-water, including through 1) being a by-product of industrial processes for industries such as rubber manufacturing, leather tanning, pesticide manufacturing, food processing, foundries and dye manufacturing, 2) sewage treatment plant effluent, 3) runoff from agricultural production and 4) being a contaminant in pesticide formulations. Furthermore, the addition of nitrites and nitrates to foodstuffs to reinforce the preserving effect of smoking, salting or cooking can lead to the formation of nitrosamines (EFSA, 2003).

The ingestion of drinking-water that contains NDMA appears to contribute only a small fraction to the overall NDMA exposure (Environment Canada & Health Canada, 2001). Rough estimates of the exposure to various sources of NDMA in Canada indicate that water contributes less than 10% to the overall exposure (IPCS, 2002). A report from the USEPA (Fristachi & Rice, 2005) indicates that the trace levels of NDMA in drinking-water contribute from 0.001% to 0.55% (or less than 1%) to overall human exposure to NDMA.

Based on a worst-case estimation of exposure to NDMA-contaminated air, water and food, the daily NDMA intake of a 20- to 59-year-old would be 0.005–0.016 µg/kg bw per day (IPCS, 2002). Daily intake of NDMA from ingestion of drinking-water was estimated at 0.0003–0.001 µg/kg bw per day, based on a mean NDMA concentration of 0.012 µg/l and a maximum concentration of 0.04 µg/l obtained from 20 samples from four water treatment plants using a pre-blended polyamine/alum product during the treatment process (IPCS, 2002). The low-end value is similar to those observed in some chloramine-treated drinking-water, which shows that human exposure to NDMA via drinking-water is likely to provide a relative contribution below 10% of total exposure.

In a home not containing environmental tobacco smoke, the major source of exposure to NDMA is food, at 0.0043–0.011 µg/kg bw per day (WHO, 2006b). If there is regular indoor exposure to environmental tobacco smoke, then this source would exceed all the other sources combined by almost an order of magnitude, at 0.05 µg/kg bw per day (WHO, 2006b).

Risk characterization

It can be concluded that the formation of nitrosamines is attributable to several mechanisms, interaction with active chlorine compounds being only a minor one. Although there are no data available on nitrosamine residues in food resulting from disinfection processes, they are likely to be minimal compared with other sources of exposure. Therefore, no health concerns are identified.

3.1.4.10 Trihalomethanes (THMs)

Introduction

THMs are generally the most prevalent by-products of drinking-water disinfection by chlorine (IPCS, 2000). A variety of non-neoplastic toxic effects have been associated with short-term and long-term exposure of experimental animals to high doses of THMs. The four most common THMs—chloroform, BDCM, DBCM and bromoform—have been shown to be carcinogenic to rodents in high-dose chronic studies, and therefore cancer following chronic exposure is the primary hazard of concern for this class of DBPs (IPCS, 2000).

The description of the toxicology of THMs in this section is based mainly on Environmental Health Criteria 216 (IPCS, 2000) and references therein.

Chloroform

Chloroform is generally the predominant THM in chlorinated water and is also the most extensively studied chemical of this class (IPCS, 2000).

Toxicological data

Owing to the weight of evidence indicating that chloroform can induce cancer in animals only after chronic exposure to cytotoxic doses, it is clear that exposures to low concentrations of chloroform in drinking-water do not pose carcinogenic risks (IPCS, 2000). Direct DNA reactivity and mutagenicity cannot be considered to be key factors in chloroform-induced carcinogenesis in experimental animals. A substantial body of data demonstrates a lack of direct *in vivo* or *in vitro* genotoxicity of chloroform. If THMs produce their genotoxic effects primarily via the glutathione conjugation mechanism, the results of Pegram et al. (1997) indicate that chloroform would be mutagenic in mammals only at lethal doses. There is, however, compelling evidence to support a mode of action for tumour induction based on metabolism of chloroform by the target cell population, followed by cytotoxicity of oxidative metabolites and regenerative cell proliferation. A number of recent studies support the hypothesis that chloroform acts to produce cancer in rodents through a non-genotoxic/cytotoxic mode of action, with carcinogenesis resulting from events secondary to chloroform-induced cytolethality and regenerative cell proliferation (Larson, Wolf & Butterworth, 1994a,b; Pereira, 1994; Larson et al., 1996; Templin et al., 1996a,b,c, 1998). These studies have shown that organ toxicity and regenerative hyperplasia are associated with the tumorigenicity of chloroform and are apparently the key steps in its carcinogenic mode of action. Thus, sustained toxicity would result in tumour development. Chloroform induces liver and kidney tumours in long-term rodent cancer bioassays only at doses that induce frank cytotoxicity in these target organs. Furthermore, there are no instances of chloroform-induced

tumours that are not preceded by this pattern of dose-dependent toxic responses (Golden et al., 1997).

The NOAEL for cytolethality and regenerative hyperplasia in female mice was 10 mg/kg bw per day after administration of chloroform in doses of 0, 3, 10, 34, 238 or 477 mg/kg bw per day in corn oil (5 days/week) for 3 weeks (Larson, Wolf & Butterworth, 1994b). Based on the mode of action evidence for chloroform carcinogenicity and applying an uncertainty factor of 1000 (10 each for intraspecies and interspecies variation and 10 for the short duration of the study) to this NOAEL for cytotoxicity in mice, a TDI of 10 µg/kg bw per day was derived for chloroform (IPCS, 2000). Subsequently, IPCS (2004) proposed a TDI of 15 µg/kg bw per day, based upon a study in which fatty cysts developed in the liver of dogs given chloroform orally at 15 mg/kg bw per day for 7.5 years. This slightly higher TDI was adopted in the more recent WHO drinking-water guidelines (WHO, 2005b).

Dietary exposure

For the purpose of the exposure assessment, presented in Table 3.8, a chloroform concentration of 0.3 mg/kg was used, representing the highest level found in cooked chicken (see section 2.6.3).

Table 3.8. Estimates of per capita dietary exposure to chloroform, following the dipping of chicken in chlorine, based on 13 GEMS/Food consumption cluster diets

	Exposure (µg/kg bw per day) ^{a,b,c}												
	A	B	C	D	E	F	G	H	I	J	K	L	M
Chicken meat	0.03	0.22	0.14	0.11	0.19	0.13	0.06	0.22	0.08	0.02	0.32	0.13	0.48
Poultry ^d	0.04	0.29	0.16	0.12	0.31	0.14	0.09	0.66	0.13	0.02	0.73	0.14	0.58

^a Assuming a 60-kg average body weight.

^b WHO consumption cluster diets based on food balance sheet data; August 2006 version used (<http://www.who.int/entity/foodsafety/chem/ClusterDietsAug06.xls>).

^c Concentration of 0.3 mg/kg in chicken and other poultry was used for the exposure assessment.

^d The poultry exposure assessment has been presented on the assumption that the dipping use of chlorine is also applied to other poultry.

Occurrence data relating to the concentration of the four most important THMs in drinking-water in North America are summarized in Table 2.4 in chapter 2. An estimate of mean dietary exposure arising from the consumption of drinking-water has been calculated and is presented in Table 3.9.

Risk characterization

The estimated range of dietary exposure to chloroform from active chlorine-treated poultry, based on the highest detected concentration in cooked chicken, is up to 0.73 µg/kg bw per day. Adding this to the highest estimated intake from drinking-water (0.53 µg/kg bw per day) results in a total dietary exposure that is well below the TDI of 10 µg/kg bw per day (or the higher TDI of 15 µg/kg bw per day, based on a study in dogs; IPCS, 2004).

Bromodichloromethane (BDCM)

Toxicological data

Of the brominated THMs, BDCM is of particular interest because it has produced tumours in both rats and mice and at several sites (liver, kidney, large intestine) after gavage in corn oil (NTP, 1987). The induction of colon tumours in rats by BDCM is also interesting because of the epidemiological associations of THM with colorectal cancer (IPCS, 2000).

BDCM and other brominated THMs are also weak mutagens (Pegram et al., 1997; IARC, 1999a). In the NTP (1987) study, BDCM caused tumours at lower doses and at more target sites compared with any of the other THMs (IPCS, 2000).

Table 3.9. Mean dietary exposure to THMs from the consumption of drinking-water^a

Country	Exposure (µg/kg bw per day)			
	Chloroform	BDCM	DBCM	Bromoform
Australia	0.228	0.143	0.093	0.030
Belgium	0.023	0.014	0.009	0.003
Czech Republic	0.061	0.038	0.025	0.008
Denmark	0.182	0.114	0.074	0.024
Finland	0.184	0.115	0.075	0.024
France	0.069	0.043	0.028	0.009
Germany	0.015	0.009	0.006	0.002
Hungary	0.000	0.000	0.000	0.000
Iceland	0.141	0.088	0.057	0.019
Ireland	0.061	0.038	0.025	0.008
Italy	0.050	0.031	0.020	0.007
Netherlands	0.045	0.028	0.018	0.006
Norway	0.068	0.043	0.028	0.009
Slovakia	0.048	0.030	0.019	0.006
Sweden	0.105	0.066	0.043	0.014
United Kingdom	0.043	0.027	0.018	0.006
USA	0.228	0.142	0.093	0.030
WHO	0.533	0.333	0.217	0.070

^a The mean concentrations of the DBPs from the 12 drinking-water utilities in the USA and Canada were used in the estimate of dietary exposure.

In a 2-year bioassay, BDCM was given by corn oil gavage 5 days/week to F344 rats and B6C3F1 mice (50 animals per sex per group) at doses of 0, 50 or 100 mg/kg bw per day (male and female rats), 0, 25 or 50 mg/kg bw per day (male mice) or 0, 75 or 150 mg/kg bw per day (female mice) (NTP, 1987). BDCM induced tumours, in conjunction with cytotoxicity and increased proliferation, in the kidneys of mice and rats at doses of 50 and 100 mg/kg bw per day, respectively (NTP, 1987). Large intestinal tumours in rats occurred after exposure to both 50 and 100 mg/kg bw per day.

However, a more recent study by NTP (2006) of BDCM given in drinking-water to male F344/N rats and female B6C3F1 mice gave no indication of carcinogenicity. In this 2-year drinking-water study, there was no evidence of carcinogenic activity of BDCM in male F344/N rats exposed to target concentrations of 0, 175, 350 or 700 mg/l (equivalent to average daily BDCM doses of approximately 0, 6, 12 or 25 mg/kg bw). There was no evidence of carcinogenic activity of BDCM in female B6C3F1 mice exposed to target concentrations of 0, 175, 350 or 700 mg/l (equivalent to average daily BDCM doses of approximately 0, 9, 18 or 36 mg/kg bw). In this study, no effects on survival rates and no non-neoplastic effects were found in either rats or mice (NTP, 2006). In the rats, the body weights were similar in the exposed groups and the control animals. In the mice, all exposed groups showed lower final body weights than controls, but that was attributed to decreased water consumption because of poor palatability of the dosed water (NTP, 2006).

Factors such as the stability of BDCM in water, the influence of the corn oil vehicle, different rates of absorption and delivery of parent compound to target organs, and different rates of metabolism after gavage and drinking-water exposure may have contributed to the contrasting results in the two studies (NTP, 2006). The results of in vitro mutagenicity studies with BDCM were mixed, with negative effects in *Salmonella* and for chromosomal aberrations in CHO cells, but positive results for mutations in mouse lymphoma cells and sister chromatid exchange in CHO cells, in the presence but not the absence of metabolic activation. In vivo studies of chromosome damage were negative (NTP, 2006).

Dietary exposure

Dietary exposure to BDCM may occur as a result of the use of DBDMH in the processing of poultry or from the treatment of beef with aqueous solutions of DBDMH. Dietary exposure to BDCM from the consumption of beef and poultry treated with DBDMH can be estimated using the CSFII 1994–1996, 1998. The consumption of beef and poultry at the 90% percentile (94% eaters) is 150 g/person per day. Using this value and assuming that the residue level of 0.0004 µg/g (see section 2.8.2.3) represents a worst-case value for BDCM residue on beef and poultry gives an exposure to BDCM of 0.06 µg/person per day, or 0.001 µg/kg bw per day for a 60-kg person.

Risk characterization

The margin between the lowest dose of BDCM found to cause tumours in rats and mice when administered by gavage in corn oil (50 mg/kg bw per day) and the estimated human dietary exposure resulting from residues in treated meat is in the region of 50 million. No effects were observed in the more recent carcinogenicity study with BDCM administered in drinking-water to male rats and female mice at doses up to approximately 25 and 36 mg/kg bw per day, respectively (NTP, 2006).

In view of the lack of mutagenicity in vivo and the lack of carcinogenicity in the recent NTP study with administration of BDCM in drinking-water, it is considered highly unlikely that BDCM residues present a concern for health.

Dibromochloromethane (DBCM)

Toxicological data

In a 2-year corn oil gavage study, DBCM was given for 5 days/week to F344/N rats at doses of 0, 40 or 80 mg/kg bw per day and to B6C3F1 mice at doses of 0, 50 or 100 mg/kg bw per day (NTP, 1985). DBCM induced hepatic tumours in female mice, but not in rats, at a dose of 100 mg/kg bw per day (NTP, 1985).

The brominated THMs are considered to be weakly mutagenic, with activation involving glutathione conjugation. DBCM and bromoform have been reported to be more potent than other brominated THMs (DeMarini et al., 1997; Pegram et al., 1997). However, WHO (2005b) considered the evidence of genotoxicity to be inconclusive. IARC (1991) has classified DBCM in Group 3 (not classifiable as to its carcinogenicity to humans).

In previous evaluations, it has been suggested that the corn oil vehicle may play a role in the induction of tumours in female mice by affecting the bioavailability of DBCM in the long-term study (WHO, 1996). A NOAEL for DBCM of 30 mg/kg bw per day was established in a 13-week corn oil gavage study, based on the absence of histopathological effects in the liver of rats (NTP, 1985). Based on this NOAEL and using an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for the short duration of the study and possible carcinogenicity), a TDI for DBCM of 30 µg/kg bw per day was derived (IPCS, 2000). In a subsequent evaluation, the NOAEL was corrected to allow for

gavage exposure on 5 days/week, resulting in establishment of a TDI of 21.4 µg/kg bw per day (WHO, 2005b).

Dietary exposure

DBCM is a potential DBP resulting from the use of DBDMH in the processing of poultry and beef. Dietary exposure to DBCM from the consumption of beef and poultry treated with DBDMH can be estimated using the CSFII 1994–1996, 1998. The consumption of beef and poultry at the 90% percentile (94% eaters) is 150 g/person per day. Using this value and assuming that the residue level of 0.0004 µg/g meat (see section 2.8.2.3) represents a worst-case value for DBCM residue on beef and poultry gives an exposure to DBCM of 0.06 µg/person per day, or 0.001 µg/kg bw per day for a 60-kg person.

Risk characterization

The estimated dietary exposure of 0.001 µg/kg bw per day (upper bound) is considerably below the DBCM TDI of 21.4 µg/kg bw per day, and therefore no health concerns were identified.

Bromoform

Toxicological data

In a 2-year corn oil gavage study, bromoform was given to F344/N rats (50 per sex per dose) and female B6C3F1 mice (50 per dose) at doses of 0, 100 or 200 mg/kg bw per day, 5 days/week (NTP, 1989). Male mice (50 per dose) received doses of 0, 50 or 100 mg/kg bw per day. Bromoform induced a small increase in tumours of the large intestine in rats at a dose of 200 mg/kg bw per day (NTP, 1989).

Bromoform was weakly mutagenic in a number of assays, with activation mediated via glutathione conjugation (DeMarini et al., 1997; Pegram et al., 1997). However, WHO (2005b) considered the evidence of genotoxicity to be inconclusive. IARC (1999b) has classified bromoform in Group 3 (not classifiable as to its carcinogenicity to humans).

A NOAEL for bromoform is 25 mg/kg bw per day based on the absence of liver lesions in rats after 13 weeks of dosing by corn oil (NTP, 1989). Based on this NOAEL and using an uncertainty factor of 1000 (10 each for interspecies and intraspecies variation and 10 for the short duration of the study and possible carcinogenicity), a TDI for bromoform of 25 µg/kg bw per day was derived (IPCS, 2000). In a subsequent evaluation, the NOAEL was corrected to allow for gavage exposure on 5 days/week, resulting in establishment of a TDI of 17.9 µg/kg bw per day (WHO, 2005b).

Dietary exposure

Bromoform is a potential DBP resulting from the use of DBDMH in the processing of poultry and beef. Dietary exposure to bromoform from the consumption of beef and poultry treated with DBDMH can be estimated using the CSFII 1994–1996, 1998. The consumption of beef and poultry at the 90% percentile (94% eaters) is 150 g/person per day. Using this value and assuming that the bromoform residue level of 0.005 µg/g meat (see section 2.8.2.3) represents a worst-case value for bromoform residue on beef and poultry gives an exposure to bromoform of 0.8 µg/person per day, or 0.013 µg/kg bw per day for a 60-kg person.

Risk characterization

The estimated dietary exposure of 0.013 µg/kg bw per day is considerably below the bromoform TDI of 17.9 µg/kg bw per day, and therefore no health concerns were identified.

3.2 Epidemiological review

3.2.1 Introduction

Several disease outbreaks associated with microbially contaminated foods have occurred in a number of countries in recent years, including outbreaks of foodborne illness associated with verotoxigenic *Escherichia coli* and *Listeria monocytogenes* in processed meat products and *E. coli* O157:H7 in spinach (see chapter 4). However, it is unknown whether any of these outbreaks could be attributed to a lack of proper disinfection procedures during food processing rather than a lack of good hygienic practices. Therefore, the expert meeting did not further consider epidemiological studies of pathogen outbreaks associated with food.

In addition, no epidemiological studies on the health effects associated with exposure to disinfectants and DBPs in food products have been identified. Instead, all epidemiological studies to date have focused on DBPs in drinking-water. Therefore, this section focuses on epidemiological studies of DBPs, mainly chlorination by-products, in drinking-water; one study deals with ozonation.

Epidemiological studies on disinfectants and DBPs in drinking-water and swimming pools have been conducted since the 1970s, when it became clear that DBPs could be formed as part of the disinfection process. The focus of epidemiological studies has generally been on the DBPs rather than the disinfectants as a putative agent. As the DBPs occur as a mixture, the epidemiological studies have compared health risks for water type (e.g. groundwater versus surface water), the absence versus presence of some disinfection process (e.g. chlorination versus chloramination) or the level of DBPs, often indicated by THMs, the most common group of DBPs. However, little information is generally provided by the studies on how these indicator variables (i.e. THMs) relate to the underlying mixture of the more than 600 known by-products (Richardson, 1998). Some studies have examined the effects of individual by-products (e.g. individual THMs or HAAs), but if there is little information on the correlation with other DBPs, then it is unclear whether these specific compounds relate to the observed risks or still act as a marker. Furthermore, many epidemiological studies have not specifically taken into account the amount of water ingested, whereas few have specifically taken into account exposure routes other than ingestion (e.g. inhalation, dermal absorption) that may contribute significantly to the uptake of substances such as THMs during, for example, showering, bathing and swimming (e.g. Backer et al., 2000; Nieuwenhuijsen, Toledano & Elliott, 2000; Lynberg et al., 2001; Miles et al., 2002; Nuckols et al., 2005; Gordon et al., 2006; Leavens et al., 2007). The review below should be read in the light of these comments.

As most epidemiological studies of DBPs and cancer were conducted before 2004, they have been extensively described and evaluated in the IPCS (2000) and IARC (2004) documents on disinfectants and DBPs. These studies will not be further discussed beyond what the two documents concluded. New studies since 2004 will be described. As many of the reproductive epidemiological studies on DBPs have taken place after 2000, a more in-depth description of these studies will be given.

3.2.2 IPCS (2000) conclusions

IPCS (2000) performed a detailed evaluation of the epidemiological studies on disinfectants and DBPs and summarized the findings as described below.

Epidemiological studies have not identified an increased risk of cardiovascular disease associated with chlorinated or chloraminated drinking-water.

Based on the entire cancer–chlorinated drinking-water epidemiological database, there is better evidence for an association between exposure to chlorinated surface water and bladder cancer than for other types of cancer. However, the latest published study by Cantor et al. (1998) noted several inconsistencies in results among the studies for smokers/non-smokers and males/females, and the evidence is still considered insufficient to allow a judgement as to whether the association is causal and which water contaminants may be important. Evidence for a role of THMs is weak. Poole (1997) also noted that “The basic conclusion of the present report is that the hypothesis of a causal relationship between consumption of chlorination by-products and the risk of any cancer, including bladder cancer and rectal cancer, is still an open question”.

The overall findings of Cantor et al. (1998) support the hypothesis of an association between bladder cancer and duration of use of chlorinated surface water or groundwater and estimated THM exposures, but aspects of these results caution against a simple interpretation and raise additional questions about the nature of the association. An increase in bladder cancer risk was found with duration of chlorinated groundwater use, as well as with total duration of chlorinated drinking-water (surface water plus groundwater) use, with relative risks similar to those observed with chlorinated surface water. This finding is unexpected, because the levels of by-products from most chlorinated groundwaters are much lower than those in treated surface water. In addition, risk was found to increase with duration of chlorinated surface water use among ever-smokers, but not women. This raises questions of internal consistency, as well as consistency with other findings. In contrast, Cantor et al. (1998) found associations for both sexes, primarily among never-smokers. Cantor, Hoover & Hartge (1985) noted:

In Ontario, King and Marrett [1996] noted somewhat higher risk estimates for never-smokers associated with duration of chlorinated surface water. In Colorado, McGeehin et al. [1993] reported similar patterns of risk among smokers and never-smokers, and among men and women. Finally, in a case–control study from Washington County, Maryland, Freedman et al. [1997] reported results that parallel the current findings, namely that the risk associated with chlorinated surface water was primarily observed among men and among smokers. Reasons for differences among these observations and differences with results from our study are unclear. A possible explanation for the apparent discrepancies in findings for smokers and never-smokers among studies may reside in water quality and water treatment differences in the respective study areas, with resulting variations in the chemical composition of byproduct mixtures. Nevertheless, results should not differ by sex.

IPCS (2000) concluded that the existing epidemiological data were insufficient to allow a conclusion that the observed associations between bladder or any other cancer and chlorinated drinking-water or THMs are causal or provide an accurate estimate of the magnitude of risk. Any association between exposure to chlorinated surface water, THMs or the mutagenicity of drinking-water and cancer of the colon, rectum, pancreas, brain and other sites cannot be evaluated at this time because of inadequate epidemiological evidence. However, the findings from well-conducted studies associating bladder cancer with chlorinated water and THMs cannot be completely dismissed, even though inconsistencies have been noted for risks among men and women and among smokers and non-smokers. Because of the large number of people exposed to chlorinated drinking-water, it is important to resolve this issue using studies designed with sound epidemiological principles. Additional studies to resolve the questions about the associations that have been reported for chlorinated surface water, THMs, fluid and tap water consumption, and bladder cancer and reproductive and developmental effects must focus on the resolution of various problems noted in previous studies, especially consideration of exposures to other DBPs.

IPCS (2000) noted that the existing epidemiological data are insufficient to allow the importance of the observed associations of chlorinated drinking-water or THMs with adverse

pregnancy outcomes to be assessed. Although several studies have suggested that increased risks of neural tube defects and miscarriage may be associated with THMs or selected THM species, additional studies are needed to determine whether the observed associations are spurious.

A recently convened scientific panel (USEPA, 1997) concluded that the results of published epidemiological studies do not provide convincing evidence that DBPs cause adverse pregnancy outcomes. The panel recommended that additional studies be conducted, specifically that the Waller et al. (1998) study be expanded to include additional exposure information about by-products other than THMs and that a similar study be conducted in another geographic area.

3.2.3 IARC (2004) conclusions

IARC (2004) evaluated the carcinogenicity of some disinfectants and DBPs that are found in most chlorinated and chloraminated drinking-water (chloral hydrate, DCA, TCA, MX and monochloramine) and concluded that several studies were identified that analysed risk with respect to one or more measures of exposure to complex mixtures of these DBPs. No data specifically on these substances were available to the IARC working group.

3.2.4 Evaluation of studies published since IPCS (2000) and IARC (2004)

3.2.4.1 Cancer

Villanueva et al. (2003) conducted a meta-analysis to evaluate whether consumption of chlorinated drinking-water was associated with bladder cancer. They selected studies evaluating individual consumption of chlorinated drinking-water and bladder cancer, extracted from each study risk estimates for intermediate and long-term (>40 years) consumption of chlorinated water, stratified by sex when possible, and performed meta-analysis for the two exposure levels. They included six case-control studies (6084 incident bladder cancer cases, 10 816 controls) and two cohort studies (124 incident bladder cancer cases). Ever consumption of chlorinated drinking-water was associated with an increased risk of bladder cancer in men (combined odds ratio [OR] = 1.4, 95% confidence interval [CI] = 1.1–1.9) and women (combined OR = 1.2, 95% CI = 0.7–1.8). The combined OR for mid-term exposure in both sexes was 1.1 (95% CI = 1.0–1.2) and for long-term exposure was 1.4 (95% CI = 1.2–1.7). The combined estimate of the slope for a linear increase in risk was 1.13 (95% CI = 1.08–1.20) for 20 years and 1.27 (95% CI = 1.15–1.43) for 40 years of exposure in both sexes.

Ranmuthugala et al. (2003) conducted a cohort study in 1997 in three Australian communities with varying levels of DBPs in the water supply. Exposure was assessed using both available dose (total THM concentration in the water supply) and intake dose (calculated by adjusting for individual variations in ingestion, inhalation and dermal absorption). Micronuclei in urinary bladder epithelial cells were used as a preclinical biomarker of genotoxicity. Cells were scored for micronuclei for 228 participants, of whom 63% were exposed to DBPs and 37% were unexposed. Available dose of total THMs for the exposed group ranged from 38 to 157 µg/l, whereas intake dose ranged from 3 to 469 µg/kg bw per day. Relative risk for DNA damage to bladder cells, per 10 µg/l of available dose of total THMs, was 1.01 (95% CI = 0.97–1.06) for smokers and 0.996 (95% CI = 0.961–1.032) for non-smokers. Relative risk, per 10 µg/kg bw per day of intake dose of total THMs, was 0.99 (95% CI = 0.96–1.03) for smokers and 1.003 (95% CI = 0.984–1.023) for non-smokers.

Villanueva et al. (2004) pooled the primary data from six case-control studies of bladder cancer that used THMs as a marker for DBPs. Two studies were included from the USA and one each from Canada, Finland, France and Italy. Inclusion criteria were the availability of detailed data on THM exposure and individual water consumption. The analysis included 2806 cases and 5254 controls, all of whom had measures of known exposure for at least 70% of the exposure window of 40 years before the interview. Cumulative exposure to THMs was estimated by combining individual year-by-year average THM level and daily tap water consumption. There was an adjusted OR of 1.24 (95% CI = 1.09–1.41) in men exposed to an average THM concentration of more than 1 µg/l compared with those who had lower or no exposure. Estimated relative risks increased with increasing exposure, with an OR of 1.44 (95% CI = 1.20–1.73) for exposure higher than 50 µg/l. Similar results were found with other indices of THM exposure. Among women, THM exposure was not associated with bladder cancer risk (OR = 0.95, 95% CI = 0.76–1.20). ORs for cumulative THM exposure are given in Table 3.10. Cumulative exposure was estimated by combining individual year-by-year average THM level and daily tap water consumption.

Table 3.10. Pooled analysis of bladder cancer and cumulative exposure to THMs^a

THM exposure level (mg)	Male ORs	Female ORs
0–15	1.00	1.00
>15–50	1.22	0.92
>50–400	1.28	0.94
>400–1000	1.31	1.02
>1000	1.50	0.92

^a After Villanueva et al. (2004).

Chevrier, Junod & Cordier (2004) used data from a case-control study of bladder cancer conducted between 1985 and 1987 in seven French hospitals. They compared 281 cases and 272 controls for whom they could reconstruct at least 70% of the residential exposure to drinking-water contaminants over a 30-year period. They found that the risk of bladder cancer decreased as duration of exposure to ozonated water increased (OR = 0.60, 95% CI = 0.3–1.3, for 1–9 years; OR = 0.31, 95% CI = 0.1–0.7, for 10 years or more). Simultaneously, the risk of bladder cancer increased with duration of exposure to chlorinated surface water (OR = 2.02, 95% CI = 1.0–4.3, for 0 versus ≥29 years), with the estimated THM content of the water (OR = 2.99, 95% CI = 1.1–8.5, for <1 versus >50 µg/l) and cumulative exposure to THMs (OR = 3.39, 95% CI = 1.2–9.6, for 0 versus >1500 (µg/l)·year).

Do et al. (2005) reported results from a population-based case-control study of 486 incident cases of pancreatic cancer and 3596 age- and sex-matched controls. Exposure to chlorination by-products was estimated by linking lifetime residential histories to two different databases containing information on chlorination by-product levels in municipal water supplies. Logistic regression analysis found no evidence of increased pancreatic cancer risk at higher chlorination by-product concentrations (all ORs <1.3). Null findings were also obtained assuming a latency period for pancreatic cancer induction of 3, 8 or 13 years.

Villanueva et al. (2007) examined whether bladder cancer risk was associated with exposure to THMs through ingestion of water and through inhalation and dermal absorption during showering, bathing and swimming in pools. Lifetime personal information on water consumption and water-related habits was collected for 1219 cases and 1271 controls in a 1998–2001 case-control study in Spain and was linked with THM levels in geographic study areas. Long-term THM exposure was associated with a 2-fold increase in bladder cancer risk,

with an OR of 2.10 (95% CI = 1.09–4.02) for average household THM levels of $>49 \mu\text{g/l}$ versus $\leq 8 \mu\text{g/l}$. Compared with subjects not drinking chlorinated water, subjects with THM exposure of $>35 \mu\text{g/day}$ through ingestion had an OR of 1.35 (95% CI = 0.92–1.99). The OR for duration of shower or bath weighted by residential THM level was 1.83 (95% CI = 1.17–2.87) for the highest compared with the lowest quartile. Swimming in pools was associated with an OR of 1.57 (95% CI = 1.18–2.09). Furthermore, they identified genetically susceptible groups, such as those with glutathione *S*-transferase enzymes GSTT1 and GSTZ1 (Cantor et al., 2006).

Bove, Rogerson & Vena (2007b) examined the relationship between the estimated concentrations of THMs in drinking-water and the risk for urinary bladder cancer in a case–control study of 567 white men aged 35–90 years in western New York State, USA. They used logistic regression to estimate ORs and to assess the effects of THM consumption on cancer risk. Higher levels of consumption of THMs led to increased risk for cancer of the urinary bladder (OR = 2.34, 95% CI = 1.01–3.66). Results were most significant for bromoform (OR = 3.05, 95% CI = 1.51–5.69), and risk was highest (OR = 5.85, 95% CI = 1.93–17.46) for those who consumed the greatest amount of water at points within the distribution system with the oldest post-disinfected tap water.

Bove, Rogerson & Vena (2007a) assessed the effects of estimated exposure to some of the components of the THM group on the ORs and probabilities for rectal cancer in white males in a case–control study of 128 cases and 253 controls, conducted in Monroe County, western New York State, USA. The spatial patterns of THMs and individual measures of tap water consumption provided exposure estimates. The risk for rectal cancer did not increase with the total level of THMs, but increasing levels of bromoform (measured in $\mu\text{g/day}$) did correspond with an increase in the risk (OR = 1.85, 95% CI = 1.25–2.74) for rectal cancer. The highest quartiles of estimated consumption of bromoform (1.69–15.43 $\mu\text{g/day}$) led to increased risk for rectal cancer (OR = 2.32, 95% CI = 1.22–4.39). Two other THMs were marginally associated with an increase in risk—DBCM (OR = 1.78, 95% CI = 1.00–3.19) and BDCM (OR = 1.15, 95% CI = 1.00–1.32).

Karagas et al. (2008) conducted an exploratory analysis of the hypothesis that exposure to DBPs may enhance risk of cancers of skin. They used data accrued in a completed population-based case–control study of keratinocyte-derived malignancies—basal cell carcinomas (BCC) and squamous cell carcinomas (SCC)—from New Hampshire, USA, originally designed to examine the effects of drinking-water arsenic. Newly diagnosed cases of BCC and SCC were identified through a state-wide network of dermatologists, dermatopathologists and pathologists, and age- and sex-matched controls were selected from population lists. The study comprised 293 SCC cases, 603 BCC cases and 540 controls. Residents of towns or cities with multiple water systems were assigned the average THM value weighted by the proportion of the population served by these systems. Among individuals who reported using public water systems, the ORs for those with levels above $40 \mu\text{g/l}$ were 2.4 (95% CI = 0.9–6.7) for BCC and 2.1 (95% CI = 0.7–7.0) for SCC compared with those below $1 \mu\text{g/l}$.

3.2.4.2 Reproductive outcomes

A summary of the results of reproductive epidemiological studies is given in Table 3.11.

Table 3.11. Summary of epidemiological studies on chlorinated DBPs and adverse reproductive outcomes

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Aschengrau, Zierler & Cohen (1989)	Massachusetts, USA Sample population: 1677	286 spontaneous abortions	Surface water versus groundwater Chlorination versus chloramination	Smoking habits Contraceptive use Medical and obstetrical history Metals	Surface water versus groundwater 2.2 (1.3–3.6)
Kramer et al. (1992)	Iowa, USA 151 towns with a single water source 1989–1990 Sample population: 4028	588 (total) 159 LBW 342 pre-term delivery 187 IUGR/SGA	Based on maternal residential address and one municipal water survey to estimate individual THM levels (2 or 3 exposure categories)	Maternal age Parity Marital status Education Smoking Prenatal care	No versus medium (1–9 µg/l) versus high (≥10 µg/l): Chloroform LBW: 1 versus 1.1 (0.7–1.6) versus 1.3 (0.8–2.2) IUGR: 1 versus 1.3 (0.9–1.8) versus 1.8 (1.1–2.9) DBCM IUGR: 1 versus 1.2 (0.8–1.7) versus 1.7 (0.9–2.9)
Aschengrau, Zierler & Cohen (1993)	Massachusetts, USA 2 hospitals 1977–1980 Sample population: 2348	1171 (total) 1039 major congenital malformations Urinary tract defects Respiratory tract defects 77 stillbirths 55 neonatal deaths	Based on maternal residential address to ascertain type of water supply, chlorination versus chloramination and groundwater/mixed water versus surface water	Maternal age Pregnancy history Alcohol Ethnicity Hospital payment Other water contaminants	Chlorinated versus chloraminated: Stillbirth: 2.6 (0.9–7.5) Neonatal deaths: 1.1 (95% CI not provided) Congenital malformations: - major malformations: 1.5 (0.7–2.1) - respiratory defects: 3.2 (1.1–9.5) - urinary tract defects: 4.1 (1.2–14.1)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Bove et al. (1995)	New Jersey, USA 75 towns with a public water supply 1985–1988 Sample population: 81 602	29 268 (total) <i>Live births:</i> 1853 LBW 905 VLBW 4082 SGA 7167 pre-term 594 fetal deaths <i>All births: defects:</i> 669 surveillance 118 CNS defects 83 oral cleft 56 NTD 108 major cardiac	Based on maternal residential address and municipal water surveys to estimate monthly TTHM levels (5 or 6 exposure categories)	Maternal age Ethnicity Sex of baby Primipara Prenatal care Education Previous stillbirth or miscarriage Other contaminants	TTHM levels >100 µg/l versus ≤20 µg/l: LBW: 1.4 (50% CI 1.2–1.7) IUGR/SGA: 1.5 (90% CI 1.2–1.9) TTHM levels >80 µg/l versus ≤20 µg/l: Surveillance register defects: 1.6 (90% CI 1.2–2.0) CNS defects: 2.6 (90% CI 1.5–4.3) NTD: 3.0 (90% CI 1.3–6.6) Major cardiac defects: 1.8 (90% CI 1.0– 3.3) TTHM levels >100 µg/l versus ≤20 µg/l: Oral cleft defects: 3.2 (90% CI 1.2–7.3)
Savitz, Andrews & Pastore (1995)	North Carolina, USA 6 hospitals 1988–1991 Sample population: 1003	548 (total) 126 spontaneous abortion 244 pre-term 178 LBW	Based on maternal residential address and quarterly municipal water surveys to estimate average TTHM levels Analysis of: a) surface water versus groundwater source b) TTHM levels (3 exposure categories) c) consumption during pregnancy d) water source x amount e) TTHM dose (level x amount)	Maternal age Ethnicity Hospital Education Marital status Poverty level Smoking Alcohol consumption Employment Nausea	TTHM concentration 40.8–59.9 versus 81.1–168.8 µg/l: Spontaneous abortion: 1.2 (0.6–2.4) TTHM concentration 40.8–63.3 versus 82.8–168.8 µg/l: LBW: 1.3 (0.8–2.1) Per 50 µg/l incremental change in TTHM concentration: Spontaneous abortion: 1.7 (1.1–2.7)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Kanitz et al. (1996)	Liguria, Italy 2 hospitals 1988–1989 Sample population: 676	548 live births in “exposed” area 50 pre-term 141 caesarean section 133 neonatal jaundice 20 LBW 288 small body length 370 small cranial circumference	Based on maternal residential address to ascertain type of water source (chlorine dioxide and/or hypochlorite versus not treated)	Maternal age Education Smoking Alcohol Sex of child	Sodium hypochlorite-treated (TTHM concentration 8–16 µg/l) versus non- treated water: Neonatal jaundice: 1.1 (0.7–2.8) LBW: 6.0 (0.6–12.6) Small body length: 2.3 (1.3–4.2) Small cranial circumference: 3.5 (2.1– 8.5)
Gallagher et al. (1998)	Colorado, USA 28 census blocks in 2 water districts 1990–1993 Sample population: 1244 live births	72 LBW 29 term LBW 68 pre-term delivery	Based on maternal residential address and municipal water surveys Estimate of household TTHM level during last trimester based on hydraulic modelling (4 exposure categories)	Maternal age Smoking Marital status Parity Education Employment Prenatal care	High TTHM level (≥61 µg/l) versus lowest (≤20 µg/l): LBW: 2.1 (1.0–4.8) Term LBW: 5.9 (2.0–17.0)
Waller et al. (1998)	California, USA 3 regions of surface water, groundwater and mixed drinking- water 1989–1991 Sample population: 5144 pregnancies	499 spontaneous abortions	Based on maternal residential address and quarterly municipal water surveys to estimate average TTHM and individual THM levels Analysis based on: a) THM levels (3 or 10 exposure categories) b) consumption during first trimester from interview (2 exposure categories)	Maternal age Gestational age Smoking History of pregnancy loss Ethnicity Employment	High TTHM dose (≥5 glasses/day + ≥75 µg/l) versus low dose (<5 glasses/day + <75 µg/l): Spontaneous abortion: 1.8 (1.1–3.0) High BDCM dose (≥5 glasses/day + ≥18 µg/l) versus low dose (<5 glasses/day + <18 µg/l): Spontaneous abortion: 3.0 (1.4–6.6)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Dodds et al. (1999)	Nova Scotia, Canada 1988–1995 Sample population: 49 842 births	4673 SGA 2393 LBW 342 VLBW 2689 pre-term delivery 77 NTD 82 cleft defect 430 major cardiac defects 197 stillbirth 96 chromosomal abnormalities	Based on maternal residential address and TTHM levels for public water facilities (3 sampling locations) modelled using linear regression on the basis of observations by year, month and facility (4 exposure categories)	Maternal age Parity Maternal smoking Attendance at prenatal classes Neighbourhood family income Sex Pregnancy and pre- delivery weight	TTHM concentration 0–49 µg/l versus >100 µg/l Stillbirth: 1.66 (1.09–2.52) Chromosomal abnormalities: 1.38 (0.73– 2.59) Small for gestation age: 1.08 (0.99–1.18) NTDs: 1.18 (0.67–2.10)
Klotz & Pyrch (1999)	New Jersey, USA 1993–1994 Sample population: all births, of which 112 cases and 248 controls selected	112 NTD	Based on residential address and public water facility TTHM data and tap water sampling for TTHMs, HANs and HAAs (3–5 exposure categories)	Sociodemographics Pregnancy and medical history Parental occupational Use of vitamins	TTHM public monitoring data, known residence and isolated cases <5 µg/l versus 40+ µg/l NTDs: 2.1 (1.1–4.0)
Magnus et al. (1999)	Norway Sample population: 141 077	2608 all birth defects 62 NTD 250 major cardiac defects 91 respiratory defects 122 urinary defects 143 oral cleft	Chlorination yes versus no Colour high versus low (in chlorinated water, average TTHMs = 9.4 µg/l, average HAAs = 14.6 µg/l)	Maternal age Parity Geographical placement Population density Industry profile	No chlorination low colour versus chlorination high colour All birth defects: 1.14 (0.99–1.31) Urinary tract defects: 1.99 (1.10–3.57) NTDs: 1.26 (0.61–2.62) Major cardiac defects: 1.05 (0.76–1.46) Respiratory tract defects: 1.07 (0.52– 2.19)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Källén & Robert (2000)	Sweden 1985–1994 Sample population: No chlorination: 74 324 singletons Sodium hypochlorite: 24 731 singletons Chlorine dioxide: 15 429 singletons	Multiple births Gestational duration Birth weight Intrauterine growth Body length Head circumference Body mass index Infant survival up to 1 year Perinatal death Apgar score Neonatal jaundice Congenital malformations, including NTDs Childhood cancer Hypothyroidism	No versus sodium hypochlorite (no versus chlorine dioxide)	Year of birth Maternal age Parity Maternal education Maternal smoking Congenital malformations and childhood cancer Maternal age Year of birth	No versus sodium hypochlorite LBW: 1.15 (1.05–1.26) <32 weeks' gestation: 1.22 (1.00–1.48) <37 weeks' gestation: 1.09 (1.01–1.17) <43 cm length: 1.97 (1.30–2.97) <47 cm length: 1.25 (1.10–1.43) Body mass index >16 kg/m ² : 1.27 (1.19– 1.37) <31 cm head circumference: 1.46 (1.07– 1.98) Spine malformation: 3.2 (1.0–10.0)
King, Dodds & Allen (2000)	Nova Scotia, Canada 1988–1995 Sample population: 49 756	214 stillbirths (72 asphyxia-related stillbirths)	Based on maternal residential address and TTHM, chloroform and BDCM levels for public water facilities (3 sampling locations) modelled using linear regression on the basis of observations by year, month and facility (4 exposure categories) ($r =$ 0.44 for TTHM and BDCM)	Maternal age Parity Maternal smoking Attendance at prenatal classes Neighbourhood family income Sex Pregnancy and pre- delivery weight	Chloroform concentration 0–49 µg/l versus >100 µg/l Stillbirth: 1.56 (1.04–2.34) Asphyxia-related stillbirth: 3.15 (1.64– 6.03) BDCM concentration <5 µg/l versus >20 µg/l Stillbirth: 1.98 (1.23–3.49) Asphyxia-related stillbirth: 1.75 (0.72– 4.22)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Yang et al. (2000a)	China, Province of Taiwan Sample population: 18 025 first-parity births Chlorinated: 10 007 Non-chlorinated: 8018	LBW Pre-term delivery (<37 weeks)	Chlorinated (>95% population served chlorinated water) versus non-chlorinated (<5% population served chlorinated water)	Maternal age Marital status Maternal education Sex	Chlorinated versus non-chlorinated Pre-term delivery: 1.34 (1.15–1.56)
Yang et al. (2000b)	China, Province of Taiwan Sample population: Chlorinated: 24 882 Non-chlorinated: 20 460	Sex ratio	Chlorinated (>95% population served chlorinated water) versus non-chlorinated (<5% population served chlorinated water)		No association
Dodds & King (2001)	Nova Scotia, Canada 1988–1995 Sample population: 49 842 births	77 NTDs 430 cardiovascular anomalies 82 cleft defects 96 chromosomal abnormalities	Based on maternal residential address and TTHM, chloroform and BDCM levels for public water facilities (3 sampling locations) modelled using linear regression on the basis of observations by year, month and facility (4 exposure categories) ($r =$ 0.44 for TTHM and BDCM)	Maternal age Parity Maternal smoking Attendance at prenatal classes Neighbourhood family income Sex Pregnancy and pre- delivery weight	BDCM concentration ≥ 20 $\mu\text{g/l}$ versus < 5 $\mu\text{g/l}$ NTDs: 2.5 (1.2–5.1)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Jaakkola et al. (2001)	Norway Sample population: 137 145	6249 LBW ? SGA 7886 pre-term delivery	Chlorination yes versus no Colour high versus low (in chlorinated water, average TTHMs = 9.4 µg/l, average HAAs = 14.6 µg/l)	Maternal age Parity Geographical placement Population density Industry profile	No chlorination low colour versus chlorination high colour Pre-term delivery: 0.91 (0.84–0.99)
Waller et al. (2001)	See Waller et al. (1998)	See Waller et al. (1998)	See Waller et al. (1998)	See Waller et al. (1998)	Reanalysis of Waller et al. (1998) Utility-wide subset sample highest OR High TTHM dose (≥5 glasses/day + ≥75 µg/l) versus low dose (≥5 glasses/day + <75 µg/l): Spontaneous abortion: 5.1 (1.8–14.7) Little relationship with showering
Cedergren et al. (2002)	Sweden Sample population: 58 669	Cardiac defects	TTHM concentration >10 µg/l versus ≤10 µg/l in surface water Hypochlorite and chlorine dioxide versus hypochlorite in surface water Groundwater versus surface water	Maternal age Parity Smoking Education	TTHM concentration >10 µg/l versus ≤10 µg/l Cardiac defects: 1.30 (1.08–1.56) Groundwater versus surface water Cardiac defects: 1.32 (1.10–1.58) Hypochlorite and chlorine dioxide versus hypochlorite Cardiac defects: 1.85 (1.42–2.39)
Hwang, Magnus & Jaakkola (2002)	Norway Sample population: 285 631	Any birth defect NTD - anencephalus - spina bifida - hydrocephalus Cardiac defects	Chlorination (yes/no) and level of water colour (mg Pt/l: <10, 10–19.9, ≥20)	Maternal age Parity Socioeconomic status: - centrality - population density	Chlorination (yes) and level of water colour: <10 versus ≥20 mg Pt/l All birth defects: 1.18 (1.02–1.36) Ventricular septal defect: 1.81 (1.05–3.09) Chlorination (yes) and level of water colour: <10 versus ≥10 mg Pt/l

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
		<ul style="list-style-type: none"> - ventricular septal defects - atrial septal defects Respiratory defects Oral cleft defects - Cleft palate - Cleft lip Urinary tract defect - Obstructive urinary tract defect 			All birth defects: 1.13 (1.01–1.25) Cardiac defects: 1.37 (1.00–1.89) Respiratory defects: 1.89 (1.00–3.58) Urinary tract defects: 1.46 (1.00–2.13)
Nieuwen-huijsen, Northstone & Golding (2002)	England Sample population: 11 462	Birth weight	Amount of swimming (h)	Maternal age Maternal education Smoking Alcohol use Drug use Gestational age Ethnicity Infant sex	No association
Wright, Schwartz & Dockery (2003)	Massachusetts, USA Sample population: 56 513	Birth weight LBW SGA Gestational age Pre-term delivery	TTHM concentration 0–60, >60–80, >80 µg/l or per 20 µg/l increase in TTHM concentration	Maternal age Maternal education Ethnicity Smoking Parental care Parity Infant sex	TTHM concentration 0–60 or >80 µg/l Birth weight: –32 g (–47 to –18) SGA: 1.14 (1.02–1.26) Gestational age (weeks): 0.08 (0.01–0.14) per 20 µg/l increase in TTHM concentration Birth weight: –2.8 g (–5.5 to –0.2) Gestational age: 0.02 (0.01–0.03)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Shaw et al. (2003)	California, USA Sample population: Study 1: 538 NTD cases and 539 controls Study 2: 265 NTD cases, 207 conotruncal heart defect cases, 409 orofacial cleft cases and 481 controls	Study 1: NTDs (anencephaly and spina bifida) Study 2: NTDs (anencephaly and spina bifida), conotruncal heart defects, orofacial clefts	Study 1 and study 2: Continuous TTHM Categorical: 0, 1–24, 25–49, 50–74 and ≥ 75 $\mu\text{g/l}$ Also study 1: ≥ 50 versus < 50 $\mu\text{g/l}$ and < 5 glasses ≥ 50 versus < 50 $\mu\text{g/l}$ and > 5 glasses Study 1: Chloroform ≥ 12.2 versus < 12.2 $\mu\text{g/l}$ BDCM ≥ 4.2 versus < 4.2 $\mu\text{g/l}$ DBCM ≥ 1.7 versus < 1.7 $\mu\text{g/l}$ Study 2: Chloroform ≥ 15.0 versus < 15.0 $\mu\text{g/l}$ BDCM ≥ 9.6 versus < 9.6 $\mu\text{g/l}$ DBCM ≥ 3.6 versus < 3.6 $\mu\text{g/l}$	Ethnicity Education Body mass index Use of vitamins Methylenetetra- hydrofolate reductase genotype	Study 1: NTDs NTD risk inversely related to TTHM exposure but only occasionally significant for one category Chloroform concentration ≥ 12.2 versus < 12.2 $\mu\text{g/l}$: 0.50 (0.34–0.75) BDCM concentration ≥ 4.2 versus < 4.2 $\mu\text{g/l}$: 0.66 (0.45–0.97) DBCM concentration ≥ 1.7 versus < 1.7 $\mu\text{g/l}$: 0.69 (0.47–1.0) Study 2: Multiple cleft palate/lip Chloroform concentration ≥ 15.0 versus < 15.0 $\mu\text{g/l}$: 0.21 (0.05–0.90)
Aggazzotti et al. (2004)	Italy 9 towns Sample population: 1194 subjects	343 pre-term delivery 239 SGA at term	Water sampling directly at mothers' homes to determine THM levels and chlorite/chlorate levels Questionnaire on personal habits to determine: - type of water consumption - frequency of bath/shower - swimming pool attendance	Maternal age Education Sex Smoking Alcohol Coffee	Pre-term delivery No significant associations Term SGA > 200 $\mu\text{g/l}$ low inhalation exposure versus < 200 $\mu\text{g/l}$: 1.52 (0.91–2.52) > 200 $\mu\text{g/l}$ high inhalation exposure versus < 200 $\mu\text{g/l}$: 1.70 (0.97–3.00)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Dodds et al. (2004)	Nova Scotia and eastern Ontario, Canada Sample population: 112 stillbirths and 398 live birth controls	Stillbirth	Various indices: 0, 1–49, 50–79 and >80 µg/l for TTHM and chloroform 0, 1–4, 5–9 and >9 µg/l for BDCM Quintiles for total exposure (ingestion/showering/bathing) for TTHM, chloroform and BDCM Concentration and duration	Age Province Household income	Stillbirth: TTHM concentration >80 µg/l versus 0: 2.2 (1.1–4.4) TTHM highest versus lowest quintile: 2.4 (1.2–4.6) Drinking 5+ drinks per day and THM 50+ µg/l versus <1 drink and THM = 0: 4.0 (1.4–11) Chloroform and BDCM generally follow TTHM trend
Infante- Rivard (2004)	Montreal, Quebec, Canada Sample population: 493 cases, 472 controls	IUGR (10th percentile)	Regulatory data on THMs, >90th percentile versus ≤90th percentile	Gestational age Sex Race Mother's weight gain Body mass index Smoking Primiparity Pre-eclampsia Previous IUGR	IUGR No association with THMs only, but with CYP2E1*5 (G1259C): 13.2 (1.19–146.7) in newborns
Wright, Schwartz & Dockery (2004)	Massachusetts, USA Sample population: 196 000 registry based	Birth weight Gestational age SGA Pre-term delivery	TTHM Individual THMs HAAs MX Mutagenicity		SGA TTHM concentration >74 versus ≤33 µg/l: 1.13 (1.07–1.20) Chloroform concentration >63 versus ≤26 µg/l: 1.11 (1.04–1.17) BDCM concentration >13 versus ≤5 µg/l: 1.15 (1.08–1.22) >2250 versus ≤1250 revertants/l (elevated mutagenic activity): 1.25 (1.04–1.51)

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Similar results for birth weight					
Yang (2004)	China, Province of Taiwan Sample population: 182 796	LBW Pre-term delivery	15 non-chlorinating municipalities and 128 chlorinating municipalities	Maternal age Education Gestational age Birth weight Sex	Pre-term delivery Non-chlorinating municipalities versus chlorinating municipalities: 1.37 (1.20– 1.56)
Hinckley, Bachand & Reif (2005)	Sample population: 48 119	LBW, IUGR, pre-term delivery	THMs and HAAs	Maternal age Ethnicity Education Parity Smoking Kessner index	IUGR TTHM concentration ≥ 53 versus <40 $\mu\text{g/l}$: 1.09 (1.00–1.18) Term LBW DBA concentration ≥ 5 versus <4 $\mu\text{g/l}$: 1.49 (1.09–2.04) IUGR DCA concentration ≥ 8 versus <6 $\mu\text{g/l}$: 1.28 (1.08–1.51) TCA concentration ≥ 6 versus <4 $\mu\text{g/l}$: 1.19 (1.01–1.41) Weeks 37–40 IUGR DCA concentration ≥ 8 versus <6 $\mu\text{g/l}$: 1.27 (1.02–1.59) Weeks 33–36 Term LBW DBA concentration ≥ 5 versus <4 $\mu\text{g/l}$: 1.49 (1.10–2.02)
King et al. (2005)	Nova Scotia and eastern Ontario, Canada	Stillbirth	HAAs	Maternal age Province Income	Stillbirth No significant results after adjustments for THMs

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
	Sample population: 112 cases, 398 controls			Occupation Smoking	
Porter et al. (2005)	Maryland, USA 4 regions Sample population: 15 416 births	IUGR	THMs and HAAs	Smoking Ethnicity Prenatal care Alcohol Marital status	No association
Toledano et al. (2005)	3 water regions in United Kingdom Sample population: 920 571 stillbirths and live births (1993– 1998) and 969 304 live births (1992– 1998)	Stillbirth LBW VLBW	THMs	Maternal age Deprivation	Stillbirths TTHM concentration ≥ 60 versus < 30 $\mu\text{g/l}$: 1.11 (1.00–1.23)
Lewis, Suffet & Ritz (2006)	Sample population: 36 259 births	Term LBW	THMs (weekly)	Trimester Age Sex Marital status Ethnicity Education Parity Smoking Conception/birth	Term LBW Second trimester: All: TTHM concentration ≥ 70 versus < 40 $\mu\text{g/l}$: 1.50 (1.07–2.10) Per 10 $\mu\text{g/l}$ TTHM concentration: 1.08 (1.00–1.20) Non-Caucasians: TTHM concentration ≥ 70 versus < 40

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
				season Maternal disease	$\mu\text{g/l}$: 1.60 (1.03–2.47) Per 10 $\mu\text{g/l}$ TTHM concentration: 1.10 (1.00–1.22)
Savitz et al. (2006)	Sample population: 2409	Spontaneous abortion	THMs, HAAs, total organic halides	Maternal age, race, ethnicity, education, marital status, income, smoking, alcohol intake, caffeine consumption, body mass index, age at menarche, employment status, diabetes, pregnancy loss history, induced abortion history, vitamin use	No association
Lewis et al. (2007)	Sample population: 37 498	Pre-term birth	THMs	Maternal age Ethnicity Education Previous birth Marital status Maternal disease Income Kessner index Sex	No association (with some exception for some groups on government pay)
Yang et al. (2007)	Sample population: 90 848	LBW, IUGR, pre-term delivery	THMs	Maternal age Maternal education Marital status Only first birth	No association

Reference	Study details (location, time, sample size)	Cases	Exposure assessment	Other risk factors included	Main positive findings OR (95% CI)
Nieuwen- huijsen et al. (2008)	Sample population: 2 605 226	Congenital anomalies	THMs	Maternal age Deprivation Sex	<p>Isolated ventricular septal defects</p> <p>TTHM concentration ≥ 60 versus < 30 $\mu\text{g/l}$: 1.43 (1.00–2.04)</p> <p>Subset isolated major cardiovascular defects</p> <p>Bromoform concentration 2–< 4 versus < 2 $\mu\text{g/l}$: 1.13 (0.99–1.29)</p> <p>Bromoform concentration ≥ 4 versus < 2 $\mu\text{g/l}$: 1.18 (1.00–1.39)</p> <p>Isolated gastroschisis</p> <p>Bromoform concentration 2–< 4 versus < 2 $\mu\text{g/l}$: 1.11 (0.85–1.45)</p> <p>Bromoform concentration ≥ 4 versus < 2 $\mu\text{g/l}$: 1.38 (1.00–1.92)</p>

CNS, central nervous system; IUGR, intrauterine growth retardation (restriction); LBW, low birth weight; NTD, neural tube defect; SGA, small for gestational age; TTHM, total trihalomethanes; VLBW, very low birth weight

A number of studies found statistically significant positive associations between THMs and neural tube defects, one of the most studied groups of congenital anomalies (Bove et al., 1995; Klotz & Pyrch, 1999; Dodds & King, 2001), whereas others did not (Dodds et al., 1999; Magnus et al., 1999; Källén & Robert, 2000; Hwang, Magnus & Jaakkola, 2002; Shaw et al., 2003; Nieuwenhuijsen et al., 2008). Klotz & Pyrch (1999) found a statistically significant association between total THM levels in the water and neural tube defects, but not with HAN and HAA levels. Also, the effects were most pronounced in offspring from women who did not take supplementary vitamins, but these findings were not confirmed by the Shaw et al. (2003) study. Inclusion of information on ingestion, showering, bathing and swimming made little difference to the risk estimates.

Hwang, Magnus & Jaakkola (2002) and Cedergren et al. (2002) found significant associations between chlorinated water and levels of total THMs above 10 µg/l, respectively, and respiratory congenital anomalies, but other studies did not find such an association (Bove et al., 1995; Dodds et al., 1999; Magnus et al., 1999; Källén & Robert, 2000; Dodds & King, 2001; Shaw et al., 2003; Nieuwenhuijsen et al., 2008). Studies on chlorinated water and respiratory congenital anomalies have been rare, but two studies found a significant positive association (Aschengrau, Zierler & Cohen, 1993; Hwang, Magnus & Jaakkola, 2002), whereas one did not (Nieuwenhuijsen et al., 2008). Similarly, for urinary tract defects, three studies reported statistically significant associations (Aschengrau, Zierler & Cohen, 1993; Magnus et al., 1999; Hwang, Magnus & Jaakkola, 2002), and one did not (Nieuwenhuijsen et al., 2008). Studies on oral cleft or cleft palate have largely been negative, except for the study by Bove et al. (1995). In a meta-analysis, Hwang & Jaakkola (2003) reported evidence for an effect of exposure to chlorination by-products on the risk of neural tube and urinary system defects, but results for respiratory system, major cardiac and oral cleft defects were heterogeneous and inconclusive. The exposure index they used, though, was fairly crude, without actual levels of DBPs. The meta-analyses also did not include the largest study to date, and larger than all the previous studies combined, by Nieuwenhuijsen et al. (2008), which reported no association between THM levels and cleft palate/lip, abdominal wall, major cardiac, neural tube, urinary and respiratory defects; except for a restricted set of anomalies with isolated defects, there were excess risks in the highest exposure categories of total THMs for ventricular septal defects and of bromoform for major cardiovascular defects and gastroschisis.

Only a few studies have assessed the relationship between DBPs and spontaneous abortion. A California, USA, study has attracted the most attention, as it found a statistically significant association between total THMs and BDCM and spontaneous abortion (Waller et al., 1998). The ORs were even larger after reanalysis when restricting it to subjects with more confidence in the exposure data (Waller et al., 2001). In a study trying to replicate these results, Savitz et al. (2006) found no evidence for an association between a number of DBPs and spontaneous abortion, even though the exposure assessment was more refined.

A number of Canadian studies and one English study found statistically positive associations between DBPs and stillbirths (Dodds et al., 1999, 2004; King, Dodds & Allen, 2000; Toledano et al., 2005). However, a small case-control study by Dodds et al. (2004) did not show a monotonic relationship between THM levels and stillbirth, and they did not find an association between HAAs and stillbirth (King et al., 2005).

Studies on pre-term delivery have generally shown no association with DBPs (Bove et al., 1995; Savitz et al., 1995; Gallagher et al., 1998; Wright, Schwartz & Dockery, 2003, 2004; Aggazzotti et al., 2004; Hinckley, Bachand & Reif, 2005; Lewis et al., 2007; Yang et al., 2007), with the exception of the study by Yang et al. (2000a) and Yang (2004). Study results on low birth weight have been mixed, with some studies reporting statistically significant associations (Bove et al., 1995; Gallagher et al., 1998; Källén & Robert, 2000;

Lewis, Suffet & Ritz, 2006) and others not (Kramer et al., 1992; Savitz et al., 1995; Kanitz et al., 1996; Dodds et al., 1999; Jaakkola et al., 2001; Wright, Schwartz & Dockery, 2003; Toledano et al., 2005; Yang et al., 2007). Studies on small for gestational age and/or intrauterine growth retardation or restriction showed some more consistent results, and a good proportion of them have found statistically significant associations (Kramer et al., 1992; Bove et al., 1995; Gallagher et al., 1998; Wright, Schwartz & Dockery, 2003, 2004; Aggazzotti et al., 2004; Hinckley, Bachand & Reif, 2005), whereas others did not (Porter et al., 2005; Yang et al., 2007). Wright, Schwartz & Dockery (2004) found statistically significant associations with THMs and a measure of mutagenicity, but not with HAAs or MX. Infante-Rivard (2004) found that the association between THMs and intrauterine growth retardation or restriction was modified by a metabolic polymorphism, with newborns without the CYP2E1 (G1259C) variant at high risk.

Two small epidemiological studies have investigated the relationship between DBPs and semen quality. Fenster et al. (2003) found that total THM levels were not associated with decrements in semen quality. The per cent normal morphology decreased and the per cent head defects increased at higher levels of an ingestion metric; at the highest level of the ingestion metric, the investigators observed a small difference in per cent morphologically normal sperm compared with the lowest level. BDCM exposure was inversely related to linearity (a motility parameter). Luben et al. (2007) studied the relationship between exposure to classes of DBPs and sperm concentration and morphology, as well as DNA integrity and chromatin maturity, but found no association or consistent pattern of increased abnormal semen quality with elevated exposure to THMs or HAAs.

The above studies generally have occurred in areas where they used chlorination or chloramination as the main water treatment. When chlorine dioxide is used as the disinfecting agent, chlorite and chlorate are the main DBPs. Aggazzotti et al. (2004) conducted a case-control study in nine Italian provinces and found a small increase in the risk of small for gestational age at term and high levels of chlorite in drinking-water. Tuthill et al. (1982) conducted a study that was difficult to interpret, but only pre-term delivery appeared to be higher in water treated with chlorine dioxide compared with chlorinated water, and there were no statistical differences in jaundice, birth weight and defects or stillbirths. Kanitz et al. (1996) found an increase in jaundice and pre-term delivery and an increase in low birth weight, small body length and cranial circumference in chlorine dioxide-treated water compared with non-treated water, but the effects were similar to those observed with chlorinated water, and the study was small. Källén & Robert (2000) found no increase in jaundice, pre-term delivery, birth weight and other characteristics, death or malformations in chlorine dioxide-treated water. Cedergren et al. (2002) found an increased risk for cardiac defects in hypochlorite- and chlorine dioxide-treated water compared with only hypochlorite-treated water.

3.2.5 *Summary*

The overall evidence from a number of recent studies suggests an association between exposure to DBPs and the risk of bladder cancer. There have been a number of studies on colon cancer and other cancers, but the results have been mixed and are inconclusive.

In a pooled analysis of six large epidemiological studies on bladder cancer in relation to drinking-water DBPs, it is suggested that the risk of bladder cancer among men may be increased by 30% above a lifetime intake of 15 mg total THMs (used as a marker of the total DBPs) from drinking-water (Villanueva et al., 2004). This is equivalent to a daily intake of 1 µg/day of THMs from drinking-water, which is about 3 µg/day (or in the order of 1 µg/day for chloroform) if we assume that drinking-water represents only one third of all sources of

THMs (other sources being showering, bathing or swimming in pools). This estimate of chloroform exposure is close to the estimate of intake of chloroform from food that could be derived from data on poultry processing (see section 3.1).

The expert meeting noted, however, that information in the study was related to the profile of DBPs found in drinking-water and that the relationship between these DBPs and those found in food is not known.

The studies on small for gestational age have generally shown a significant excess risk, but the results for other reproductive outcomes have generally been inconsistent and inconclusive.

3.3 References

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4. THE EFFECT OF DISINFECTANTS IN FOOD PROCESSING ON MICROBIOLOGICAL SAFETY AND HEALTH

4.1 Introduction

Chlorinated compounds are used extensively in the food industry as disinfectants to control both spoilage bacteria and pathogenic bacteria on food. Their use is designed either to prevent an increase in the microbiological load on foods or to reduce the microbiological load on foods. In the former capacity, chlorinated compounds are introduced into food processing water or used to disinfect food contact surfaces to control the buildup of bacteria and prevent cross-contamination of foods. In the latter capacity, they are directly applied to the surface of foods to inactivate contaminating microorganisms. Details on the specific use of chlorine in the food industry are provided in chapter 1.

The focus in this chapter is on evaluating the effect of chlorinated compounds and certain other disinfectants on the reduction in the prevalence and numbers of pathogenic microorganisms on food. Considered are specific uses (as described in chapter 1) and those pathogenic bacteria that are known hazards associated with the food commodities reviewed. Although disinfectant chemicals will also control spoilage bacteria and, hence, increase the shelf life and stability of foods, this aspect is not considered here, as it has no direct impact on health risks.

Although there is now a considerable body of scientific literature on disinfectants, not all studies have indicated a beneficial effect (i.e. reduction in pathogen load), and the evidence obtained must be examined critically in relation to the relevance of the study to practical processing conditions. To differentiate between evidence from different studies, it is necessary to develop criteria to distinguish their relative contribution to the general body of evidence.

It is generally accepted that studies whereby pathogenic bacteria are inoculated onto food prior to assessing disinfectants generate data that overestimate the activity of the disinfectant compared with data from studies where the pathogen contamination is natural. This tends to be a result of inefficient attachment of pathogens to food using artificial inoculation methods. Therefore, for the purposes of assessing data in this chapter, studies using inoculation of food with pathogens were considered to contribute less to the body of evidence on disinfectant effectiveness than those studies using natural contamination. Similarly, studies that generate data on the effect of disinfectants using industrial-scale equipment are more likely to accurately describe disinfectant effects in practice compared with studies conducted in laboratories using experimental equipment. Thus, studies in industrial settings generally contribute more to the body of evidence.

The data on pathogen reduction achieved by food disinfectants that have been identified in this chapter were assessed using the matrix shown in Table 4.1. In each case, adjustments were made to this general categorization to accommodate the specific details of the study, such as suitable controls or clear articulation of the disinfection conditions.

Table 4.1. Relative strength of the contribution of study data to the general body of evidence based on study type

	Natural contamination	Inoculated studies
Industrial data	High ^a	–
Pilot-scale data ^b	High ^c	Medium ^d
Laboratory data	Medium ^d	Low ^e

^a Ideal data also quantify counts and prevalence of pathogens with statistical analysis.

^b Experiments using industrial equipment in non-industrial settings.

^c If the pilot process is representative of the industrial process; otherwise, evidence makes a “medium” contribution to the body of evidence.

^d Data would not be sufficient to inform a quantitative microbial risk assessment or to allow definitive conclusions on risk reduction.

^e Data are indicative of a disinfectant effect that may be reproducible in practice, but on their own do not allow definitive conclusions on risk reduction.

4.2 Poultry

4.2.1 Pathogens

Several pathogenic bacteria have been associated with raw poultry. These are *Salmonella enterica* subsp. *enterica*, *Campylobacter* spp., *Clostridium perfringens*, *Listeria monocytogenes*, *Staphylococcus aureus*, pathogenic *Escherichia coli* and *Yersinia enterocolitica* (Cox et al., 2005). However, the main pathogenic bacteria associated with human illness resulting from the consumption of poultry and poultry products are species of the genera *Salmonella* and *Campylobacter*.

Campylobacter is the leading cause of zoonotic enteric infections in most developed and developing countries (Aarestrup & Engberg, 2001). The reported incidence rates of *Campylobacter* infections vary widely among countries; in 2004, rates ranged from 12.8 cases per 100 000 inhabitants in the United States of America (USA) to 299.1 cases per 100 000 inhabitants in New Zealand. Some of the variation may in part be explained by differences in surveillance systems, diagnostic methods and means of reporting, so caution should be used when drawing inferences from these data. Estimates of campylobacteriosis in developing countries, developed from laboratory-based surveillance studies in the general population, range from 5% to 20%, with significantly higher incidence rates in children (Coker et al., 2002).

Over 2500 *Salmonella enterica* serotypes are recognized, and all are regarded as capable of producing disease in humans. Worldwide, salmonellosis is a leading cause of enteric infectious disease attributable to foods. Illnesses caused by the majority of *Salmonella* serotypes range from mild to severe gastroenteritis and, in some patients, bacteraemia and a variety of associated longer-term conditions (FAO/WHO, 2002a).

Modern poultry processing is rapid, intensive and highly mechanized. As it is a wet process, there are considerable opportunities for the spread of *Salmonella* and *Campylobacter* spp. This section focuses on evaluating the evidence associated with the main disinfection processes in common use today in some countries and their effectiveness at reducing the contamination risks associated with *Salmonella* and *Campylobacter* spp. on poultry.

4.2.2 Common disinfection practices

Chlorine gas and hypochlorite are historically the common forms of chlorine that have been used in the poultry industry. However, other forms of chlorine have emerged, including

acidified sodium chlorite (ASC), chlorine dioxide and electrolysed water containing chloride ions. In addition, there are several non-chlorine-based alternative disinfectants that are available, such as trisodium phosphate (TSP), cetylpyridinium chloride and peroxyacetic acid. These disinfectants are primarily used for the purpose of post-processing sanitization of plant and equipment as well as reducing contamination of the raw product with pathogenic and spoilage bacteria and control of microbial cross-contamination. A review of commercial disinfectants used in poultry processing was conducted by Oyarzabal (2005). This review cites the approved disinfectants in the USA and their approved conditions of use. Similar conditions of use are employed in some other countries.

Whereas there are many potential chemicals and points of application during poultry processing, there are a few in common use that have been identified (chapter 1) for which the data have been summarized. These include:

- hypochlorite for carcass washing pre-chill or post-chill;
- hypochlorite in carcass chillers;
- ASC as a carcass wash pre-chill and post-chill;
- chlorine dioxide as a carcass wash or in chiller water;
- peroxyacetic acid for carcass spraying.

The following section summarizes the available information related to the effectiveness of these practices at reducing the contamination risks associated with *Salmonella* and *Campylobacter* in poultry.

4.2.3 Effectiveness of common disinfection practices

A keyword search (focusing on *Salmonella* and *Campylobacter* in poultry) of the current published scientific literature, including e-journals, was conducted. The *Journal of Food Protection*, *Poultry Science* and *Journal of Food Science* publishers' databases were also searched. The reference sections of identified papers were also used as a source of relevant papers. The results from a call for data put out by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) were considered when relevant. In total, 39 suitable scientific papers from 1965 to 2007 were obtained and reviewed for this exercise.

4.2.3.1 Hypochlorite for carcass washing pre-chill and post-chill

In a laboratory experiment using artificially inoculated poultry, Olson et al. (1981) demonstrated that dipping inoculated chicken wings in chlorinated water (20 mg/l) reduced the numbers of *Salmonella* Typhimurium from 0.91 log colony-forming units (cfu)/g to 0.54 log cfu/g and that this result was statistically significant compared with *Salmonella* numbers on wings that were not dipped.

The effectiveness of an inside–outside bird washer (IOBW) followed by chilling in tap water for 45 min at 4 °C was evaluated on a pilot scale using chicken carcasses artificially inoculated with *Salmonella* Typhimurium (Yang, Li & Slavik, 1999). Washing with a 50 mg/l chlorine solution at 20 °C (17 s spray time with 60 s contact time before wash-off) compared with washing in tap water provided a statistically significant reduction in *Salmonella* of 0.63 log cfu/carcass in only one trial of the three performed. In the second trial, the result was not statistically significant, and in the final trial, the water wash removed more *Salmonella* than the chlorine wash.

Northcutt et al. (2005) conducted similar studies on the effectiveness of chlorine washes. Carcasses were inoculated with caecal contents containing nalidixic acid-resistant *Salmonella*. Water at 21.1, 43.3 and 54.4 °C with and without available chlorine at 50 mg/l was sprayed onto carcasses for 5 s with an IOBW. Neither water temperature nor chlorine level was found to have a statistically significant effect on the counts of *Salmonella*. However, the physical action of washing alone resulted in a reduction of 0.7–1.1 log cfu/ml in *Salmonella* on the inoculated carcasses.

Stopforth et al. (2007), in an industrial study using natural contamination, showed that spraying poultry carcasses with 20–50 mg/l chlorinated water after defeathering reduced *Salmonella* prevalence by 8 percentage points, from 34% to 26%. They also showed that spraying carcasses with 20–50 mg/l chlorinated water after evisceration reduced *Salmonella* prevalence by 9 percentage points, from 45% to 36% (statistically significant). Spray application of 20–50 mg/l chlorinated water after neck removal using an IOBW reduced *Salmonella* prevalence by 5 percentage points, from 25% to 20% (not statistically significant). A second IOBW after the first IOBW using 20–50 mg/l chlorinated water reduced *Salmonella* prevalence by 4 percentage points, from 16% to 12% (not statistically significant). Spray-washing carcasses after chilling with 20–50 mg/l chlorinated water did not affect the prevalence of *Salmonella*. However, a post-chiller wash of carcasses with 20–50 mg/l chlorinated water after sizing reduced *Salmonella* prevalence by 6 percentage points, from 10% to 4% (not statistically significant). None of these treatments were compared with similar washing treatments using unchlorinated water alone, and therefore any additional effect of hypochlorite over the physical washing effect of water alone cannot be established. Evidence from other studies (e.g. Northcutt et al., 2005) suggests that the physical action of washing alone can remove pathogenic bacteria inoculated onto poultry samples, although the washing effect on natural contamination is not clear.

Villarreal, Baker & Regenstein (1990) studied the effect of a commercial carcass washer (chlorine concentration 20 mg/l) on natural *Salmonella* contamination of turkey carcasses. *Salmonella*-positive carcass prevalence rates dropped from 75% and 65% to 10% and 20%, respectively, using a spray carcass rinse with chlorine at 20 mg/l. This reduction was statistically significant compared with unwashed carcasses, but there was no control using washing in unchlorinated water.

The effectiveness of a chlorine carcass wash was evaluated in a study in which poultry carcasses were inoculated with caecal material containing *Campylobacter* (Northcutt et al., 2005). Water at 21.1, 43.3 and 54.4 °C with and without available chlorine at 50 mg/l was sprayed onto carcasses for 5 s with an IOBW. Neither water temperature nor chlorine level was found to have a statistically significant effect on the counts of *Campylobacter*. The physical action of washing alone resulted in a reduction of 2.1–2.8 log cfu of *Campylobacter* per carcass, although numbers were not reduced below those of the natural *Campylobacter* load on carcasses prior to inoculation. In another study on naturally contaminated poultry in a commercial plant, an IOBW with hypochlorinated water resulted in a *Campylobacter* reduction of 0.7 log cfu/carcass (statistically significant) and 0.34 log cfu/carcass (not statistically significant) in two experiments, but the prevalence of *Campylobacter*-contaminated carcasses was not affected (Oyarzabal et al., 2004). However, no unchlorinated washing controls were evaluated.

Chlorine was found to be effective against *Campylobacter* in a laboratory study of extended washing conducted on inoculated chicken breast skin (Park, Hung & Brackett, 2002). Chicken wing sections were inoculated with *Campylobacter* and immersed in the test solutions of chlorine (~50 mg/l) with a deionized water control at 4 °C and 23 °C for 10 and 30 min with agitation before analysis. *Campylobacter* was reduced by 1.14 and 1.21 log cfu/g at 23 °C for 10 and 30 min, respectively, in deionized water alone. Hypochlorite resulted in

further reductions of 1.64 and 1.76 log cfu/g at 23 °C for 10 and 30 min, respectively, and 1.47 and 1.6 log cfu/g at 4 °C for 10 and 30 min, respectively, in comparison with washing in deionized water alone. However, the contact times in this experiment were substantially longer than those employed in commercial premises.

Bashor et al. (2004) made a comprehensive study of carcass washing in four poultry processing plants. A single IOBW with 25 mg/l chlorinated water reduced *Campylobacter* numbers by 0.31 log cfu/carcass, and a series of three IOBW units reduced *Campylobacter* numbers by 0.45 log cfu/carcass. The prevalence of *Campylobacter*-positive carcasses was reduced from 86.6% pre-wash to 80% post-triple wash. Similar results were achieved in a second plant using a similar setup of three IOBW units in series, but all with a higher level of chlorinated water, at 35 mg/l. A reduction in *Campylobacter* of 0.63 log cfu/carcass was observed after the three washing units, and the prevalence of *Campylobacter*-positive carcasses was reduced from 83% pre-wash to 80% post-triple wash. Unfortunately, statistical analysis of the between-plant effects of the different chlorine concentrations was not reported by the authors. The effect of washing alone in water without any chemical addition was not reported, but from other studies cited above, it is possible that the physical washing action alone contributed substantially to the reductions achieved.

Summary

Table 4.2 summarizes the effects of hypochlorite on *Salmonella* and *Campylobacter* during carcass washing before and after chilling.

Industrial studies by Stopforth et al. (2007) and Villareal, Baker & Regenstein (1990) demonstrated an effect of washing carcasses in hypochlorite solution on the prevalence of *Salmonella*. However, these did not include an evaluation of the effect on *Salmonella* numbers of washing in water alone in the absence of chlorine. Other studies (Yang, Li & Slavik, 1999; Northcutt et al., 2005) showed that washing in water alone resulted in most of the reductions in *Salmonella* inoculated onto poultry. Therefore, it is not possible to make a definitive statement on the effectiveness of hypochlorite against *Salmonella* during carcass washing on an industrial scale based on these studies. It is likely that washing in water alone is a moderately effective intervention and that hypochlorite does not provide a significant additional effect.

Laboratory-based experiments have shown reductions in *Campylobacter* on carcasses of less than 2 log units, but only over extended washing times (up to 30 min). Other experiments using more practical conditions show reductions of less than 1 log unit on *Campylobacter* in comparison with no washing. However, when compared with washing in water alone, there was no effect on *Campylobacter* inoculated onto carcasses washed in water with hypochlorite (Northcutt et al., 2005). The industrial studies by Bashor et al. (2004) showed log reductions in *Campylobacter* in the order of 0.5 log units and prevalence reductions of between 3 and 7 percentage points after extensive washing in a series of three IOBW units. However, the action of washing in water alone was not evaluated. Therefore, as with *Salmonella*, it is likely that washing in water alone is a moderately effective intervention and that hypochlorite does not provide a significant additional effect.

The removal of pathogenic bacteria from poultry carcasses during physical washing procedures on an industrial scale is predominantly a feature of the physical action of the water rather than the use of hypochlorite in the water.

Table 4.2. Studies of hypochlorite for poultry carcass washing pre-chill and post-chill

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
20 mg/l (manual spray)	<i>Salmonella</i>	Industrial	Natural	High	75% reduced to 10% ^a 65% reduced to 20% ^a	Villarreal, Baker & Regenstein (1990)
20–50 mg/l (various spray-washing methods pre-chill and post-chill)	<i>Salmonella</i>	Industrial	Natural	High	Between 4 and 8 percentage point reduction, depending on method ^a	Stopforth et al. (2007)
50 mg/l	<i>Salmonella</i>	Pilot	Inoculated	Medium	No consistent log reduction over water washing alone	Yang, Li & Slavik (1999)
50 mg/l	<i>Salmonella</i>	Pilot	Inoculated	Medium	No log reduction over water washing alone	Northcutt et al. (2005)
20 mg/l	<i>Salmonella</i>	Experimental	Inoculated	Low	0.37 log reduction ^a	Olson et al. (1981)
Not stated	<i>Campylobacter</i>	Industrial	Natural	Medium ^b	0.7 log reduction ^a 0.34 log reduction ^a	Oyarzabal et al. (2004)
50 mg/l	<i>Campylobacter</i>	Pilot	Inoculated	Medium	No log reduction over water washing alone	Northcutt et al. (2005)
50 mg/l (4 °C and 23 °C), 10 min and 30 min wash	<i>Campylobacter</i>	Experimental	Inoculated	Low	1.47–1.76 log reductions over water washing alone	Park, Hung & Brackett (2002)
25 mg/l (three washers in sequence)	<i>Campylobacter</i>	Industrial	Natural	High	0.31 log reduction (one washer), 0.45 log reduction (three washers), 6.6 percentage point reduction (after three washers) ^a	Bashor et al. (2004)
35 mg/l (three washers in sequence)	<i>Campylobacter</i>	Industrial	Natural	High	0.63 log reduction (three washers), 3 percentage point reduction (after three washers) ^a	Bashor et al. (2004)

^a Reductions were not compared with a control using water washing alone, and therefore it is not possible to separate the reduction resulting from the physical action of spraying carcasses with water and any additional effect of using hypochlorite in the wash water.

^b Contribution rating reduced because no conditions of use or concentration of chlorine provided.

4.2.3.2 Hypochlorite in carcass chillers

Hypochlorite is routinely used in poultry process lines in countries where chilling by water immersion is allowed. It is added to the chiller water to prevent the buildup of bacteria in the water during processing. Several studies have produced quantitative data on the effect of chlorinated chiller water both on the reduction of *Salmonella* and *Campylobacter* numbers on contaminated poultry carcasses and also in prevention of cross-contamination of uncontaminated carcasses from bacteria released into the chiller water from contaminated carcasses.

The effect of sodium hypochlorite (50 mg/l) in chiller water was evaluated in a study conducted on a pilot and commercial scale (Russell & Axtell, 2005). In a pilot-scale poultry chiller (5 °C, 1 h), mean log counts of nalidixic acid-resistant strains of *Salmonella* inoculated onto chicken carcasses were not reduced by hypochlorite. Immersion chilling in tap water alone reduced the count from 2.9 to 1.6 log cfu/ml. The addition of chlorine to the tap water had no additional effect over tap water alone. The statistical significance of these differences was not reported.

Thomson, Cox & Bailey (1976) conducted a laboratory study into the effects of water treated with sodium hypochlorite on a nalidixic acid-resistant marker strain of *Salmonella* Typhimurium. Inoculated carcasses were pre-chilled in a stirred water tank at 18 °C for 3 min before being transferred to a chilling regime consisting of a stirred chill tank at 18 °C for 10 min and then a second chill tank containing slush ice for 20 min. When the pre-chill and chill treatments with chlorine at 50 mg/l were compared with chilling in water alone with no pre-chill treatment, the carcass prevalence of the marker strain *Salmonella* dropped from 85% to 45% for inoculated carcasses and from 15% to 2% for uninoculated carcasses. This demonstrated an effect of chlorine and pre-chill agitation on *Salmonella* prevalence for infected carcasses as well as prevention of cross-contamination of uninfected carcasses. However, it is not possible to separate the individual effects of chlorine and pre-chill agitation because of a lack of a suitable control.

In a later study, Thomson et al. (1979) again used carcasses inoculated with the nalidixic acid-resistant marker strain of *Salmonella* Typhimurium. Here, inoculated carcasses were pre-chilled in a stirred water tank at 18 °C for 10 min before being transferred to a stirred chill tank containing slush ice for 20 min. The water in the tanks was chlorinated to an available chlorine level of 20 or 50 mg/l at pH 6.0. They noted that there was no statistically significant effect on the prevalence of *Salmonella* recovered from inoculated carcasses at either 20 or 50 mg/l. Uninoculated carcasses processed alongside inoculated carcasses were contaminated with the marker strain of *Salmonella* at a prevalence rate of 80% in the absence of chlorine. However, there was a statistically significant reduction in the prevalence of *Salmonella*-positive uninoculated carcasses at both chlorine concentrations: at 20 mg/l (to 33% at a flow rate of 1.9 litres per carcass and 58% at a flow rate of 0.95 litres per carcass) and at 50 mg/l (to 10% at a flow rate of 1.9 litres per carcass and 8% at a flow rate of 0.95 litre per carcass).

In a further study, the mean prevalence of *Salmonella*-positive carcasses was unaffected by chilling in water containing chlorine at 20–50 mg/l at pH 6.5–7.0 (Stopforth et al., 2007). Similarly, no statistically significant changes in the mean prevalence of *Salmonella*-positive carcasses were observed after immersion chilling poultry carcasses in water containing chlorine at 25 mg/l at the inflow and 9 mg/l at the outflow (James et al., 1992). However, this study showed that chilling in water without chlorination resulted in an increase in *Salmonella* prevalence on carcasses from 48% to 72%.

Lillard (1980) studied the effects of hypochlorite in chiller water on the prevalence of *Salmonella*-positive poultry carcasses. Chilling carcasses in water with chlorine at 20 and 34

mg/l resulted in an average carcass *Salmonella* prevalence rate reduction from 14.3% in untreated water to between 4.5% and 1.9% in chlorinated water. The effect of chlorine concentration was statistically insignificant.

Yang, Li & Johnson (2001) studied the effect of chlorine in chiller water on the death kinetics of inoculated nalidixic acid-resistant *Salmonella* Typhimurium on chicken skin. They reported that a 50 mg/l addition of chlorine resulted in a residual free chlorine level of 34 mg/l after 1 min, decreasing to 20 mg/l after 50 min, and this had little effect on the death kinetics of *Salmonella* (D-value 78.7 min). With older chiller water, where organic material had built up, the residual concentration of free chlorine was approximately zero after 1 min, and here the D-value for *Salmonella* on chicken skin increased to 167.7 min. This clearly illustrates the inactivation of chlorine by organic matter, its effect on *Salmonella* and the need to maintain chlorine addition to chiller water during processing to achieve the necessary free chlorine concentration.

In a study in an industrial plant by Bashor et al. (2004), a reduction in *Campylobacter* of 0.13 log cfu/carcass was achieved after chilling in water with chlorine at 25 mg/l, and the prevalence of *Campylobacter*-positive carcasses was reduced from 80% post-wash to 73.3% post-chill. In a second plant using a chill tank with a higher level of chlorinated water, at 35 mg/l, a reduction in *Campylobacter* of 0.25 log cfu/carcass was observed after chilling. The prevalence of *Campylobacter*-positive carcasses was reduced from 80% post-wash to 70% post-chill. Unfortunately, statistical analysis of the between-plant effects of the different chlorine concentrations was not reported by the authors.

The effect of chlorine in chiller water on the death kinetics of inoculated *Campylobacter jejuni* was studied on chicken skin (Yang, Li & Johnson, 2001). Chilling in chlorinated water with 50 mg/l added chlorine (free chlorine residual level of 34 mg/l after 1 min, decreasing to 20 mg/l after 50 min) resulted in a D-value for *Campylobacter* on chicken skin of 73 min. However, using older chiller water initially with chlorine at 50 mg/l, where organic material had built up, the residual concentration of free chlorine was approximately zero after 1 min. Chilling in this water resulted in a D-value for *Campylobacter* on chicken skin of 344.8 min. A similar result was seen with *Salmonella*, confirming the need to maintain free residual chlorine levels in chiller water during processing. However, Yang, Li & Johnson (2001) demonstrated that chlorine was effective at killing free *Campylobacter* in chiller water but did not examine the effect that this might have had on carcass prevalence.

In another study on naturally contaminated poultry in a commercial plant, a chiller with chlorinated water resulted in a *Campylobacter* reduction of 1.09 log cfu/carcass (statistically significant) and 1.3 log cfu/carcass (statistically significant) in two experiments. The prevalence of *Campylobacter*-contaminated carcasses was not affected in the first experiment but was reduced from 95% to 77.5% in the second experiment (Oyarzabal et al., 2004). However, no unchlorinated chiller water controls were evaluated.

Mead, Hudson & Hinton (1995) examined the effect of the chlorination of process water at several stages in the poultry slaughter process using hypochlorite in the chiller water and chlorine gas to chlorinate in-plant water (the forms of chlorine were not stated in the paper but were confirmed by personal communication). Water was chlorinated at the killing machine, the three defeathering machines, the head puller, conveyor belt to evisceration line, evisceration machines and other machinery in contact with birds, as well as in the chiller, to between 28 and 38 mg/l as available chlorine. Carcass neck skin samples were tested for *Campylobacter*. Individual process steps were not tested for their effect on *Campylobacter* reduction; instead, this was done for the process as a whole. Therefore, the effect of chlorine alone cannot be evaluated. However, a comparison of flocks before and after process changes involved only those flocks with similar levels of caecal carriage of *Campylobacter*. Before changes, 100% of samples were positive for *Campylobacter* after exsanguinations, with a log

geometric average count of 3.7 log cfu/g, and 91% of samples were positive after packing, with a log geometric average count of 1.8 log cfu/g. Following changes, 100% of samples were still positive after exsanguinations, with a log geometric average count of 3.9 log cfu/g, but 85% of samples were positive after packing, with a log geometric average count of 1.2 log cfu/g.

Summary

Table 4.3 summarizes the studies on the effect of hypochlorite in chiller tanks of *Salmonella* and *Campylobacter* on poultry. Studies evaluating the numbers of *Salmonella* on carcasses before and after chilling are few. However, Russell & Axtell (2005) noted a reduction in *Salmonella* numbers inoculated onto carcasses caused by the physical movement of carcasses in the chiller water rather than the presence of hypochlorite in the chiller water. Experiments by Thomson et al. (1979) showed that greater reductions in the prevalence of *Salmonella* (inoculated) on carcasses were achieved with chlorinated water than with non-chlorinated water, by a combination of pre-chill and chill treatments.

Overall, the studies show that if chlorine is not present in chiller water, then the prevalence of *Salmonella* on carcasses increases because of cross-contamination. This is supported by Lillard (1980), who showed that the prevalence of *Salmonella* in chiller water treated with chlorine at 34 and 20 mg/l was reduced from 41.7% (untreated water) to “not detected” and 17.3%, respectively. Other data not elaborated here also demonstrate the effectiveness of chlorine in killing free *Salmonella* and *Campylobacter* in chiller water (Yang, Li & Johnson, 2001).

The effects of chlorinated chiller water on the prevalence of *Campylobacter*-contaminated carcasses and also mean contamination concentrations per carcass seem to be slightly greater than the effects on *Salmonella*, but reports are inconsistent. Small reductions in both numbers and prevalence of *Campylobacter* on carcasses were observed when chiller water was chlorinated.

Rapid inactivation of chlorine by organic matter greatly reduced its ability to kill *Campylobacter* and *Salmonella* in the chiller water itself. Hence, chlorine must be continually dosed into chiller water to maintain residual activity.

4.2.3.3 ASC as a carcass wash pre-chill and post-chill

The effectiveness of ASC was evaluated by Stopforth et al. (2007) as part of a study on multiple sequential interventions conducted in three poultry processing plants in the USA. Spray application of ASC (500–1200 mg/l as sodium chlorite acidified with citric acid to pH 2.5–2.9) reduced the prevalence of *Salmonella* on carcasses from 17% to 9% (statistically significant). Dipping carcass parts in ASC had an even bigger effect, reducing the prevalence from 29% to 1%. Controls to evaluate the physical effect of dipping and spraying carcasses in water alone were not included.

Spray treatment of poultry carcasses with ASC followed by chilling was studied in five poultry plants in the USA (Kere-Kemp et al., 2001). Carcasses that were visibly contaminated with faecal matter were tested after evisceration, after the IOBW, after spray treatment with ASC (1100 mg/l as sodium chlorite acidified with citric acid at 9000 mg/l, pH 2.5, for 15 s at 14–18 °C) and after chilling. The IOBW reduced the prevalence of *Salmonella*-positive carcasses from 37.3% to 31.4%. Treatment with the IOBW followed by ASC spray resulted in a reduction in the prevalence of *Salmonella*-positive carcasses from 37.3% to 10%. Controls to evaluate the physical effect of spraying carcasses in water alone were not included.

Table 4.3. Studies of hypochlorite in poultry carcass chillers

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
50 mg/l	<i>Salmonella</i>	Pilot	Inoculated	Medium	1.3 log reduction in water alone; no additional effect of hypochlorite	Russell & Axtell (2005)
50 mg/l (18 °C pre-chill in tank with stirring and two-stage chill in water, then ice slush)	<i>Salmonella</i>	Pilot	Inoculated	Medium	85% reduced to 45% (inoculated carcasses) 15% reduced to 2% (uninoculated carcasses)	Thomson, Cox & Bailey (1976)
20 and 50 mg/l (18 °C pre-chill in tank with stirring chill in ice slush)	<i>Salmonella</i>	Pilot	Inoculated	Medium	No change in prevalence (inoculated carcasses) 80% reduced to 33% or 10% (uninoculated carcasses)	Thomson et al. (1979)
20–50 mg/l (chiller tank pH 6.5–7.0)	<i>Salmonella</i>	Industrial	Natural	High	No reduction in prevalence	Stopforth et al. (2007)
25 mg/l (drag-through chiller)	<i>Salmonella</i>	Industrial	Natural	High	48% increased to 72% (unchlorinated water) No change in prevalence (chlorinated water)	James et al. (1992)
20–34 mg/l (chiller tank)	<i>Salmonella</i>	Industrial	Natural	High	14.4% (untreated water) reduced to between 4.5% and 1.9% (concentration of chlorine insignificant)	Lillard (1980)
25 mg/l (chiller tank)	<i>Campylobacter</i>	Industrial	Natural	High	0.13 log reduction, 80% reduced to 73.3% ^a	Bashor et al. (2004)
35 mg/l (chiller tank)	<i>Campylobacter</i>	Industrial	Natural	High	0.25 log reduction, 80% reduced to 70% ^a	Bashor et al. (2004)
Not stated	<i>Campylobacter</i>	Industrial	Natural	Medium ^b	1.09 log reduction, no change in prevalence ^a 1.3 log reduction, 95% reduced to 77.5% ^a	Oyarzabal et al. (2004)

^a Reductions were not compared with a control using water chilling alone, and therefore it is not possible to separate the reduction resulting from the physical action of carcass agitation in water and any additional effect of using hypochlorite in the chiller water.

^b Contribution rating reduced because no conditions of use or concentration of chlorine provided.

The effect of ASC on *Salmonella* Enteritidis was also studied on inoculated chicken legs followed by chill storage at 3 °C over 5 days (Del Río et al., 2007). Sodium chlorite (1200 mg/l) was acidified with citric acid to pH 2.7 and applied to the inoculated legs as a dip for 15 min. Treatment resulted in mean log reductions over untreated controls of 2.05, 2.42, 2.25 and 1.65 log cfu/g skin on sampling days 0, 1, 3 and 5, respectively. However, the mean log reductions were not significantly different from each other on any one sampling day. A water dip control achieved a 0.33 log cfu/g reduction in *S. Enteritidis*, but in that case, the pathogen grew on the samples during storage over the 5-day period. Sexton et al. (2007) studied ASC treatment of chicken carcasses in a plant after the screw chiller using birds naturally contaminated with *Salmonella*. Sodium chlorite (900 mg/l) was acidified with citric acid to pH 2.5–2.6. Carcasses were dipped in the treatment solution after chilling for 20 s before testing after a maximum of 4 h. The prevalence of *Salmonella*-positive carcasses dropped from 90% to 10% after treatment. However, the log mean count on positive carcasses remained similar between untreated carcasses ($-1.8 \log \text{ cfu/cm}^2$; standard deviation [SD] $0.56 \log \text{ cfu/cm}^2$) and treated carcasses ($-1.85 \log \text{ cfu/cm}^2$; SD $0.55 \log \text{ cfu/cm}^2$). Controls to evaluate the physical effect of the dipping carcasses in water alone were not included.

ASC carcass treatment followed by chilling was studied in an industrial setting for activity against *Campylobacter* (Kere-Kemp et al., 2001). Carcasses that were visibly contaminated with faecal matter were sampled after evisceration, after IOBW, after ASC spray treatment and after chilling. Sodium chlorite (1100 mg/l) acidified with citric acid (9000 mg/l, pH 2.5) was sprayed (15 s) onto carcasses at 14–18 °C. The IOBW reduced the *Campylobacter* numbers on contaminated carcasses by an average of 1.08 log cfu/carcass but did not affect the prevalence of *Campylobacter*-positive carcasses (73.2% post-evisceration versus 74.8% post-IOBW). The IOBW followed by ASC spray treatment resulted in a reduction in *Campylobacter* of 2.56 log cfu/carcass, and the prevalence of *Campylobacter*-positive carcasses was reduced from 73.2% to 49.1%. Controls to evaluate the physical effect of the spraying of carcasses with water alone were not included.

ASC was studied for its effects on *Campylobacter* inoculated onto chicken breast skin in a laboratory study (Arritt et al., 2002). ASC (0.1% volume by volume [v/v]) was sprayed as a fine mist onto skin samples for 3 s with 0.5, 3 and 10 min contact time. Treatment with water alone resulted in a reduction in *Campylobacter* of 0.15 log cfu/skin sample, whereas treatment with ASC resulted in a reduction of 1.52 log cfu/skin sample. These reductions were mean reductions across all contact times, as contact time was found to have no significant effect on the ability of the antimicrobial agent to kill *Campylobacter*. Arritt et al. (2002) also demonstrated that the antimicrobial agents were even more effective at killing *Campylobacter* when the bacteria were applied to skin samples after application of the antimicrobial agent.

The activity of ASC (900 mg/l as sodium chlorite acidified with citric acid to pH 2.5–2.6) was also tested as a carcass dip on carcasses naturally contaminated with *Campylobacter* after a screw chiller in a commercial plant (Sexton et al., 2007). The prevalence of naturally contaminated *Campylobacter*-positive carcasses was reduced from 100% to 23% by ASC treatment of carcasses, and the mean count on positive carcasses dropped from $1.59 \log \text{ cfu/cm}^2$ (SD $0.51 \log \text{ cfu/cm}^2$) to $-2.21 \log \text{ cfu/cm}^2$ (SD $0.17 \log \text{ cfu/cm}^2$) compared with untreated control carcasses. The effect of a control dip in water alone was not reported. Oyarzabal et al. (2004) studied the use of an ASC dip for controlling *Campylobacter* on broiler carcasses after chilling in a commercial plant. ASC (600–800 mg/l as sodium chlorite acidified to pH 2.5–2.7) was used as a carcass dip with 15 s contact time. Mean log reduction of *Campylobacter* was 0.92 log cfu/carcass, and prevalence rates dropped from 100% of carcasses to 12.5%, compared with untreated carcasses. In a second experiment, mean log

reduction of *Campylobacter* was 1.2 log cfu/carcass, and prevalence rates dropped from 77.5% of carcasses to 2.5%, compared with untreated carcasses. The effect of a control dip in water alone was not reported. Bashor et al. (2004) studied the effectiveness of an ASC spray treatment against *Campylobacter* in a commercial plant. They found that ASC reduced *Campylobacter* populations on average by 1.26 log units. The effect of a carcass spray with water alone was not studied. Overall, in these three studies, the absence of controls for carcass washing in water alone makes it difficult to draw definitive conclusions regarding the effect of including ASC in the wash water independent of the physical effects of spraying or dipping.

The effect of chlorine and Alcide (a product containing an activator of 16.7% lactic acid and a base containing 3.03% sodium chlorite) on *Salmonella* on turkey carcasses was evaluated in a process plant (Villarreal, Baker & Regenstein, 1990).¹ *Salmonella* prevalence was reduced to zero from 75% and 65% following chlorine rinse (20 mg/l) and chilling of the rinsed carcasses in iced water containing the Alcide solution (1 part Alcide base : 200 parts water : 1 part Alcide activator). However, dip-rinsing carcasses for 20 s in Alcide (1 part Alcide base : 20 parts water : 1 part Alcide activator), with or without chilling in water with the Alcide solution, also reduced the contaminated carcass prevalence rate from 75% and 65% to zero. No controls were used to study the effect of rinsing and chilling carcasses in untreated water alone.

In a study of post-chill carcass treatment, chicken skin samples inoculated with *Campylobacter jejuni* were exposed to ASC (0.1% sodium chlorite, 0.9% citric acid, pH 2.43) for up to 5 days (Ozdemir, Gugukoglu & Koluman, 2006). Reductions in *Campylobacter* compared with immersion in tap water alone were 1.9, 2.5, >3.3 and >3.0 log cfu/g skin after 0, 1, 3 and 5 days of chill storage at 4 °C, respectively. Similar results were also found using a second inoculated strain of *C. jejuni*.

Summary

Table 4.4 summarizes the effects of ASC on *Salmonella* and *Campylobacter* on poultry. ASC is an effective means of reducing the prevalence of *Salmonella*-contaminated carcasses during spray or dip treatments both pre-chill and post-chill. However, reliable data on the effect of ASC on numbers of *Salmonella* on carcasses were not found.

ASC was shown to be more effective against *Campylobacter*. As a spray or dip either pre-chill or post-chill, it resulted in log reductions of around 1.5 log cfu/g in industrial settings. The prevalence of *Campylobacter* was also reduced significantly. ASC activity appeared to extend into chill storage, but quantitative results were available only from laboratory-based experiments rather than commercial situations.

Most studies, particularly those conducted in the industrial setting, suffered from the lack of a control for the physical action of water alone as a spray or dip. However, evidence from a laboratory study that contained this control suggested that there was only a small effect on inoculated *Salmonella* of 0.15 log cfu/skin sample (Arritt et al., 2002). Also, studies tended not to use IOBW or high-volume sprays, and therefore they would be less likely to exert a physical reduction effect on bacteria on carcasses.

¹ The expert meeting recognizes that Villarreal, Baker & Regenstein (1990) considered Alcide to be a slow-release chlorine dioxide product. However, more recent understanding of the chemistry involved indicates that the appropriate active chemical should more correctly be referred to as either chlorous acid or ASC (S. Burnett, personal communication, 2009).

Table 4.4. ASC for poultry carcass washing pre-chill and post-chill

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
500–1200 mg/l as sodium chlorite, pH 2.5–2.9 with citric acid (pre-chill spray)	<i>Salmonella</i>	Industrial	Natural	High	17% reduced to 9% ^a	Stopforth et al. (2007)
500–1200 mg/l as sodium chlorite, pH 2.5–2.9 with citric acid (pre-chill dip)	<i>Salmonella</i>	Industrial	Natural	High	29% reduced to 1% ^a	Stopforth et al. (2007)
1100 mg/l as sodium chlorite, pH 2.5 (15 s pre-chill spray)	<i>Salmonella</i>	Industrial	Natural	High	31.4% reduced to 10% ^a	Kere-Kemp et al. (2001)
1200 mg/l as sodium chlorite, pH 2.7 with citric acid (dip)	<i>S. Enteritidis</i>	Laboratory	Inoculated	Low	Additional 1.65–2.42 log reduction over 0.33 log cfu/g reduction (water dip alone)	Del Río et al. (2007)
900 mg/l as sodium chlorite, pH 2.5–2.6 with citric acid (post-chill dip)	<i>Salmonella</i>	Pilot	Natural	High	90% reduced to 10%, no change in log mean counts ^a	Sexton et al. (2007)
1100 mg/l as sodium chlorite, pH 2.5 (15 s pre-chill spray)	<i>Campylobacter</i>	Industrial	Natural	High	1.48 log reduction above the effect of an IOBW alone, 73.2% reduced to 49.1% ^a	Kere-Kemp et al. (2001)
0.1% v/v (spray as fine mist)	<i>Campylobacter</i>	Laboratory	Inoculated	Low	0.15 log reduction (water control) 1.52 log reduction (ASC)	Arritt et al. (2002)
1200 mg/l as sodium chlorite, pH 2.5	<i>Campylobacter</i>	Industrial	Natural	High	1.26 log reduction, 87% reduced to 63% ^a	Bashor et al. (2004)
900 mg/l as sodium chlorite, pH 2.5–2.6 with citric acid (post-chill dip)	<i>Campylobacter</i>	Pilot	Natural	High	100% reduced to 23%, 3.8 log reduction ^a	Sexton et al. (2007)

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
Chlorine rinse (20 mg/l), then chilled in water with 1 part Alcide : 200 parts water : 1 part activator	<i>Salmonella</i>	Pilot	Natural	High	75% and 65% reduced to “not detected” (chlorine rinse 20 mg/l and chill in chlorinated water, 75% and 65% reduced to 25%) ^a	Villarreal, Baker & Regenstein (1990)
1 part Alcide : 20 parts water : 1 part activator (pre-chill dip)	<i>Salmonella</i>	Pilot	Natural	High	65% and 75% reduced to “not detected” ^a	Villarreal, Baker & Regenstein (1990)
600–800 mg/l as sodium chlorite, pH 2.5–2.7 (post-chill dip)	<i>Campylobacter</i>	Industrial	Natural	High	0.92 log reduction, 100% reduced to 12.5% ^a 1.2 log reduction, 77.5% reduced to 2.5% ^a	Oyarzabal et al. (2004)

^a Reductions were not compared with a control using water spray/dip alone, and therefore it is not possible to separate the reduction resulting from the physical action of water spray/dip and any additional effect of using ASC (see summary text for discussion).

4.2.3.4 Chlorine dioxide as a carcass wash or in chiller water

There are few studies examining the effect of chlorine dioxide on bacteria in poultry, and even fewer on pathogenic bacteria. These are summarized in Table 4.5.

Lillard (1980) studied the effects of chlorine dioxide in chiller water on the prevalence of *Salmonella*-positive poultry carcasses. Chilling carcasses in water with chlorine dioxide at 3 and 5 mg/l resulted in a reduction of the average carcass *Salmonella* prevalence rate from 14.3% with untreated water to 2.1% and 1%, respectively. The effect of chlorine dioxide concentration was statistically insignificant. Lillard (1980) also showed that the prevalence of *Salmonella* in chiller water treated with chlorine dioxide at 3 and 5 mg/l was reduced from 41.7% in the untreated water control to not detected and 25%, respectively. In another study, Thiessen, Osborne & Ogg (1984) reported that the prevalence rates of *Salmonella* on carcasses were reduced from 97.3% in untreated water to not detected, with residual chlorine dioxide at 1.33 mg/l or higher in the chiller water. Significant reductions of *Salmonella* were also reported in the chiller water itself with chlorine dioxide present.

Overall, the limited data set available suggests that chlorine dioxide is effective against *Salmonella* and *Campylobacter* on poultry. It is also active against *Salmonella* in chiller water and would therefore help to reduce cross-contamination.

4.2.3.5 Peroxyacetic acid for carcass spraying

The only data available on the effectiveness of peroxyacetic acid at reducing pathogens on poultry are laboratory-based data with artificial inoculation (see Table 4.6). Del Río et al. (2007) studied the effect of peroxyacetic acid (220 mg/l, pH 3.75) on *Salmonella* inoculated on poultry legs during an experimental dipping process. *Salmonella* was reduced by 0.36 ± 0.7 log cfu/g from 6.93 ± 0.47 log cfu/g by a 15 min dip. Subsequent storage over 5 days showed a statistically significant increase in the reduction achieved, up to 1.1 ± 0.59 log cfu/g. However, a control dipped in water alone resulted in a reduction of 0.33 ± 0.35 log cfu/g. Therefore, there was virtually no effect of peroxyacetic acid. Over 5-day storage, *Salmonella* on the water-dipped legs grew, whereas *Salmonella* on the peroxyacetic acid-dipped legs continued to die off.

In a study conducted by Ecolab (unpublished data, 2001), *S. Typhimurium* artificially inoculated on chicken skin was reduced by 0.75 log cfu/g after spray treatment with peroxyacetic acid at a concentration of 200 mg/l. The same study found that dipping chicken parts in peroxyacetic acid also had an effect, with wing and liver contamination reduced by 0.32 cfu/g and 0.45 log cfu/g, respectively. The statistical significance of these results was not reported, however, and there was no water spray control.

It appears from these limited data that peroxyacetic acid is not as effective as other antimicrobial agents against *Salmonella*. However, prevalence was not tested, and studies in industrial settings were not found. Peroxyacetic acid may have use as a means of preventing *Salmonella* growth on processed poultry, but more studies would be required. The lack of spray-wash controls with water alone to evaluate the effect of the physical action of water on pathogens on carcasses means that definitive conclusions on the effectiveness of peroxyacetic acid cannot be drawn. No data on the effect of peroxyacetic acid on *Campylobacter* were found in the search conducted.

Table 4.5. Chlorine dioxide in chiller water for poultry

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
3 mg/l as chlorine dioxide (0.3–0.6 mg/l as free residual chlorine) (chiller water)	<i>Salmonella</i>	Industrial	Natural	High	14.3% (untreated water) reduced to 2.1%, numbers on positive carcasses 0.4–48 cells/g reduced to <0.4 cells/g	Lillard (1980)
5 mg/l as chlorine dioxide (0.5–1.0 mg/l as free residual chlorine) (chiller water)	<i>Salmonella</i>	Industrial	Natural	High	14.3% (untreated water) reduced to 1%, numbers on positive carcasses 0.4–48 cells/g reduced to <0.4 cells/g	Lillard (1980)
1.33 mg/l	<i>Salmonella</i>	Industrial	Natural	High	97.7% reduced to not detected	Thiessen, Usborne & Ogg (1984)

^a Reductions were not compared with a control using water spray/dip alone, and therefore it is not possible to separate the reduction resulting from the physical action of water spray/dip and any additional effect of using chlorine dioxide.

Table 4.6. Peroxyacetic acid as a wash or dip for poultry

Conditions of use	Pathogen	Setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence	Reference
200 mg/l (skin spray)	<i>S. Typhimurium</i>	Laboratory	Inoculated	Low	0.75 log reduction ^a	Ecolab, unpublished data, 2001
200 mg/l (wing immersion)	<i>S. Typhimurium</i>	Laboratory	Inoculated	Low	0.32 log reduction ^a	Ecolab, unpublished data, 2001
200 mg/l (liver immersion)	<i>S. Typhimurium</i>	Laboratory	Inoculated	Low	0.48 log reduction ^a	Ecolab, unpublished data, 2001
220 mg/l (leg dipping, 15 min)	<i>S. Enteritidis</i>	Laboratory	Inoculated	Low	0.36 log reduction (peroxyacetic acid) 0.33 log reduction (water alone)	Del Río et al. (2007)

^a Reductions were not compared with a control using water spray/dip alone, and therefore it is not possible to separate the reduction resulting from the physical action of water spray/dip and any additional effect of using peroxyacetic acid.

4.2.4 Quantitative microbial risk assessment to evaluate the public health impact of the use of disinfectants in poultry processing

To evaluate the effect of chlorinated disinfectants on microbiological risk, it is necessary to establish the risks to health that certain food commodities pose in the absence of these chemicals. In the case of poultry, two quantitative risk assessment models have been previously developed for FAO/WHO, one on *Salmonella* and one on *Campylobacter* (FAO/WHO, 2002a,b). Only the *Campylobacter* model is suitable for illustrating the possible impact of food disinfectant use on public health outcomes. It has been possible to adapt this model to incorporate quantitative data on the effect of chlorine-based disinfectants on these *Campylobacter* in poultry production systems. As a result, a quantitative estimate of the risk reduction brought about by the use of chlorine-based disinfectants has been possible. However, in other food commodities reviewed—namely, red meat, fish and fishery products and fresh produce—no suitable quantitative risk assessment models were available.

The detailed model use and risk reduction outcome is shown in Appendix 1.

4.3 Red meat

4.3.1 Pathogens

Red meat is an important vehicle of foodborne human illness in many parts of the world and may be contaminated with a range of pathogenic bacteria (Skovgaard, 1999). When present, the organisms are usually carried asymptomatically in the alimentary tract and on the skin or hide of animals. Meat can become contaminated at any of the stages involved in slaughter and carcass dressing or subsequently during handling or further processing in different parts of the supply chain. The principal pathogens of concern in primary processed meats are *Salmonella*, *Campylobacter* and verotoxigenic *Escherichia coli* (VTEC). VTEC are mainly associated with ruminants, especially cattle and sheep. VTEC are also a risk in some fermented products, and outbreaks of disease associated with this pathogen in salami-type products have been reported in a number of countries due to uncontrolled fermentations. Strains of *Listeria monocytogenes* are also commonly found in the primary processed product, but their public health significance in this context remains unclear. In further processed products, *L. monocytogenes* is of substantial concern, and a number of outbreaks of disease associated with this pathogen in these products have been reported.

4.3.2 Common disinfection practices

With respect to primary meat processing, a spray-chilling system is used in some abattoirs to reduce water loss and increase the chilling rate of carcasses by evaporative cooling, thus ensuring that the deep muscle reaches 10.0 °C within 24 h and 7.2 °C within 36 h (National Advisory Committee on Microbiological Criteria in Foods, 1993). During the first 12 h of chilling at about −3 °C, carcasses may be exposed intermittently (e.g. for 2 min every 30 min) to a fine mist of chilled water containing free chlorine concentrations up to 50 mg/l. Although this is not strictly an antimicrobial treatment, it was thought to contribute to the control of pathogenic and spoilage bacteria on the meat (Swift & Company, 1973; Dickson & Anderson, 1992). Other chemical-based antimicrobial treatment of carcasses is likely to be applied before the chilling process, with the aim of maximizing the effect on microbial contamination. These treatments vary, but generally include spraying of whole carcasses, primal or subprimal cuts, organs and trim with various antimicrobial chemicals

(including chlorine-based ones) in water. In the case of primal cuts, subprimal cuts and organs, immersion in water with antimicrobial compounds may also occur. Carcasses may also be sprayed with antimicrobial agents, which can be chlorine based, prior to hide removal in an attempt to reduce transfer of microorganisms from the hide to the surface of the meat. In the case of further processed products, contamination with *L. monocytogenes* often occurs post-cooking. Attempts to control this pathogen generally entail spraying the meat with, or immersing it in, a solution of antimicrobial chemical. Although chlorine-based products have been experimentally used in this context, their application in commercial processing facilities is very infrequent. In contrast, chlorine-based products may be used to control microorganisms on food contact surfaces during processing in both primary and secondary red meat processing in many parts of the world. This use, however, is often sporadic, and the degree of transfer of antimicrobial compounds to the meat remains undetermined. The most common antimicrobials used are hypochlorite, ASC and lactic acid (see chapter 1).

4.3.3 Effectiveness of common disinfection practices

Several studies have been carried out on pre-chill carcasses of beef, lamb and pork to determine the effects of spray-washing with superchlorinated water on either aerobic plate counts or counts of specific indicator bacteria. For example, Kotula et al. (1974) used chlorine at 200 mg/l at either 12.8 °C or 51.7 °C over a pH range of 4–7. When carcasses were sampled 45 min after treatment, aerobic plate counts were reduced by 1–2 log units, extending to more than 2 log units after 24 h. By increasing the washing pressure from 85 to 498.5 kPa, counts were reduced by more than 2 and 3 log units after 45 min and 24 h, respectively. Similar results were obtained by other workers (reviewed by Dickson & Anderson, 1992), and reductions in count ranged from 1 to 3 log units, depending on the experimental conditions. In other studies, however, there was no significant effect of chlorine on carcass contamination, and this may have been due to the initial presence of unusually low numbers of organisms or to the treatment conditions used.

There have been few studies on the effectiveness of chlorine-containing compounds against specific pathogens of concern, and even fewer in processing plants. Emswiler-Rose & Kotula (1984) used a model system rather than carcass meat to determine the chlorine sensitivity of pure cultures of various organisms. In each case, an agar plate was spread-inoculated with the test organism, and a disc of filter paper soaked in a chlorine solution at a specific concentration was placed on the surface. After incubation of the plate, the diameter of any zone of inhibition was measured. The lowest chlorine concentration at which inhibition occurred under these conditions was 78 mg/l for *Campylobacter jejuni*, 177 mg/l for *Yersinia enterocolitica* and 362 mg/l for *Salmonella* Typhimurium.

Cutter & Siragusa (1995) reported that an 800 mg/l chlorine spray-wash reduced counts of *E. coli* O157:H7 on inoculated beef carcass tissue by only 1.04 log cfu/cm², and spray treatments with 50, 100, 250 or 500 mg/l resulted in reductions of <1 log cfu/cm². Inoculated beef carcass tissue was also used by Stopforth et al. (2004) to determine the effect of chlorine sprays on acid-habituated and non-habituated *E. coli* O157:H7 under simulated chilling conditions. The meat samples were held at –3 °C for 10 h and sprayed for 30 s every 30 min with a 500 mg/l sodium hypochlorite solution at 4 °C. The samples were then transferred to 1 °C for a further 38 h. With acid-habituated cells, chlorine had no significant effect on the counts obtained immediately after spraying, but there was a 1.2 log cfu/cm² reduction after the full 48 h, a result comparable to that obtained by spraying plain water. Similarly, chlorine reduced counts of non-habituated cells by 0.6 log cfu/cm² and by a further 1.2 log cfu/cm² after 48 h. Again, the effects resembled those observed with water alone.

The efficacy of chlorine dioxide as a carcass decontaminant for beef was studied by Cutter & Dorsa (1995). Fresh beef carcass tissue was inoculated with bovine faeces and spray-treated in a pilot-scale washer for 10 s at 16 °C and 520 kPa, using chlorine dioxide at concentrations ranging from 0 to 20 mg/l. Regardless of chlorine dioxide concentration, bacterial populations were reduced by no more than 0.93 log cfu/cm², and the results were not statistically different from those obtained with plain water. Even with a chlorine dioxide concentration of 20 mg/l and an increase in water pressure to 690 kPa for up to 60 s, count reductions were no greater than those achieved with water. It was concluded that spray treatment with chlorine dioxide was no more effective than water for reducing bacterial contamination of beef.

Two forms of ASC were studied by Castillo et al. (1999), one activated by phosphoric acid, the other by citric acid. Trials involved inoculation of various sites on hot-boned beef carcasses, using either *E. coli* O157:H7 or *S. Typhimurium*. For both pathogens, counts were reduced by 3.8–3.9 log units when a water wash was followed by spraying with phosphoric acid-activated ASC and by 4.5–4.6 log units after spray-washing with citric acid-activated ASC. The corresponding reduction with water alone was 2.3 log units. All sites on the carcass were treated effectively, apart from the inside round, which showed lower reductions. With both forms of ASC, there was a clear reduction in count for organisms that spread beyond the initial inoculation site. In a study entailing the dipping of meat inoculated with *E. coli* O157:H7 or *S. Typhimurium* into ASC, a similar reduction in number (1.4–2.1 log units) as for the spray treatment for both of the pathogens was obtained (Harris et al., 2006).

The study of Stopforth et al. (2004) utilized samples of beef carcass tissue that were inoculated with either acid-habituated or non-habituated strains of *E. coli* O157:H7. Exposure to simulated conditions of carcass chilling involved –3 °C for 10 h, followed by 1 °C for a further 38 h. During the initial 10 h period, carcass samples were sprayed for 30 s every 30 min with either water or 0.12% ASC. The effect of ASC treatment was similar for both acid-habituated and non-habituated cells. Immediately after treatment, there was a 1.7–2.2 log reduction in count and a further decline of 0.9–1.1 log after the full 48 h of chilling, which was about 2.0 log units greater than that achieved with water alone.

Lactic acid is a non-chlorine-containing compound commonly used in sprays and washes for the control of pathogens during primary processing of red meat. Harris et al. (2006) demonstrated that the dipping of meat inoculated with *E. coli* O157:H7 or *S. Typhimurium* into 2% lactic acid gave a reduction in numbers (1.5–2.0 log units) similar to that achieved with ASC at 1200 mg/l. In another study, Sawyer et al. (2008) showed a 1.3–1.6 log unit reduction in numbers of the same two pathogens on meat dipped in a 2.5% lactic acid solution.

Although there is little information in the literature on the effect of chlorine usage in abattoirs on specific pathogens on meat, experiments with the model system of Emswiler-Rose & Kotula (1984) showed that *C. jejuni* was among the more chlorine sensitive of the organisms tested and notably more so than some strains of *Salmonella*. However, the studies on poultry described previously suggest that this difference in chlorine sensitivity is of little consequence in relation to spray treatment of carcasses. Under commercial conditions, spray-washing pre-chill red meat carcasses with chlorine has had a variable effect on aerobic plate counts or counts of indicator bacteria, and some studies have found no effect. Whether used in spray-cooling of carcasses or in a separate spray-washing process, there was little or no effect of chlorine on *E. coli* O157:H7, even at a concentration of 800 mg/l, and spray-washing with chlorine dioxide was similarly ineffective. Hence, both chlorine and chlorine dioxide, when used in these ways, have only a minimal effect on pathogens associated with beef carcasses, and therefore risk reduction is likely to be negligible.

Of the chlorine-containing products tested, only ASC, especially when activated by citric acid, was an effective antimicrobial in both spray-washing and spray-cooling systems, and counts of *E. coli* O157:H7 were reduced by approximately 2 log units on inoculated beef carcass tissue. These findings parallel those on poultry and the effects of ASC on *Salmonella* and *Campylobacter* described previously. As the incidence of enteric pathogens on raw red meat is usually low, use of ASC would be expected to have a significant effect in reducing risk, although only to a small extent, because the treatment tends to be less effective on naturally occurring contaminants than it is on inoculated organisms.

In some countries, lactic acid is commonly used during processing as an antimicrobial agent for red meat. However, studies on this compound suffer from the same limitations as for those on chlorine-containing compounds—namely, a lack of data on effectiveness under commercial conditions. In practice, lactic acid is likely to be as effective as ASC. This has been confirmed, for example, by Harris et al. (2006), who compared the efficacy of the two against the same pathogens, tested under identical conditions. From the available data, lactic acid appears to be a suitable alternative to chlorine-based compounds for reducing pathogen contamination of red meat.

Summary

Although no in-plant studies have been reported, Table 4.7 summarizes some laboratory-based work that has examined the effects of commonly used antimicrobial agents on pathogens present on meat.

Overall, spray treatment of the meat with hypochlorite at 50–800 mg/l reduced counts of *E. coli* O157 by only 0.1–1.0 log units and therefore was largely ineffective. By contrast, ASC applied as a spray or dip treatment at 1200 mg/l yielded a 1.4–1.5 log reduction in *E. coli* O157 and a 1.6–2.1 log reduction in *Salmonella*, suggesting that the treatment would be beneficial under practical conditions. Similar results were obtained with lactic acid, which could be used as an alternative to ASC.

4.4 Fishery products

4.4.1 Product

Fishery products are highly diverse, ranging from raw whole fish to ready-to-eat products. Fish and fishery products are generally considered safe, and surveillance data from a few developed countries show that these products account for only a small percentage of foodborne illnesses. During 1992–2003 in England and Wales, fish and shellfish accounted for 14% of foodborne illnesses, whereas desserts accounted for 15%, poultry 24% and red meat 20% (Hughes, Gillespie & O'Brien, 2007). In the USA, seafood accounts for only 10–19% of foodborne illnesses (Butt, Aldridge & Sanders, 2004). Most of these illnesses are associated with consumption of live bivalve molluscs or are due to histamine in some marine fish, and chlorine has no specific use to overcome these hazards. However, ready-to-eat fishery products such as cold-smoked fish have been occasionally implicated in illnesses due to *Listeria monocytogenes* (Rocourt, Jacquet & Reilly, 2000).

Table 4.7. Relevant antimicrobial chemical effectiveness studies against important pathogens on red meat

Conditions of use	Pathogen	Study setting	Contamination type	Contribution to body of evidence	Effect on numbers and prevalence ^a	Control used ^a	Reference
Hypochlorite							
50 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	0.74 log	Water (0.57 log)	Cutter & Siragusa (1995)
100 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	0.49 log	Water (0.57 log)	Cutter & Siragusa (1995)
250 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	0.79 log	Water (0.57 log)	Cutter & Siragusa (1995)
500 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	0.51 log	Water (0.57 log)	Cutter & Siragusa (1995)
800 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	1.04 log	Water (0.57 log)	Cutter & Siragusa (1995)
50 mg/l (spray)	<i>E. coli</i> O157 (acid habituated)	Laboratory	Inoculated	Low	0.1 log	Water (0.3 log)	Stopforth et al. (2004)
50 mg/l (spray)	<i>E. coli</i> O157 (non-acid habituated)	Laboratory	Inoculated	Low	0.6 log	Water (0.5 log)	Stopforth et al. (2004)
ASC							
1200 mg/l (dip)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	1.4 log	Water	Harris et al. (2006)
1200 mg/l (dip)	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.1 log	Water	Harris et al. (2006)
1200 mg/l (spray)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	3.8 log	Water (2.3 log)	Castillo et al. (1999)
1200 mg/l (spray)	<i>Salmonella</i>	Laboratory	Inoculated	Low	3.9 log	Water (2.3 log)	Castillo et al. (1999)
Lactic acid							
2% (dip)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	1.5 log	Water	Harris et al. (2006)
2% (dip)	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.0 log	Water	Harris et al. (2006)
2.5% (dip)	<i>E. coli</i> O157	Laboratory	Inoculated	Low	1.3 log	Water	Sawyer et al. (2008)
2.5% (dip)	<i>Salmonella</i>	Laboratory	Inoculated	Low	1.6 log	Water	Sawyer et al. (2008)

^a Effects are given as log cfu/ml or log cfu/g reduction of organisms in all cases.

Use of hazard analysis and critical control point (HACCP)-based approaches has led to marked improvements in the safety of fish and fishery products, and a sanitation plan is a prerequisite for implementation of HACCP. The sanitation plan includes safety of processing water, hygiene of food contact surfaces, prevention of cross-contamination, hand washing, employee health and exclusion of pests as important components. Chlorine usage is important to ensure water safety, hygiene of food contact surfaces and prevention of cross-contamination. The FAO/WHO risk assessment of choleraenic *Vibrio cholerae* O1 in warm-water shrimp in international trade (FAO/WHO, 2005) considered data on detection of this pathogen in warm-water shrimp imported by the USA, Japan and Denmark during 1995–2000. Of over 20 000 samples analysed, only 2 samples in 1995 (early period of HACCP implementation) were positive for this pathogen. On the other hand, *V. cholerae* O1 has been reported at a much higher frequency from domestically marketed shrimp and fish in southern Asia (Chen et al., 2004; Saravanan et al., 2007) and occasionally in Latin America (De Paola et al., 1993), when hygienic practices have been inadequate.

4.4.2 Pathogens

There are very few human pathogenic microorganisms (e.g. *Vibrio parahaemolyticus*) that are naturally associated with fish and fishery products. In fish that are cultured in coastal environments or inland in fresh water, pathogens such as *Listeria monocytogenes* and *Salmonella* could be of concern because of their presence in the environment. *Vibrio parahaemolyticus* is generally present at low levels—for example, 10^2 /g or lower in shrimp (Karunasagar, Venugopal & Karunasagar, 1984) and ~88/g in finfish (Chan et al., 1989). The infective dose for *V. parahaemolyticus* is $\sim 10^6$ cells (FAO/WHO, in press); therefore, multiplication in seafood is necessary before an infective dose is reached. *Listeria monocytogenes* is widespread in the aquatic environment and has been frequently isolated from several fish species (Huss, Jorgensen & Vogel, 2000). It may colonize the fish processing environment and may be difficult to eliminate (Huss, Jorgensen & Vogel, 2000). Its prevalence in fish smoking plants typically ranges from 10% to 40%, but may sometimes reach 100% (Jorgensen & Huss, 1998; Autio et al., 1999).

4.4.3 Common disinfection practices

Usage of chlorine in most types of fish processing industry is mainly as a hygienic processing aid rather than as a decontamination treatment. Mostly calcium or sodium hypochlorite is used to treat water used for washing fish and for making ice. For these purposes, water containing chlorine at concentrations below 10 mg/l is generally used. However, for cleaning boxes, cleaning fish processing tables and washing floors, water containing chlorine concentrations of 50–200 mg/l is used. Use of chlorine to reduce pathogen levels is common in the fish processing industry to produce ready-to-eat products such as cold-smoked fish fillets or shrimp for the sushi and sashimi market. In cold-smoked fish, *L. monocytogenes* is the target organism; in sashimi-grade shrimp, *V. parahaemolyticus* is the target pathogen. In these industries, use of chlorine dips at levels ranging from 50 to 200 mg/l has been reported. *Listeria monocytogenes* is particularly difficult to eliminate from the processing environment, and a decontamination step using chlorine at levels of 100–200 mg/l has been recommended to control this pathogen (El-Kest & Marth, 1988). This is a common practice in the industry producing ready-to-eat smoked fish.

4.4.4 Effectiveness of common disinfection practices

Washing fish using chlorinated water is important to clean the fish surface. Use of non-potable water at this stage could result in contamination of fish with pathogens such as *Salmonella* or choleraogenic *Vibrio cholerae* O1. Chlorination of processing water would eliminate these waterborne pathogens and prevent contamination of fish. Chlorination of drinking-water played an important role in the elimination of typhoid fever in Europe and the USA. Washing of fish would also reduce the microbial load on the surface of the fish. Reduction in surface microflora of fish by washing could contribute to improved shelf-life of fish (Shewan, 1971). In the case of pathogens such as *V. parahaemolyticus* and *V. vulnificus*, which are indigenous to coastal and estuarine environments, about 90% reduction in levels can be achieved by washing shrimp with water containing chlorine at 10 mg/l (Table 4.8). Washing of contaminated surfaces with potable water brought about 2 log reductions in levels of *Salmonella*, *V. parahaemolyticus*, *V. vulnificus*, *V. cholerae*, *Escherichia coli* and *Staphylococcus aureus*, and washing these surfaces with water containing residual chlorine levels of 100 mg/l completely eliminated the pathogens (Dinesh, 1991).

Listeria monocytogenes is a pathogen that is widely distributed in the environment and may be present in fish. This organism is of concern in ready-to-eat products such as smoked fish, because it is known to persist in the fish processing environment and may contaminate cold-smoked fish after processing (FAO/WHO, 2004). Use of water containing chlorine at 20–30 mg/l for thawing frozen salmon has been found to reduce the level of *L. monocytogenes* (Eklund et al., 1997). Under laboratory conditions, chlorine at levels of 20–25 mg/l has been shown to be effective in killing both *E. coli* and *L. monocytogenes* in a fish model system. Shin, Chang & Kang (2004) reported a 2–3 log reduction in levels of *L. monocytogenes* in fish stored in ice made with water containing chlorine dioxide at 20–100 mg/l. Bremer & Osborne (1998) evaluated an industrial-scale finfish washing system using gilled and gutted king salmon (*Oncorhynchus tshawytscha*). Exposure of salmon to free chlorine at 200 mg/l at a turnover rate for the total wash solution of 2.25 cycles/h for 120 min resulted in a 96–99% decrease in total plate count. Further, washing could eliminate 99.79% of *L. monocytogenes* cells that had been artificially inoculated on the surface of gilled and gutted fish. A study in Iceland (Cormier et al., 2007) showed that implementation of HACCP in plants producing ready-to-eat shrimp and lobster minimized the probability of finding *L. monocytogenes* in ready-to-eat products. Although use of chlorine in the fish smoking industry will not result in a product that is free from this pathogen, the prevalence and numbers of pathogens are significantly reduced. Cases of human illness are due to foods containing more than 10^2 cells of *L. monocytogenes* per gram, and measures that reduce the frequency of contamination would imply a proportional reduction in the rates of illness, provided the proportion of high contamination is reduced similarly (FAO/WHO, 2004). Available data suggest that use of chlorine can reduce prevalence and also reduce the number of organisms, hence contributing to risk reductions.

In the case of *V. parahaemolyticus*, the infective dose is $\sim 10^6$ cells (FAO/WHO, in press); therefore, multiplication in seafood is necessary before an infective dose is reached. Washing fish in chlorinated water would bring about over a 90% reduction in levels of *V. parahaemolyticus* (Table 4.8), thus greatly reducing the human health risk due to this organism.

Table 4.8. Studies showing pathogen reduction following use of chlorine in fish processing

Conditions of use	Pathogen	Study setting	Contamination type	Contribution to body of evidence	Effect on numbers and/or prevalence	Reference
Washing of fish in water containing chlorine at 200 mg/l	<i>L. monocytogenes</i>	Pilot	Inoculation	Medium	99.79% reduction	Bremer & Osborne (1998)
Thawing frozen fish in water containing chlorine at 20–25 mg/l	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	Elimination	Eklund et al. (1997)
Fish storage in ice containing chlorine dioxide at 20–100 mg/l	<i>L. monocytogenes</i> , <i>S. Typhimurium</i> , <i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2–3 log reduction	Shin, Chang & Kang (2004)
Immersion of shrimp in water containing chlorine at 50 mg/l for 30 min	<i>V. parahaemolyticus</i>	Laboratory	Natural	Medium	85–97% reduction	Chaiyakosa et al. (2007)
Washing shrimp in water containing chlorine at 10 mg/l	<i>V. parahaemolyticus</i> , <i>V. cholerae</i> , <i>V. vulnificus</i> , <i>Salmonella</i>	Laboratory	Inoculation	Low	>90% reduction	Dinesh (1991)
Washing of processing surface with water containing chlorine at 100 mg/l	<i>V. parahaemolyticus</i> , <i>V. cholerae</i> , <i>V. vulnificus</i> , <i>Salmonella</i>	Laboratory	Inoculation	Low	Elimination	Dinesh (1991)

4.5 Fresh produce

4.5.1 Product

Fresh produce includes fruits and vegetables that are consumed with little or no further processing or preparation by the consumer. Produce can be distributed and sold loose or pre-packed in either unprocessed or minimally processed form. Many products are ready to eat, and no further antimicrobial process is applied before consumption.

4.5.2 Pathogens

The Centre for Science in the Public Interest in the USA compiles a database of outbreaks associated with foods. Between 1990 and 2005, this database captured information on 639 outbreaks of foodborne illness due to produce, involving 31 496 illnesses (CSPI, 2008). The most publicized outbreak in recent years occurred in the USA in 2006: spinach from the Salinas Valley in California was contaminated with *Escherichia coli* O157:H7. In 26 states, 204 persons were infected with *E. coli* O157:H7, 102 were hospitalized, 31 developed haemolytic-uraemic syndrome and 3 died.

Fresh produce becomes contaminated primarily in the field during production via contaminated water (irrigation, pesticide application, flooding), by contact with soil and soil improvers contaminated with animal or human faeces, as a result of the presence of livestock or wildlife in the production areas or from the equipment or workers during harvesting. Contamination is also possible during post-harvest operations by cross-contamination from contaminated wash water, from contaminated food contact surfaces or from workers and equipment. Microorganisms associated with fresh produce are controlled by a combination of good agricultural practices during production, good hygienic practices during harvesting and packing, processing and distribution, as well as the use of antimicrobial chemicals during processing and a cold chain during distribution.

A non-exhaustive list of the main pathogenic microorganisms that have been associated with human illness as a result of the consumption of fresh produce includes VTEC, *Salmonella* spp., *Shigella* spp., *Cryptosporidium* spp., *Yersinia enterocolitica*, *Listeria monocytogenes*, *Giardia lamblia* and *Cyclospora cayetanensis*, as well as various enteric viruses.

4.5.3 Common disinfection practices

Chlorinated compounds are perhaps the most universal disinfectants used in the fresh produce industry. Chlorine is used to decontaminate processing equipment, to control the microbial load in wash waters as well as in the disinfection of food contact surfaces and the fresh produce itself. Chapter 1 identified that the most commonly used chlorinated compounds in the fresh produce industry are sodium/calcium hypochlorite and aqueous chlorine dioxide. Chlorine delivered by use of hypochlorous acid and hypochlorite is used by the industry at levels between 25 and 200 mg/l (contact time <2 min) as post-harvest spray or dip and then at concentrations of between 10 and 50 mg/l in flume water (contact time 0.5–15 min). The aqueous form of chlorine dioxide is also used by the industry at up to 3 mg/l in flume water. The fresh produce industry also uses peroxyacetic acid as an alternative to chlorine at about 40 mg/l in flume water.

The use of other disinfectants, such as ASC, gaseous chlorine dioxide, ozone and hydrogen peroxide, is less common in the industry, or the disinfectants have been examined only at the experimental phase.

4.5.4 Effectiveness of common disinfection practices

In this section, data have been identified that concern the effect of those disinfectants considered in common industrial use in chapter 1 and summarized in the previous section. These data were identified during literature searches conducted by FAO/WHO and also from information provided to these organizations in the call for data accompanying this expert meeting. They may not constitute all of the available studies on pathogens on fresh produce, but they do provide a representative cross-section of data.

4.5.4.1 Hypochlorite in flume water and as a dip/spray

Table 4.9 summarizes these studies and the strength of their individual contribution to the body of evidence concerning the effect of chlorine. Treatments (up to 200 mg/l) with chlorine solutions can reduce populations of pathogens by up to 2 log units compared with water washing generally. In contrast, Wu et al. (2000) reported that treatment of whole parsley leaves with free chlorine at 150 mg/l reduced the populations of *Shigella sonnei* by more than 6 log cfu/g. It is clear that each bacterial species exhibits different sensitivity to chlorine. The physical structure of the vegetable also has an impact on the efficacy of chlorine. In addition, there are a variety of methods (e.g. time for inoculation of pathogens and treatment with chlorine, temperature, concentration of chlorine) used to study the effect of chlorine on fresh produce. Different experimental methods will affect the results. Akbas & Olmez (2007) reported that increasing the treatment time from 2 to 5 min did not result in any further significant decrease in *Escherichia coli* population on lettuce pieces. Li et al. (2001) reported that survival of *E. coli* O157:H7 on lettuce pieces after agitation in a chlorine solution of 20 mg/l at 20 °C and 50 °C was not significantly different. Although the effect of the different conditions individually might be small, the combination might have a greater impact on the result.

Although there are many studies providing data on pathogen reduction on produce due to chlorine, they are confined to experimental methods; as such, they would make a smaller contribution to the body of evidence on the likely effect of chlorine used in practice during spray-washing of produce or in flume water. No identified studies have examined the effect of chlorine in flume water on the prevalence of pathogens on produce; hence, definitive conclusions cannot be drawn on its effect on preventing cross-contamination due to pathogens in the process water or on contact surfaces.

The primary health concern with fresh produce is foodborne illness from the consumption of ready-to-eat leafy green vegetables such as lettuce and spinach. The data shown in Table 4.9 for leafy greens suggest that chlorine use at levels between 20 and 200 mg/l for contact times between 1 and 10 min results in reductions of between 0.2 and 1.7 log units of *L. monocytogenes*, 0.3 and 2 log units of *Salmonella*, 0.3 and 1.7 log units of *E. coli* O157 and 0.2 and 6.0 log units of *Shigella* over washing in water alone. In general, larger reductions are achieved at higher concentrations of chlorine, but data seem too inconsistent to be definitive. Data are also inconsistent between studies on the effect of contact time. Those studies that included a water wash control showed log reductions in pathogens between 0.5 and 1.0 log units, depending on the type of leafy green tested and the pathogen species. Given that these experiments use pathogens artificially inoculated onto produce, it is likely that these effects are an overestimate of the effects of chlorine in washes or flume water in the industrial setting.

Table 4.9. Studies showing pathogen reduction after produce treatment with chlorine via hypochlorite

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
100 mg/l, dipping (2 min)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.5 log	Water (0.6 log)	Akbas & Olmez (2007)
100 mg/l, dipping (5 min)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.7 log	Water (0.7 log)	Akbas & Olmez (2007)
20 mg/l, dipping (30 s)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1–1.2 log	No treatment	Li et al. (2001)
300 mg/l (3 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation (internalized in leaves by vacuum perfusion)	Low	0.5 log	No treatment	Niemira (2007)
600 mg/l (3 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation (internalized in leaves by vacuum perfusion)	Low	0.5 log	No treatment	Niemira (2007)
300 mg/l (3 min)	Spinach pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation (internalized in leaves by vacuum perfusion)	Low	0.5 log	No treatment	Niemira (2007)
600 mg/l (3 min)	Spinach pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation (internalized in leaves by vacuum perfusion)	Low	0.5 log	No treatment	Niemira (2007)
25 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	0.2 log	Tap water	Zhang & Farber (1996)
50 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	0.8 log	Tap water	Zhang & Farber (1996)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
100 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.0 log	Tap water	Zhang & Farber (1996)
200 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.3 log	Tap water	Zhang & Farber (1996)
25 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	0.6 log	Tap water	Zhang & Farber (1996)
50 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.0 log	Tap water	Zhang & Farber (1996)
100 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.2 log	Tap water	Zhang & Farber (1996)
200 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.7 log	Tap water	Zhang & Farber (1996)
200 mg/l, immersion (10 min)	Lettuce pieces	<i>Salmonella</i>	Laboratory	Inoculation	Low	1.0 log	Distilled water (0.7 log)	Kondo, Murata & Isshiki (2006)
200 mg/l, immersion (10 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	1.2 log	Distilled water (0.7 log)	Kondo, Murata & Isshiki (2006)
200 mg/l, immersion (10 min)	Lettuce pieces	<i>S. aureus</i>	Laboratory	Inoculation	Low	1.4 log	Distilled water (1.1 log)	Kondo, Murata & Isshiki (2006)
100 mg/l, stirring (10 min)	Lettuce pieces	<i>Y. enterocolitica</i>	Laboratory	Inoculation	Low	2.36–2.68 log	Distilled water	Escudero et al. (1999)
100 mg/l, stirring (10 min)	Lettuce pieces	<i>Y. enterocolitica</i>	Laboratory	Inoculation	Low	2.55–3.15 log	Distilled water	Escudero et al. (1999)
200 mg/l, agitation (1 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	0.86–0.88 log	No treatment and water (0.58–0.59 log)	Koseki et al. (2003)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
200 mg/l, agitation (1 min)	Lettuce pieces	<i>Salmonella</i>	Laboratory	Inoculation	Low	0.96–1.04 log	No treatment and water (0.53–0.67 log)	Koseki et al. (2003)
20 mg/l, agitation (20 °C, 1 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	1.0 log	No treatment and immersion in water (0.7 log)	Li et al. (2001)
120 mg/l, shaking (40 s)	Shredded lettuce	<i>Salmonella</i>	Laboratory	Inoculation	Low	0.8 log	Deionized water	Weissinger, Chantarapanont & Beuchat (2000)
200 mg/l, shaking (40 s)	Shredded lettuce	<i>Salmonella</i>	Laboratory	Inoculation	Low	0.8 log	Deionized water	Weissinger, Chantarapanont & Beuchat (2000)
100 mg/l, wash (1 min)	Shredded lettuce	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	0.7 log	Water (0.5 log)	Hellstrom et al. (2006)
100 mg/l, mixing (5 min)	Chinese cabbage pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2.0–2.7 log	Water (0.7–1.0 log)	Inatsu et al. (2005)
100 mg/l, immersion (5 min)	Parsley bunches	<i>Salmonella</i>	Laboratory	Inoculation	Low	1.7–2.0 log	Deionized water	Lapidot, Romling & Yaron (2006)
200 mg/l, immersion (5 min)	Parsley bunches	<i>Salmonella</i>	Laboratory	Inoculation	Low	1.7–2.0 log	Deionized water	Lapidot, Romling & Yaron (2006)
800 mg/l, immersion (5 min)	Parsley bunches	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.2–2.6 log	Deionized water	Lapidot, Romling & Yaron (2006)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
1600 mg/l, immersion (5 min)	Parsley bunches	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.6–3.0 log	Deionized water	Lapidot, Romling & Yaron (2006)
5 mg/l, agitation (5 min)	Parsley bunches	<i>Shigella</i>	Laboratory	Inoculation	Low	1.2 log	Deionized water	Wu et al. (2000)
10 mg/l, agitation (5 min)	Parsley bunches	<i>Shigella</i>	Laboratory	Inoculation	Low	2.3 log	Deionized water	Wu et al. (2000)
100 mg/l, agitation (5 min)	Parsley bunches	<i>Shigella</i>	Laboratory	Inoculation	Low	4.3 log	Deionized water	Wu et al. (2000)
150 mg/l, agitation (5 min)	Parsley bunches	<i>Shigella</i>	Laboratory	Inoculation	Low	>6 log	Deionized water	Wu et al. (2000)
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2.4 log	Water (1.0 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	2.2 log	Water (0.6 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.1 log	Water (0.6 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2.3 log	Water (1.0 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	2.1 log	Water (1.4 log)	Stopforth et al. (2008)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
Sodium hypochlorite (50 mg/l) + citric acid to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.8 log	Water (1.1 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2.3 log	Water (1.0 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	2.0 log	Water (0.6 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (60 s)	Leafy greens (many varieties)	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.2 log	Water (0.6 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>E. coli</i> O157:H7	Laboratory	Inoculation	Low	2.5 log	Water (1.0 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>L. monocytogenes</i>	Laboratory	Inoculation	Low	1.7 log	Water (1.4 log)	Stopforth et al. (2008)
Sodium hypochlorite (50 mg/l) + sodium acid sulfate to pH 6.5, agitation (90 s)	Leafy greens (many varieties)	<i>Salmonella</i>	Laboratory	Inoculation	Low	2.1 log	Water (1.1 log)	Stopforth et al. (2008)
Sodium hypochlorite at 25 mg/l (2 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.56 log	No treatment	Pirovani et al. (2000)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
Sodium hypochlorite at 75 mg/l (2 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.82–0.95 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 125 mg/l (2 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.62 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 25 mg/l (5 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.62–0.80 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 75 mg/l (5 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.75–0.84 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 125 mg/l (5 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.96–1.00 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 25 mg/l (8 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.60 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 75 mg/l (8 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	0.98–1.01 log	No treatment	Pirovani et al. (2000)
Sodium hypochlorite at 125 mg/l (8 min)	Spinach	<i>Salmonella</i> Hadar	Laboratory	Inoculation	Low	1.30 log	No treatment	Pirovani et al. (2000)

^a Effects are given as log cfu/ml or log cfu/g reduction of organisms in all cases.

4.5.4.2 Aqueous chlorine dioxide in flume water and as a spray/dip

There is less information about the effectiveness of chlorine dioxide compared with hypochlorite as a disinfectant for fresh produce. The effect of chlorine dioxide on pathogenic bacteria on fresh produce is shown in Table 4.10. Zhang & Farber (1996) showed that concentrations of chlorine dioxide in water up to 5 mg/l could inactivate up to 90% of *L. monocytogenes*. Inactivation of *Salmonella* and *E. coli* O157 was similar with chlorine dioxide at 20 mg/l, around 1 log unit over water alone, with a slightly greater effect on apples than on lettuce (Huang et al., 2006). Han et al. (2001) showed that there was little effect of chlorine dioxide at 0.3 mg/l on *L. monocytogenes* on green peppers. Treatment of uninjured green pepper surfaces with chlorine dioxide at 3 mg/l resulted in a 2.3 log reduction of *L. monocytogenes*, whereas no effect was seen on injured green pepper surfaces.

From the limited data available, at the chlorine dioxide concentrations below 3 mg/l that are commonly used in the fresh produce industry, the effect on pathogens is limited to no more than 1 log unit over and above water treatment alone. Data on *Salmonella* and *E. coli* O157 are available only at high experimental concentrations, but even then, inactivation was low. It appears that aqueous chlorine dioxide is no more effective than chlorine at reducing the numbers of pathogens on leafy greens.

4.5.4.3 Peroxyacetic acid in flume water and as a spray/dip

Peroxyacetic acid is used in the fresh produce industry in flume water as an alternative to chlorine. However, data on its effect on pathogen reduction on fresh produce are limited. Table 4.11 shows data quantifying the effects on pathogens. Oh, Dancer & Kang (2005) demonstrated that peroxyacetic acid at 40 mg/l reduced *E. coli* O157 and *L. monocytogenes* by 0.8 and 0.3 log, respectively, with 10 min contact time, but *Salmonella* was more susceptible (2.5 log reduction). To achieve reductions in the other pathogens similar to those in *Salmonella*, it was necessary to increase contact time to 30 min, whereupon similar log reductions of between 2 and 3 log units were achieved for all pathogens studied. Higher reductions of up to 4.5 log units were detected with contact times of 60 min, but this is unrealistic in the industrial setting when peroxyacetic acid is used in flume water. Other studies show similar results. Generally, peroxyacetic acid seems more effective at killing pathogens than chlorine with similar contact times. However, the effect of water alone in these studies was not reported, although other studies on other disinfectants suggest that water may result in up to a 1 log reduction in pathogens alone without disinfectant.

Under commercial conditions, as described in chapter 1, the extent of pathogen reduction by peroxyacetic acid in flume water would depend on the pathogen and would range from 0.3 to 2.5 log units.

Table 4.10. Studies showing pathogen reduction after produce treatment with aqueous chlorine dioxide

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
500 mg/l, mixing (15 min)	Chinese cabbage	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	0.9–1.2 log	Water (0.4–0.6 log)	Inatsu et al. (2005)
20 mg/l, stirring (10 min)	Lettuce leaves	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	2.3 log	Water (1.3 log)	Huang et al. (2006)
20 mg/l, stirring (10 min)	Lettuce leaves	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.2 log	Water (1.5 log)	Huang et al. (2006)
20 mg/l + sonication 170 Hz, stirring	Lettuce leaves	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	2 log	Water (1.3 log)	Huang et al. (2006)
20 mg/l + sonication 170 Hz, stirring	Lettuce leaves	<i>Salmonella</i>	Laboratory	Inoculated	Low	3.2 log	Water (1.5 log)	Huang et al. (2006)
20 mg/l, stirring (10 min)	Apples	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	2 log	Water (0.5 log)	Huang et al. (2006)
20 mg/l, stirring (10 min)	Apples	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.5 log	Water (0.5 log)	Huang et al. (2006)
20 mg/l + sonication 170 Hz, stirring	Apples	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	4 log	Water (0.5 log)	Huang et al. (2006)
20 mg/l + sonication 170 Hz, stirring	Apples	<i>Salmonella</i>	Laboratory	Inoculated	Low	4 log	Water (0.5 log)	Huang et al. (2006)
10 mg/l, agitation (10 min)	Lettuce pieces	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	1.55 log	Water (0.88 log)	Singh et al. (2002)
1 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	<0 log	Tap water	Zhang & Farber (1996)
2 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.6 log	Tap water	Zhang & Farber (1996)
3 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.4 log	Tap water	Zhang & Farber (1996)
5 mg/l, stirring (10 min, 4 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	1.1 log	Tap water	Zhang & Farber (1996)

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
1 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0 log	Tap water	Zhang & Farber (1996)
2 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.5 log	Tap water	Zhang & Farber (1996)
3 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.4 log	Tap water	Zhang & Farber (1996)
5 mg/l, stirring (10 min, 22 °C)	Lettuce pieces	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.8 log	Tap water	Zhang & Farber (1996)
0.3 mg/l, agitation (10 min)	Green pepper pieces (injured)	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.54 log/5 g	Water (0.51 log/5 g)	Han et al. (2001)
0.3 mg/l, agitation (10 min)	Green pepper pieces (uninjured)	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	1.87 log/5 g	Water (1.53 log/5 g)	Han et al. (2001)
3.0 mg/l, agitation (10 min)	Green pepper pieces (injured)	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.44 log/5 g	Water (0.39 log/5 g)	Han et al. (2001)
3.0 mg/l, agitation (10 min)	Green pepper pieces (uninjured)	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	3.67 log/5 g	Water (1.35 log/5 g)	Han et al. (2001)

^a Effects are given as log cfu/ml or log cfu/g reduction of organisms in all cases.

Table 4.11. Studies showing pathogen reduction after produce treatment with peroxyacetic acid

Conditions of use	Fresh produce	Pathogen	Study setting	Study type	Contribution to the body of evidence	Effect on numbers and/or prevalence ^a	Control used ^a	Reference
40 mg/l, 10 min	Lettuce leaves	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	0.8 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 10 min	Lettuce leaves	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	0.3 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 10 min	Lettuce leaves	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.5 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 30 min	Lettuce leaves	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	2.2 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 30 min	Lettuce leaves	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	3.3 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 30 min	Lettuce leaves	<i>Salmonella</i>	Laboratory	Inoculated	Low	2.7 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 60 min	Lettuce leaves	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	3.4 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 60 min	Lettuce leaves	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	4.5 log	No	Oh, Dancer & Kang (2005)
40 mg/l, 60 min	Lettuce leaves	<i>Salmonella</i>	Laboratory	Inoculated	Low	3.8 log	No	Oh, Dancer & Kang (2005)
50 mg/l, 60 s	Precut iceberg lettuce	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	1.7 log	Potable water	Hellstrom et al. (2006)
80 mg/l, 2–5 min	Lettuce leaves (whole and shredded)	<i>E. coli</i> O157:H7	Laboratory	Inoculated	Low	~4.4 log	Tap water	Rodgers et al. (2004)
80 mg/l, 2–5 min	Lettuce leaves (whole and shredded)	<i>L. monocytogenes</i>	Laboratory	Inoculated	Low	~4.4 log	Tap water	Rodgers et al. (2004)

^a Effects are given as log cfu/ml or log cfu/g reduction of organisms in all cases.

4.6 Food contact surfaces

The purpose of the disinfectant on food contact surfaces is to reduce cross-contamination where pathogens attached to equipment become dislodged and attach to the surfaces of food in contact with them. The standard method of assessing the effect of disinfectants is by suspension tests with the bacteria of concern. Here, different concentrations of the disinfectant are used to establish the minimum inhibitory concentration. However, in practice, spoilage and pathogenic bacteria attach to surfaces and can form a biofilm. Biofilms respond differently to disinfectants compared with bacteria in suspension. This section considers the effects of disinfectants only on biofilms either in industrial situations or under laboratory conditions using bacteria grown on model contact surfaces such as stainless steel coupons. This assessment is not a comprehensive review of the subject, but aims to quantify the general effects of key disinfectants.

4.6.1 Studies on test surfaces

Sodium hypochlorite is the most common surface disinfectant used in the food industry. Joseph et al. (2001) studied hypochlorite effects against biofilms of *Salmonella* on plastic, cement and stainless steel surfaces. Biofilms on plastic challenged with chlorine solutions at concentrations up to 100 mg/l for up to 25 min resulted in reductions in *Salmonella* from less than 2 log units (chlorine at 10 mg/l for 25 min) up to 7.53 log units (chlorine at 100 mg/l for 20 min). On cement, *Salmonella* biofilm numbers were reduced by 3.53 log units (chlorine at 100 mg/l for 20 min), reflecting the difficulty in sanitizing porous surfaces. On steel, *Salmonella* biofilm numbers were reduced by 5.47 log units (chlorine at 100 mg/l for 15 min). Ramesh et al. (2002) studied the effect of several disinfectants on *Salmonella* numbers in 4-day-old biofilms grown on galvanized steel surfaces. Sodium hypochlorite at 250 mg/l for 2 min resulted in a reduction of 7.18 log cfu/cm².

Listeria monocytogenes has been shown to adhere to various surfaces after a short contact time at 4 °C and 20 °C (Mafu et al., 1990a). Biofilms of *L. monocytogenes* grown on stainless steel and plastic surfaces were challenged with sodium hypochlorite in a study by Jeyasekaran, Karunasagar & Karunasagar (2000). A 100 mg/l chlorine solution resulted in an additional 3.27 log cfu/cm² reduction from 5.72 log cfu/cm² over the effect of the water control on stainless steel. However, on plastic, the same concentration of chlorine resulted in only a 0.75 log cfu/cm² reduction from 5.16 log cfu/cm² over the effect of the water control. Clearly, plastic surfaces were more difficult to disinfect. Higher concentrations of chlorine (200 mg/l) resulted in an additional 5.72 and 2.3 log cfu/cm² reduction on stainless steel and plastic, respectively, over the effect of a water control. Another study on *L. monocytogenes* was conducted by Mustapha & Liewen (1989). Concentrations of chlorine up to 800 mg/l resulted in a reduction in *L. monocytogenes* biofilm numbers on stainless steel of between 1 and >4 log cfu/ml. Smooth stainless steel was found to be easier to disinfect than pitted stainless steel. Meylheuc, Renault & Bellon-Fontaine (2006) also studied the effect of sodium hypochlorite on *L. monocytogenes*. They reported a 3.9 and 4.0 log reduction in *L. monocytogenes* on stainless steel for cells grown at 20 °C and 37 °C, respectively, using a solution with active chlorine at 1.23 mg/l and a 5 min contact time. On polytetrafluoroethylene with the same solution, log reductions were 3.4 and 3.5 log cfu for cells grown at 20 °C and 37 °C, respectively. Mafu et al. (1990b) found that hypochlorite at 100 mg/l as chlorine was effective as a sanitizer against *L. monocytogenes* on food contact surfaces.

Other disinfectants, such as peroxyacetic acid, hydrogen peroxide, iodophores and quaternary ammonium compounds (QACs), have also been tested against pathogenic bacteria in biofilms on hard surfaces. QACs (50–800 mg/l) were tested against *L. monocytogenes* in

biofilms (Mustapha & Liewen, 1989). QACs at 50 mg/l were effective at reducing *L. monocytogenes* biofilm numbers by >4 log cfu/ml on smooth and pitted stainless steel. Peroxyacetic acid was found to be effective against *L. monocytogenes* as 4 h adherent mixed culture biofilm with *Pseudomonas* on stainless steel. The mixed culture attachment was 10^8 cfu/cm², and this was reduced to 4 cfu/cm² after 1 min contact with peroxyacetic acid at 40 mg/l (Fatemi & Frank, 1999). A combination of peroxyacetic acid and hydrogen peroxide was tested against *L. monocytogenes* cells adhered to stainless steel or polytetrafluoroethylene (Meylheuc, Renault & Bellon-Fontaine, 2006). Peroxyacetic acid/hydrogen peroxide containing peroxyacetic acid at 5.13 mg/l resulted in a 3.6 and 3.0 log reduction for cells grown at 20 °C and 37 °C, respectively, on stainless steel. On polytetrafluoroethylene, log reductions of 3.7 and 3 log cfu were reported for cells grown at 20 °C and 37 °C, respectively. Iodophors were studied against *Salmonella* biofilms (Joseph et al., 2001). Available iodine concentrations between 1 and 50 mg/l were used with contact times between 5 and 25 min. A maximum 3.5 log cfu/cm² reduction was achieved with iodine (I₂) at 50 mg/l for 5 min on plastic. A 6 log cfu/cm² reduction was achieved with iodine at 50 mg/l for 25 min on cement. A 5.5 log cfu/cm² reduction was achieved with iodine at 50 mg/l for 20 min on stainless steel. Jeyasekaran, Karunasagar & Karunasagar (2000) studied the effect of iodophors on biofilms of *L. monocytogenes*. An iodophor solution of 10 mg/l resulted in an additional 1.78 log cfu/cm² reduction from 5.72 log cfu/cm² over the effect of the water control on stainless steel. However, on plastic, the same concentration of iodophor resulted in only a 0.18 log cfu/cm² reduction from 5.16 log cfu/cm² over the effect of the water control. Higher concentrations of iodophor (20 mg/l) resulted in an additional 3.21 and 1.77 log cfu/cm² reduction on stainless steel and plastic, respectively, over the effect of a water control.

Frank, Ehlers & Wicker (2003) tested a number of disinfectants against *L. monocytogenes* biofilms grown on stainless steel and coated in chicken serum albumin and rendered chicken fat. Static cleaning with sodium hypochlorite at 200 mg/l resulted in log reductions in the coated biofilm of 4.27, 4.56 and 5.41 log units at 1, 10 and 30 min exposure, respectively. QACs (2 ml/l) resulted in log reductions in the coated biofilm of 4.78, 5.56 and 6.06 log units at 1, 10 and 30 min exposure, respectively. ASC (7.5% with 6% phosphoric acid) resulted in log reductions in the coated biofilm of 5.76, 6.32 and 6.16 log units at 1, 10 and 30 min exposure, respectively. Peroxyacetic acid (2 ml/l) resulted in log reductions in the coated biofilm of 4.48, 4.59 and 5.26 log units at 1, 10 and 30 min exposure, respectively.

4.6.2 Studies on industrial equipment surfaces

Mead, Hudson & Hinton (1994) demonstrated that an antimicrobial-resistant *E. coli*-inoculated knife in an automatic poultry killer spread contamination to at least 500 poultry carcasses; chlorinated water spray (10 mg/l) resulted in contamination of 250–400 carcasses at levels 0.4–1.3 log units lower than with the unwashed knife. Similar results were detected with the head puller, which spread contamination to 500 carcasses, but a water spray with chlorine at 25 mg/l stopped the spread after only 25–100 carcasses. Superchlorinated water may prevent biofilm formation on working surfaces and equipment, reducing the likelihood of cross-contamination and facilitating post-processing cleaning (Arnold, 2005). Bailey et al. (1986) found that using chlorine at 40 mg/l in wash water to combat bacteria in a chicken fat matrix on stainless steel reduced numbers of *Salmonella* by 96% compared with a 50% reduction by using an unchlorinated water spray.

Disinfectants are also used in the meat industry to decontaminate equipment surfaces, especially knives (Taormina & Dorsa, 2007). Knives were inoculated with raw pork residues and the pathogens *Escherichia coli* O157, *Salmonella* Typhimurium or *Clostridium*

perfringens. Blades were dipped for 1–15 s in hot water (82.2 °C), warm water (48.9 °C) or warm disinfectant (neutral or acid QAC at 400 mg/l or peroxyacetic acid in combination with hydrogen peroxide [peroxyacetic acid at 165 mg/l and hydrogen peroxide at 700 mg/l]). Reductions on knives dipped for 1 s were less than 1 log unit, with no significant difference between treatments. Reductions in *E. coli* O157 after 15 s in hot water, neutral QAC, acid QAC or peroxyacetic acid were 3.02, 2.38, 3.04 and 1.52 log units, respectively. Reductions in *S. Typhimurium* after 15 s in hot water, neutral QAC, acid QAC or peroxyacetic acid were 2.39, 1.49, 1.66 and 1.34 log units, respectively. Reductions in *C. perfringens* after 15 s in hot water, neutral QAC, acid QAC or peroxyacetic acid were 2.03, 1.50, 1.18 and 1.41 log units, respectively.

In the fish processing industry, hypochlorite is mostly used in Thailand, India, Bangladesh and Indonesia at concentrations of 20–100 mg/l for decontamination of container and table surfaces. A study of tote box cleaning (Powney & Dunsmore, 1986) demonstrated that fish fillets with low counts stored in clean boxes took 10 days to reach 10^7 cfu/g, whereas in dirty boxes they took only 7 days to reach the same numbers. Several cleaning regimes were assessed, including chlorinated alkaline detergent, a phosphoric acid detergent and an acidic QAC compound detergent/sanitizer. In a study on the general microbial ecology of fish processing plants, Bagge-Ravn et al. (2003) observed that in four different fish industries (two of cold-smoked salmon, semipreserved herring and caviar), disinfection was carried out with hypochlorite in three of them (alone or in association with other products); only in one industry was the disinfecting agent peroxyacetic acid.

Summary

Cross-contamination is a complex process that is difficult to quantify in experimental and industrial settings. The experiment by Mead, Hudson & Hinton (1994) in poultry plants provides one of the best examples of how surface decontamination can prevent cross-contamination of food. It is difficult to quantify the effects of cross-contamination on pathogen numbers on food, but it is widely recognized that the use of disinfectants in food processing is important to prevent cross-contamination and therefore reduce consumer exposure to pathogens.

Data on the quantitative effects of disinfectants on food pathogens are available based on studies in industrial, pilot and laboratory settings. These data are not always equivalent. Assessment of the effectiveness of disinfectants based on studies in industrial settings is difficult. This is because the microflora, including pathogens, in the process environment is already being controlled by the ongoing use of disinfectant. Hence, attempting to measure the effectiveness at individual steps does not accurately reflect what would happen if no disinfectants had ever been used in the process prior to the study. The end result of this is that the incremental effectiveness of the individual control steps is underestimated.

Laboratory studies demonstrate that biofilms of *Salmonella* and *L. monocytogenes* can be inactivated by a range of disinfectants at suitable concentrations with appropriate contact times. Taormina & Dorsa (2007) demonstrated the effectiveness of disinfectants against *E. coli* O157, *S. Typhimurium* and *C. perfringens* on knives. Hypochlorite is effective at concentrations between 100 and 200 mg/l, depending on the porosity and smoothness of the surface being treated. Peroxyacetic acid is also an effective disinfectant alone and in combination with hydrogen peroxide. QACs are effective at concentrations up to 50 mg/l. Iodophors are active against *Salmonella* and *L. monocytogenes* but seem less effective than chlorine when used at concentrations up to 20 mg/l. Limited data on ASC show that this chemical also has surface disinfectant potential.

4.7 References

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Appendix 1: Risk modelling of the effect of chlorinated compounds on *Campylobacter* in poultry

This appendix illustrates how risk assessment (which consists of four steps: hazard identification, hazard characterization, exposure assessment and risk characterization), risk modelling and its outputs can be incorporated into the risk–benefit decision-making process. The overall objectives of a risk model are to translate the level or frequency of contamination of a product into a human health risk outcome. In the current illustration, the impact of the use of chlorine during poultry processing on *Campylobacter* contamination can be translated into an estimate of infections avoided. Translating the impact of an intervention on pathogens on a product to the human health outcome is helpful, because it allows us to compare different interventions acting in different ways and at different points in the process into a common metric for comparison across strategies or when conducting a cost–benefit assessment.

Campylobacter risk model description

FAO/WHO (2002b) developed a risk model for *Campylobacter* in poultry, which can be adapted and applied in the current project, as the basis for estimating the risk from *Campylobacter* in poultry and to quantify the potential implications of the use of chlorine in the processing of poultry in terms of risk reductions.

The risk modelling part of any microbial risk assessment can be divided into two primary components: the exposure assessment (which estimates the prevalence and level of a pathogen by considering processing effects as well as human consumption and behaviour); and the hazard characterization (which translates the outputs from the exposure assessment into a human health outcome, typically done using a dose–response relationship).

An overview of the risk assessment model for *Campylobacter* in broilers developed by FAO/WHO (2002b) is outlined in Figure 4A.1. The model considered the occurrence and number of *Campylobacter* present in chicken products throughout the process and up to the point of consumption. The stages from rearing of broilers to the consumption of chicken products are grouped into four main modules: 1) Farm & Transport, 2) Processing, 3) Storage and 4) Preparation. The exposure assessment initially evaluates the frequency and levels of *Campylobacter* on the farm, estimating the probability that a random flock is *Campylobacter* positive, the within-flock prevalence and the levels of colonization and contamination of the broilers (internally and externally). Subsequently, the stages of transport, processing, storage and preparation by the consumer are explored and combined to predict the overall impact that these stages will have upon the contaminating *Campylobacter* load on a random chicken carcass or product to determine the final exposure level.

The risk model relies on a human feeding trial study that was conducted (Black et al., 1988) using just over 100 healthy young adult volunteers (in the USA) in order to derive the dose–response relationship. Data for *C. jejuni* A3249 and 81-176 were pooled and fit to the beta-Poisson dose–response model. The response being measured in the model is infection; however, in order to estimate the probability of illness, the conditional probability of illness following infection was estimated using a dose-independent probability derived from the same study. The dose–response relationship is shown in Figure 4A.2.

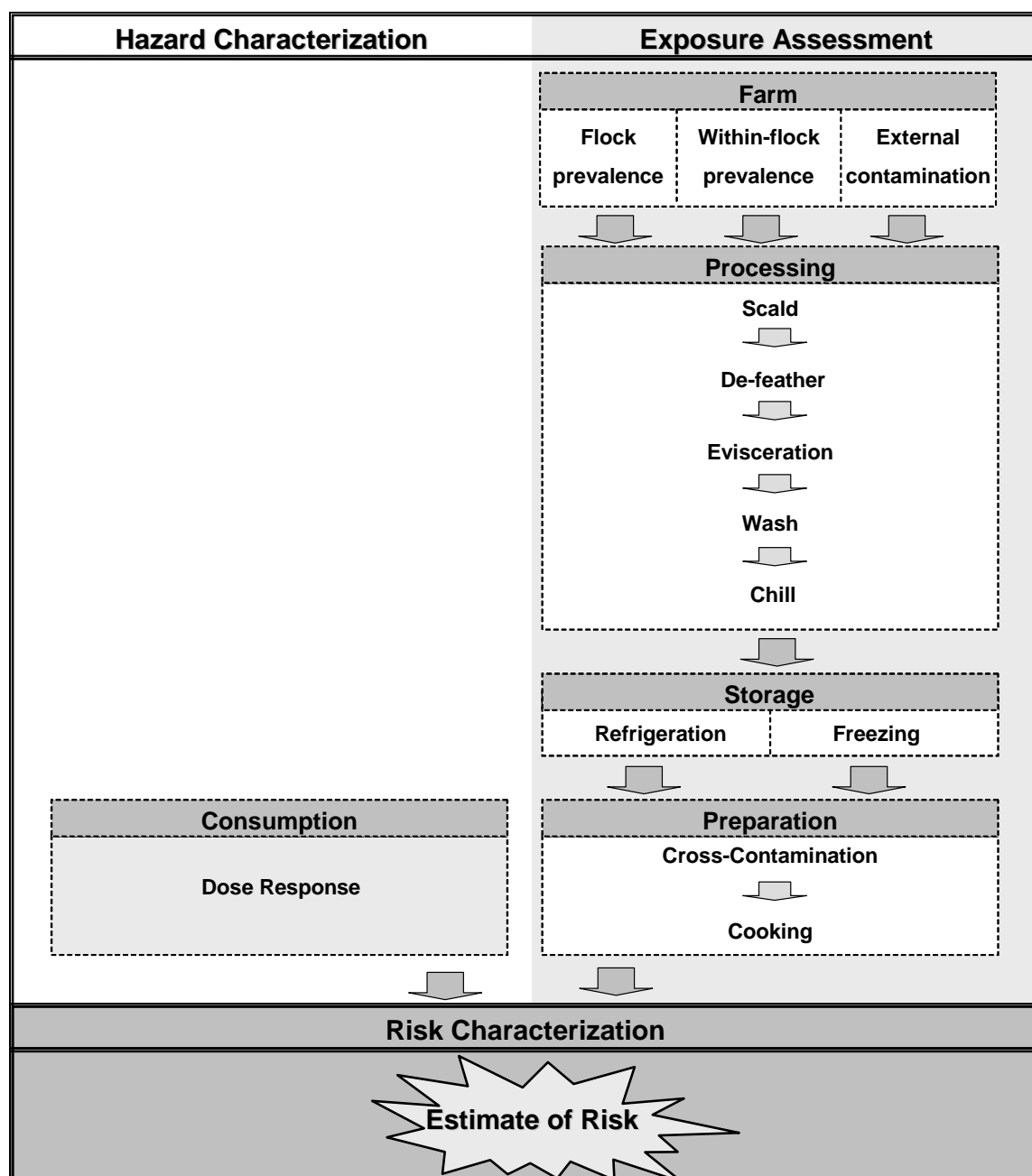


Figure 4A.1. Graphical representation of a *Campylobacter* in poultry exposure assessment. The model developed by FAO/WHO (2002b) begins at the end of the hazard characterization, the second step of risk assessment.

Model application

The FAO/WHO (2002b) risk model focuses on both fresh and frozen whole broilers prepared and consumed in the home and can be analysed using Monte Carlo simulation implemented with @RISK software.

Every iteration of the model tracks a randomly selected chicken from the farm, through processing, storage, preparation and cooking, to consumption, and the exposures that arise as a result of preparing that serving. In the model, chickens are probabilistically assigned to be either contaminated or not contaminated given the on-farm prevalence of *Campylobacter*. Chickens originating from negative and positive flocks are then

simultaneously simulated, the number of *Campylobacter* organisms present on the resulting product is estimated from statistical distributions based on reported data, and the changes in the level of contamination from farm to fork are modelled. The variability in these processes is described by probability distributions derived from published and unpublished data. In addition, the model also estimates the conversion of previously negative chickens into positive chickens as a result of cross-contamination, or vice versa.

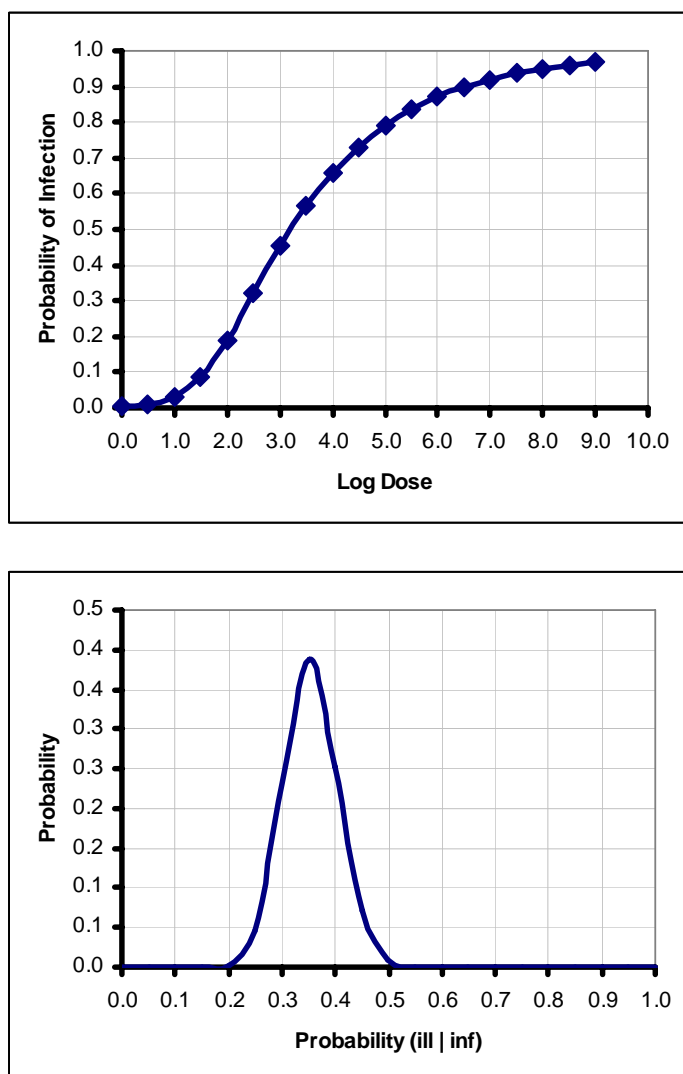


Figure 4A.2. FAO/WHO (2002b) dose–response model used to estimate the probability of infection upon exposure to *Campylobacter* and conditional probability of illness upon infection

Ultimately, the objective of the risk model is to translate pathogen contamination rates and levels, and their subsequent reductions as a result of an intervention, into a human health outcome. In order to do this using the existing model, some modifications were made. These modifications were primarily a simplification of the model to create a more efficient model that would still be appropriate for current purposes. Specifically, the FAO/WHO (2002b) model included detailed bird-by-bird contamination transfer at various stages of the processing plant with a very detailed and mechanistic model of the defeathering process, which tended to be very computationally expensive.

As the current project was primarily interested in the impact of chlorine on the contamination levels exiting the plant, and as the most frequent use of chlorine in the processing plant occurs during washing or chilling, both of which happen near the end of the process, the earlier processes were collapsed. The existing model was simulated for 10 000 iterations using an input value of 80% for on-farm prevalence with all other inputs at their default settings, and the resulting pre-washing prevalence and contamination distribution were estimated (Figure 4A.3). The concentration on carcasses originating from positive flocks was described using a normal distribution with a mean of 3.8 log cfu/carcass and standard deviation of 1.3 log cfu/carcass, whereas the concentration on carcasses originating from negative flocks was described with a normal distribution with a mean of 1.62 log cfu/carcass and a standard deviation of 1.3 log cfu/carcass. These distributions were then used as the starting point for all subsequent simulations used to estimate the effect of chlorine use on pathogen risk. In essence, the baseline model against which all results are compared is one for which the prevalence of *Campylobacter*-contaminated flocks on farms is 80%.

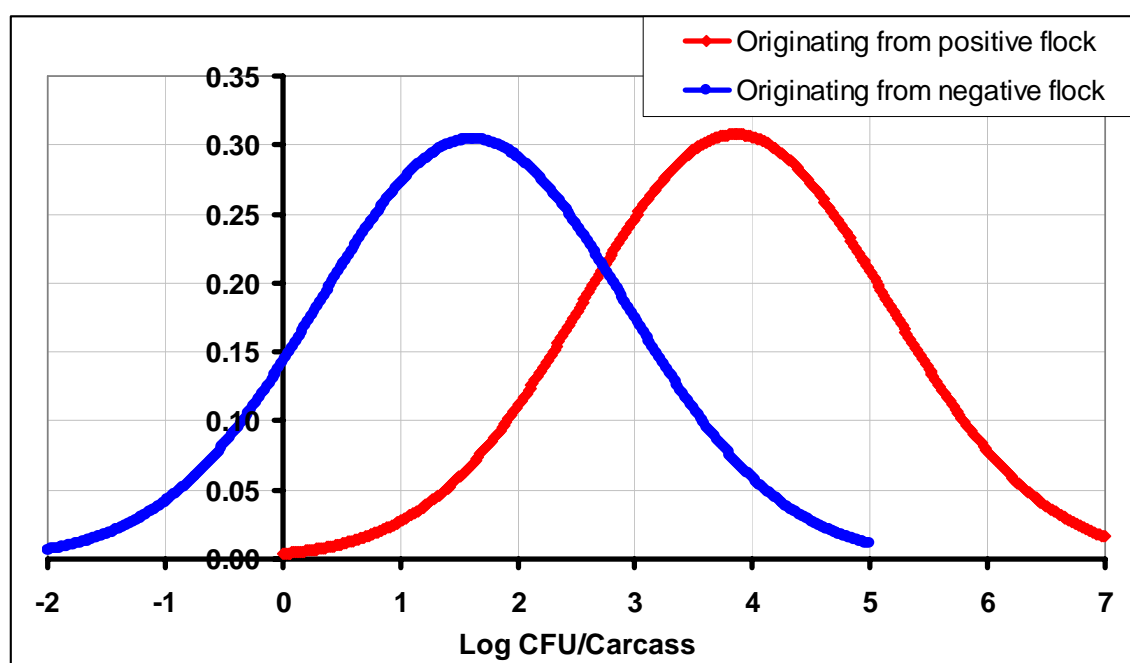


Figure 4A.3. Resulting distributions for contamination levels on chickens prior to washing used as inputs to the modified model

The impact of chlorine use during chicken processing and its subsequent estimated public health impact through the reduction of pathogen risk are presented in the following scenarios. The detailed quantitative data on the effect of chlorine on *Campylobacter* on poultry carcasses have been summarized previously in this chapter. The following scenarios are constructed based on a subset of the information in order to illustrate how pathogen reduction estimates, reported at various points in the process, can be translated into a common human health risk outcome.

Model scenarios

The following scenarios were constructed based on the data presented and applied to the modified risk model, in order to estimate the potential risk reduction as a result of the use of chlorine or other disinfectants in poultry processing.

Baseline scenario

The baseline scenario represents the risk estimates generated based on the current model without any additional steps to the described process. The baseline model, summarized graphically in Figure 4A.1, includes a washing step with plain water and a chilling step in water with no free chlorine.

1) Use of chlorine in an IOBW

As summarized previously, the primary effect from washing is the physical removal of contamination rather than a chemical decontamination effect. Northcutt et al. (2005) evaluated the effectiveness of a chlorine carcass wash in a study where poultry carcasses were inoculated with caecal material containing *Campylobacter*. Water at various temperatures with and without available chlorine at 50 mg/l was sprayed onto carcasses for 5 s with an IOBW. Neither water temperature nor chlorine level was found to have a statistically significant effect on the counts of *Campylobacter*. Although the effect was not statistically significant, the use of chlorine produced on average approximately 0.1 log greater reduction compared with just water alone. As this appendix is an illustrative exercise, we can assume that the effect of adding chlorine to the wash water could produce anywhere from no effect to a generous 0.1 log reduction.

2) Use of an ASC spray decontamination wash (based on Kere-Kemp et al., 2001; Bashor et al., 2004; Oyarzabal et al., 2004; Sexton et al., 2007)

This scenario estimates the effect of an additional decontamination step during processing that consists of the use of ASC at concentrations ranging from 600 to 1200 mg/l, resulting in log reductions from 0.9 to 3.8 log.

Most studies, particularly those conducted in the industrial setting, suffered from the lack of a control for the physical action of water alone as a spray or dip. However, evidence from a laboratory study that contained this control suggested that there was no significant effect on *Salmonella* (Arritt et al., 2002). Also, studies tended not to use IOBW or high-volume sprays, and therefore they would be less likely to exert a physical reduction effect.

3) Use of an alternative to chlorine-based disinfectant spray (based on Bashor et al., 2004)

This scenario estimates the impact on pathogen risk of using an alternative to chlorine-based disinfectant spray. The use of TSP (12% solution) was studied by Bashor et al. (2004) and was found to reduce *Campylobacter* by approximately 1 log when sprayed on carcasses for 15 s.

This study suffered from the lack of a control for the physical action of water alone as a spray or dip. However, evidence from a laboratory study that contained this control suggested that there was no significant effect on *Salmonella* (Arritt et al., 2002). Also, studies tended not to use IOBW or high-volume sprays, and therefore they would be less likely to exert a physical reduction effect.

4) The use of chlorine in the chill tank

This scenario is based on one used in the FAO/WHO (2002b) risk assessment model, which assumes that when there is sufficient free chlorine in the chill tank, the frequency with which cross-contamination occurs is reduced (50–75% of the time); when it does occur, the amount of cross-contamination is less (0–4 log without chlorine to 0–3 log with chlorine). This is supported by the results of Yang, Li & Johnson (2001) presented below, in which the use of chlorine in the chill tank had a very short D-value.

The data available from the literature search that are relevant to the use of chlorine in the chill tank and its impact on the load of *Campylobacter* on carcasses do not provide any directly usable information for incorporation into the risk model. Although various authors have shown that there is a reduction in the contamination levels on carcasses exiting the chill tank, there is no clear way to determine how much of an effect the use of water alone might have had. One study done by Yang, Li & Johnson (2001) using inoculated *Campylobacter* on chicken does provide some indication of the effect that chlorine has on carcass contamination levels. These authors found that the chilling of chicken in water containing chlorine at 50 mg/l had a D-value of 73 min for *Campylobacter* contamination on the chicken. In other words, it would take 73 min to produce a 1 log reduction on chicken carcasses immersed in chiller water containing chlorine at 50 mg/l. When these authors looked at chiller water with a higher amount of organic content (as might be expected as the processing operation continues), the D-value was increased to 344 min. Based on this study, the chilling of carcasses using chlorinated chiller water is unlikely to be a significant decontamination step.

The biggest potential impact from the use of chlorine in chill tanks is not necessarily from the reduction in contamination on already contaminated chickens, but the prevention of or reduction in cross-contamination from *Campylobacter* being deposited on either uncontaminated or previously very low level contaminated chicken.

Yang, Li & Johnson (2001) also conducted a study to look at reduction of *Campylobacter* in chiller water as a function of chlorine concentration. These results are presented in Table 4A.1.

Table 4A.1. Effect of chlorine concentration in chiller water on the survival of *Campylobacter* as a function of chlorine concentration and water age (organic material buildup)

Chemical	Concentration (mg/l)	Water age (h)	D-value (min)
Chlorine	10	0	17.2
Chlorine	30	0	1.3
Chlorine	50	0	0.5
Chlorine	10	8	113.6
Chlorine	30	8	15.2
Chlorine	50	8	6.0

These results indicate that *Campylobacter* can be rapidly deactivated in chlorinated chill tank water, provided the amount of free chlorine is sufficient to overcome the organic material that builds up during processing. At a concentration of 50 mg/l, we would expect 90% reductions in the water within 30 s, whereas this would get extended to about 6 min when the organic load increases. Continuous dosing to ensure a sufficient free chlorine concentration in the water would be required in order for the cross-contamination to be prevented, as evidenced by the fact that a chlorine concentration of 10 mg/l has a D-value of 17.2 min in 0-h-old water, whereas the D-value gets extended to 113.6 min in 8-h-old water.

The results from incorporating these scenarios into the model are presented in Table 4A.2.

Conclusions

It is difficult to determine the risk reduction achievable by the use of disinfectants and therefore the impact of these chemicals on public health. Models that estimate these effects, like the one used in this work, carry a high degree of uncertainty as a result of the lack of appropriate data.

Table 4A.2. Summary of model estimates of relative risk reduction

Scenario description	Mean risk estimate	Estimated reduction in risk (%)
Baseline: Fresh chicken produced without chlorine in either the chill tank or during washing	1.63E-03	–
Scenario 1: Use of an IOBW with chlorine at 50 mg/l	1.57E-03	4 ^a
Scenario 2: Use of ASC decontamination spray	4.82E-04	71 ^b
Scenario 3: Use of a chlorine alternative TSP decontamination spray	7.49E-04	54 ^b
Scenario 4: Use of chlorine in chill tank at concentration to ensure sufficient free chlorine	5.10E-04	69
Scenario 5: Combination of Scenarios 1 and 4 (chlorine in wash water and chill tank)	4.76E-04	71 ^{a,b}
Scenario 6: Combination of Scenarios 2 and 4 (ASC decontamination spray and chlorine in chill tank)	4.58E-05	97 ^b
Scenario 7: Combination of Scenarios 3 and 4 (TSP decontamination spray and chlorine in chill tank)	1.26E-04	92 ^b

^a Chlorine had no statistically significant additional effect compared with unchlorinated water alone. The effect was due to the physical action of washing.

^b It is important to recognize that these studies did not compare the effect of a carcass spray or dip with water alone against the effect when the chemical agent was used. As a result, the true additional effect of the disinfectant in the spray/dip water cannot be assessed.

The use of an IOBW can result in significant reductions in *Campylobacter* numbers; however, the addition of chlorine to the water has no real significant additional effect (Northcutt et al., 2005). The model estimates that if an allowance is given to assume up to 0.1 log additional reduction due to chlorine addition in the wash water, then this translates to a *Campylobacter* risk reduction of 4% compared with the baseline scenario. This upper range in risk reduction (benefit) would need to be carefully tempered with the potential additional risk from adding chlorine to the wash water. Specifically, is the questionable and minimal benefit greater than the corresponding risks that would be calculated?

When ASC is used as a disinfectant spray, this results in an estimated 71% reduction in the risk of campylobacteriosis. However, data are not available that allow the effect of the ASC to be disaggregated from the physical effect of spraying/dipping carcasses in water alone. However, data from other studies suggest that the removal of bacteria from carcasses by the physical action of water is minimal (e.g. Arritt et al., 2002) unless high-pressure, high-volume water is used, as in an IOBW (Northcutt et al., 2005). The use of a TSP spray-wash was estimated to result in a 54% reduction in mean risk of campylobacteriosis, although this estimate is also subject to caveats similar to those in the estimate with ASC discussed previously.

The use of chlorine as a disinfectant to remove *Campylobacter* from chill tank water and hence prevent cross-contamination resulted in an estimated mean risk reduction in campylobacteriosis of 69%. When combined with an ASC or TSP carcass wash, use of chlorine in the chill tank resulted in an estimated mean risk reduction in campylobacteriosis of 97% and 92%, respectively, subject to the caveat discussed previously for the ASC and TSP carcass wash scenario. The combination of IOBW carcass wash with carcass chilling in chlorinated water resulted in an estimated mean risk reduction in campylobacteriosis of 71%. The model therefore demonstrates the enhanced risk reduction that can be achieved by the use of multiple interventions in series during poultry processing.

5. UNINTENDED CONSEQUENCES

The primary intended benefits of disinfection processes are the reduction of microbial foodborne disease risk and the control of contamination of food by pathogenic and non-pathogenic microorganisms during food production and food processing. However, use of antimicrobial compounds in the food processing industry can have consequences other than those intended. These include the development of antimicrobial resistance, the disruption of normal microflora, and nutritional and organoleptic changes in treated foods. Studies on the nature of such unintended consequences are described in this chapter.

5.1 Development of antimicrobial resistance

Microorganisms exposed to sublethal concentrations of antimicrobial compounds may develop the ability to survive in the presence of normally lethal concentrations. As acquired resistance to one type of antimicrobial agent may confer protection against other types, the widespread use of biocides by the food industry has led to concern about its impact on the development of resistance to therapeutic drugs. Sanitizers used by the food industry inactivate microorganisms by reacting at multiple sites within the cell. Therefore, microorganisms cannot develop resistance to these agents through modification of a specific target site, as is the case for therapeutic antimicrobial compounds. However, there are reports of microorganisms developing tolerance to chemical sanitizers after sublethal exposure in the laboratory, and sanitizer-tolerant microorganisms have been isolated from processing plant environments (Meyer, 2006).

Active chlorine compounds and peroxides kill through oxidation brought about by the generation of free radicals. As multiple free radicals may be produced, their specific interactions with cell components are complex. The specific mechanism by which hypochlorous acid kills bacterial cells is still unknown (Mokgatia, Gouws & Brozel, 2002). As multiple components of the cell are susceptible to oxidative damage, tolerance to oxidative sanitizers is based on the ability of the cell to neutralize free radicals, counter the effects of oxidative damage and excrete polymers that inactivate the biocide before it reaches the cell. Mokgatia, Gouws & Brozel (2002) isolated a hypochlorous acid-tolerant strain of *Salmonella* from a poultry processing plant. The tolerance was related to increased catalase and membrane-bound dehydrogenase production and increased ability to repair deoxyribonucleic acid (DNA). Hypochlorous acid tolerance in *Listeria monocytogenes* induced by exposure to sublethal levels in the laboratory is associated with increased biofilm formation (Folsom & Frank, 2007). Cells within a biofilm are protected from inactivation by the production of exocellular polymers. Published research has not associated the development of tolerance to hypochlorous acid with the acquisition of resistance to therapeutic antimicrobial compounds.

More information is available on acquired tolerance to quaternary ammonium compounds (QACs) compared with chlorine tolerance, perhaps because microorganisms exhibiting this characteristic are more frequently isolated from processing plant environments than are microorganisms that tolerate active chlorine biocides. QACs inactivate bacteria by modifying the cell membrane, causing loss of control over permeability (Block, 2001). Mullapudi, Siletsky & Kathariou (2008) found a high prevalence (51–60% of isolates) of benzalkonium chloride-tolerant *L. monocytogenes* in turkey processing plants, whereas Aase et al. (2000) observed 10% prevalence in strains isolated from poultry processing

environments. Some strains of *L. monocytogenes* adapt to sublethal exposure to QACs through stimulation of proton motive force-dependent efflux (Aase et al., 2000). Mereghetti et al. (2000) found evidence that the efflux pump-associated QAC resistance gene is not plasmid-borne, but Romanova, Favrin & Griffiths (2002) concluded that the gene (*mdrL*) can be both plasmid and chromosomal. Mereghetti et al. (2000) also found evidence that QAC tolerance in *L. monocytogenes* is associated with modification to the cell wall, as did To et al. (2002). These modifications involve changes to surface antigens and cell membrane fatty acids. Lunden et al. (2003) observed that the adaptive response of *L. monocytogenes* to various processing plant biocides resulted in cross-protection towards related and unrelated biocides. There is little information on the public health implications of pathogens acquiring QAC tolerance. Mullapudi, Siletsky & Kathariou (2008) reported that an outbreak strain of *L. monocytogenes* exhibited tolerance to benzalkonium chloride. However, there is no evidence that QAC tolerance in pathogens is associated with resistance to therapeutic agents or otherwise increased public health risk. Meyer (2006) concluded that there is no need for rotational use of biocides in food processing facilities, as biocide-tolerant microorganisms isolated from these environments remain susceptible to recommended usage levels.

A recent report from the European Food Safety Authority (EFSA, 2008) assessed the possible effect of chlorine dioxide, acidified sodium chlorite (ASC), trisodium phosphate (TSP) and peroxyacids on the emergence of antimicrobial resistance. These biocides are widely used in the food industry as alternatives to hypochlorous acid-based biocides. This report concluded that there is no published information to indicate that the use of these substances to treat poultry carcasses would lead to the development of resistance to therapeutic antimicrobial compounds.

5.2 Disruption of normal microflora

The use of active chlorine in food processing water is targeted at preventing the spread of pathogenic microorganisms and reducing levels of pathogens on food and equipment. However, active chlorine exhibits nonspecific activity and therefore also reduces levels of normal microflora. Possible negative consequences of disruption of native microflora include a reduction of microbial competition, which might allow increased growth of pathogen, and an increase in shelf life, which would provide more time for pathogen growth before loss of sensory quality.

One example where an application of technology that increases shelf life has a demonstrated potential to increase public health risk is the use of modified atmosphere packaging (MAP) for fresh produce. Berrang, Brackett & Beuchat (1989) observed that the application of MAP for some vegetables does not slow the growth of *Listeria monocytogenes*; because of this, the increase in shelf life may result in greater public health risk. No information is available to indicate that increases in shelf life resulting from use of active chlorine in food processing provide the opportunity for additional pathogen growth. Unlike MAP, there is no evidence that the use of active chlorine alters the growth environment of the food, and, unlike MAP, the initial pathogen load in the produce may be reduced.

The possibility that reduced microbial competition to chlorine treatment could allow increased growth of pathogens should also be considered. Many fruits and vegetables are sufficiently acidic to provide yeasts and moulds a competitive growth advantage over pathogens. Growth of yeasts and moulds can increase the pH of the fruit or vegetable or degrade the cellular structure so that growth of pathogens is increased (Beuchat, 2002). Wells & Butterfield (1997) found that *Salmonella* was potentially present in 18–20% of 401 fresh fruit and vegetable samples affected by soft rot that were obtained at market, whereas only 9–

10% of 402 healthy samples were potentially positive for the pathogen. When they induced soft rot in carrot, pepper and potato, *Salmonella* growth increased 10-fold. Brandl (2008) observed that soft rot due to growth of *Erwinia chrysanthemi* enhanced growth of *Escherichia coli* O157:H7 on lettuce. However, others have isolated native microflora from fresh produce that inhibits growth of pathogens. For example, *Salmonella syringae* prevented growth of *E. coli* O157:H7 in apple wounds (Janisiewicz, Conway & Leverentz, 1999), and Liao & Fett (2001) found that 6 of 120 isolates from fresh produce were able to inhibit growth of at least one human pathogen. Current evidence indicates that native microflora that inhibits growth of pathogens on fresh produce is less common than native microflora that has either no effect or a growth-promoting effect on pathogens. There are no data indicating that the disruption of native microflora on fresh fruits and vegetables by washing in chlorinated water as practised in the food industry would enhance the growth or survival of pathogenic microflora in the commercial product.

Use of chlorinated water in poultry processing will reduce the population of both normal and pathogenic microflora on the carcass. Patterson (1968) investigated the consequences of this microflora disruption and found that the spoilage microflora of chicken carcasses washed with chlorine at 200 and 400 mg/l was similar to that of water-washed carcasses. He concluded that chlorine-treated carcasses posed no greater risk to public health as a result of microflora disruption. There are no data indicating that the disruption of native microflora on poultry carcasses by chlorine treatment as practised in the food industry would enhance the growth or survival of pathogenic bacteria.

5.3 Nutritional and organoleptic changes in treated foods

This section covers the unintended effects of chlorine-based disinfectants and other alternatives, such as peroxyacids or ozone, in food production and food processing, focusing on nutritional and organoleptic changes in treated foods.

5.3.1 Effects on nutritional quality of treated foods

Little information is available at present in the scientific literature on the effect of the use of disinfectants on the nutritional quality of muscle foods. Most of the published studies have been performed with vegetables, probably because of their high surface to volume ratio, which can potentially facilitate more intense effects on nutritional components.

5.3.1.1 Meat, poultry, fish and fishery products

Poultry carcasses treated with ASC under exaggerated conditions showed amino acid and fatty acid profiles similar to those of controls. Lipid peroxidation, measured as an increase in thiobarbituric acid reactive substances (TBARS), was observed in the skin but not in the muscle (EFSA, 2005). Poultry carcasses treated with peroxyacids showed no significant alteration in either TBARS or fatty acid profiles in raw or cooked samples (EFSA, 2005). Beef trimmings for production of ground beef treated with chlorine dioxide (200 mg/l solution) showed oxidation profiles, measured as TBARS, similar to those of controls (Jiménez-Villarreal et al., 2003a).

The effect of chlorine dioxide treatment (20, 40, 100 and 200 mg/l in 3.5% brine for 5 min) on nutrients was evaluated in salmon and red grouper (Kim et al., 1998). Treatment did not result in variation in composition of major nutrients (protein and lipid) or moisture content, but decreased the concentrations of some vitamins. Red grouper had a higher initial

content of thiamine and riboflavin compared with salmon, and the relative effects were also more pronounced. The reduction in thiamine content for both fishes appeared to be dose related and reached almost 60% at 200 mg/l. Red grouper and salmon showed a reduction in riboflavin content (more than 30% and 15%, respectively). Niacin content did not correlate to the concentration of chlorine dioxide, and the mineral content was unaffected by the chlorine dioxide treatment (Kim et al., 1998).

5.3.1.2 Fresh fruits and vegetables

The content of L-ascorbic acid in shredded cabbage treated with hypochlorite (200 µg/l) was reduced by 30% (Sawai et al., 2001). Reduced concentrations of vitamin C (36%) and β -carotene (56%) were noted for fresh-cut iceberg lettuce treated with chlorine (dipped in 100 mg/ml chlorine solution at 20 °C for 2 min, pH 8.6) after 12 days of storage (Akbas & Ölmez, 2007). However, there were similar reductions in controls. Chlorine treatment (100 mg/l, pH 6.5) of rocket (arugula) leaves reduced vitamin C content by around 15% and 20% after 12 days of storage under air or MAP, respectively, in comparison with water-treated controls. The content of total polyphenols was not affected, but the total glucosinolate content was halved in treated produce after a 12-day storage under MAP (Martínez-Sánchez et al., 2006). Shredded carrots washed with chlorinated water (free chlorine at 100 mg/l) showed a 20% decrease in sugars, especially sucrose, probably due to leaching (Klaiber et al., 2004).

Shredded carrots were washed with ASC (100 mg/l at pH 2.71, 250 mg/l at pH 2.55 and 500 mg/l at pH 2.47) and stored up to 21 days at 5 °C. Other sanitizers included in the study were sodium hypochlorite (200 mg/l at pH 6.5) and peroxyacetic acid (40 mg/l at pH 3.72) (Ruiz-Cruz et al., 2007). In general, all sanitizers tended to retain antioxidant capacity. The shredded carrots washed with ASC at 250 mg/l and pH 2.55 showed a higher retention of antioxidant capacity than controls during the storage at 5 °C, which may be due to the retention of phenolic and flavonoid compounds and also carotenes. In fact, the reduction of carotenes was lower in treated produce compared with controls washed with water. The treatment also reduced the activity of peroxidase, and this may explain the observed control of whitening and maintenance of firmness in treated carrots (Ruiz-Cruz et al., 2007). In rocket (arugula) leaves washed with ASC at 250 mg/l and pH 2.63 (stored 8 and 12 days at 4 °C), no difference in vitamin C content compared with controls washed with water was reported after 8 days of storage under air or MAP. After 12 days of MAP storage, a 45% decrease in vitamin C content was noted in treated produce in comparison with controls (Martínez-Sánchez et al., 2006). Storage under MAP reduced the content of total polyphenols (more markedly than controls), mainly due to acylated flavonoid glycoside degradation. The total glucosinolate content was significantly reduced in ASC-treated leaves after 5 days of storage under MAP in comparison with the controls (Martínez-Sánchez et al., 2006).

Treatments with ozone or peroxyacids generate very reactive oxygen species that are potentially able to react with food components, such as amino acids (histidine, tryptophan, cysteine, cystine and methionine), vitamins (β -carotene, riboflavin, ascorbic acid, vitamin D and tocopherols), lipids (unsaturated fatty acids), sugars (glucose, fructose, sucrose and maltose) (Choe & Min, 2006) and even cell wall polysaccharides. However, it must be taken into account that while these treatments are strongly oxidative, they are limited to the external surface of the food, so that any expected effect on such nutrients would be restricted mainly to those located on the surface. Significant losses of vitamin C and β -carotene (30% and 55%, respectively) have been reported after 18 days of storage of fresh iceberg lettuce initially treated with ozone (4 mg/l for 2 min), but similar effects were seen in controls (Akbas & Ölmez, 2007). The vitamin C content of ozone-treated (up to 0.18 mg/l for 5 min) fresh-cut

celery was higher after 3, 6 and 9 days of refrigerated storage than those in controls (Zhang et al., 2005). In the same study, a decrease of total sugars was reported with time of storage, but there was no difference in relation to the control. Rocket (arugula) leaves washed with ozonated water (10 mg/l) or peroxyacetic acid solution (300 mg/l) showed reduced vitamin C content with storage—about 28% and 12%, respectively, when stored for 12 days under air, and about 40% and 30%, respectively, when stored for 12 days under MAP (Martínez-Sánchez et al., 2006). Peroxyacid treatment reduced the total glucosinolate content by 30% and 60% after 8 and 12 days, respectively, under MAP, but did not affect the total polyphenols content (Martínez-Sánchez et al., 2006). Ozone treatment reduced the total glucosinolate content by 55% and total polyphenolic content by 25% after 8 days' storage under MAP (Martínez-Sánchez et al., 2006). Treatment of fresh-cut tomatoes with hydrogen peroxide (dipping in up to 0.4 mol/l hydrogen peroxide solutions for 1 min) resulted in reduced phenolic and antioxidant levels (11% and 31%, respectively, in comparison with controls) after 7 days of storage at 4–6 °C. Reductions in vitamin C and lycopene contents were also reported, about 20% and 10%, respectively, at 1 day of storage, but the differences compared with controls were almost negligible after 7 days of refrigerated storage (Kim, Luo & Tao, 2007).

The use of disinfectants under typical conditions—hydrogen peroxide (5% for 30 min), hypochlorite (500 mg/l at pH 7.6 for 30 min), aqueous-phase ozone (8 mg/l for 30 min) and gaseous ozone (40 mg/l for 60 min)—resulted in significant losses of biothiols in vegetables (Qiang et al., 2005). These thiols are antioxidants and may act as such once consumed. This finding is important, as biothiols are present inside the vegetables. A hypothesis is that antioxidants near the surface have been previously oxidized, and therefore further oxidation can take place. The assayed biothiols were reduced glutathione, *N*-acetyl-L-cysteine, captopril, cysteine, homocysteine, γ -L-glutamyl-L-cysteine and oxidized glutathione. The effect and extent of the losses were dependent on the disinfectant and type of vegetable (Qiang et al., 2005). Higher losses were noted for all analysed biothiols in spinach, especially after peroxide treatment, with 70% biothiol reduction. Around 50% losses were reported after ozone and free chlorine treatments. Around 60–70% of the reduced glutathione was oxidized in red pepper. Reduction of *N*-acetyl-L-cysteine in cucumber was around 30% for all treatments. Smaller effects were reported in green beans and asparagus (Qiang et al., 2005).

5.3.2 Effects on organoleptic quality of treated foods

5.3.2.1 Meat and poultry

Meat treated with chlorinated water has been reported to increase more in weight than meat treated with non-chlorinated water (Cunningham & Lawrence, 1977). Also, chicken skin absorbed more water (130% in weight after 2 h in chlorinated water) than lean meat or fat.

Poultry carcasses were exposed to a chiller bath with chlorinated water (hypochlorous acid at 18 mg/l). Light (breast) and dark (leg/thigh) meats were removed and minced. Minces of patties were baked at 177 °C for 25 min. After cooling, patties were stored for 0, 1, 2 and 3 days under refrigeration and reheated at 177 °C for 20 min. Dark patties (from leg/thigh) did not show any difference for any of the sensory attributes in relation to the controls. Warmed-over flavour notes were observed in cooked chlorinated and non-chlorinated light patties (from breast); these off-flavours were higher for non-chlorinated samples till day 2, but after 2 days, off-flavours increased rapidly in chlorinated samples during storage and were significantly higher than in non-chlorinated samples (Erickson, 1999). The reason may

be the slowing down of initiation reactions for warmed-over flavour. In summary, chlorination did not affect the flavour of cooked, reheated dark chicken patties but had effects on light chicken patties consisting of a delay of warmed-over flavour up to 2 days of storage but an opposite effect after 3 days (Erickson, 1999). Concentrations of chlorine up to 200 mg/l have not been reported to cause an adverse effect on the appearance, taste or odour of the meat (SCVPH, 1998).

The use of chlorine dioxide (USDA, 2002a), ASC (USDA, 2002b) or peroxyacids (USDA, 2002c) as respective antimicrobial agents in poultry process water, under the prescribed and controlled conditions of use, have been reported to not alter the sensory properties of poultry. Some slight effects have been reported, such as a change in the colour of chicken breast skin from pinkish-white to greyish-white, but with no effect (no off-flavours) upon oven cooking (Thiessen, Usborne & Orr, 1984). Slight bleaching was also reported on the surface of turkey carcasses after chlorine dioxide treatment (Villarreal, Baker & Regenstein, 1990).

ASC treatments (1200 mg/l for 5 s) in the form of dips or sprays on the surface of dressed broilers were reported not to affect water holding capacity, appearance, smell, tenderness or overall acceptability (Sinhamahapatra et al., 2004). However, in another study in which chicken legs were treated with ASC (dipping into 1200 mg/l ASC solution, pH 2.7, for 15 min at 18 °C), legs turned slightly whiter initially, but no differences in smell or overall acceptability were found (Del Río et al., 2007). In the same study, it was reported that sensory quality (colour, smell and general acceptability) was improved in relation to the controls when the legs were stored at 3 °C for up to 5 days. A mild transitory whitening of the poultry skin after ASC treatment (1200 mg/l) has been also reported (Kemp, Aldrich & Waldroup, 2000). ASC treatment (300 mg/l) also maintained the organoleptic quality (colour, odour and taste) of raw ground beef, even in the cooked product. In both cases, the analysis was performed at 5, 8 and 12 days after the initial treatment; however, a more intense ASC treatment (600 mg/l) had a significant effect ($P < 0.05$) on raw and cooked ground beef, giving worse colour and odour in relation to the control (Bosilevac et al., 2004).

Beef trimmings were treated with chlorine dioxide (200 mg/l). The prepared ground beef had colour parameters (L , a and b), pH, TBARS, beef odour and off-odours similar to those of controls and followed the same trend up to 7 days' display (Jiménez-Villarreal et al., 2003a). When preparing ground beef patties, similar results were observed, except a little worse off-odour and better juiciness in the chlorine dioxide-treated beef trimmings (Jiménez-Villarreal et al., 2003b).

Peroxyacids can exert some slight whitening on poultry carcass surface that can be reverted after 24 h. Acids were reported to accumulate in the skin, affecting odour and flavour, such as a vinegar-like odour when peroxyacetic acid was used (SCVPH, 2003). However, chicken legs treated with peroxyacids (dipping into 220 mg/l peroxyacid solution, pH 3.75, for 15 min at 18 °C) did not show significant sensory differences compared with the untreated legs in terms of colour, smell or overall acceptability (Del Río et al., 2007).

Chicken legs treated with TSP at concentrations below 10% did not produce noticeable off-flavours or discoloration. So, chicken legs treated with TSP (dipping into 12% weight by volume TSP solution, pH 13.0, for 15 min at 18 °C) did not show significant sensory differences, or were even better after 5 days of storage at 3 °C, compared with the untreated legs in terms of colour, smell or overall acceptability (Del Río et al., 2007). However, chicken legs treated with higher concentrations had a detectable chemical odour and showed darker, less red and less yellow legs compared with untreated legs (Kim et al., 1999a).

5.3.2.2 Fish and fishery products

ASC treatment of salmon fillets (dipping in ASC at >100 mg/l, pH 3.24, for 1 min) resulted in a visible loss of colour. A similar change happened with another ASC treatment (50 mg/l, pH 3.29, for 2 min) that produced a very apparent change of colour, which would result in rejection by consumers. However, a reduction of the treatment to just 1 min did not result in a visible change of colour, even though the treated ASC solution had a light pink colour combined with a small degree of turbidity (Su & Morrissey, 2003).

Chlorine dioxide treatment of sea scallops did not show discernible effects until the scallops were exposed to concentrations above 3.8 mg/l for more than 10 min. Development of slime and loss of surface sheen were then noticeable, giving the product a drier appearance. Also, seepage about the product was evident (Kim et al., 1999b). Fillets of mahi-mahi experienced changes in colour from the preferred ruby-red to darker reddish brown. A bleaching effect was noticed at chlorine dioxide concentrations of 7.6 mg/l or higher, but was judged still acceptable. Chlorine dioxide treatment of shrimps did not cause discernible effects for the first 2 days of storage, and appearance was even better than control between 2 and 5 days. The exposure of shell-on shrimp to chlorine dioxide did not influence the sensory attributes. For all these treatments, the solutions experienced noticeable changes of colour, which were attributed to the formation of chlorinated reaction products (Kim et al., 1999b).

5.3.2.3 Fresh fruits and vegetables

Processing of vegetables, especially physical stress during cutting procedures, creates wound signals. These may elicit physiological and biochemical reactions in tissues (adjacent and distant). These changes may be varied and can contribute to the accumulation of phenolic compounds that may serve as substrates to polyphenol oxidase and peroxidase, resulting in ortho-quinones that in turn can polymerize and form brown pigments (Baur et al., 2004a). Browning is one of the major causes of loss of quality in cut vegetables. Another important quality factor is the decrease in firmness and loss of integrity (Rico et al., 2006).

Phenolic metabolism may be affected by washings with sanitizers. Washing of shredded lettuce with chlorinated water (free chlorine at 100–200 mg/l) significantly reduced the activity of phenylalanine ammonia-lyase. The visual quality, the cut edge vascular tissue browning and favourable aroma preservation during 7 days of storage of shredded iceberg lettuces washed with chlorinated water were reported as better than when using tap water or ozone for washings. In this study, no off-odours or off-flavours caused by chlorine were perceived by the test panel (Baur et al., 2004b). Fresh-cut iceberg lettuce samples treated with chlorine (dipping in 100 mg/ml chlorine solution at 20 °C for 2 min, pH 8.6) or ozone (4 mg/l) did not reveal initial changes in colour, texture or moisture. Colour reduction followed a similar trend for all treatments as for the untreated samples during the 12 days of storage at 4 °C. Reported changes consisted of increases in *a* value (loss of green pigment), decreases in *b* value (loss of yellowness) and decreases in *L* value (lightness), which might be caused by phenolic oxidation or bacterial spoilage. No changes in texture and moisture were reported (Akbas & Ölmez, 2007). Sequential washes of sliced green bell peppers with chlorinated water (100 µg/l) produced a significant reduction in acetaldehyde, soluble solids (mostly sugars) and total phenols in relation to the non-washed controls (Toivonen & Stan, 2004). However, firmness retention was improved in washed slices, this being attributed to the removal of stress-related compounds produced during the cutting operation.

Fresh cilantro bunches were washed with 1-methylcyclopropene at 1.5 mg/l and then cut and washed for 1 min in either sodium hypochlorite (100 mg/l) or ASC (100 mg/l), dried, packaged and stored for up to 14 days. The control samples washed with water showed the

lowest quality score and high levels of yellowing. In contrast, samples washed with sanitizers had no off-odour and had higher colour score, near the initial green, and fresh appearance, with no yellowing or dehydration (Kim et al., 2007).

Apple slices treated with ASC (1.5–6 g/l dipped for 1 min) showed a smaller decrease in lightness (*L*) when stored for up to 24 h at 20 °C, indicating that treated slices showed significantly less browning than the water-treated control (Lu et al., 2007). However, this effect was not observed when the storage was prolonged to 14 days. Rocket (arugula) leaves washed with ASC (250 mg/l) and stored under air or under low oxygen and high carbon dioxide (MAP) were reported to keep a sensory quality (colour and visual quality) similar to that of controls washed with water (Martínez-Sánchez et al., 2006). ASC treatments (250 mg/l, pH 2.55, and 500 mg/l, pH 2.47) of shredded carrots and storage for up to 21 days at 5 °C showed a control of whitening and firmness maintenance (Ruiz-Cruz et al., 2007). ASC treatment of fermented Chinese cabbage (500 mg/l ASC pre-wash for 15 min) did not significantly influence the sensory (colour, odour, taste and texture) parameters analysed (Inatsu et al., 2005).

Chlorine dioxide treatment has been reported to cause browning of lettuce and cabbage attributed to oxidation of phenols by polyphenol oxidase (Sy et al., 2005), even though this enzyme appears to be inactivated by chlorine dioxide in apples (Fu et al., 2007). Gaseous chlorine dioxide was evaluated for its effectiveness to extend the shelf life of minimally processed lettuce and cabbage previously immersed in a cysteine solution to inhibit browning from occurring during chlorine dioxide treatment (Gómez-López et al., 2008). Chlorine dioxide treatment did not affect the respiration rate of iceberg lettuce but enhanced the respiration rate of cabbage. This change could be due to modifications of the metabolism of the tissue, probably due to oxidation of plant constituents. The previous addition of cysteine was effective in avoiding the development of brown pigments. Treated lettuce stored for 4 days at 7 °C under MAP showed higher off-odour and bad flavour above the acceptability limit as well as surface browning. Treated cabbage stored under similar conditions did not show variations in relation to controls and remained sensorily acceptable until 9 days of storage. However, practical application of cysteine before chlorine dioxide treatment is impaired due to its effect on the decontamination efficacy of chlorine dioxide (Gómez-López et al., 2008). Other authors have also observed significant discoloration of lettuce leaves after treatment with chlorine dioxide gas (0.5 mg/l for 2 min) in comparison with control samples at 0 days. The yellow-green colour changed to white-brown, and the *a* value (green to redness) increased for most treated samples. This effect was enhanced at higher concentrations of chlorine dioxide (0.5 mg/l for 10 min or 5 mg/l for 2 or 10 min) (Mahmoud & Linton, 2008). Significant discoloration of lettuce leaves was also reported at concentrations of chlorine dioxide higher than 0.2 mg/l for 60 min (D'Lima & Linton, 2002).

Several types of berries treated with chlorine dioxide gas (4.1 mg/l for 30 min and stored for up to 10 days at 8 °C) did not show significant changes in sensory quality (Sy, McWatters & Beuchat, 2005). Appearance, colour, aroma and overall quality of control and treated blueberries were not significantly different at day 0, and reductions in values were also similar during storage. The sensory attributes of treated strawberries and raspberries were significantly lower than controls at day 0. Sensory quality decreased during storage, but no differences were observed between treated and untreated samples. Initial bleached spots observed in treated samples of strawberries at day 0 were not evident after storage (Sy, McWatters & Beuchat, 2005).

Fresh-cut vegetables (cabbage, carrot and lettuce) treated with chlorine dioxide (1.4 mg/l for 10.5 min and then stored at 10 °C for 10 days) showed significant adverse changes in sensory quality (appearance, colour, aroma and overall quality) after 3 days of storage, particularly for lettuce leaves (Sy et al., 2005). Sensory quality also decreased during

further storage, but no differences were observed between treated and untreated samples, with some exceptions: treated fresh-cut carrots showed slight whitening in colour and significant adverse effects for all tested parameters, whereas fresh-cut lettuce showed slight brown discoloration and fresh-cut cabbage showed increased brown discoloration. In contrast, carrots treated with gaseous chlorine dioxide (1.3 mg/l at 28 °C for 6 min) and stored under MAP did not show significant sensory effects compared with the untreated samples (Gómez-López et al., 2007). Lettuce leaves treated with chlorine dioxide gas (for 30 min, 1 h and 3 h) did not show any visible difference in visual quality compared with the untreated control lettuce after 18 days of storage at 4 °C (Lee, Costello & Kang, 2004).

Various fruits (apple, tomato, onion and peach) were treated with chlorine dioxide gas (1.4 mg/l for 6 min) and stored at 21 °C for 10 days (tomatoes and peaches), 31 days (onions) and 41 days (apples) (Sy et al., 2005). Sensory quality (appearance, colour, aroma and overall quality) of peaches was significantly adversely affected by the treatment, which was evident even at 0 days; the quality of treated peach deteriorated very rapidly and markedly, so that the scores were unacceptable at 3 days. No significant differences were observed for tomatoes (even a trend towards better scores) or onions. Apples showed significant adverse effects of treatment for appearance, colour and overall quality after 9 days (Sy et al., 2005). Carrots treated with chlorine dioxide gas (1.3 mg/l at 1 min) and then stored under MAP at 7 °C for 8 days did not show significant differences compared with untreated carrots (Gómez-López et al., 2007). After 7 days, treated samples were unacceptable due to odour. In this case, no whitening was reported, in contrast to the results reported by Sy et al. (2005).

Potato strips were washed with several sanitizers and then either vacuum packaged or kept under adequate MAP, with the exception of samples treated with hypochlorite, and stored for 14 days at 4 °C. The treatments consisted of total chlorine (80 mg/l, adjusted to pH 6.5, from 10% sodium hypochlorite), sodium sulfite (2 g/l), peroxyacetic acid (300 mg/l), total ozone dose (20 mg/l, pH 7.5), and total ozone dose + peroxyacetic acid (20 mg/l + 300 mg/l, respectively) (Beltrán et al., 2005a). The respiratory activity was similar for all the treatments. Neither of the washing treatments resulted in browning promotion at 0 days. After 5 days, a moderate degree of browning was observed in peroxyacetic acid-treated and MAP-packaged samples. Only sodium sulfite-treated samples kept the initial visual appearance; the treatment controlled the browning at 5 days but produced off-odours. Fresh-cut potatoes treated with ozone, sodium sulfite and ozone-peroxyacetic acid and kept under vacuum had good results, with no browning and with full typical aroma and turgid texture. On the contrary, hypochlorite-treated potatoes gave some browning at 5 days. Vacuum packaging preserved the appearance better than MAP. Tomato slices treated with hydrogen peroxide (up to 0.4 mol/l for 1 min and stored up to 7 days at 4 °C) exhibited reduced red colour (Kim, Luo & Tao, 2007). Rocket (arugula) leaves were washed with various sanitizers (chlorine at 100 mg/l at pH 6.5, ASC at 250 mg/l at pH 2.6, lactic acid at 20 ml/l, ozone at 10 mg/l and peroxyacetic acid at 300 mg/l) and then stored at 4 °C under air or MAP (Martínez-Sánchez et al., 2006). Lactic acid treatment was detrimental to sensory quality. The visual quality, texture and freshness decreased during storage in a similar pattern as for the other assayed sanitizers, even though MAP storage generally gave significantly worse results. No off-odours were detected in any treatment.

Gaseous ozone treatment (21 400 mg/m³ for 30 min) did not affect the global sensory quality (visual quality, colour, translucency and soluble solids content) of fresh-cut cantaloupe melon after 8 days of storage under MAP at 5 °C; only aroma and firmness were slightly affected (Selma et al., 2008). Ozone-treated carrots showed a lighter (higher *L* values) and less intense (lower chromatic values) colour than control carrots. These effects increased with the ozone concentration (Liew & Prange, 1994). Other authors who have studied the effect of pre-washing of carrots with either chlorinated water (free chlorine at 200

mg/l for uncut and 100 mg/l for shredded carrot) or ozonated water (1.3 mg/l for uncut carrots) did not report significant sensory effects (colour, odour, texture or sweetness) (Klaiber et al., 2004). The authors reported a significant reduction in sweetness only for the shredded carrots treated with chlorinated water (free chlorine at 100 mg/l) as a consequence of about 20% loss of sugars due to sugar leaching caused by washing of the shredded carrots. The flavour of the carrots was also reported to be reduced. Fresh-cut lettuce treated with ozone showed excellent visual quality during storage, with no browning (Beltrán et al., 2005b).

In asparagus, some enzymes, such as phenylalanine ammonia-lyase and peroxidases, control lignification, which in turn is related to the toughening that occurs a few days after harvest and is a major factor for the determination of the spear quality. Ozone treatment (1 mg/l for 30 min) of fresh-cut green asparagus partially inhibited enzyme activity, and the levels of lignin, cellulose and hemicellulose, which play important roles in the texture attributes of the asparagus cell walls, increased at a slower rate than controls (An, Zhang & Lu, 2007). Polyphenol oxidase was partially inhibited by ozone treatment (up to 0.18 mg/l for 5 min), showing a concentration dependence in fresh-cut celery. The sensory quality (colour, visible structural integrity and general appearance) was reported to be better in ozone-treated celeries than in non-treated controls (Zhang et al., 2005). Polyphenol oxidase and pectin methylesterase activities in fresh-cut lettuce were also partially inhibited by ozone treatment (1 mg/l for 1 min and subsequent refrigerated storage for 10 days). The reduction of the methylesterase activity gave some negative effect on texture, as it was correlated with a lower crispness, whereas the fresh appearance was rated similar to the initial values until 7 days of storage (Rico et al., 2006). Fresh-cut salads consisting of chopped lettuce, shredded carrots and red cabbage were treated with ozone (2.5 mg/l for 10 min) or chlorine (100 mg/l as free chlorine for 10 min), and packages were kept under refrigeration for up to 25 days. Visual evaluation by a test panel reported browning, loss of integrity and overall poor appearance after 16 days in chlorine-treated salads. Ozone-treated salads showed slower degradation, with acceptable values at 21 days (García, Mount & Davidson, 2003).

5.4 Summary of findings

The nutrient contents and sensory quality of foods may be affected by treatments with disinfectants, even though the consequences show a large variability and to some extent contradictory results. The effects depend mainly on the type of food and mode of preparation, the type of sanitizer and conditions of the treatment (concentration, pH, time, temperature, full procedure), washing procedures and storage conditions (type of package, film permeability, time, temperature). In view of so many variables involved, recommendations should be given on a case-by-case basis.

Nutritional effects appear to be mainly focused on some vitamins (β -carotene, riboflavin, thiamine, ascorbic acid and tocopherols) and thiols (reduced and oxidized glutathione, captopril, *N*-acetyl-L-cysteine, γ -L-glutamyl-L-cysteine) that are particularly sensitive, especially in fruits and vegetables. Chlorine, ozone and peroxyacetic acid appear to be the most damaging for such vitamins and important antioxidant thiols. Some losses of sugars have also been reported after treatment with chlorine. Reductions of total polyphenols and glucosinolates have been reported during storage after the sanitizer treatment of vegetables.

Sensory quality, particularly colour, may be affected, depending on the intensity of the treatment. Some whitening in muscle foods and discoloration (browning) in vegetables and fruits have been reported. Even though there are some contradictory results in the

literature, the general trend shows that ASC and ozone treatments appear to keep and even improve the sensory quality during storage of fruits and vegetables, whereas chlorine dioxide and peroxyacids appear to be ineffective in preventing brown discoloration caused by phenolic oxidation, or even promote it. Off-odours may be detected during storage after specific treatment conditions for some sanitizers.

5.5 References

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6. RISK–BENEFIT ASSESSMENT

6.1 Introduction

Risk–benefit assessment can be defined as an activity that weighs the probability and severity of harm in a particular exposure scenario against the probability and magnitude of benefit as a basis for risk management decisions and communication to the public. Risk–benefit assessment can be performed to inform policy-makers, regulatory authorities and risk managers or consumers. The request for risk–benefit assessment must be unequivocally formulated, preferably in a dialogue between manager and assessor.

Risk–benefit assessment integrates the results of two separate activities: risk assessment and benefit assessment. Definitions and procedures for risk assessment have been well established in the scientific literature and in procedures adopted by international bodies, such as the Codex Alimentarius Commission. Similar definitions are not available for benefit assessment, but it is recommended that benefit assessment follows the same steps as risk assessment (e.g. EFSA, 2006). A general approach to risk–benefit assessment can be proposed (Table 6.1).

Table 6.1. General approach to risk–benefit assessment

Risk	Benefit
Hazard identification	Positive health effect identification ^a
Hazard characterization	Positive health effect characterization ^a
Exposure assessment	Exposure assessment
Risk characterization	Benefit characterization
Risk–benefit assessment	

^a A positive health effect (benefit) may also result from an intervention that leads to the reduction of the level of a hazard in food (i.e. a reduction in risk).

Risks and benefits should be assessed similarly and separately and for different population groups if necessary. The presentation of the results (risk characterization, benefit characterization, risk–benefit assessment) can be descriptive, semiquantitative or—if sufficient data are available—quantitative. Weighing of benefits against risks needs to take into account the time frame in which the effects become apparent and the severity and/or magnitude of these effects.

6.2 Current activities relating to risk–benefit analysis

Risk–benefit assessment is an actively developing field. Published studies have considered the risks and benefits associated with fish consumption (Ponce et al., 2000; FSA, 2004; Tuomisto et al., 2004; Cohen et al., 2005; Foran et al., 2005; Gochfeld & Burger, 2005; Hansen & Gilman, 2005; Verbeke et al., 2005; Norwegian Scientific Committee for Food Safety, 2006; Maycock & Benford, 2007), the risks and benefits of increased dietary exposure to folic acid (Lawrence, 2005; FSANZ, 2006; Hoekstra et al., 2007) and micronutrients (Renwick et al., 2004; Keijer et al., 2005; Shenkin, 2006).

The European Food Safety Authority (EFSA) Scientific Committee is preparing guidelines, and several European Union projects are ongoing: HiWATE (Health Impacts of Long-Term Exposure to Disinfection By-Products in Drinking Water; <http://www.hiwate.eu/>), INTARESE (Integrated Assessment of Health Risk of Environmental Stressors in Europe; <http://www.intarese.org/>), BENERIS (Benefit–Risk Assessment for Food: an Iterative Value-of-Information Approach; <http://www.beneris.eu/>), QALIBRA (Quality of life – integrated benefit and risk analysis; <http://www.qalibra.eu/>) and BRAFO (Benefit–Risk Analysis for Foods; <http://www.brafo.org/brafo/>). These projects study different aspects of risk–benefit analysis.

Only one published study on risk–benefit assessment of disinfectants was available. Havelaar et al. (2000) compared the risks of bromate formation due to ozonation of drinking-water with the benefits of reducing the concentration of viable *Cryptosporidium parvum*. Disability-adjusted life years (DALYs)—a metric that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health—were used to quantify the risks and benefits, and it was concluded that the health benefits of preventing gastroenteritis in the general population and premature death in patients with acquired immunodeficiency syndrome outweighed health losses by premature death from renal cell cancer. The application of DALYs in principle allowed a more explicit comparison of the public health risks and benefits of different management options. In practice, the application of DALYs was hampered by a substantial degree of uncertainty. The methodology used by Havelaar et al. (2000) was applied to optimize the ozone dosage in a drinking-water plant near Paris, France (Dilé-Mary et al., 2002).

6.3 Evaluation of the risks and benefits of disinfectants used in food production and processing

In the case of chlorine-based disinfectants used in food production and processing, there may be several benefits. From a public health perspective, the reduced exposure to pathogens is the key benefit. Other benefits, such as longer shelf life, are not considered here. The key potential risks are related to the increased exposure to chemical residues. Other potential risks, such as reduced consumer acceptance, are not considered in this assessment. Similar potential risks and benefits apply to other non-chlorine-containing chemical disinfectants, such as peroxyacetic acid.

Foodborne diseases are an important cause of morbidity and mortality worldwide, but the full extent and cost of unsafe food, and especially the burden arising from chemical and parasitic contaminants in food, are currently still unknown. Recently, the World Health Organization (WHO) has established the Foodborne Disease Burden Epidemiology Reference Group, which engages in estimating the global burden of foodborne illness using summary health metrics that combine morbidity, mortality and disability in the form of the DALY (Stein et al., 2007).

Several countries have published estimates of the incidence of illness related to the occurrence of pathogens in food. For example, it is estimated that in Australia, contaminated food caused approximately 5.4 million cases of gastroenteritis per year, along with 6000 non-gastrointestinal illnesses, 42 000 episodes of long-term effects (chronic sequelae) and 125 cases of premature mortality (Abelson, Potter Forbes & Hall, 2006). Such estimates can be based on reported cases, corrected for an estimate of the under-reporting ratio (e.g. USA—Mead et al., 1999; Australia—Hall et al., 2005), or can be based on population-based studies on the incidence of infectious intestinal illness (e.g. United Kingdom—Wheeler et al., 1999; Adak, Long & O'Brien, 2002; Adak et al., 2005; the Netherlands—De Wit et al., 2001).

These studies include attribution of a proportion of identified cases to food, as most pathogens can also be transmitted by other pathways, such as water, direct animal contact or between humans. Attribution studies may also include evaluation of the proportion of cases that is attributable to different food groups (beef, pork, poultry meat, fish, produce, etc.; Adak, Long & O'Brien, 2002; Hoffmann et al., 2007; Havelaar et al., 2008). Estimates for the disease burden (in DALYs) are available for the Netherlands (Kemmeren et al., 2006; Vijgen et al., 2007), whereas several countries (e.g. USA—USDA, 2009; Australia—Hall et al., 2005; the Netherlands—Kemmeren et al., 2006; Vijgen et al., 2007) have presented estimates of the costs associated with foodborne illness. In general, epidemiological information on foodborne illness is available at an aggregated level (“foodborne” or broad food categories, such as red meats, poultry, produce, etc.). At the level of specific food product–pathogen combinations, such information cannot be based on epidemiological studies, but would require the development of specific risk assessment models, with epidemiological information being used to calibrate or validate the risk assessment models. The public health impact of applying disinfectants in the food-chain can then be assessed using risk assessment models, as illustrated in Appendix 1 to chapter 4.

In general, it is difficult to attribute low levels of contaminant residues in food to the incidence of adverse health outcomes in the population, primarily because of the chronic nature of the potential health end-point. A conservative approach is usually taken whereby a chemical risk assessment is undertaken based on toxicological and other data. A limited number of countries have tried to characterize the adverse health outcomes associated with chemical residues across the population. In particular, the Netherlands has made an estimate of the number of DALYS that may result from the presence of naturally occurring contaminants (e.g. allergens and mycotoxins) and chemicals (e.g. nitrate and acrylamide) that arise in the production and processing of food (Baars, van Leeuwen & Kramers, 2006). No national assessment of potential adverse health outcomes across populations for disinfectants or their by-products was available to the expert meeting.

6.4 Approach taken by the expert meeting

The expert meeting developed a stepwise approach to risk–benefit analysis of chlorine-based compounds and alternative disinfectants used in food production and processing. This consisted of the following steps:

- listing the most predominant application practices used in food production and processing (i.e. use scenarios; see chapter 1 for details on the various uses of the disinfectants);
- performing risk assessments for the residues arising from each of the use scenarios; these residues may include both the parent disinfectant and its by-products (see chapter 3 for details);
- performing benefit assessments from pathogen reduction in the food (see chapter 4 for details).

The expert meeting identified some important gaps in the available data. These data gaps constrained the scope of the risk–benefit assessments. Consequently, the expert meeting agreed on a number of recommendations for further scientific studies and the development of standardized practices (see chapter 7). Where scientific data were available, an assessment of risk and/or benefit was undertaken, and the expert meeting categorized these situations in one of the following four categories:

- 1) No health concern identified; no benefits identified.
- 2) No health concern identified; benefits identified.
- 3) Health concern identified; no benefits identified.
- 4) Health concern identified; benefits identified.

Only use scenarios for which it was concluded that there are both health concerns and benefits were considered to need further evaluation. However, the expert meeting did not identify any use scenarios that were of this type (i.e. both health concerns and benefits identified).

6.5 Uncertainties

6.5.1 Chemical risk assessment

In the toxicological assessment, sufficient data or existing authoritative toxicological reviews were available to the expert meeting to allow the identification of a health reference value for most of the disinfectants identified in the scenarios as well as some by-products. However, the occurrence data (i.e. concentration in food) available for disinfectants and their by-products in food were relatively limited. These data are necessary to estimate the dietary exposure arising from the consumption of treated food. There is therefore a relatively high level of uncertainty associated with the dietary exposure assessments, although conservative assumptions were generally applied to compensate for this. In some cases, particularly for the disinfection by-products (DBPs) in food, there were very limited occurrence data available. For these DBPs, no dietary exposure assessment could be performed, and hence no complete risk assessment could be prepared. The data available on occurrence of DBPs on food were used to conclude on the likelihood of any health concerns, and the degree of uncertainty and conservatism is documented in chapter 3 where appropriate. The level of uncertainty and conservatism needs to be taken into consideration in the risk–benefit assessments.

There are only limited occurrence data available for trihalomethanes (THMs), some of which are genotoxic and carcinogenic. As THMs can be formed with hypochlorite but not with chlorine dioxide or acidified sodium chlorite (ASC), there is more uncertainty associated with the safety of the hypochlorite treatments than with that of the other processes, although definite data are not available.

6.5.2 Microbial risk assessment

The microbiological risk assessment contained a number of sources of uncertainty. The key sources were:

- data gaps where no experimental data were identified;
- lack of data on industrial-scale processes and the associated uncertainty of using only experimental data;
- use of data from studies in which the food was inoculated with the pathogen, rather than being naturally contaminated;
- inconsistencies between individual studies and the variability of these data;
- lack of appropriate controls used in studies.

These uncertainties were taken into consideration when evaluating the evidence and arriving at a risk–benefit conclusion, as shown in Table 6.2.

6.6 Results

From Table 6.2, it can be concluded that, where data were available, no health concerns were identified in relation to residues of disinfectants or the occurrence of DBPs. There were few scenarios in which some benefits were identified. These were the use of ASC to reduce counts of *Campylobacter* and *Salmonella* on poultry carcasses prior to chilling and the use of sodium hypochlorite or chlorine dioxide in chiller water for poultry to prevent cross-contamination. For other scenarios, the only documented benefits are based on laboratory studies using seeded cultures, and this evidence was considered insufficient to allow a conclusion to be reached about their effectiveness in practice.

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Table 6.2. Risk–benefit assessment

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Poultry (Sequential scenario) ^a	Hypochlorite	Pre-chill carcass spray, 20–50 mg/l (including sequential treatment using three washers)	THMs and other organohalogens expected; data on chloroform only	No health concern identified (limited data)	<i>Salmonella</i> <i>Campylobacter</i>	No effect over washing in water alone discernible	No health concern identified; no benefit identified
		Chiller water, 50 mg/l as chlorine, aimed at 5 mg/l residual			<i>Salmonella</i> <i>Campylobacter</i>	Little to no reduction in numbers, but effective method for preventing cross-contamination of carcasses from chiller water	No health concern identified; benefits identified

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Poultry (Sequential scenario) ^a	ASC	Pre-chill spray or dip, 500–1200 mg/l, pH 2.5–2.9	Chlorite Chlorate	No health concern identified	<i>Salmonella</i>	Some evidence for prevalence reduction	No health concern identified; benefits identified
					<i>Campylobacter</i>	Some evidence for prevalence reduction and up to 1.2 log reduction	
	Hypochlorite	Chiller, 20–50 mg/l as chlorine	THMs and other organohalogens expected; data on chloroform only	No health concern identified (limited data)	<i>Salmonella</i> <i>Campylobacter</i>	Little to no reduction in numbers, but effective method for preventing cross-contamination	
	ASC	Post-chill dip, 500–1200 mg/l, pH 2.5–2.9	Chlorite Chlorate	No health concern identified	<i>Salmonella</i>	Some evidence for prevalence reduction	
					<i>Campylobacter</i>	Some evidence for prevalence reduction and up to 1.2 log reduction	
Poultry (Sequential scenario) ^b	Hypochlorite	Pre-chill rinse, 20 mg/l	THMs and other organohalogens expected; data on chloroform only	No health concern identified (limited data)	<i>Salmonella</i>	No effect over washing in water alone discernible	No health concern identified; no benefit identified
	ASC (Alcide)	Chiller, 1 part Alcide base : 200 parts water : 1 part Alcide activator	Chlorite Chlorate	No health concern identified	<i>Salmonella</i>	Some evidence for prevalence reduction	No health concern identified; benefits identified

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Poultry	ASC (Alcide)	Pre-chill dip, 1 part Alcide base : 20 parts water : 1 part Alcide activator	Chlorite Chlorate	No health concern identified	<i>Salmonella</i>	Some evidence for prevalence reduction	No health concern identified; benefits identified
Poultry	Chlorine dioxide	Chiller water, 3–5 mg/l as chlorine dioxide	Chlorite Chlorate	No health concern identified	<i>Salmonella</i>	No data on reduction in numbers, but an effective method for preventing cross-contamination of carcasses from chiller water	No health concern identified; benefits identified
Poultry	Peroxyacetic acid	Spray, 200 mg/l	HEDP	No health concern identified	<i>Salmonella</i>	Little to no effect on contamination levels over water washing alone (laboratory inoculation studies only)	No health concern identified; no benefits identified
Red meat	Hypochlorite	Carcass spray, 50–500 mg/l	THMs and other organohalogens expected; data on chloroform only	No health concern identified (limited data)	<i>E. coli</i> O157:H7	Little to no effect compared with water alone	No health concern identified; no benefits identified

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Red meat	ASC	Dip or spray, 1200 mg/l	Chlorite Chlorate	No health concern identified	<i>E. coli</i> O157:H7	1.4–1.5 log reduction (laboratory inoculation studies only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
					<i>Salmonella</i>	1.6–2.1 log reduction (laboratory inoculation studies only)	
Red meat	Lactic acid (as food-grade acid)	Dip, 2–2.5%	Lactate ^c	No health concern identified	<i>E. coli</i> O157:H7	1.3–1.5 log reduction (laboratory inoculation studies only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
					<i>Salmonella</i>	1.6–2.0 log reduction (laboratory inoculation studies only)	
Shrimp	Hypochlorite	Immersion of shrimp in water containing 50 mg/l (for 30 min in laboratory studies)	THMs and other organohalogenes expected; data on chloroform only	No health concern identified (limited data)	<i>V. parahaemolyticus</i>	Up to 1.5 log reduction (laboratory-based natural contamination studies)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
Fish and fishery products	Hypochlorite	Thawing fish in water containing 20–25 mg/l, or washing in water containing 200 mg/l	THMs and other organohalogenes expected; data on chloroform only	No health concern identified (limited data)	<i>L. monocytogenes</i>	Up to approximately 2.5 log reduction (laboratory inoculation studies only)	No health concern identified (limited data); potential benefits identified (only laboratory-based studies; more data needed)

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Fish and fishery products	Chlorine dioxide	Fish storage in ice made with water containing chlorine dioxide at 20–100 mg/l	Chlorite Chlorate	No health concern identified	<i>Salmonella</i> Typhimurium <i>L. monocytogenes</i> <i>E. coli</i> O157:H7	2–3 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
Leafy greens	Hypochlorite	20–200 mg/l dips and sprays with contact times between 1 and 10 min	THMs and other organohalogens expected	No health concern identified (limited data)	<i>L. monocytogenes</i>	0.2–1.7 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
					<i>Salmonella</i>	0.3–2.0 log reduction (laboratory inoculation study only)	
					<i>E. coli</i> O157:H7	0.3–1.7 log reduction (laboratory inoculation study only)	
					<i>Shigella</i>	0.2–6.0 log reduction (laboratory inoculation study only)	
Leafy greens	Chlorine dioxide	20 mg/l with 10–15 min contact time	Chlorite Chlorate	No health concern identified	<i>E. coli</i> O157:H7	Up to 1 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
					<i>Salmonella</i>	Up to 0.7 log reduction (laboratory inoculation study only)	

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Leafy greens	Chlorine dioxide	1–5 mg/l with 10 min contact time	Chlorite Chlorate	No health concern identified	<i>L. monocytogenes</i>	Up to 1.1 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
Apples	Chlorine dioxide	20 mg/l with 10 min contact time	Chlorite Chlorate	No health concern identified	<i>E. coli</i> O157:H7	Up to 1.5 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies, more data needed)
					<i>Salmonella</i>	Up to 2.0 log reduction (laboratory inoculation study only)	
Green peppers	Chlorine dioxide	0.3–3 mg/l with 10 min contact time	Chlorite Chlorate	No health concern identified	<i>L. monocytogenes</i>	Up to 2.3 log reduction (laboratory inoculation study only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Fresh produce	Peroxyacetic acid	40–80 mg/l with 10–60 min contact time	HEDP	No health concern identified	<i>E. coli</i> O157:H7	Up to 4.4 log reduction (laboratory inoculation studies, no control for effect of water alone)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
					<i>Salmonella</i>	Up to 3.8 log reduction (laboratory inoculation studies, no control for effect of water alone)	
					<i>L. monocytogenes</i>	Up to 4.5 log reduction (laboratory inoculation studies, no control for effect of water alone)	
Seeds for sprouting	Hypochlorite	20 000 mg/l	THMs and other organohalogens expected	No health concern identified (limited data)		No data identified	No health concern identified; no benefits identified (no data)
Hydroponics	Hypochlorite	2 mg/l in irrigation water	THMs and other organohalogens expected	No health concern identified (limited data)		No data identified	No health concern identified; no benefits identified (no data)
Food contact surfaces	Chloramine-T	0.5%	None expected	No health concern identified		No data identified	No health concern identified; no benefits identified (no data)

Commodity	Chemical	Process parameters	Chemical risk assessment		Microbial risk assessment		Risk–benefit assessment
			Residue(s)	Conclusion	Pathogen(s)	Conclusion	
Food contact surfaces	Dichloroisocyanurate	0.005%	Cyanuric acid	No health concern identified		No data identified	No health concern identified; no benefits identified (no data)
Food contact surfaces	Iodophors	10–20 mg/l on plastic and metal surfaces	Iodine	No health concern identified	<i>L. monocytogenes</i>	0.18–3.21 log reduction (laboratory-grown biofilm studies only)	No health concern identified; potential benefits identified (only laboratory-based studies; more data needed)
Food contact surfaces	Hypochlorite	10–200 mg/l on porous and non-porous hard surfaces	THMs possible	No health concern identified (limited data)	<i>Salmonella</i>	0.75–7.5 log reduction (laboratory-grown biofilm studies only); 1 log reduction on biofilm in industrial setting	No health concern identified; potential benefits identified
					<i>L. monocytogenes</i>	0.75–5.7 log reduction (laboratory-grown biofilm studies only)	

ASC, acidified sodium chlorite; HEDP, 1-hydroxyethylidene-1,1-diphosphonic acid; THMs, trihalomethanes

^a Indicates that this is part of a series of processing steps used when chicken is water chilled. These steps are designed primarily to chill the carcass and not as a decontamination step; however, the use of chlorine during this step can be used as a risk mitigation method.

^b Indicates that this is a sequence of steps tested in studies that included a pre-rinse and the addition of Alcide (ASC) in the chill tanks.

^c Lactate is a natural constituent of food and the human body, so the expert meeting did not consider a separate risk assessment to be necessary.

6.7 References

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7. CONCLUSIONS AND RECOMMENDATIONS

The expert meeting's conclusions, key sources of uncertainty and recommendations for further scientific studies to fill gaps in knowledge and for the development of standardized practice are provided below, by chapter.

7.1 Description of current processes

- Poultry and fresh produce are the food products that have the most direct exposure to chlorine-containing disinfectants. The use of chlorine-based compounds in the fish and fishery product industry is mainly focused on the end-point disinfection of contact surfaces, and direct application to the edible portions of fish and shellfish is limited. The use of chlorine-containing disinfectants in red meat processing is uncommon.
- Sodium hypochlorite is the most widely used disinfectant, in particular in the production and processing of poultry meat, fresh produce (such as leafy greens), fish and fishery products, sprouts and hydroponics.
- Acidified sodium chlorite (ASC) solutions are commonly used as an alternative to sodium hypochlorite in specific poultry processing steps.
- Non-chlorine-based alternatives include (in addition to physical treatments, which were not considered) peroxyacids in poultry production and organic acids in meat production. These alternatives are effective disinfectants in some use scenarios.
- Active chlorine compounds are broadly used in food processing facilities to disinfect food contact surfaces prior to and during food processing operations in order to control cross-contamination and to obtain pathogen reduction. Requirements related to completing the cleaning and sanitization cycle with a potable water rinse vary globally from region to region and from country to country.
- The application of chlorine directly to food products to reduce virus levels has not been reported to date.

Recommendations

- Disinfectant treatment of water used in food processing must not be used to mask poor hygienic practices. It is recommended that disinfectants be used within the framework of good hygienic practices and a hazard analysis and critical control point (HACCP) system where applicable and subject to adequate process controls.

7.2 Chemistry of compounds used

- Chlorine (hypochlorite and hypochlorous acid) and chloramines, to a lesser degree, produce small quantities of oxidized and chlorinated disinfection by-products (DBPs); other disinfectants produce more oxidized products and lesser quantities of chlorinated by-products.
- There are limited data on the types and quantities of DBPs present as food residues after disinfection. Although most of the reported data on organic DBP formation on foods

involved chloroform measurements only, it can be assumed that if chloroform was detected, other trihalomethanes (THMs) and other DBPs were also formed.

- Substantial data are available on DBPs in drinking-water, but such data have limited applicability to scenarios of disinfection processes in food production and processing. Extrapolations from chloroform, other THMs and other DBPs in drinking-water to foods are difficult to make because the conditions of the chemical interactions, dosages, contact times, temperature and precursors are different.
- In addition, the chemical composition of food is more complex than that of water, and the contact/exposure conditions for disinfectants used in food processing are different. This may lead to the formation of different types and quantities of DBPs in treated foods compared with water.
- Cooking is likely to reduce the quantities of volatile compounds, such as chloroform, in foods.
- Nitrosamines are not likely to be present in most disinfected water used for food processing. If present, the quantities would be very small, especially in relation to the amount of nitrosamines commonly found in foods and produced by cooking.
- Under some oxidation conditions, bromide can be converted to hypobromous acid, which would shift the composition of DBPs to organobromine compounds. Chlorination of seawater or any water that contains bromide may lead to the formation of organobromine compounds; ozonation would also produce bromate.

Recommendations

- More research is needed on the formation, identity and amounts of DBPs in foods at consumption, reflecting the effects of processing, cooking, storage and other factors. Such studies should be interpreted in conjunction with the microbiological risk and shelf life benefits of the use of disinfectants.
- The formation of organobromines and bromate as a result of water chlorination should be studied further (e.g. in saltwater fish and shrimp processing).

7.3 Chemical risk assessment

- There is a lack of data on the by-products present in foods or in processing water following the use of chlorine-containing disinfectants. There is therefore a high degree of uncertainty in the dietary exposure assessments, although conservative assumptions were generally applied to compensate for this. Data on by-products were available for drinking-water, although these data have limited applicability to food.
- No epidemiological studies on the health effects of exposure to disinfectants and DBPs in food have been identified. The evidence from studies of drinking-water suggests an association between DBPs and increased risk of bladder cancer; however, the relationship between DBPs in drinking-water and those in food is not known.
- The toxicology of chlorine-containing compounds and alternatives has been extensively reviewed based on currently available risk assessments. For the identified residues of disinfectants and by-products, the estimated exposures did not raise toxicological concerns. The evidence with respect to hypochlorite use in poultry, fish and shellfish was weak, owing to a lack of qualitative and quantitative information on THMs.

Key sources of uncertainties

- Very limited data were available on the use of some of the substances (i.e. on which food commodities they were used, at which doses, etc.).
- Very few data were available for a number of DBPs in food, other than drinking-water.
- The authoritative international assessments used for chemical risk assessment and dietary exposure assessment may be some years old and therefore not always up to date.
- THMs, some of which are genotoxic and carcinogenic, are expected to result from hypochlorite use. However, data are available only for chloroform, which indicates the presence of other THMs, or are completely lacking.
- The concentrations of some DBPs could be decreased by volatilization during cooking or by degradation in the saliva or stomach, but quantitative data on such effects are lacking.

Recommendations

- Further research is needed on the toxicological effects of DBPs formed in water and in food.
- Studies of disinfectant residues and DBPs are needed, particularly for foods that might have substantial residues present when consumed.

7.4 Microbiological risk assessment

- Cross-contamination is a complex process that is difficult to quantify in experimental and industrial settings. It is difficult to quantify the effects of cross-contamination on pathogen numbers on food, but the use of disinfectants in food processing is important to prevent cross-contamination and thereby reduce consumer exposure to pathogens.
- Data on the quantitative effects of disinfectants on food pathogens are available based on studies in industrial, pilot and laboratory settings. These data are not always equivalent. It is considered that experimental studies using inoculated pathogens on food products may overestimate the effect of the disinfectant chemical on pathogens. However, this may not be the case when studying disinfectant use in wash or flume waters.
- ASC as a pre-chill and post-chill dip/wash is an effective disinfectant for reducing pathogens in poultry processing.
- In order to translate the impact of pathogen reductions into public health benefits, a risk assessment model is required. The Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) have a model available for *Campylobacter* in chicken. This model was used to test various scenarios, resulting in estimates of up to 70% reduction in campylobacteriosis risk from the use of ASC as a decontamination spray and up to approximately 97% reduction in campylobacteriosis risk from the use of a combination of chlorine in the immersion chill tank and an ASC decontamination spray.
- Laboratory studies have demonstrated that biofilms containing *Salmonella* spp. and *L. monocytogenes* can be inactivated by a range of disinfectants at suitable concentrations with appropriate contact times. The effectiveness of disinfectants against *Escherichia coli* O157, *Salmonella* Typhimurium and *Clostridium perfringens* on cutting tools has also been demonstrated.
- Assessment of the effectiveness of disinfectants based on studies in industrial settings is difficult. This is because the microflora, including pathogens, in the process environment

is already being controlled by the ongoing use of disinfectants. Hence, attempting to measure the effectiveness at individual steps does not accurately reflect what would happen if no disinfectants had been used in the process prior to the study. The end result is that assessments of the effectiveness of disinfectants based on studies in industrial settings are likely to underestimate the incremental effectiveness of the individual control steps.

Key sources of uncertainties

- There is a lack of data on industrial-scale processes and uncertainty associated with using only experimental data.
- Data from studies in which food is inoculated with a pathogen rather than being naturally contaminated tend to overestimate the efficacy of a disinfectant.
- There are inconsistencies between individual studies, and data are often variable within studies.
- It is difficult to quantify the effects of cross-contamination on pathogen numbers on food.
- Translation of pathogen reduction information into public health outcomes requires the use of quantitative microbial risk assessment models, which ideally should be done on a national level. These models are not always available or suitable. However, the public health impact on a relative basis can be achieved using international models (e.g. the FAO/WHO *Campylobacter* in poultry model).
- Data are available on individual disinfection steps in a process, but data are often lacking on the combined disinfection effects of serial or sequential control strategies.

Recommendations

- There is a need to develop more standardized protocols for studies of microbial reduction in the main food processing scenarios outlined in the report to address the problems of comparability of the results.

7.5 Unintended consequences

- There are no published reports indicating that the use of active chlorine or currently used alternatives to active chlorine are associated with acquired antimicrobial resistance to therapeutic agents. Chlorine and non-chlorine alternatives, including peroxyacids, ozone and other oxidants, as well as surfactants, including trisodium phosphate (TSP) and quaternary ammonium compounds (QACs), have nonspecific modes of action for which microorganisms may develop tolerance. However, this potential tolerance has not been associated with acquired antimicrobial resistance or the failure of biocides to be effective when used as recommended.
- Treatment of fresh fruits and vegetables and poultry carcasses with active chlorine can reduce the normal microflora of the produce. Currently available data indicate that such reduction in normal microflora does not result in increased survival or growth of pathogenic microorganisms.
- The nutrient contents (some vitamins and antioxidants) of foods may be affected by treatments with disinfectants, even though the effects are variable and sometimes contradictory. The effects depend on the type of food and mode of preparation, the type of disinfectant and conditions of use, and further processing (washing, type of packaging

and conditions of storage). The reported changes in nutrient content due to disinfectant use are low in relation to the normal dietary intake of these nutrients.

- The effect of disinfectant use on the sensory quality of foods is expected to be low when the disinfectant is used as recommended. Some studies show that ASC and ozone treatments appear to keep and even improve the sensory quality during storage of fruits and vegetables, whereas chlorine dioxide and peroxyacids appear to be ineffective in preventing, or even promote, the brown discoloration caused by phenolic oxidation.

Recommendations

- In view of the many variables involved in determining the effects of disinfection treatments on nutrient content and sensory quality of food, recommendations for best practices can be given only on a case-by-case basis.

7.6 Risk–benefit assessment

- Risk–benefit assessment is an activity that weighs the probability and severity of harm in a particular exposure scenario against the probability and magnitude of benefit. The expert meeting assessed the risks associated with exposure to the residues arising from the predominant application practices used in food production and processing and the benefits from pathogen reduction in the food.
- In principle, the results of risk–benefit assessments could be in four possible categories:
 - 1) No health concern identified; no benefits identified
 - 2) No health concern identified; benefits identified
 - 3) Health concern identified; no benefits identified
 - 4) Health concern identified; benefits identified

Only use scenarios resulting in category 4 (i.e. there are both health concerns and benefits) would need further evaluation and weighing of the risks and benefits.

- Based on the available data, no health concerns were identified from an evaluation of the toxicity and dietary exposure. This applies to both the disinfectant residues and, where data were available, the by-product residues. However, as discussed in chapters 2 and 3, there is greater uncertainty with respect to the use of hypochlorite than to the use of other chlorine and alternative disinfectants, owing to the potential formation of DBPs that are genotoxic and carcinogenic.
- There is evidence for reduction of pathogens on poultry carcasses and red meats by application of ASC and chlorine dioxide and by application of sodium hypochlorite in smoked fish production. There is some evidence for reduction of cross-contamination by the application of disinfectants (in particular sodium hypochlorite) in wash and flume waters.

ANNEX 1: LIST OF PARTICIPANTS

Joint FAO/WHO expert meeting on the benefits and risks of the use of chlorine-containing disinfectants in food production and food processing

Ann Arbor, Michigan, USA, 27–30 May 2008

LIST OF PARTICIPANTS

Experts

- Professor Gabriel O. Adegoke, Department of Food Technology, University of Ibadan, Ibadan, Nigeria (*unable to participate*)
- Dr Wayne A. Anderson, Food Safety Authority of Ireland (FSAI), Dublin, Ireland
- Dr Bassam Annous, Eastern Regional Research Center, Agricultural Research Service, United States Department of Agriculture, Wyndmoor, PA, USA
- Dr Kirk B. Arvidson, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA
- Dr Gail Baccus-Taylor, Food Science and Technology Unit, Faculty of Engineering, University of the West Indies, St Augustine, Trinidad and Tobago
- Dr Diane Benford, Food Standards Agency, London, England
- Dr Scott L. Burnett, Ecolab Research Center, Eagan, MN, USA
- Associate Professor Sylvaine Cordier, Groupe d'Etude de la Reproduction chez l'Homme et les Mammifères (GERHM), Institut National de la Santé et de la recherche médicale, Unit 625, Université de Rennes, Rennes, France
- Dr Joseph A. Cotruvo, Consultant, Washington, DC, USA
- Mr Stephen J. Crossley, Consultant, Harrogate, England
- Dr Michael J. DiNovi, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA
- Dr Gary Dykes, Food Safety & Quality, Food Science Australia, Brisbane, Australia
- Mr Aamir M. Fazil, Public Health Agency of Canada, Guelph, Ontario, Canada
- Professor Joseph F. Frank, Food Science and Technology Department, University of Georgia, Athens, GA, USA
- Dr Michael Graz, Consultant, Biophys Ltd, Chepstow, England
- Professor Arie H. Havelaar, Laboratory for Zoonoses and Environmental Microbiology, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
- Dr Hyoungh S. Lee, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA
- Mr Hector Lupin, Consultant (retired Senior Officer, Fisheries and Aquaculture Department, Food and Agriculture Organization of the United Nations), Rome, Italy
- Dr Inger-Lise Steffensen, Department of Food Safety and Nutrition, Norwegian Institute of Public Health (NIPH), Oslo, Norway

Professor Fidel Toldrá, Instituto de Agroquímica y Tecnología de Alimentos (CSIC), Valencia, Spain

Dr Varaporn Vuddhakul, Department of Microbiology, Faculty of Science, Prince of Songkla University, Hat Yai, Thailand

Secretariat

Dr Annamaria Bruno, Codex Secretariat, Nutrition and Consumer Protection Division, Food and Agriculture Organization of the United Nations, Rome, Italy

Dr Myoengsin Choi, Department of Food Safety and Zoonoses, World Health Organization, Geneva, Switzerland

Dr Iddya Karunasagar, Fish Products and Industry Division, Food and Agriculture Organization of the United Nations, Rome, Italy

Dr Angelika Tritscher, Joint Secretary to JECFA and JMPR, Department of Food Safety and Zoonoses, World Health Organization, Geneva, Switzerland

Dr Annika Wennberg, Joint Secretary to JECFA, Nutrition and Consumer Protection Division, Food and Agriculture Organization of the United Nations, Rome, Italy

ANNEX 2: LIST OF DRAFTERS

Chapter 1

Dr Bassam Annous, Eastern Regional Research Center, Agricultural Research Service, United States Department of Agriculture, Wyndmoor, PA, USA

Dr Mark Berrang, Russell Research Center, Agricultural Research Service, United States Department of Agriculture, University of Georgia, Athens, GA, USA

Dr Scott L. Burnett, Ecolab Research Center, Eagan, MN, USA

Dr Gary Dykes, Food Safety & Quality, Food Science Australia, Brisbane, Australia

Professor Joseph F. Frank, Food Science and Technology Department, University of Georgia, Athens, GA, USA

Dr Michael Graz, Consultant, Biophys Ltd, Chepstow, England

Dr Iddya Karunasagar, Fish Products and Industry Division, Food and Agriculture Organization of the United Nations, Rome, Italy

Mr Hector Lupin, Consultant (retired Senior Officer, Fisheries and Aquaculture Department, Food and Agriculture Organization of the United Nations), Rome, Italy

Associate Professor Karl Matthews, Department of Food Science, Rutgers University, New Brunswick, NJ, USA

Mr Alan Reilly, Deputy Chief Executive, Food Safety Authority of Ireland (FSAI), Dublin, Ireland

Mr Bob Sanderson, Jonathans Sprouts Inc., Marion, MA, USA

Associate Professor Youbin Zheng, Department of Environmental Biology, University of Guelph, Guelph, Ontario, Canada

Chapter 2

Dr Kirk B. Arvidson, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Dr Richard Bull, Consultant, Richland, WA, USA

Dr Joseph A. Cotruvo, Consultant, Washington, DC, USA

Dr Hyoung S. Lee, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Professor Fidel Toldrá, Instituto de Agroquímica y Tecnología de Alimentos (CSIC), Valencia, Spain

Chapter 3

Dr Kirk B. Arvidson, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Dr Diane Benford, Food Standards Agency, London, England

Dr Sylvaine Cordier, Groupe d'Etude de la Reproduction chez l'Homme et les Mammifères (GERHM), Institut National de la Santé et de la recherche médicale, Unit 625, Université de Rennes, Rennes, France

Mr Stephen J. Crossley, Consultant, Harrogate, England

Dr Michael J. DiNovi, Center for Food Safety and Applied Nutrition, Food and Drug Administration, United States Department of Health and Human Services, College Park, MD, USA

Dr Jean-Charles LeBlanc, French Food Safety Agency (AFSSA), Maisons Alfort, France

Professor Mark J. Nieuwenhuijsen, Center for Research in Environmental Epidemiology (CREAL), Barcelona, Spain

Dr Inger-Lise Steffensen, Department of Food Safety and Nutrition, Norwegian Institute of Public Health (NIPH), Oslo, Norway

Chapter 4

Dr Wayne A. Anderson, Food Safety Authority of Ireland (FSAI), Dublin, Ireland

Mr Aamir M. Fazil, Public Health Agency of Canada, Guelph, Ontario, Canada

Mr Hector Lupin, Consultant (retired Senior Officer, Fisheries and Aquaculture Department, Food and Agriculture Organization of the United Nations), Rome, Italy

Mr Geoff Mead, Consultant, Harbutts, Bathampton, Bath, England

Mr Alan Reilly, Deputy Chief Executive, Food Safety Authority of Ireland (FSAI), Dublin, Ireland

Chapter 5

Professor Fidel Toldrá, Instituto de Agroquímica y Tecnología de Alimentos (CSIC), Valencia, Spain

Professor Joseph F. Frank, Food Science and Technology Department, University of Georgia, Athens, GA, USA

Chapter 6

Dr Diane Benford, Food Standards Agency, London, England

Mr Stephen J. Crossley, Consultant, Harrogate, England

Professor Arie H. Havelaar, Laboratory for Zoonoses and Environmental Microbiology, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands

ANNEX 3: LIST OF ACRONYMS AND ABBREVIATIONS

ADI	acceptable daily intake
ASC	acidified sodium chlorite
BCAN	bromochloroacetonitrile
BCC	basal cell carcinoma
BDCM	bromodichloromethane
BEMX-1	(<i>E</i>)-2-chloro-3-(bromochloromethyl)-4-oxobutenoic acid
BEMX-2	(<i>E</i>)-2-chloro-3-(dibromomethyl)-4-oxobutenoic acid
BEMX-3	(<i>E</i>)-2-bromo-3-(dibromomethyl)-4-oxobutenoic acid
BMD	benchmark dose
BMD ₁₀	benchmark dose for a 10% increase in effect
BMDL ₁₀	95% lower confidence limit on the benchmark dose for a 10% increase in effect
BMX-1	3-chloro-4-(bromochloromethyl)-5-hydroxy-2(5H)-furanone
BMX-2	3-chloro-4-(dibromomethyl)-5-hydroxy-2(5H)-furanone
BMX-3	3-bromo-4-(dibromomethyl)-5-hydroxy-2(5H)-furanone
bw	body weight
CAS	Chemical Abstracts Service
cfu	colony-forming unit
CHO	Chinese hamster ovary
CI	confidence interval
CNS	central nervous system
CPC	cetylpyridinium chloride
CSFII	Continuing Survey of Food Intakes by Individuals (USA)
CYP	cytochrome P450
DALY	disability-adjusted life year
DBA	dibromoacetic acid
DBAN	dibromoacetonitrile
DBCM	dibromochloromethane
DBDMH	1,3-dibromo-5,5-dimethylhydantoin
DBP	disinfection by-product
DCA	dichloroacetic acid
DCAN	dichloroacetonitrile
DMH	dimethylhydantoin
DNA	deoxyribonucleic acid
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EMX	(<i>E</i>)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GC/MS	gas chromatography/mass spectrometry
GDWQ	Guidelines for Drinking-water Quality (WHO)
GEMS/Food	Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme
GLP	Good Laboratory Practice
GRAS	generally recognized as safe
GST	glutathione <i>S</i> -transferase

GV	guideline value
HAA	haloacetic acid
HACCP	hazard analysis and critical control point
HAN	haloacetonitrile
HEDP	1-hydroxyethylidene-1,1-diphosphonic acid
HP	hydrogen peroxide
IARC	International Agency for Research on Cancer
IOBW	inside–outside bird washer
IPCS	International Programme on Chemical Safety (WHO)
IRIS	Integrated Risk Information System
IUGR	intrauterine growth retardation (restriction)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LAE	ethyl lauroyl arginate
LBW	low birth weight
LO(A)EL	lowest-observed-(adverse-)effect level
LOD	limit of detection
MAP	modified atmosphere packaging
MCL	maximum contaminant level (USA)
MTDI	maximum tolerable daily intake
MX	3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone
NA	not available
NaDCC	sodium dichloroisocyanurate
nd	not detected
NDEA	<i>N</i> -nitrosodiethylamine
NDELA	<i>N</i> -nitrosodiethanolamine
NDMA	<i>N</i> -nitrodimethylamine
NDPA	<i>N</i> -nitrosodiphenylamine
NMOR	<i>N</i> -nitrosomorpholine
NO(A)EL	no-observed-(adverse-)effect level
NOM	natural organic matter
NPIP	<i>N</i> -nitrosopiperidine
NPRO	<i>N</i> -nitrosoproline
NPYR	<i>N</i> -nitrosopyrrolidine
NTD	neural tube defect
NTP	National Toxicology Program (USA)
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio
ox-EMX	(<i>E</i>)-2-chloro-3-(dichloromethyl)-butenedioic acid
ox-MX	2-chloro-3-(dichloromethyl)-butenedioic acid
PMTDI	provisional maximum tolerable daily intake
POA	peroxyacetic acid/hydrogen peroxide
PTSA	<i>p</i> -toluenesulfonamide
QAC	quaternary ammonium compound
red-MX	3-chloro-4-(dichloromethyl)-2(5H)-furanone
SCC	squamous cell carcinoma
SCF	the former Scientific Committee for Food in the European Union
SD	standard deviation
SGA	small for gestational age
SI	Système international d'unités
spp.	species

T ₃	triiodothyronine
T ₄	thyroxine
TBARS	2-thiobarbituric acid reactive substances
TCA	trichloroacetic acid
TCAN	trichloroacetonitrile
TDI	tolerable daily intake
THM	trihalomethane
TSH	thyroid stimulating hormone
TSP	trisodium phosphate
TTHM	total trihalomethanes
USA	United States of America
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UV	ultraviolet
VLBW	very low birth weight
VTEC	verotoxigenic <i>Escherichia coli</i>
v/v	volume by volume
WHO	World Health Organization
ZMX	(Z)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid

ANNEX 4: GLOSSARY

Acceptable daily intake (ADI): An estimate of the amount of a substance in food or drinking-water, expressed on a body weight basis (usually milligrams per kilogram body weight), that can be ingested daily over a lifetime by humans without appreciable health risks.

Acceptable daily intake “not limited”: A term no longer used by the Joint FAO/WHO Expert Committee on Food Additives, which has the same meaning as acceptable daily intake “not specified”.

Acceptable daily intake “not specified”: A term applicable to a food substance of very low toxicity that, on the basis of the available chemical, biochemical and toxicological data as well as the total dietary intake of the substance, does not, in the opinion of the Joint FAO/WHO Expert Committee on Food Additives, represent a hazard to health. For that reason, the establishment of an acceptable daily intake expressed in numerical form is not deemed necessary.

Acquired resistance: Resistance to an antimicrobial treatment that is passed on to progeny.

Active chlorine: Chlorine in a form that is readily available for chemical reaction with microorganisms.

Antimicrobial: A disinfectant; an agent that kills or inactivates microorganisms.

Aquaculture: The farming during part or the whole of their life cycle of all aquatic animals, except mammalian species, aquatic reptiles and amphibians, intended for human consumption.

Bacteriocin: A peptide or small protein produced by bacteria that inhibits the growth of closely related strains or species.

Benefit assessment: An activity that estimates the probability and magnitude of benefit in a particular exposure scenario as a basis for risk management decisions and communication to the public.

Biocide: An active substance that inactivates microorganisms on animate or inanimate surfaces or in foods.

Biofilm: Microbial growth as a thin layer on a surface, including associated extracellular products.

By-product: A secondary or incidental product deriving from a manufacturing process, a chemical reaction or a biochemical pathway, not the primary product or service being produced. *See also* Disinfection by-products.

Chiller: A tank or vat containing cooled water or slush ice, used for cooling (e.g. poultry carcasses) in the food industry; sometimes used in series, with the first tank used for prechilling with tap water.

Chlorine alternative: A treatment or substance that replaces the use of chlorine-based compounds in a specified process by accomplishing the same functions without generating active chlorine compounds.

Colony-forming unit: A measure of viable cells in which a colony represents an aggregate of cells derived from a single progenitor cell.

Colour parameters (L, a and b): Descriptors of a globally recognized colour system, in which L represents lightness and a and b are colour space coordinates. They provide a standard, approximately uniform colour scale (known as the CIELAB colour scale) so that colours can be easily compared.

Cross-contamination: The transfer of microorganisms from an individual food item (animal carcass, single fish, whole fruit or vegetable, or single cut piece of these items) to another individual food item through air, water, handlers, contact with equipment surfaces or direct contact between individual items. This may occur between units within a batch or between batches.

D-value: A measure of the amount of time needed to provide a 1 log reduction in the number of microorganisms. A D-value of 73 min means that it would take 73 min to produce a 1 log reduction.

D₁₀ value: The radiation dose needed to inactivate 1 log of a target microorganism (measured in kilograys).

DALY: A time-based measure (disability-adjusted life year) that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health.

Depuration: A short-term process commonly used to reduce low levels of bacterial contamination in filter-feeding shellfish. Long-term relaying is required if there is the risk of high levels of contamination.

Disability-adjusted life year: *See* DALY.

Disinfectant: A substance used in aqueous solutions in food production and processing to eliminate or reduce the number of microorganisms on the food in washing, chilling and other processes. In some countries, a distinction is made between disinfection and sanitization, but for the purpose of this document, no such distinction is made.

Disinfection: The reduction by means of chemical agents and/or physical methods of the number of microorganisms in the environment to a level that does not compromise food safety or suitability.

Disinfection by-products (DBPs): Chemical compounds formed during disinfection processes, other than the original substances introduced in the aqueous solution used for disinfection.

End-point disinfection: The final treatment of a food product with disinfectant solution before retail distribution or the disinfection of a food contact surface immediately before use.

Flume: An elevated trough or pipe filled with wash water that keeps the product immersed for a certain minimum time as required by the treatment.

Further processed: A meat or poultry product that has undergone further processing, such as smoking, cooking or curing.

GEMS/Food consumption cluster diets: Per capita consumption of raw and semiprocessed agricultural commodities expressed in grams per person per day for distinct groups of the world's population that share similar dietary patterns. Based on food balance sheet data from the Food and Agriculture Organization of the United Nations, the diets were generated using a cluster analysis, which assigned countries to one of the 13 cluster diets.

Generally recognized as safe (GRAS): A designation used by the United States Food and Drug Administration, stating that a chemical or substance added to food is considered safe by experts and so is exempted from the usual Federal Food, Drug, and Cosmetic Act (i.e. the law in the USA that authorizes the United States Environmental Protection Agency to oversee the safety of foods, drugs and cosmetics) food additive tolerance requirements.

Hazard characterization: The qualitative and, wherever possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties.

Hazard identification: The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system or (sub)population.

Infective dose: That amount of pathogenic organisms that will cause infection in susceptible subjects.

Iodophor: A mixture of iodine and surface-active agents that act as carriers and solubilizers for the iodine.

Log unit: “Log” stands for logarithm, which is the exponent of 10. For example, log 2 represents 10^2 or 10×10 or 100.

Log reduction: Log reduction stands for a 10-fold or one decimal or 90% reduction in numbers of recoverable bacteria in a test food vehicle. For example, a 1 log reduction would reduce the number of bacteria by 90%. This means, for example, that 100 bacteria would be reduced to 10 or 10 reduced to 1.

Lowest-observed-(adverse-)effect level (LO(A)EL): Lowest concentration or amount of a substance, found by experiment or observation, that causes an (adverse) alteration of morphology, functional capacity, growth, development or lifespan of the target organism distinguishable from normal (control) organisms of the same species and strain under the same defined conditions of exposure.

Margin of exposure: The ratio of the no-observed-adverse-effect level (NOAEL) or benchmark dose lower confidence limit for the critical effect to the theoretical, predicted or estimated exposure dose or concentration.

Margin of safety: The margin between the health-based guidance value (e.g. acceptable daily intake, tolerable daily intake) and the actual or estimated exposure dose or concentration. For some experts, the margin of safety has the same meaning as the margin of exposure.

Maximum tolerable daily intake (MTDI): *See* Provisional maximum tolerable daily intake (PMTDI).

Maximum tolerated dose (MTD): A high dose used in chronic toxicity testing that is expected, on the basis of an adequate subchronic study, to produce limited toxicity when administered for the duration of the test period.

Modified atmosphere packaging: A packaging technology for increasing shelf life in which the internal atmosphere is modified by reducing oxygen and replacing it with either carbon dioxide or nitrogen gas.

No-observed-(adverse-)effect level (NO(A)EL): Greatest concentration or amount of a substance, found by experiment or observation, that causes no detectable (adverse) alteration of morphology, functional capacity, growth, development or lifespan of the target organism under defined conditions of exposure.

Potable water: Drinking-water of sufficiently high quality that it can be consumed or used without risk of immediate or long-term harm.

Provisional maximum tolerable daily intake (PMTDI): The reference value, established by the Joint FAO/WHO Expert Committee on Food Additives, used to indicate the safe level of intake of a contaminant with no cumulative properties. Its value represents permissible human exposure as a result of the natural occurrence of the substance in food and drinking-water. In the case of trace elements that are both essential nutrients and unavoidable constituents of food, a range is expressed, the lower value representing the level of essentiality and the upper value the PMTDI. The tolerable intake is generally referred to as “provisional”, as there is often a paucity of data on the consequences of human exposure at low levels, and new data may result in a change to the tolerable level.

Residue: Chemicals that remain in or on food after, for example, disinfection, pesticide application, etc.

Resistance: An increased, genetic-based ability of a microorganism to survive a recommended usage level of an antimicrobial compound, resulting in a high

likelihood of treatment failure. This is similar to the definition of “clinical resistance” used by the European Food Safety Authority.

Risk assessment: A process intended to calculate or estimate the risk to a given target organism, system or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. The risk assessment process includes four steps: hazard identification, hazard characterization, exposure assessment and risk characterization.

Risk–benefit assessment: An activity that weighs the probability and severity of harm in a particular exposure scenario against the probability and magnitude of benefit as a basis for risk management decisions and communication to the public.

Risk characterization: The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system or (sub)population, under defined exposure conditions.

Spoilage microorganism: Microorganisms that cause undesirable changes to the colour, odour, taste and texture of food.

Superchlorination: Use of high chlorine dosage to ensure sufficient free chlorine residual to inactivate harmful microorganisms.

Target microorganism: A microbial species, genus or group for which lack of control during a specified process could result in adverse public health consequences.

2-Thiobarbituric acid reactive substances (TBARS): Biological specimens contain a mixture of TBARS, including lipid hydroperoxides and aldehydes, which increase as a result of oxidative stress. Plasma concentrations of TBARS are an index of lipid peroxidation and oxidative stress.

Tolerable daily intake (TDI): Analogous to acceptable daily intake (an estimate of the amount of a contaminant in food or drinking-water, expressed on a body weight basis, which can be ingested daily over a lifetime by humans without appreciable health risks). The term tolerable is used for agents that are not deliberately added, such as contaminants in food.

Tolerance: Reduced susceptibility of a microorganism to an antimicrobial treatment, usually determined as an increase in the minimum inhibitory concentration or minimum bactericidal concentration, that does not result in treatment failure, if the treatment is applied as recommended.

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Attachment 9



19 March 2010
[8-10]

FINAL ASSESSMENT REPORT

PROPOSAL P282

PRIMARY PRODUCTION & PROCESSING STANDARD FOR POULTRY MEAT

For Information on matters relating to this Assessment Report or the assessment process generally, please refer to <http://www.foodstandards.gov.au/foodstandards/changingthecode/>

Executive Summary

Purpose

FSANZ has prepared this Final Assessment Report¹ on Proposal P282 which includes draft variations to the *Australia New Zealand Food Standards Code* (the Code).

This Report is prepared in accordance with the principles of best practice regulation recommended by the Council of Australian Governments: identifying the problem that has prompted government action; the objectives of such action and possible options for achieving the objectives. An impact analysis of the risk management options has been conducted and a preferred option recommended.

FSANZ's decision is to vary the Code by introducing a primary production and processing standard for poultry meat and to introduce a preliminary Standard (Standard 4.1.1) to augment the Chapter 4 standards. Minor amendments are also recommended to Standard 1.6.2 – Processing Requirements, Standard 2.2.1 – Meat and Meat Products and Standard 4.2.3 – Production and Processing Standard for Meat.

Introduction

This Final Assessment Report represents the final stage in addressing food safety within the poultry meat supply chain. The work has progressed with the advice and guidance of a Standard Development Committee comprising representatives from the poultry industry, government regulators and consumers.

The Problem

FSANZ undertook a scientific risk assessment of the public health and safety of poultry meat in Australia (FSANZ, 2005). This assessment concluded that the main microbiological hazards associated with poultry meat are contamination with *Salmonella* and *Campylobacter*.

In Australia, raw poultry meat purchased by the consumer is very likely to be contaminated with *Campylobacter* (90%) and to a lesser extent, *Salmonella* (43%, with 13% being non-Sofia *Salmonella* serovars²). The higher the prevalence and concentration of these two bacteria being present on raw poultry, the greater the likelihood these pathogens could be present at the point of consumption and therefore a greater likelihood of illness occurring.

Campylobacteriosis is the most commonly notified food-borne illness in Australia and it is estimated that approximately 30% of cases (or 83,100 cases per year³) can be attributed to contaminated poultry (Stafford et al, 2007). Similar data are not available for *Salmonella* but a proportion of the estimated 81,000 food-borne cases of salmonellosis in Australia per year could be reasonably expected to come from contaminated chicken.

¹ This Report has been prepared according to the FSANZ standard development process as was in force prior to 1 July 2007.

² *Salmonella* Sofia is the most commonly isolated serovar in chicken in Australia and it is not normally pathogenic to humans.

³ This is 30% of the estimated 277,000 total cases of campylobacteriosis that occurs each year in Australia (Hall et al, 2005).

Chicken meat has been identified internationally as one of the most important food vehicles for these two organisms (FAO and WHO, 2009).

Raw poultry contaminated with *Salmonella* or *Campylobacter* can cause illness if the poultry meat consumed is undercooked or contamination from the raw poultry is transferred to cooked poultry or other food that is ready-to-eat. Cross contamination between raw and ready-to-eat food is a particular concern with *Campylobacter*, as only small numbers of the bacteria are needed to cause human illness.

There are regulatory measures in place for the primary processing of poultry within an Australian Standard (AS 4465-2005), which require poultry processors to develop and implement Hazard Analysis Critical Control Point (HACCP) programs. A properly developed and implemented HACCP program should be sufficient to ensure the likelihood of poultry being contaminated with *Salmonella* and *Campylobacter* during the slaughtering process is kept to a minimum.

Industry reports that the majority of poultry growers comply with industry developed biosecurity manuals such as the *National Biosecurity Manual for Contract Meat Chicken Farming*. This manual specifies the biosecurity measures necessary to prevent the introduction of infectious diseases to poultry and the spread of disease from an infected area to an uninfected area. These measures include controls needed to minimise flock infection with *Campylobacter* and *Salmonella*.

FSANZ coordinated a national study to obtain information on the likelihood of live chickens being contaminated with *Salmonella* and *Campylobacter* and also the likelihood of the chicken being contaminated after it has been slaughtered (FSANZ, 2010). Overall, the results indicated that a large percentage of live chickens entering processing plants are infected with *Campylobacter* (84%) and, to a much lesser extent, *Salmonella* (13% with 7.5% positive for non-Sofia serovars). Samples taken at the end of primary processing gave a similar prevalence for *Campylobacter* (84%). However, the samples tested were higher for the prevalence of *Salmonella* at the end of processing (37% with 22% positive for non-Sofia serovars). The levels of *Campylobacter* on the carcass were reasonably high (~500 per 100 cm²) and for *Salmonella*, low (~1 per 100 cm²).

Overseas studies show that steps can be taken to lower both the prevalence and concentration of *Salmonella* and *Campylobacter* on-farm and at primary processing. New Zealand has been able to demonstrate a 50% reduction in cases of *Campylobacter* infection caused by food, as a result of its intervention strategy (NZFSA, 2009). This reduction has been achieved partly by improving biosecurity measures on-farm and, in particular, controls during primary processing.

Objective

The objective of this Proposal was to reduce the incidence of food-borne illness from *Campylobacter* and *Salmonella* by minimising the prevalence and concentration of these two pathogens in poultry.

Options

In order to decide the most cost-effective approach for achieving the objective, FSANZ proposed risk management options. These options included the *status quo* as a comparative measure against which appropriate non-regulatory and regulatory approaches can be assessed. Four options were proposed.

Option 1 – Status quo

No change made to the existing regulatory regime.

Option 2 – consumer education

A specific education campaign developed with the aim of improving consumer handling and cooking of poultry.

Option 3 – industry self-regulation

Poultry growers would be encouraged to follow control measures that specifically address food safety issues at the primary production level. Processors would continue to comply with the current regulatory requirements.

Option 4 – through chain food safety management consisting of regulatory elements on farm and on processors

Poultry growers and processors would be required to comply with regulatory requirements for the primary production and processing of poultry by way of an amendment to the Code.

Impact analysis

All Australian Government departments and agencies need to demonstrate that their proposals deliver net benefits to the community. This includes an analysis of the impact of each proposed risk management option on different affected parties. The parties likely to be affected by the proposed options are consumers of poultry meat and poultry products, businesses involved in the production, distribution and sale of poultry meat and poultry products and state and territory agencies.

Option 1 (*status quo*) does not introduce any new measures to lower the likelihood of the community contracting campylobacteriosis and salmonellosis from the consumption of poultry. The adoption of the *status quo* option is estimated to cost the community a figure in the range of \$AUD 14 m⁴ to \$74 m annually, which is the estimated current cost burden associated with illness from poultry contaminated with *Campylobacter* or *Salmonella*. Option 2 could reduce poultry associated illness from *Campylobacter* and *Salmonella* by 3%, according to a Dutch Government study (Havelaar et al, 2007). This option is estimated to provide a maximum benefit to the community of around \$2 m with a sensitivity analysis indicating a benefit of \$0 to \$3.4 m⁵. However, any such benefit could be short lived as the impact of the education campaign is expected to lessen over time.

⁴ Unless otherwise stated, all dollar amounts are in Australian dollars.

⁵ Sensitivity analysis involves estimating a range of outcomes (high, low and medium case) depending on the uncertainty in data and assumptions.

Option 3 (industry self-regulation), as per option 4, has the potential to reduce flock prevalence of poultry with *Campylobacter* and *Salmonella* over that possible under the *status quo*. This is achieved by encouraging poultry growers to have improved biosecurity systems in place and for industry to report to government on compliance levels. However the benefits of this option are not expected to be as high as those for option 4. Higher compliance levels are expected under option 4 because poultry growers are legally obligated to comply with biosecurity measures and penalties will apply for non-compliance.

Option 4 is the preferred option as it represents the most cost effective way of reducing the likelihood of food-borne illness occurring from the consumption of poultry. It provides a greater incentive to poultry growers to comply with biosecurity measures by legally obligating them to have these measures in place. It also introduces independent oversight by government and penalties for non-compliance. Poultry growers and transporters would be required to put in place measures to reduce flock infection with *Campylobacter* and *Salmonella*. This lowers the likelihood, and degree to which, raw poultry will be contaminated with *Campylobacter* and *Salmonella* and hence the likelihood that illness will occur.

Data provided by the Australian Chicken Meat Federation indicate compliance with a Standard for Poultry Meat will result in the industry incurring an initial cost of \$11 m in the first year and \$4 m each year thereafter. Allowing for the fact that the benefits of initial infrastructure investments will be realised over a number of years, to achieve a positive net benefit over five years would require at least a 14.5% reduction in illness or 13% if considered over 10 years (based on net present value calculations at a 7% discount rate). International experience, while not directly comparable, would suggest that reductions in excess of these percentages might be achievable.

Decision

To approve draft Standards 4.1.1 – Primary Production and Processing Standards Preliminary Provisions and 4.2.2 – Primary Production and Processing Standard for Poultry Meat and make consequential amendments to Standards 1.6.2 – Processing Requirements, 2.2.1 – Meat and Meat Products and 4.2.3 – Production and Processing Standard for Meat.

Reasons for Decision

At Final Assessment, FSANZ has approved draft variations to the Code. The amendments:

- address public health and safety concerns raised in the Scientific Assessment of the Public Health and Safety of Poultry Meat in Australia
- are consistent with the section 18 objectives of the FSANZ Act to protect public health and safety
- provide a nationally consistent legislative framework for a whole-of-chain approach to poultry and poultry product safety

- take into account existing state and territory requirements, providing a consolidated set of requirements based on scientific assessment
- provide measures that are outcome-based and would not impose any unwarranted overall additional costs to industry over existing requirements.

Implementation and review

Implementation is the responsibility of the States and Territories. The Implementation Sub-Committee (ISC) is facilitating the consistent national implementation of the Standard for Poultry Meat.

A two-year implementation timeframe has been adopted, from the date the Primary Production and Processing Standard for Poultry Meat is gazetted.

FSANZ coordinated a baseline survey on the prevalence and concentration of *Salmonella* and *Campylobacter* in chicken meat on-farm and at primary processing (FSANZ, 2010). FSANZ proposes that a follow up survey be undertaken, two to three years after the implementation of the Standard, to determine whether the Standard has been successful in lowering the prevalence and concentration of *Salmonella* and *Campylobacter* in poultry.

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SUPPORTING DOCUMENTS

The following material, which was used in the preparation of this Final Assessment Report, is available on the FSANZ website at

<http://www.foodstandards.gov.au/foodstandards/proposals/proposalp282primaryp2442.cfm>.

SD1: Cost benefit scenarios for P282 – Primary Production & Processing Standard for Poultry Meat

1. INTRODUCTION

The Australian Government has agreed that Food Standards Australia New Zealand (FSANZ) should consider food safety throughout all parts of the food supply chain for all industry sectors. FSANZ has been developing primary production and processing standards for identified industry sectors for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

A primary production and processing standard, incorporated into Chapter 4 of the Code and applicable in Australia, is a set of obligations on primary producers and processors of food commodities. These obligations include measures to control food safety hazards that could occur during the production and processing of food. Development and application of primary production and processing standards to industry sectors is dependent on analysis of the public health and safety risks, economic and social factors and current regulatory and industry practices.

To date, FSANZ has developed primary production and processing standards for the seafood and dairy sectors and is currently assessing the development of standards for the egg, raw milk products, meat and seed sprouts sectors.

This Final Assessment Report represents the last stage in the development of P282 – Primary Production & Processing Standard for Poultry Meat. A Standard Development Committee (SDC) consisting of representatives from the industry, government regulators and consumers was established by FSANZ to assist and advise with this Proposal. The Draft Assessment Report⁶, released in December 2005 included a scientific assessment of the risk to public health and safety from the consumption of poultry meat products and proposed risk management options, and their analysis, for consultation.

This Report summarises the submissions from the second round of public consultation and details the response to those submissions (Attachment 3). In addition, this Report includes the proposed amendments to the Code.

1.1 Poultry meat

1.1.1 Scope

Following advice from the SDC, this Proposal examined major avian species consumed in Australia – including chickens, ducks, turkeys, geese, pigeons, quail, pheasants and guinea fowls. Wild caught birds (e.g. magpie geese and mutton birds) where processed in a registered establishment were also considered. However, ratites (emus and ostriches) were not included as they are processed using different methods and the vast majority are processed in export-registered premises which are already regulated. Ratite meat and eggs, and products thereof, will be considered under a separate Proposal at a later date.

⁶ <http://www.foodstandards.gov.au/foodstandards/proposals/proposalp282primaryp2442.cfm>

1.2.1 The production chain

Primary production of poultry includes all steps from the importation of fertilised eggs to the transport of live birds to the slaughter facility⁷ (Figure 1). Differences in primary production between chicken meat and other poultry meat species are often observed in the type of housing/facilities used, composition of feed and age at which poultry are slaughtered⁸. There are also different requirements for the importation of fertile eggs, with only chicken, duck and turkey eggs permitted to be imported into Australia.

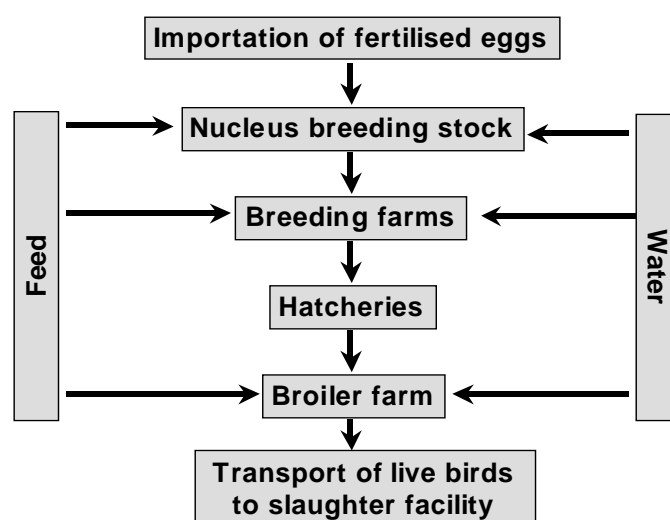


Figure 1: Stages in the primary production of poultry for human consumption

Processing of poultry includes the slaughtering of live poultry, portioning and any value adding such as crumbing and marinating (Figure 2). Poultry processing establishments vary in size from highly automated, large poultry processing establishments processing 4000-9000 poultry per hour to smaller, mainly manual or semi-automated establishments processing less than 1000 poultry per day.

Increasingly, dressed poultry carcasses undergo further processing through portioning and value-adding which may occur at the initial processing establishment, other further processing establishments or at poultry retail establishments.

⁷ Further detail of the poultry meat industry can be found in the Initial Assessment Report for Proposal P282. The report is available on the FSANZ website at http://www.foodstandards.gov.au/srcfiles/P282_Poultry_PPPS_IAR_Final.pdf.

⁸ A summary of processes involved in the production of a number of different non-chicken poultry species is included in a report from the Rural Research and Development Corporation, RIRDC Report Number 03/023. <http://www.rirdc.gov.au>

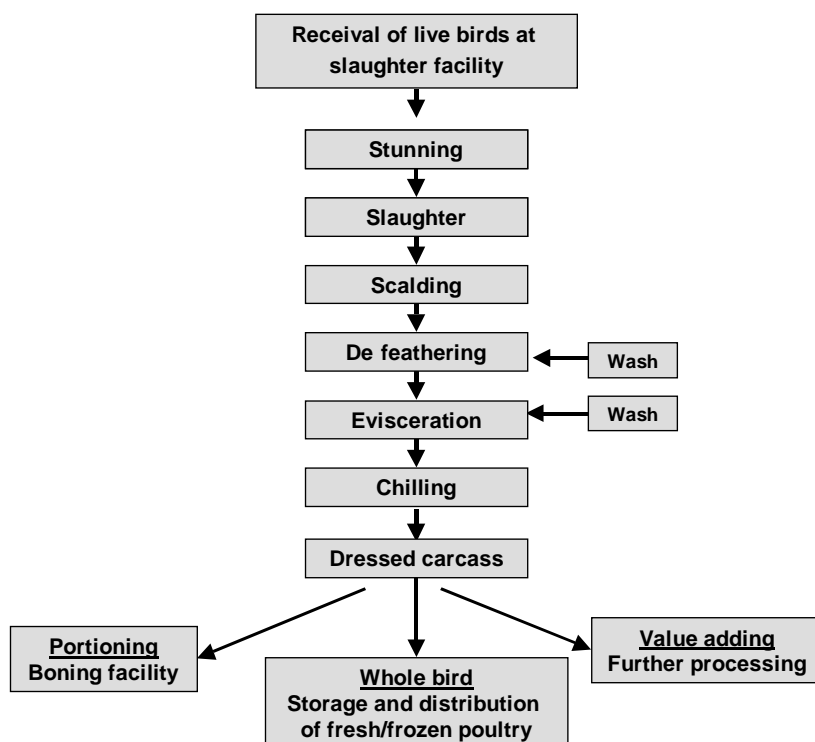


Figure 2: Stages in the processing of poultry for human consumption

1.2 The Problem

In Australia there is an unacceptably high number of food-borne illness cases occurring as a result of the high likelihood of raw poultry being contaminated with *Campylobacter* and, to a lesser extent, *Salmonella*. The higher the prevalence and concentration of these two bacteria on raw poultry, the more likely it is that illness will occur.

1.2.1 Public health risk

FSANZ undertook a scientific risk assessment of the public health and safety of poultry meat in Australia (FSANZ, 2005). This assessment concluded that the main microbiological hazards associated with poultry meat are contamination with *Salmonella* and *Campylobacter*. Commercial chicken meat has been identified as one of the most important food vehicles for these organisms (FAO and WHO, 2009).

Raw poultry contaminated with *Salmonella* or *Campylobacter* can cause illness if the poultry meat consumed is undercooked or contamination from raw poultry is transferred to cooked poultry or other food that is ready-to-eat. Cross contamination between raw and ready-to-eat food is a particular concern with *Campylobacter*, as ingestion of only small numbers of the bacteria are likely to cause illness.

The symptoms of *Salmonella* and *Campylobacter* infection are similar and generally consist of self-limiting gastroenteritis, sometimes requiring hospitalisation. In a small proportion of cases, infection can lead to more severe, long term illness such as septicaemia, reactive arthritis or Guillain-Barré syndrome, a potentially life-threatening neurological disorder.

Campylobacteriosis is the most commonly report notified disease in Australia, followed by salmonellosis. In the 2007 Annual Report of the OzFoodNet Network, campylobacteriosis was the most frequently notified illness with 16,984 notifications, or 120 cases per 100,000 population (The OzFoodNet Working Group, 2008). Salmonellosis was the second most frequently notified illness at 9,484 notifications or 45 cases per 100,000 population (The OzFoodNet Working Group, 2008). These figures represent the number of notified cases and not the numbers of actual cases. Many cases of campylobacteriosis and salmonellosis are not reported as they are not confirmed by microbiological testing.

OzFoodNet, the food-borne disease surveillance network operating in Australia, undertook a study to estimate the amount of food-borne gastroenteritis in a typical year. This study estimated that in a typical year (around the year 2000) there were approximately 277,000 **total** cases of campylobacteriosis (95% credible interval 89,800-463,000) and 92,000 **total** cases of salmonellosis (95% credible interval 26,000-158,000) (Hall et al, 2005). The report also estimated that proportion of the total cases that could be attributed to food. For *Campylobacter* this was estimated to be 75%⁹ or 208, 000 (95% credible interval 67,000 – 350,000) and for *Salmonella* 87%¹⁰ or 81,000 (95% credible interval 23,000-138,000).

It is difficult to estimate what proportion of *Campylobacter* and *Salmonella* cases can be attributed to contaminated poultry. However, it has been estimated that poultry meat may account for ~30% of the **total** number of *Campylobacter* cases that occur each year in Australia (Stafford et al, 2007), which, if the estimates from the OzFoodNet study discussed above are used, would equate to 83,100 cases per year i.e. 30% of the estimated 277,000 **total** *Campylobacter* cases. No similar data are available for *Salmonella*. However, poultry is one of the implicated foods in *Salmonella* outbreaks. In a review of reported salmonellosis outbreaks in Australia during 1995-2000, poultry meat was associated with 13% of the identified salmonellosis outbreaks and 8% of the total outbreak cases (Dalton et al, 2004).

1.2.2 Factors contributing to risk

Poultry become infected with *Salmonella* and *Campylobacter* on-farm. With *Salmonella*, day old chicks can be infected if they are sourced from contaminated breeder flocks. Poultry can also become infected with both *Salmonella* and *Campylobacter* horizontally, that is by contamination being introduced into a broiler shed.

Research was conducted by the Rural Industries Research and Development Corporation (RIRDC) on risk factors for *Campylobacter* in broilers (Miflin, 2001). Potential sources of *Campylobacter* were shown to be external to the shed. Wild birds, sheep, cattle and mice were all shown to be potential carriers of *Campylobacter*. However, one of the greatest risks to flocks being colonised with *Campylobacter* was shown to be depopulation¹¹. In particular, this study found that crates, in which caught poultry are placed, introduce *Campylobacter* into the shed and thereby infect the remaining poultry. While crates are normally cleaned daily, they are not routinely cleaned and disinfected between sheds and farms being depopulated on the same day. Once introduced into a shed, *Campylobacter* spreads rapidly and will infect the majority of remaining poultry within 3-6 days (Miflin, 2001).

⁹ 95% credible interval of 67%-83%.

¹⁰ 95% credible interval of 81%-93%.

¹¹ Depopulation is the practice of removing part of a broiler flock for slaughter. This means one flock can supply broilers of different ages (and therefore sizes) to meet market demands.

This rapid spread of *Campylobacter* throughout the flock is a result of high levels of shedding and faecal-oral transmission, assisted by shared water and feed (Lee and Newell, 2006). While day old chicks can be infected with *Salmonella* from infected breeder flocks, the major avenue by which *Salmonella* is introduced into poultry flocks is considered to be poultry feed (FSANZ, 2005). While heat-treatment of feed will lower the risk of *Salmonella* being present, contamination can still occur post processing. Birds and rodents can contaminate the raw ingredients of poultry feed as well as the heat-treated feed. As with *Campylobacter*, once poultry within a flock are infected, the *Salmonella* infection spreads rapidly to the remaining poultry in the flock.

Both *Salmonella* and *Campylobacter* colonise the gastrointestinal tract of poultry and infected birds can shed large numbers of the organism in their faeces without the birds being affected. Contamination of the poultry carcass can occur when the poultry are slaughtered, particularly during the scalding, plucking and evisceration processes (FAO and WHO, 2009). During evisceration, the content of the intestines can be spilt over onto the carcass. External faecal contamination on skin and feathers will also contribute to contamination of the carcass. Poultry carcasses are also normally chilled in a large water bath, referred to as 'spin chilling', which can further spread contamination if the spin chillers are not correctly maintained.

FSANZ coordinated a national study to obtain information on the likelihood of live chickens being contaminated on-farm with *Salmonella* and *Campylobacter* and also the likelihood of the chicken being contaminated after it has been slaughtered¹² (FSANZ, 2010). Samples were taken in 2007-2008. Overall, the results indicated that a large percentage of the live chickens entering the processing plants are infected with *Campylobacter* (84%) and to a much lesser extent, *Salmonella* (13% with 7.5% positive for non-Sofia serovars). Samples taken at the end of primary processing gave a similar prevalence for *Campylobacter* (84%). However, the samples tested were higher for the prevalence of *Salmonella* at the end of processing (37% with 22% positive for non-Sofia serovars). The levels of *Campylobacter* on the carcass were reasonably high (~500 per 100 cm²) and for *Salmonella*, low (~1 per 100 cm²).

These results are similar to the results from a retail baseline microbiological survey carried out in 2005-2006 in South Australia and New South Wales, which looked at contamination levels in raw chicken meat, purchased at retail outlets (Pointon et al, 2008). The study found that raw chicken is likely to be contaminated with *Campylobacter* (90%) and to a lesser extent *Salmonella* (43% with 13% being non-Sofia serovars).

1.2.3 How is the risk addressed under current regulatory and non-regulatory measures?

1.2.3.1 Regulatory measures

On-farm

There are currently no regulatory measures in place for poultry growers to minimise the likelihood of poultry being contaminated with *Salmonella* and *Campylobacter* on-farm.

¹² Live chickens and chicken meat were tested as chicken meat is consumed in far greater quantities than other poultry. Per capita consumption of chicken meat was estimated to have reached 37 kg/person in 2007-2008, compared to other poultry being 2.2 kg/person (ACMF, 2009).

Primary processing

In March 1995, the (then) Agriculture and Resource Management Council of Australia and New Zealand¹³ determined that aspects of all existing national meat industry codes relevant to human health would be mandated by amendment of legislation in all States and Territories. This decision was given effect by appointment of a Steering Group¹⁴, which reviewed existing codes of hygienic practices (in relation to meat) to express mandatory national standards in outcome terms. The mandatory requirements were specified within Australian Standards and require process control to be achieved through the application of HACCP¹⁵ methodology as defined by the Codex Alimentarius Commission.

The Australian Standard, AS 4465-2005 *Construction of Premises and Hygienic Production of Poultry Meat for Human Consumption*, requires poultry processors to develop and implement HACCP programs and also includes specific requirements relating to the design and construction of the premises, the processing of poultry, health and hygiene requirements and cleaning and sanitising. A properly-developed and implemented HACCP program should be sufficient to ensure the likelihood of poultry being contaminated with *Salmonella* and *Campylobacter* during the slaughtering process is kept to a minimum.

Retail/Food Service

All food businesses in Australia are required to comply with the Food Safety Standards within the Code. Standard 3.2.2 – Food Safety Practices and General Requirements specifies what steps food businesses must take to ensure food is handled safely. With respect to poultry, this includes cooking it thoroughly and ensuring that contamination from raw poultry is not transferred to cooked poultry or other ready-to-eat food.

1.2.3.2 Non-regulatory measures

On-farm

Currently, the majority of chicken and turkey growers comply with an industry manual, *National Biosecurity Manual for Contract Meat Chicken Farming*. This manual was developed by the Australian Chicken Meat Federation in 2002 and forms part of, or is directly or indirectly referred to, in most contracts governing the farming of chicken on behalf of chicken processors. This manual specifies the biosecurity measures necessary to prevent the introduction of infectious diseases to poultry and the spread of disease from an infected area to an uninfected area. This includes controls needed to minimise flock infection with *Campylobacter* and *Salmonella*. Duck growers also follow a similar manual.

¹³ This Council has been replaced by the Primary Industries Ministerial Council and consists of the Australian/State/Territory and New Zealand government ministers responsible for agriculture, food, fibre, forestry, fisheries and aquaculture industries/production and rural adjustment policy.

¹⁴ The Steering Group comprised Chairmen and Chief Executives of State and Territory meat hygiene authorities, the Australian Quarantine Inspection Service, meat industry organisations, food safety technical advisers and the (then) Australia New Zealand Food Authority.

¹⁵ The Hazard Analysis and Critical Control Point (HACCP) system ensures the safety of food by requiring potential food safety hazards to be controlled at every step of a food's production and to keep records to demonstrate this is occurring.

A new National Biosecurity Manual for Poultry Production has been written, in part, to assist poultry growers meet their legal obligations under the proposed Standard for Poultry Meat. The new Biosecurity Manual was developed by a consultative group with representatives from the poultry industry and relevant state and commonwealth government departments. It was published by the Australian Government Department of Agriculture, Fisheries and Forestry (DAFF) in May 2009 (DAFF, 2009) and applies to meat chickens, the egg industry and growers of ducks, turkeys, game birds, emus and ostriches. It recognises the importance that biosecurity plays in minimising the incidence and spread of microorganisms of public health significance.

This new Biosecurity Manual is similar to the current biosecurity manuals in place within the poultry industry but is clearer to follow and more detailed, see section 4.3. It includes requirements for staff training and more information on water treatment, rodent control, pick-up and transport and movement of personnel and equipment.

The intention is that each part of the poultry industry adapts the generic poultry biosecurity manual to reflect the requirements as they apply to their industry. For example, the Australian Chicken Meat Federation has updated its 2002 biosecurity manual in line with the new Biosecurity Manual and is seeking approval of the revised manual with the Animal Health Committee¹⁶. Once the revised manual is approved, the new manual is likely to be referred to directly or indirectly in most contracts governing the farming of chickens, when new contracts are agreed to with chicken growers (contracts are normally in place for five years).

Consumers

The food safety management strategies for consumers of poultry meat and poultry meat products are primarily education and information dissemination. The messages include cooking poultry thoroughly until it appears cooked and juices run clear. They also include advice on separating raw and cooked foods.

1.2.3.1 International measures

The Codex Alimentarius Commission is currently developing guidelines for the control of *Salmonella* and *Campylobacter* in poultry from ‘primary production-to-consumption’, with potential control measures being considered at each step in the process. The draft guidelines consist of three sections: one addressing good hygiene practices; another covering hazard-based control measures; and a third focusing on risk-based control measures. These guidelines were considered at the Fort-first session of the Codex Committee on Food Hygiene in November 2009 and were returned to the working group for re-drafting¹⁷.

To ensure the development of the above guidelines was underpinned with the most robust scientific data, the 40th Session of CCFH requested the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO) to provide them with the necessary scientific advice.

¹⁶ The Animal Health Committee (AHC) is a committee that sits under the National Biosecurity Committee and reports to the Primary Industries Standing Committee. The AHC comprises of the Chief Veterinary Officers of the Commonwealth, states and territories and New Zealand along with representatives from the Australian Animal Health Laboratory (CSIRO), Animal Health Australia and Biosecurity Australia.

¹⁷ Further information is available from the Codex Alimentarius Commission’s website www.codexalimentarius.net.

In response to this request, FAO and WHO convened an *ad hoc* Technical Meeting from 4-8 May 2009 in Rome Italy. A report from this meeting has been published¹⁸. This report is an independent assessment and review of all available scientific information on control of *Campylobacter* and *Salmonella* at relevant stages of the broiler supply chain and has been referenced in this Final Assessment Report, where appropriate.

1.2.4 Do the current regulatory and non-regulatory measures adequately address the risk?

The FSANZ coordinated national chicken meat survey on the prevalence and concentration of *Salmonella* and *Campylobacter* on-farm and at primary processing found that chickens are contaminated at the on-farm stage of the chicken meat supply chain and this contamination is carried through to the chicken carcasses at the end of the slaughtering process. In an earlier, retail study, similar contamination levels were found on chicken meat at retail outlets. This indicates that the contamination originating from infected flocks on-farm is carried through to the chicken meat being purchased by the consumer.

During the slaughtering of poultry, steps can be taken to minimise the likelihood of poultry carcasses being contaminated with *Salmonella* and *Campylobacter*. As evidenced by the survey results, the likelihood of poultry carcasses remaining contaminated following the slaughtering process is also high, particularly with *Campylobacter*.

The RIRDC study illustrates the importance of biosecurity measures being in place on farm to minimise contamination being introduced into poultry flocks (Miflin, 2001). While most poultry growers are obligated, under contract, to have biosecurity measures in place, this approach has not proven successful in lowering flock prevalence with *Campylobacter*.

Countries that have improved practices and procedures on-farm and at slaughtering facilities have successfully reduced the amount of *Salmonella* and *Campylobacter* in raw chicken and consequently human illness from these pathogens. Countries that have interventions in place on-farm to lower the prevalence of either *Campylobacter* or *Salmonella* include New Zealand, the United Kingdom, Sweden, Netherlands, Iceland and Norway. The majority also have a regulatory backing and require biosecurity to be improved on-farm. With the exception of the UK, where the interventions growers are voluntary, these interventions have resulted in significant reductions in the flock prevalence of *Campylobacter*. See section 4.4 for further detail.

For example, in New Zealand a *Campylobacter* reduction strategy was implemented in 2006 and specific poultry processing targets set in 2008 (NZFSA, Dec 2008). Poultry processors must ensure that at the end of processing, their poultry carcasses meet the specified microbiological criteria¹⁹ (NZFSA, Jan 2008). This strategy has seen cases of *Campylobacter* infection caused by food being reduced by 50% (NZFSA, 2009).

Food-borne illness data show that the mishandling of poultry must be occurring relatively often both in the home and in food service and retail outlets as an estimated 83,100 cases of *Campylobacter* can be attributed to poultry each year (see section 1.2.1).

¹⁸ The report is available from the FAO website. <http://ftp.fao.org/ag/agn/jemra/MRA1911Nov09.pdf>

¹⁹ Standard (sized) processors must sample three poultry carcasses per day and are required to achieve microbiological criteria for *Campylobacter* of an 80th percentile of 1200 CFU/carcass, 3.08 log₁₀CFU/carcass.

If raw poultry is heavily contaminated, the contamination can be spread more easily from the raw poultry to the cooked poultry or other ready-to-eat foods and cause illness (see section 1.2.2).

The FSANZ, *Scientific Assessment of the Public Health and Safety of Poultry Meat in Australia*, found that measures to reduce prevalence and levels of *Salmonella* and *Campylobacter* on carcasses reduced the estimated number of cases of human illness (FSANZ, 2005). If cases of campylobacteriosis and salmonellosis are to be reduced, stronger measures further back in the poultry meat supply chain are needed to reduce the prevalence and concentration of these two pathogens on raw poultry.

1.2.5 Summary of the Problem

In Australia, raw poultry purchased by the consumer is very likely to be contaminated with *Campylobacter* (90%) and to a lesser extent, *Salmonella* (43% with 13% being non-Sofia). Campylobacteriosis is the most commonly notified food-borne illness in Australia and it is estimated that approximately 30% of cases can be attributed to contaminated poultry. This equates to 83,100 cases per year. *Campylobacter* and *Salmonella* cause gastroenteritis, which in some cases results in more serious illness.

Poultry mainly become infected with *Salmonella* and *Campylobacter* as a result of these bacteria contaminating the growing sheds. Once poultry become infected, the majority of the flock can become infected rapidly. There are many possible sources of contamination in Australia, including contaminated feed for *Salmonella*, and for *Campylobacter*, the process of depopulating poultry and in particular, the crates used to hold and transport poultry to processing facilities. Poultry infected by *Salmonella* and *Campylobacter* still appear healthy and therefore flock yields are not affected. Therefore, unless tested, there is no way of differentiating between infected and non-infected flocks.

The findings from both the FSANZ baseline survey and the retail study show that poultry are infected on-farm and this contamination is carried through to the processing plant and then to the retail product. The poultry may then be mishandled, causing illness.

Overseas studies show that steps can be taken to lower both the prevalence and concentration of *Salmonella* and *Campylobacter* on-farm and at primary processing in poultry, thereby reducing the likelihood of illness occurring.

While Australia has comprehensive regulatory measures in place for the primary processing of poultry, there are no regulatory measures for the growing of poultry on-farms. If cases of campylobacteriosis and salmonellosis are to be reduced, stronger measures are needed earlier in the poultry meat supply chain.

2. OBJECTIVES

2.1 Objective of the Proposal

The objective of this Proposal is to reduce the incidence of food-borne illness from *Campylobacter* and *Salmonella* by minimising the prevalence and concentration of these two pathogens in poultry.

2.2 Statutory considerations

There are specific legislative constraints on FSANZ as a standard setting body. These constraints will be considered in any analysis of risk management options.

2.2.1 Food Standards Australia New Zealand Act 1991

Where regulatory interventions are required (e.g. by developing or varying a food standard), FSANZ is required by its legislation to meet three primary objectives which are set out in section 18 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). These are

- the protection of public health and safety; and
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying food regulatory measures, FSANZ must also have regard to

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

2.2.2 Policy guidelines

The Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) *Overarching Policy Guideline on Primary Production and Processing Standards* specifies a number of high order principles that must be considered where a standard is developed. These principles state that standards will be outcomes-based, address food safety across the entire food chain where appropriate, ensure the cost of the overall system should be commensurate with the assessed level of risk and provide a regulatory framework that only applies to the extent justified by market failure.

3. RISK MANAGEMENT OPTIONS

In order to determine the most effective and efficient approach for achieving the objective, FSANZ has considered various risk management options. These options include the *status quo* (the situation if no action is taken) as a comparative measure against appropriate non-regulatory (consumer education), self regulatory (industry) and regulatory (government) approaches.

The preferred option at Draft Assessment was for a regulatory approach for both the primary production and primary processing stages. At the primary production stage, the preferred option was to require poultry growers to control food safety hazards. At the primary processing stage, the preferred option was to continue to require poultry processors to control their hazards through a HACCP-based food safety management system, as currently required under State/Territory legislation.

The preferred option was generally supported by the Australian Chicken Growers Council²⁰, the Australian Food and Grocery Council, the Department of Agriculture, Fisheries and Forestry, the then Australian Consumers' Association (ACA now CHOICE), Coles Myer Ltd, the Food Technology Association of Victoria and the state enforcement agencies, with the exception of South Australia.

The South Australian Department of Health, the Department of Primary Industries and Resources South Australia and the South Australian Research and Development Institute, in a joint submission, did not support the proposed Standard for Poultry Meat. They are concerned that it will entrench current industry practice that currently results in frequent supply of contaminated poultry to consumers.

The Australian Chicken Meat Federation and Bartter Enterprises supported a non-regulatory approach on-farm and strengthening critical controls during the poultry processing phase.

We have refined the options, taking into consideration the comments and issues raised during the public consultation on the Draft Assessment Report. At Final Assessment, we have included an education campaign as an option and removed the option that obligated processors to ensure growers supplying them are controlling their food safety hazards.

3.1 Option 1 – *status quo*

Option 1, the *status quo*, retains the current situation i.e. FSANZ would not make any changes to the Code or propose any other regulatory changes for broiler farms, poultry transport operators and processors to address food safety.

In maintaining the *status quo*, there would be no regulatory requirements for poultry growers to address food safety. However, these businesses could choose to follow industry-based codes and, if a contract grower, would also be subject to any contractual obligations placed on them by poultry processors²¹.

Poultry processors would continue to comply with the *Australian Standard for the Construction of Premises and Hygienic Production of Poultry Meat for Human Consumption* (AS 4465-2005). This Standard has been adopted under all state and territory regulations to manage poultry meat safety during the processing phase of the poultry meat supply chain.

²⁰ The Australian Chicken Growers Council provided its support with the reservation that there did not appear to be a clear understanding in the proposed Standard for Poultry Meat of which factors in producing poultry that growers, processors and contractors have control over. The Council's support was also conditional on the Standard being consistently implemented by the jurisdictions.

²¹ The major poultry processors contract poultry growers to supply poultry. As part of this contract of supply, the poultry growers are required to meet certain food safety obligations and the processor will audit the farms to ensure they are meeting these contractual obligations.

3.2 Option 2 – consumer education

Under this option, a specific education campaign would be developed with the aim to improve consumer handling and cooking of poultry. No new regulation would be introduced for poultry growers, transporters or processors i.e. as per the *status quo*.

3.3 Option 3 – industry self regulation

Under this option, poultry growers would be encouraged to follow control measures that specifically address food safety issues at the primary production level. Compliance could be promoted by industry associations and the state regulatory agencies. Industry would be expected to report on compliance rates with these food safety measures and the procedures in place to rectify areas of non-compliance.

For processing, the *status quo* would continue i.e. poultry processors complying with AS 4465-2005 as currently required under state and territory regulation.

3.4 Option 4 – through-chain food safety management consisting of regulatory elements on farm and on processors

Under this option, a primary production and processing standard for poultry is adopted into the Code. This standard would specify food safety obligations for growing poultry and the processing of poultry, poultry meat carcasses and poultry meat products for human consumption. It would also include the implementation of measures to control the food safety hazards and the responsibility to demonstrate compliance.

At the primary production stage, poultry producers would be required to identify and control the food safety hazards associated with the growing of poultry. Specific requirements have also been included for:

- the control of inputs
- waste disposal
- health and hygiene
- ensuring poultry handlers have the necessary food safety skills and knowledge
- the design, construction and maintenance of premises, equipment and transportation vehicles
- traceability of poultry
- sale or supply of unsuitable poultry.

At primary processing, poultry processors would be required to identify and control the food safety hazards associated with the processing of poultry and verify the effectiveness of the control measures. Specific requirements have also been included for:

- prohibition on processing unsuitable poultry
- control of inputs
- waste disposal
- ensuring persons engaged in poultry processing have the necessary food safety skills and knowledge
- traceability of poultry

- sale or supply of unsuitable poultry.

For primary processing, these requirements reflect what is already required under AS 4465 - 2005 (see section 1.2.3).

The approved draft Standard is at Attachment 1 and an explanation of the provisions is at Attachment 2.

Following is a table summarising the options.

Table 1: Summary of the options to manage poultry meat safety

Option	On-farm	Processing
Option 1 - <i>Status quo</i>	<p>No regulatory requirements on poultry growers to implement biosecurity measures on-farm.</p> <p>Currently the majority of growers implement biosecurity measures as part of contractual arrangements to supply live poultry to poultry processors.</p> <p>Industry regulated.</p>	<p>Regulatory requirements in state and territory legislation.</p> <p>Poultry processors must comply with the <i>Australian Standard for Construction of Premises and Hygienic Production of Poultry Meat for Human Consumption</i> AS 4465-2005. This Standard includes a requirement for processing to be controlled through a HACCP program.</p> <p>Government regulated.</p>
Option 2 - Consumer education	<p>No regulatory requirements i.e. <i>status quo</i> (above)</p> <p>A specific education campaign is developed with the aim of improving consumer handling and cooking of poultry meat.</p>	<p>Regulatory requirements in state and territory legislation i.e. the <i>status quo</i> (above).</p>
Option 3 - Industry self regulation	<p>No regulatory requirements</p> <p>Poultry growers would be actively encouraged to improve biosecurity measures to control <i>Salmonella</i> and <i>Campylobacter</i> on-farm and the industry encouraged to report on compliance levels.</p> <p>Industry regulated.</p>	<p>Regulatory requirements in state and territory legislation i.e. the <i>status quo</i> (above).</p> <p>Government regulated.</p>
Option 4 - Regulatory requirements in the Code – on farm and on processors	<p>Regulatory requirements in the Food Standards Code</p> <p>Poultry growers legally obligated to identify and control the food safety hazards associated with the growing of poultry.</p> <p>Government regulated.</p>	<p>Regulatory requirements in the Food Standards Code.</p> <p>Poultry processors legally obligated to identify and control the food safety hazards associated with the processing of poultry. This would include a HACCP-based food safety program as in the <i>status quo</i>.</p> <p>Government regulated.</p>

4. **IMPACT ANALYSIS**

4.1 **Option 1 – *status quo***

The major advantage of this option is that it imposes no additional costs. However, the disadvantages are that the outbreaks of poultry-related illnesses and the associated cost burden, not only on those who contract these illnesses and their families, but also on their employers and the community's medical services, remain unchanged. In addition, there is the continuing cost to government of investigation of food-borne illnesses.

4.1.1 **Primary Production**

In maintaining the *status quo*, there would be no regulatory requirements for poultry growers or poultry transport operators to address the food safety hazards associated with their operations. Poultry growers and transporters could voluntarily comply with industry codes and may also be required to meet contractual requirements relating to biosecurity that includes food safety matters.

While there is currently no regulatory requirement for biosecurity measures to ensure good animal health and food safety outcomes, there is a binding agreement in place between the governments (all states and federal) and the chicken meat and the duck industry which governs arrangements to minimise the likelihood of exotic diseases occurring and spreading. The agreement also establishes cost sharing principles in case of an outbreak of exotic diseases. This agreement, known under the name of Emergency Animal Disease Response Agreement (EADRA), requires under section 14 ("Biosecurity") that each industry party to the agreement develop, maintain and implement a biosecurity program which is reviewed by Animal Health Australia on an annual basis. Further information on this agreement is available from the Animal Health Australia website²².

This agreement means the majority of poultry growers are already obligated to have biosecurity measures in place. This obligation is achieved through the processors entering into contracts with poultry growers that require compliance with biosecurity measures. The chicken meat industry has advised that chickens which may not be grown under contract i.e. where the processor is not also the owner of the chickens, is likely to be less than 1% of growers. The game bird industry has also advised that growers are usually contracted to processors for the provision of birds. While the focus of these biosecurity measures is minimising the occurrence and spread of exotic diseases, the measures necessary to minimise flock infection with *Salmonella* and *Campylobacter* are similar.

Processors audit their own growers to ensure these contractual obligations are being met. Therefore the extent to which growers comply with biosecurity measures is assessed by the industry itself. There is no independent assessment on whether the interventions are successful and the results of the FSANZ baseline survey would indicate that they are not reducing contamination.

Currently most chicken growers comply with the *National Biosecurity Manual for Contract Meat Chicken Farming*, which was developed by the Australian Chicken Meat Federation and published in 2002 (see section 1.2.3).

²² <http://www.animalhealthaustralia.com.au/programs/eadp/eadra.cfm>

The results of a benchmark survey study conducted on behalf of FSANZ found that approximately 65% of poultry primary production businesses complied with this Biosecurity Manual²³. This figure is consistent with data collected from an industry survey, undertaken earlier this year and provided to FSANZ by the Australian Chicken Meat Federation. The industry survey found that 65% of all meat chickens are grown on farms that are fully compliant with the current National Biosecurity Manual, 28% of farms are largely compliant and 7% comply to a limited degree. The areas of non-compliance included baiting programs that were insufficient, livestock not kept away from sheds and lack of fences or lockable gates. These areas of non-compliance could impact on flock infection with *Salmonella* and *Campylobacter* noting that the level of on farm compliance was not independently verified.

The ability of the current approach²⁴ to lower flock prevalence with *Salmonella* and *Campylobacter* is uncertain. Recent survey data indicates that live chickens are very likely to be contaminated with *Campylobacter*, and, to a lesser extent *Salmonella*, and this contamination is likely to be carried through to the raw chicken that is purchased by the consumer (see section 1.2.2).

It is estimated that chicken meat may account for ~30% of *Campylobacter* cases that occur each year in Australia (Stafford et al, 2007) or 83,100 cases per year. Similar data is not available for *Salmonella* but a proportion of the estimated 81,000 food-borne cases of salmonellosis per year could be reasonably expected to come from contaminated chicken.

The current measures alone do not seem to be effective in ensuring all growers work towards reducing the likelihood of live poultry being contaminated with *Salmonella* and *Campylobacter* spp. This may be because:

- the yield of poultry infected with these pathogens is not greatly affected
- while poultry processors check that their growers are complying with biosecurity measures, there is no immediate penalty for non-compliance – industry advises that continued non-compliance may result in a loss of contract for further supply of birds
- there is no independent assessment of whether the poultry growers are complying with biosecurity measures – this assessment is made by the processor the grower is contracted to supply live poultry
- growers are not offered higher premiums for supplying poultry that is free of *Campylobacter* or *Salmonella* infections, nor offered specific incentives to lower their infection rates.

Poultry processors could provide more incentive to poultry growers by paying a higher price for poultry with lower prevalence rates. Danish growers are paid a premium for supplying *Campylobacter*-free poultry to the major processor Danpo (Miflin, 2001). Danpo then sell a *Campylobacter*-free chicken²⁵, for which Danish consumers are prepared to pay a price premium (UK Advisory Committee on the Microbiological Safety of Food, March 2005).

²³ Colmar Brunton Social Research (2005) Benchmark Research on the Poultry Meat industry – Full Report prepared for Food Standards Australia New Zealand.

²⁴ Poultry growers are contracted to poultry processors to supply live poultry. Part of this contract is to comply with biosecurity measures. The processor determines compliance.

²⁵ Danish legislation covering *Campylobacter*-free status requires that there is 95% certainty that the prevalence of *Campylobacter* is below 1%. The *Campylobacter* status of the chickens must be tested prior to slaughter. See www.danpo.dk.

To date, poultry processors in Australia have not initiated any incentive system to promote the growing of poultry that has a lower incidence of *Campylobacter* and/or *Salmonella*. As contaminated raw poultry cannot be differentiated by the consumer from uncontaminated raw poultry, the consumer is unable to make this choice without poultry processors marketing and labelling potentially safer products, as has occurred in Denmark.

While responsible operators may not need additional incentives, the lack of incentives for the industry as a whole means the levels of live poultry contaminated with *Salmonella* and *Campylobacter* being supplied to poultry processors is likely to continue to be high. The higher the prevalence of *Campylobacter* and *Salmonella* on the incoming poultry, the more difficult it is for the processor to control the levels of these pathogens during processing. Contamination present after processing is likely to be carried through to the raw poultry purchased by the consumer. While the consumer could address the hazard of contaminated raw poultry through adequate cooking and correct handling, the current illness data indicates this does not always occur.

4.1.2 Primary processing

Primary processors would continue to comply with their legal obligations under AS4465-2005, which is mandated through State and Territory regulation and is enforced by the government agencies responsible for poultry processing within each State and Territory. The Meat Standards Committee²⁶ was responsible for maintaining AS4465-2005 until it was disbanded in 2007. Currently, there is no mechanism to review, update or change the Australian Standard.

Poultry processors who meet their legal obligations under AS4465-2005 should be ensuring that the contamination of poultry with *Salmonella* and *Campylobacter* is minimised during slaughtering and processing. During slaughtering and processing, poultry meat becomes contaminated, particularly during the evisceration process, when the content of the intestines can be spilt over onto the carcass. External faecal contamination on skin and feathers will also contribute to contamination of the meat. Poultry carcasses are also normally chilled in a large water bath, referred to as 'spin chilling', which can spread contamination between carcasses if free chlorine levels are not maintained in the chilling tanks.

The higher the flock prevalence of the live poultry entering the processing facility with *Campylobacter* and *Salmonella*, the more difficult it is for the processor to minimise contamination of the raw poultry with these pathogens. More stringent requirements are needed at the primary production stage, to effectively lower the prevalence and concentration of *Campylobacter* and *Salmonella* post processing.

4.1.3 Regulatory impact – industry

The *status quo* option does not impose any new costs on industry, nor does it provide any new benefits to them.

²⁶ The Meat Standards Committee was formed in 1995 to review existing codes of hygienic practice relating to meat and mandate national meat hygiene standards in outcome terms. The Committee comprised representatives from states and territory meat hygiene authorities, the Australian Quarantine and Inspection Service, FSANZ, meat industry organisations and food safety technical advisers. The Committee reported to the Primary Industries Ministerial Council.

4.1.4 Regulatory impact – government

There would be no new enforcement costs or new benefits for government. The State and Territory enforcement agencies would continue to enforce the Australian Standard for poultry. There would be no government food safety inspection of poultry primary production businesses. Government would incur the continuing cost of investigating food-borne illness.

4.1.5 Regulatory impact – consumers/community

The estimated number of cases of campylobacteriosis from poultry in Australia each year is 83,100. It is not known what percentage of the estimated number of food-borne cases of salmonellosis (81,000) can be attributed to poultry. However, an estimate can be made based on the fact that poultry meat has been associated with 13% of identified salmonellosis outbreaks and 8% of the total cases from these outbreaks (Dalton et al, 2004). This would, amount to 6480²⁷ cases per year.

However, the element of uncertainty indicated by current studies (Hall et al 2004) makes it necessary to view the incidence of poultry-meat related illness as a range rather than a finite figure.

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Salmonellosis	1,840	6,480	11,040
Campylobacteriosis	26,040	83,100	138,900
Total number of cases per annum	27,880	89,580	149,940

The severity of poultry-meat related illness is not uniform. It is estimated that 22% of food-borne gastroenteritis cases require outpatient treatment – a visit to a General Practitioner or Hospital Emergency Department – while 2.6% require hospitalisation (Abelson et al 2006). Salmonellosis and Campylobacteriosis resulting from the consumption of poultry-meat would result in a more severe illness than general food-borne gastroenteritis. However, we have used the more conservative data pertaining to the latter, to estimate health costs.

Health costs

On the basis of the above evidence (Abelson et al 2006) the following patient management assumptions are made:

Treatment	%
Self-care	0.753318
Outpatient	0.220000
Hospitalisation	0.026667
Deaths	0.000015

It is possible to estimate the number of poultry-meat related patients in each of the above categories. For self care, the lower bound estimate will be 21,003 (27,880 x 0.753318).

²⁷ This is 8% of the estimated 81 000 food-borne cases of salmonellosis that occur each year.

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Self care	21,003	67,482	112,953
Outpatient	6,134	19,708	32,987
Hospitalisation	743	2,389	3,998
Deaths	0.315	1.34	2.24
Total number of cases per annum	27,880	89,580	149,940

The most recent figures with regards the cost of medical treatment can be derived from data provided by the Australian Institute of Health and Welfare (AIHW: Refined Diagnosis Related Group 1998-99 to 2007-08). For gastroenteritis the figures for patients in different age groups and with different degrees of severity are:

	<u>2006/07(\$)</u>	<u>2007/08(\$)</u>	<u>Average (\$)</u>
<u>With complications</u>			
Over 10 years	4,872	5,229	5,051
Under 10 years	4,220	4,677	4,449
Average costs	4,546	4,953	4,750
<u>Without complications</u>			
Over 10 years	1,551	1,739	1,645
Under 10 years	1,852	2,067	1,960
Average costs	1,702	1,903	1,802
Total Average cost	3,124	3,428	3,276

For the purpose of calculation, the medical costs arising out of a case of poultry-meat related illness, is taken as the final average i.e. \$3276.

Welfare costs

It is possible to attribute a cost to the loss of health and welfare. This can be described in monetary terms as the Willingness To Pay (WTP) to avert a food-borne illness (Mathers et. al. 1999). This is derived from the monetary value \$442 ascribed to a day of good health.

Using data available at OzFoodNet the WTP is calculated as follows:

	<u>Disability weight</u>	<u>Days with illness</u>	<u>WTP (\$)</u>
Self care	0.056	3	74
Outpatient	0.094	4	166
<u>Hospitalisation case</u>			
Time in hospital	0.402	2	355
Out of hospitals	0.056	7	173
WTP for hospital case			529

From the above, it is possible to arrive at the total cost, in terms of willingness to pay, that the community bears on account of poultry meat-related illness:

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Self care	1,554,222	4,993,668	8,358,522
Outpatient	1,018,244	3,271,528	5,475,842
Hospitalisation	393,047	1,263,781	2,114,942
Total	2,965,513	9,528,977	15,949,306

Premature mortality

It is also possible to compute the cost to the community of death on account of poultry-meat related illness. This is done by taking the value of a statistical life year (VSLY) and discounting it for projection over 40 years, which is the average period of productivity for the individual (Abelson et al 2006).

VSLY	\$108,000
Discount rate	0.03
Time period	40 years

Cost of premature mortality **\$2,496,395**

Productivity costs

To determine the economic costs in terms of loss of productivity due to patients being unable to work, the following assumptions are made. It is assumed that on average a person affected by a poultry-meat related illness loses two days of work. The forgone earning is \$250 per day, derived from the ABS's Average Weekly Earnings table for August 2009 which is reproduced below. This figure is multiplied by 0.53, the proportion of the population in the workforce, to arrive at the productivity loss.

Private sector

Full-time adult ordinary time earnings	1 179.40
Full-time adult total earnings	1 228.30

Public sector

Full-time adult ordinary time earnings	1 279.40
Full-time adult total earnings	1 320.10

Total costs

It is now possible to sum up the above and arrive at a total cost under the *status quo* for poultry-meat related illness in Australia. The health care costs are derived from the \$3,276 above, the average the medical costs arising out of a case of poultry-meat related illness.

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Health care	2,435,504	7,825,410	13,098,259
WTP	2,965,513	9,528,977	15,949,306
Premature mortality	1,043,993	3,354,406	5,614,643
Productivity loss	7,388,200	23,693,910	39,734,100
Total Cost	13,833,210	44,402,703	74,396,308

4.1.6 Conclusion

Currently, the cost to consumers from food-borne illness associated with poultry contaminated with *Campylobacter* and *Salmonella* is estimated to be in the range of \$14- \$74 m annually.

The results from the FSANZ coordinated chicken meat baseline survey and the retail study indicate that contamination from chicken flocks infected with *Salmonella* and *Campylobacter* will be present after slaughtering and processing and then carried through to the raw chicken purchased by the consumer. The source of the *Campylobacter* and *Salmonella* contamination is from live chicken being infected during the growing stage. The *status quo* does not appear to provide sufficient incentives, given the present rates of contamination, for poultry growers to continuously implement the control measures necessary to consistently produce poultry flocks that have a lower infection rate of *Campylobacter* and *Salmonella*. Scope exists, on the scientific evidence available, to decrease the rates of contamination and human illness.

4.2 Option 2 – consumer education

Under this option, a specific education campaign would be developed with the aim of improving consumer handling and cooking of poultry. No new regulation would be introduced for poultry growers, transporters or processors i.e. as per the *status quo*.

Raw poultry contaminated with *Campylobacter* and/or *Salmonella* can cause illness in two ways, the pathogens can be transferred to the cooked poultry or other ready-to-eat food and be ingested or they may survive an inadequate cooking process.

Campylobacter is readily inactivated by heat and therefore will not survive normal cooking. However, illness can occur after exposure to low numbers of *Campylobacter* cells (<500 bacterial cells) (UK Advisory Committee on the Microbiological Safety of Food, 2005). Therefore cross contamination from the raw poultry via utensils and hands to ready-to-eat food is considered the most important risk factor for *Campylobacter*. For example, if after cooking, chicken is placed on the same plate the raw chicken was on, illness may occur. Illness could also occur if a chopping board used to cut raw chicken, is used to cut salad items, without being adequately cleaned and sanitised between these two tasks.

Most strains of *Salmonella* will die off at temperatures of 60°C and above (Hocking, 2003). However, the heat resistance of *Salmonella* in foods depends on the composition, the pH and the type of acidulant, and the water activity (Hocking, 2003). The US Food Code recommends poultry is cooked to at least 74°C for 15 seconds (US Public Health Service, 2009) to destroy *Salmonella*. The infective dose for *Salmonella* in food is generally higher than *Campylobacter* though varies with the strain, the food vehicle, and the age and health status of the patient.

If *Salmonella* is present in foods with a high fat content, the infectious dose is much lower as the fat content appears to protect *Salmonella* from the lethal effects of stomach acids (Hocking, 2003). Therefore, poultry contaminated with *Salmonella* could cause illness if the cooking process is inadequate and to a lesser extent, via cross contamination.

Currently, the main national avenue in Australia for dissemination of food safety information is the Food Safety Information Council (FSIC)²⁸. The FSIC is a non-profit entity supported by the Australian Government Department of Health and Ageing, FSANZ, State and Territory health and food safety agencies, local government, and leading professional, industry and community organisations. Each year, FSIC actively promotes food safety through the distribution of information directly to requesting individuals and organisations, and at food safety, educational, health and general safety conferences, exhibitions and expos. A major part of the FSIC's campaign is Food Safety Week each November which aims to pass on simple messages to improve consumer knowledge of how to handle, store and cook food safely.

The food safety messages of the FSIC tend to be general in nature and do not normally target specific foods. With respect to cooking poultry, the FSIC recommends:

- poultry is cooked until well done, right through to the centre and no pink is visible.

To prevent cross contamination, the FSIC recommends

- using a clean plate and clean utensils for the cooked meat
- washing hands, chopping boards, knives and anything else which will come into contact with the food before starting food preparation and between preparing raw and ready-to-eat foods
- storing raw meat and poultry in a leak-proof container in the refrigerator and below ready-to-eat food so that raw juices can't contaminate it.

The FSIC food safety campaign employs community media and other low cost measures to get its message across. Its annual budget is about \$150,000 and its reach and efficacy is limited. In the Netherlands, the cost of an information campaign was estimated at €1 m per year (Havelaar et al, 2007). Extrapolating for Australia on the basis of population, a comparable campaign is estimated to cost \$2.26 m. An effective media campaign would require an on-going evaluation program which would survey public opinion prior to the introduction of the media campaign and review public opinion on a periodic basis. It is estimated that an ongoing evaluation program would require around 5%, that is, \$133,000 per annum, of the cost of the media campaign. The total cost of a media campaign would therefore be about \$2.4 m per annum.

Evidence from a consumer survey conducted in 2004-05 on poultry meat food handling practices in the home undertaken for FSANZ suggests that most consumers report to be adhering to these practices²⁹.

²⁸ Information on the Food Safety Information Council is available from the Council's website, www.foodsafety.asn.au

²⁹ In 2004, FSANZ commissioned Colmar Brunton Social Research to obtain benchmark data on awareness, knowledge and behaviour of poultry meat businesses, government enforcement officers and consumers in relation to poultry food safety issues.

Consumers are careful to avoid practices that may lead to cross-contamination of raw poultry meat and other food items, and also report a good understanding of how to determine when chicken is cooked (FSANZ, 2005).

In summary, the results relevant to handling and cooking were

- almost all respondents (98%) indicated that they do not use the same plate or surface to store cooked and uncooked poultry meat
- almost all consumers wash the utensils that they use with raw poultry (96%), wash their hands both before (94%) and after (95%) handling raw poultry, and also dry their hands after washing them (93%)
- consumers usually determine when chicken pieces are cooked when the chicken meat is no longer pink (30%), or had turned white (28%)
- consumers usually determine that a whole chicken is cooked by inserting a skewer or fork into the meat (32%), following a set recipe (28%), or waiting until the juices run clear (21%).

In this survey, consumers were also asked where they currently get information about safe handling and cooking of poultry meat. Around one-quarter of consumers said that they currently obtain information on safe food handling practices. Of these respondents, one-quarter (26%) obtain this information from their family or friends, 22% obtain this information from television and 16% find it in magazines or cookbooks. However, when prompted with options for information sources, up to 69% of consumers say that they will consider looking for information on safe food handling practices from magazines/cooking books (69%), television (67%), butcher/retailer (53%), government health department (36%), FSIC (32%) and the Internet (30%). Multiple responses were permitted.

The Colmar Brunton Social Research indicates that the majority of consumers already know how to handle and cook poultry safely and *report* that they follow the recommended safe practices. Therefore, it is questionable how successful additional consumer education will be. It is well recognised that consumers already seem to possess adequate knowledge about domestic food hygiene practices, but that this knowledge is not necessarily translated into consumer behaviours (Redmond, Griffith 2003; Fischer et al, 2007).

In its submission, the then ACA agreed that further 'generic' food safety messages will do little to improve consumer handling of poultry and that consumer education specific to poultry was needed, in conjunction with regulatory measures. In their joint submission, the South Australian Department of Health, the Department of Primary Industries and Resources South Australia and the South Australian Research and Development Institute queried whether there should be a legal requirement for raw poultry products to be labelled with handling/cooking instructions.

The Dutch Government commissioned research to investigate the potential costs and benefits of interventions to reduce the exposure of the Dutch population to *Campylobacter* from broiler chicken. A series of interventions was considered along the broiler chicken meat supply chain, including consumer education. The view was that consumer education by an 'information campaign' was not likely to be a promising strategy, mainly because the potential effect of such a campaign in terms of modified consumer behaviour is generally considered low (Havelaar et al, 2007).

Based on the limited literature, it was estimated that after an information campaign 3% (with a margin between 0 and 7%) of all non-hygienic food preparers would improve their behaviour (Havelaar et al, 2007). The decrease in the risk to consumers was calculated at 3% (with a margin of 0-5%), leading to approximately 500 prevented cases of gastroenteritis. Additionally, the cost of an information campaign was estimated at €1 m per year (~\$AUD 1.7 million) and was therefore not considered cost effective.

A study in the Netherlands investigated various methods of improving food safety in the domestic kitchen with respect to handling poultry contaminated with *Campylobacter* (Nauta et al, 2008). Some web-based information interventions were designed and tested on participant motivation and intentions to cook more safely. The most promising information intervention was tested by recruiting a set of participants who prepared a salad with chicken breast fillet carrying a known amount of tracer bacteria. The amount of tracer bacteria that could be recovered from the salad was used as a measure of hygiene. However, when the effect of this information intervention was tested, it alone had no measurable effect on the health risk. For the risk to decrease sharply, a behavioural cue needed to be embedded within the instructions for the salad preparation relevant to the prevention of cross-contamination.

The study concluded that consumer food safety interventions should focus on activation of the knowledge that consumers already possess at the moment of food preparation, rather than general food safety education (Nauta et al, 2008). However, how this could be achieved in practice at a community wide-level was not discussed and it was recommended that this be investigated in future research.

To have any chance of success, a consumer information campaign would need to be developed that was targeted at improving consumer handling and cooking of poultry, with an emphasis on minimising cross contamination. The messages would need to be delivered through television, magazine/books and at butchers/supermarkets and other retailers where poultry is sold. Based on the Nauta study, the education campaign could be enhanced by also including more specific handling instructions on the packaging of raw poultry.

4.2.1 Regulatory impact – industry

There is no direct impact on poultry growers, transporters or processors under this option, as no new regulation is recommended. However, the industry generally, through the representative industry bodies, could be encouraged to contribute to the development and cost of the education campaign. The cost to industry would also rise significantly if handling instructions were recommended for inclusion on packaged poultry.

This could best be achieved by the voluntary adoption of a label, containing handling/cooking instructions, on packaged poultry meat. In a study commissioned by FSANZ, the cost of labelling has been calculated to be \$19,424 per poultry processing unit (Cost Schedule for Food Labelling Changes by PricewaterhouseCoopers March 2008). This is the cost attributed to the setting up of a labelling facility, for a product marketed in a flexible bag or pouch. It assumes a standard label that could be incorporated in all poultry meat products leaving the processing unit, regardless of size/weight.

The poultry meat industry in Australia is centralised in ownership and organisation. The Australian Chicken Meat Federation has indicated that there are two large integrated companies supplying 70% of broiler meat consumed and approximately 20 major chicken meat processing plants. This industry structure could facilitate a voluntary labelling option.

From the above, it is calculated that for an estimated 25³⁰ poultry processing plants at a cost of \$19,424 per unit, voluntary labelling would cost \$485,600.

4.2.2 Regulatory impact – government

The government may be called upon to bear the cost of the education campaign amounting to about \$2.4 m per annum, or it may share this cost burden with industry.

In return, the government will benefit from the reduced costs in the area of health and medical care as a result of a reduction in poultry meat-related illness.

For effectiveness, any education campaign would need to be ongoing. As part of the strategy to lower the incidence of food-borne illness in the United Kingdom, and in particular *Campylobacter*, a food hygiene campaign was undertaken by the UK Food Standards Agency in June 2004 and July 2005 to coincide with the peak incidence of *Campylobacter* in human (spring/summer). It aimed to promote an increase in awareness of cross-contamination in the home. The raised awareness of cross contamination was followed by a reduction in the number of cases of *Campylobacter* in humans, although the level of decrease was short term (UK Advisory Committee on the Microbiological Safety of Food, March 2008).

4.2.3 Regulatory impact – consumers/community

Consumers would encounter no additional costs if a wholly government funded campaign is undertaken. However, consumers of poultry meat products may incur costs if industry contributes to the funding of a campaign and passes some or all of these costs on to the consumer. The cost of poultry would also increase, if labelling were to be included on poultry packages, as industry would seek to recover the costs of this labelling.

The percentage of additional industry costs passed on to the consumer is not shown separately, as these costs have already been reflected in full under in section 4.2.1 Regulatory impact – industry.

Consumers would benefit from this option because of a reduction in illness.

4.2.4 Conclusion

The cost of an education campaign, specific to the safe handling and cooking of poultry, is estimated to be approximately \$2.39 m per annum. The voluntary adoption of a warning label, containing handling/cooking instructions, on packaged poultry meat, could cost about \$485,600. The total cost of Option 2 would be around \$2.87 m in its first year.

³⁰ This includes an estimate of the total number of processing plants i.e. 20 major plants and five minor plants.

On the basis of the Dutch study cited above (Havelaar et al, 2007), a 3% decrease in the prevalence of poultry meat-related illness, both with respect to *Campylobacter* and *Salmonella*, can be expected. This would reduce the number of persons affected by poultry-meat related illness in any given year by the following figures, broken down according to the severity of such cases:

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Self care	630	2,024	3,389
Outpatient	184	591	990
Hospitalisation	22	72	120
Deaths	Nil	Nil	Nil
Total number of cases per annum	836	2,687	4,499

The reduced number of cases would result in a fall in the welfare costs calculated as Willingness To Pay:

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Self care	46,620	149,776	250,786
Outpatient	30,544	98,106	164,340
Hospitalisation	11,638	38,088	63,480
Total cost	88,802	285,970	478,606

Consequently the total costs of illness under this option will be reduced as follows:

	<u>Lower bound estimate</u>	<u>Mid point estimate</u>	<u>Upper bound estimate</u>
Health care	72,072	235,872	393,120
WTP	88,802	285,970	478,606
Productivity loss	221,540	712,055	1,192,235
Total Cost	382,414	1,233,897	2,063,961

The benefit derived from a 3% reduction in illness equates to a range of \$0.38-2.06 m.

Based on the above costs and mid-point estimate of benefits, this option is likely to involve a net cost over 10 years of \$8.6 m (calculated as the net present value using a 7% discount rate). Noting that there is significant uncertainty around the costs of illness, the net cost over 10 years could range from \$2.8-14.6 m, using the above upper and lower bound estimates of benefits.

To break even this option would need to produce around a 6% reduction in illness over a 10-year period. This would be double what was achieved in the overseas example identified above.

4.3 Option 3 – industry self regulation

Under this option, poultry growers would be encouraged to follow control measures that specifically address food safety issues at the primary production level. Compliance with the control measures could be promoted by industry associations and the state regulatory agencies. Industry would be expected to report on compliance rates and the procedures in place to rectify areas of non-compliance.

For processing, the *status quo* would continue i.e. poultry processors complying with the Australian Standard for poultry (AS 4465-2005) as currently required under state and territory regulation.

The control measures for poultry growers would need to include those identified within the Poultry Scientific Assessment as having the most impact on the infection of poultry flocks with *Campylobacter* and *Salmonella*. These were:

- measures on-farm to minimise environmental contamination of poultry from *Salmonella* and *Campylobacter*
- measures to minimise *Salmonella* contaminated feed being fed to poultry
- measures to minimise contamination of live poultry during transport.

As discussed in section 1.2.3, a revised Poultry Biosecurity Manual has already been developed and was published by DAFF in May 2009. This revised Biosecurity Manual addresses the areas highlighted within the Poultry Scientific Assessment as necessary to minimise flock infection with *Salmonella* and *Campylobacter* such as:

- the use of footbaths or dedicated footwear for each shed
- hand sanitation at the entry to each shed
- controlling access to wild birds and vermin into sheds
- keeping shed surrounds free from debris and minimising vegetation
- using potable or treated drinking water
- using closed feeding systems and protecting feed from contamination by wild birds and rodents
- clean protective clothing for personnel
- controlling contamination from visitors
- minimising contamination during pick up and transport.

While the revised Biosecurity Manual is similar to the current biosecurity manuals in place within the poultry industry it is clearer to follow and more detailed. It includes new requirements for staff training and more detail on control measures for water treatment, rodent control, pick-up and transport and movement of personnel and equipment.

The intention is that each part of the poultry industry adapts the revised Biosecurity Manual to reflect the requirements as they apply to their industry. The Australian Chicken Meat Federation has already done this for the chicken growers and once approved, compliance with the new National Farm Biosecurity Manual for Chicken Growers will become part of any new contract with growers.

Implementation and enforcement of these new biosecurity manuals, by the poultry industry, would therefore meet the criteria for a self-regulatory approach.

There would need to be a high level of compliance with the new biosecurity manuals (for each poultry sector) for this option to be effective at lowering flock infection with *Salmonella* and *Campylobacter*. FSANZ and industry surveys discussed under option 1 found that compliance rates were reasonably high with the current chicken meat manual. However, there were areas of non-compliance which could impact on flock infection with *Salmonella* and *Campylobacter*.

Poultry processors would be responsible for assessing compliance and putting in place sanctions for poultry growers who are found to be non-compliant. Currently, this approach is used for the existing chicken meat biosecurity manual. To potentially achieve higher compliance levels, over that achieved under the *status quo*, industry will need an additional incentive to comply. Therefore, this option recommends industry agrees to report to government on overall compliance levels (with respect to biosecurity measures affecting food safety) and actions being taken by industry against non compliant growers. An obligation on poultry processors to report on compliance levels may provide a greater incentive, over the *status quo*, to ensure their growers comply with the revised biosecurity manuals. This could result in greater compliance levels than the *status quo*.

4.3.1 Regulatory impact – industry

For poultry growers who are obligated (under contract) to follow revised biosecurity measures, there may be costs associated with modifying procedures/practices. While the revised biosecurity manuals will be similar to the previous ones, there is a new requirement for staff training. More detail will also be included on control measures, which may require changes to procedures. There may also be costs associated with upgrading facilities such as sheds and equipment. The extent of these costs will depend on the degree to which an individual business needs to modify procedures/practices and upgrade facilities.

There may be benefits for growers who fully comply with the biosecurity measures in the revised biosecurity manuals as they may be preferentially contracted to supply poultry to processors.

There are likely to be costs to the poultry industry to report on compliance rates with the revised biosecurity manuals and follow up on non-compliance. The industry associations, who represent each poultry sector, will have costs associated with compiling compliance data and supplying this to government.

4.3.2 Regulatory impact – government

There would be no new enforcement costs to the government.

There may be some costs to government to assess the adequacy of industry self-regulating poultry growers and transporters. Government would need to encourage the poultry industry to report to government on compliance levels with the revised biosecurity manuals and the systems in place to follow up on areas of non-compliance. Further microbiological surveys on prevalence of flocks with *Salmonella* and *Campylobacter* could also be conducted to assess whether improvements are occurring.

However, there would be costs associated with conducting these surveys.

There may be benefits to government from reduced illness rates from *Salmonella* and *Campylobacter* if biosecurity measures improve when the new biosecurity manuals across the poultry industry are implemented.

4.3.3 Regulatory impact – consumers/community

The combination of improved biosecurity measures and higher compliance rates across the poultry industry has the potential to reduce flock prevalence of poultry with *Salmonella* and *Campylobacter* over that possible under the *status quo* and thereby reduced illness rates from these pathogens.

However, as discussed under the *status quo*, an obligation to meet biosecurity measures as part of a contract with a grower may not offer sufficient incentive for poultry growers to continuously implement the biosecurity measures necessary to minimise flock infection with *Campylobacter* and *Salmonella*. While poultry growers may risk loss of contract if their biosecurity measures do not meet the processor's expected standards, this industry driven system has not resulted in low infection rates of live poultry with *Campylobacter* and *Salmonella*. As discussed under the *status quo*, this may be because there are not sufficient incentives (positive or negative) to lower flock infection rates with *Campylobacter* and *Salmonella*. Any benefit, therefore, may be minimal.

4.3.4 Conclusion

This option potentially has higher costs to industry and government than the *status quo*. Poultry growers may incur the costs to improve biosecurity measures where they are currently inadequate and the poultry industry generally will incur costs reporting to government on compliance levels. Government will incur the costs of assessing the adequacy of this industry self-regulatory system. However, this option may be more effective in lowering flock prevalence of poultry with *Salmonella* and *Campylobacter* than the *status quo* because of:

- implementation of improved biosecurity measures
- improved compliance levels as there is more incentive on poultry processors to ensure their growers are implementing the necessary biosecurity measures.

4.4 Option 4 –through-chain food safety management consisting of regulatory elements on farm and on processors

Under this option, a primary production and processing Standard for poultry is adopted into the Code (see attachment 1 for the draft Standard). This Standard would specify food safety obligations from animal production to the processing of poultry, poultry meat carcasses and poultry meat products for human consumption. It would also include the implementation of measures to control the food safety hazards and the responsibility to demonstrate compliance.

The majority of countries that have improved practices and procedures on-farm and at slaughtering facilities have successfully reduced the amount of *Salmonella* and *Campylobacter* in raw chicken.

Countries that have interventions in place to lower the prevalence of either *Campylobacter* or *Salmonella* include New Zealand, the United Kingdom (UK), Sweden, Netherlands and Denmark. The majority of these interventions are for *Campylobacter* as contaminated poultry is considered to be the main cause of campylobacteriosis.

In New Zealand the *Campylobacter* Risk Management Strategy was formally implemented in late 2006 to achieve a sustainable reduction in *Campylobacter* levels on chicken meat. In 2008, the Strategy was updated and specific poultry processing targets were set. Poultry processors must ensure that at the end of primary processing, their poultry carcasses meet the specified microbiological criteria (NZFSA, Jan 2008). When results are higher than the criteria, the processor is required to take corrective action. Details of the requirements can be found on the NZFSA website³¹. The Strategy in its entirety has seen the mean prevalence of *Campylobacter* being reduced by nearly half (from 57% in 2007 to 30.6% in 2008) and the mean levels reduce from 3.07 log₁₀CFU/carcass (1175 CFU/carcass) to 2.41 log₁₀CFU/carcass (257 CFU/carcass). This strategy has seen cases of *Campylobacter* infection caused by food, being reduced by 50% (NZFSA, 2009).

These reductions in New Zealand have been predominantly achieved by processors improving their good hygienic practices during slaughter and dressing. The increased use of processing aids has undoubtedly been a significant contribution. Further activities have included broiler growers improving control measures on farm³², improvements in packaging and providing safe food messages to food distributors, retailers and consumers.

In 2005, the UK Food Standards Agency set a strategic target of achieving a 50% reduction in the incidence of UK produced chicken testing positive for *Campylobacter* by 2010 (UK Food Standards Agency, 2009a). The baseline, against which this target was to be measured, was set at 70% based on the surveillance data available at the time (UKFSA, 2009a). A key part of the strategy to achieve the 50% reduction is the 'Cleaner Farms, Better Flocks' program which aims to improve hygiene measures on broiler farms and ensure that best practices are followed at all times (UK Food Standards Agency, 2009b). The key messages are:

- keep livestock away from poultry houses
- only allow essential visitors onto the farm
- use dedicated boots for each poultry house
- eliminate vermin
- wash and sanitise hands before and after visiting the poultry shed

In October 2009, the UK Food Standards Agency published its findings on a recent survey testing for *Campylobacter* and *Salmonella* in chicken on sale in the UK (UKFSA, 2009a). The survey was undertaken between May 2007 and September 2008. The prevalence of *Campylobacter* in chicken meat at retail (overall) was 65.2% for the 927 samples tested. *Salmonella* prevalence in chicken at retail remained low at 6.6%. This survey demonstrated that a significant proportion of chicken on sale in the UK remains contaminated and that to date, the strategy to achieve a 50% reduction in the prevalence of *Campylobacter* in retail chicken meat i.e. from 70% to 35%, has not yet been successful.

³¹ <http://www.nzfsa.govt.nz/animalproducts/legislation/notices/animal-material-product/nmd/nmd-09-schedule-1-technical-procedures.pdf>

³² At the farm level, generic aspects of biosecurity have been improved but currently it is accepted that this only results in a limited reduction in the level of contamination of slaughtered birds

The UK Food Standards Agency has not publically speculated why the implementation of the Cleaner Farms, Better Flocks campaign has not achieved the decline in flock prevalence of chickens with *Campylobacter* that was expected. The Agency has advised that there was an initial decrease in cases of campylobacteriosis following the commencement of the campaign. However, this decrease was not sustained. Compliance with this campaign is not mandatory and there is no publicly available information on the level of compliance with the recommended biosecurity measures.

A *Campylobacter* monitoring program in broiler chickens was carried out in Sweden from 2001 through to 2005. The objective was to reduce the occurrence of *Campylobacter* in the food chain through preventive measures, starting with primary production. The annual incidence of *Campylobacter*-positive slaughter batches progressively decreased from 20% in 2002 to 13% in 2005 (Hansson et al, 2007). When *Campylobacter* spp. are found in a flock, the farm of origin is advised to implement more stringent biosecurity measures to prevent subsequent flocks from being infected with *Campylobacter*. There are no statutory sanctions or penalties, but when the program started in 2001, eight of nine slaughterhouses were paying a premium for *Campylobacter*-free flocks (Hansson et al, 2007).

In the Netherlands, the *Salmonella* flock prevalence dropped from 20% in 1999 to 11% in 2002. During this period, the *Campylobacter* flock prevalence remained fairly stable at 20%. In 1997, the Dutch Products Boards for Livestock, Meat and Eggs implemented monitoring and control programs to reduce *Salmonella* and *Campylobacter* contamination of poultry meat. These programs include, amongst others, microbiological examination of flocks at each stage of the production chain, application of strict hygiene measures throughout the production chain and a logistic slaughtering procedure for broiler flocks (Van de Giessen et al, 2006).

In 2003, the Danish voluntary strategy to control *Campylobacter* was intensified. The focus was on biosecurity, allocation of meat from *Campylobacter*-negative broiler to the production of chilled products and consumer information campaigns. While it was not possible to identify the effect of each single initiative at the farm, the implementation of the control strategy did coincide with a decrease in the number of positive flocks. From 2002 to 2007, the percentage of *Campylobacter*-positive broiler flocks at slaughter decreased from 43% to 27%. The number of reported cases of campylobacteriosis also decreased by 12%. While higher decreases were expected, the market share of imported broiler meat doubled from 20% in 2002 to 40% in 2006 and *Campylobacter* is found more frequently in imported broiler meat compared to domestically produced broiler meat (Rosenquist et al, 2009).

Iceland has experienced a dramatic decrease in human cases of campylobacteriosis following implementation of control measures in broiler production (Rosenquist et al, 2009). Since strict control measures were implemented along the whole food chain (birds to humans) in 2000, campylobacteriosis cases fell from 116 cases/100 000 population to <10 cases/100 000 population (Stern NJ et al, 2003; Callicott KA et al, 2008).

The control measures in Iceland comprised biosecurity at farm, freezing of meat from *Campylobacter*-positive flocks and intensive consumer education campaigns (Rosenquist et al, 2009). The interventions in Iceland have been more effective than in other Northern European countries because only domestically produced broiler meat is consumed in Iceland (Rosenquist et al, 2009).

With the exception of the UK, the information above indicates that countries have achieved reductions in flock prevalence of poultry infected with *Campylobacter* and *Salmonella*, following targeted interventions. However, the exact level that could be achieved in Australia is difficult to estimate.

4.4.1 Primary production

The draft Standard for poultry meat requires a poultry producer (poultry grower or transporter) to:

- examine all of its processing operations to identify potential hazards and implement control measures to address those hazards
- have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.

The poultry producer must operate according to a food safety management statement that sets out how the requirements of the Standard will be complied with. Other requirements have been specified for poultry producers in relation to:

- controlling inputs
- waste disposal
- health and hygiene
- ensuring persons engaged in poultry growing or transporting have the necessary skills and knowledge in food safety and food hygiene commensurate with their work
- design, construction and maintenance of premises, equipment and transportation vehicles
- traceability
- not selling or supplying poultry that is unsuitable.

4.4.1.1 Regulatory impact at primary production – industry (poultry growers and transporters)

The specific practices a poultry primary production business would be expected to implement to fulfil the above requirements that could entail costs include:

- protecting poultry from wild birds and rodents - this would require sheds to be wild bird and rodent proofed to an extent that is practicable to achieve the required outcome and for pest control management to be in place
 - providing clean continuous drinking water for the birds
 - providing feed that has been treated to minimise *Salmonella* and stored so that it is protected from contamination introduced by pests, wild birds and other livestock
 - cleaning and disinfecting sheds in between each flock
 - cleaning pickup equipment, crates and trailers
 - providing clean and treated litter for each new flock and litter storage that protects litter from contamination introduced by birds, pests and other livestock
 - providing protective boots and clothing for personnel and visitors
 - providing appropriate facilities to dispose of dead birds
 - providing toilet and hand washing facilities for staff and visitors
 - providing adequate facilities for waste disposal including waste water disposal
- stocking density management.

There would also be costs associated with keeping records to demonstrate compliance. These would be:

- pest control
- vendor declarations in relation to feed and litter
- chemical use
- water treatment (where applicable)
- cleaning and disinfection of sheds and equipment
- waste disposal
- staff health and hygiene i.e. hand washing, foot washing and protective clothing
- staff training
- staff declarations in relation to contact with other poultry, pigs etc
- visitor log including visitor declarations and conditions
- procedures relating to pick up.

There are other practices a poultry primary production business would need to follow that would have no or minimal costs associated with them such as:

- withdrawing feed at an appropriate time prior to harvest to minimise faeces during transport and holding times
- cleaning up feed spills promptly
- minimising stress of birds during transport to minimise shedding of faeces - this includes not overcrowding and handling birds with care during loading and unloading;
- maintaining the farm in a clean and tidy condition
- separating sick or dead birds from the main flock
- ensuring poultry handlers wear protective cloth and maintain personal hygiene when working in the sheds – e.g. farm staff do not have contact with other poultry or other avian species and minimise contact with domestic and wild animals
- limiting access to sheds
- storing chemicals separately (away from feed, litter and poultry)
- maintaining appropriate records of fertile eggs and/or hatched poultry live poultry and live poultry supplied to processors.

Industry has advised that there will be costs to non-compliant poultry growers to meet the proposed Standard under this option. With a transition period of two years recommended for the proposed Standard for Poultry, compliance costs for the poultry primary production sector can be spread to minimise the impact.

One off costs

The Australian Chicken Meat Federation (ACMF) assesses that approximately 80 farms would each need to spend \$20,000 on structural improvements covering gates, fences, bird proofing, rodent stations, hand sanitizers, change facilities etc to meet their legal obligations under the proposed Standard. This totals \$1.6 m.

ACMF also assess that a maximum of 500 other farms would have to spend \$5000 on structural improvements which totals \$2.5 m.

The cost of developing and implementing a food safety management statement, estimated at \$3000 per farm, will amount to \$2.4 m for the 800 farms.

ACMF estimates that total one off costs for all poultry farms will be \$6.5 m nationally.

On-going costs

ACMF estimates that monitoring, record keeping and reporting would entail \$4.4 m nationally in personnel costs each year for farms.

Poultry growers may also incur licence and inspection/audit costs (see details below). These costs range from zero for poultry growers in Victoria, Western Australia and Tasmania to \$740 per annum in Queensland for compliant farms. New South Wales is proposing a cost of \$323 per annum for poultry growers³³ and in SA \$250/annum. Farms that do not comply will incur additional inspection/audit costs.

According to Safe Food Production Queensland, there are 70 broiler farms within this State. In Queensland, these 70 farms will incur a licence fee of \$740 per annum; a total of \$51,800 per annum.

According to available data, (Department of Agriculture, Fisheries and Forestry, November 2008) the proportion of the national chicken meat production for each State and Territory approximately reflects their respective shares of the Australian population. The number of poultry farms in the other states is calculated on this basis. Extrapolating, there would be 301 farms in New South Wales (33% of the population) where the licensing will be \$323; a total of \$97,223. In South Australia (8%) 73 farms will pay \$250 each; a total of \$18,250.

Out of an estimated 800 poultry farms Australia-wide, there are 356 in States where the governments will either bear the inspection/auditing costs or have still to determine the level of fees to be charged. By considering an average of the fees prescribed by the three states where information is available, namely Queensland, New South Wales and South Australia, we have assumed a licensing fee of \$437 for the remaining 356 farms; a total of 155,809.

In addition to the \$167,273 that State Governments in Queensland, New South Wales and South Australia will incur, we estimate that nationally, licensing/inspection/auditing costs will total \$323,082.

The on-going costs for farms in complying with the Poultry Standard will be \$4.72 m annually.

These costs are summarised below.

³³ This is an estimate only. NSW is still to consult with the poultry industry and make a final decision on licensing and inspection/audit costs.

Primary Production

Initial one off costs	Costs
Structures & Facilities	
80 non-compliant farms	\$1,600,000
500 partial compliant farms	\$2,500,000
Food Safety Management	\$ 2,400,000
Total Initial Costs	\$ 6,500,000
Ongoing / Annual Costs	
Monitoring & Record keeping	\$4,400,000
Licensing	\$323,082
Total Ongoing Costs	\$4,723,000
TOTAL COSTS	\$11,223,000

Taking the median \$44 m (see 4.1.5 above) as the cost of illness, in order to be cost-effective this option should provide a 13% reduction in poultry-meat related illness over 10 years (based on a 7% discount rate) or 14.5% over five years.

Alternatively, if a 20% reduction in illness were achieved the net benefit over five years (in present value terms using a 7% discount rate) would be \$10.5 m. If only a 10% reduction in illness were achieved there would be a net cost over five years of \$7.7 m.

Industry has also provided costs which the industry believes will be faced by feedmills if there was a requirement for *Salmonella*-free feed. The proposed Standard for Poultry Meat requires a poultry producer to take all reasonable measures to ensure inputs (such as feed) do not make the poultry unsuitable. The specific practices a poultry primary production business would be expected to implement to fulfil this requirement include providing feed that has been treated to reduce *Salmonella* and stored so that it is protected from contamination introduced by pests, wild birds and other livestock. There is no requirement for *Salmonella*-free feed.

There are also costs provided by industry based on the assumption that segregation of eggs from *Salmonella*-positive breeder flocks will be required. However hatcheries are not within the scope of the draft Standard and therefore the Standard does not require eggs to be segregated.

These costs, which are listed below, are therefore not taken into consideration in calculating the cost to industry of complying with the proposed Standard for Poultry Meat, because they are based on assumptions which FSANZ does not consider will be correct when the Standard is implemented.

FEEDMILLS

Initial one off costs	\$
Breeder feed delivery vehicle	650,000
Feed storage bins	3,500,000
Double conditioning	250,000
Air filters	125,000
TOTAL INITIAL COSTS	\$ 5,025,000
Initial Cost for 30 feedmills	\$150,750,000
Ongoing / Annual Costs	
Breeder feed delivery costs	100,000
Cleaning	83,000
Organic acid treatment	500,000
TOTAL ONGOING COSTS	\$683,000
FIRST YEAR COST FOR EACH MILL	\$5,708,333
FOR THIRTY FEEDMILLS	\$171,250,000

HATCHERIES

Ongoing / Annual Costs	\$
Streaming of eggs	52,000
Streaming of chick placements	31,000
TOTAL	\$83,000
FOR TWENTY HATCHERIES	\$1,664,000

4.4.1.2 Regulatory impact at primary production – government

Governments may charge the costs associated with licensing/enforcing/implementing the proposed new requirements for poultry producers on the respective farms; or they may chose to bear some part or all of these costs themselves. These practices may vary from state to state and over time. For the purposes of this cost analysis all such fees, real or notional, have been shown above as industry costs.

Jurisdictions will inspect/audit poultry primary production operations to assess whether the businesses are controlling their food safety hazards according to the requirements set out in the proposed Standard for poultry meat. The frequency and extent of inspections will be determined by the respective jurisdictions. Feedback from the Poultry SDC indicates that controlling authorities will limit their inspection of poultry primary production businesses to those occasions where there is concern that a poultry primary production business may not be controlling food safety hazards. This could occur when

- a poultry primary production business is supplying a poultry processor without a contract or the existing contract does not require adequate food safety controls to be in place at the farm
- information indicates that a poultry primary production business is not satisfactorily controlling its food safety hazards
- investigation is required following a suspected food-borne illness outbreak or a complaint.

With respect to licensing and inspection costs, the State and Territory enforcement agencies with responsibility for poultry growers have provided the information below. A table summarising this information follows.

- The New South Wales Food Authority licenses dairy farms (with an annual licence fee in the order of \$323 – no GST applicable) and may propose a similar licence fee for poultry farms. Currently, the dairy farm licence fee includes the cost of one audit per year. Audits are conducted on dairy farms at 1-24 month intervals, dependent on the audit outcome and resultant rating. Audit costs are \$163.50/hr (including GST) plus a flat travel component of \$40.86 (including GST). If a farm requires additional follow up audits/inspections because non-conformances are identified during a failed audit, these would be invoiced at the rate above.
- In Queensland, the preferred method for monitoring poultry growers' compliance with the proposed Standard for poultry meat is via the Preferred Supplier Arrangement. Under this arrangement, farms would be required to operate in accordance with the processor's food safety program (the processor who owns the farm). Farms would not pay accreditation fees and no audit fees would be charged for compliance audits. However, if non-conformances are detected, follow-up audits on farm would be charged at \$225/hr plus GST. Consultation is still to be undertaken with the poultry industry in Queensland and therefore this may change.
- In Victoria, the requirements will be enforced through the auditing of processors. Inspections on farm will occur where there is concern with the arrangement between the processor and the farm. Costs related to farm inspections will be absorbed by PrimeSafe³⁴ as part of compliance management.
- Western Australia is not anticipating inspecting or auditing farms on a routine basis, but will rely on the processors ensuring that suppliers comply with the proposed Standard for Poultry Meat. Farms may be assessed when evidence held by a processor indicates that there is an issue on farm that is not being adequately addressed or as part of a verification program. The *Food Act 2008* currently being implemented allows for the setting of fees for registration and fee for service, but current thought is that fees may not be applied immediately. However, this may change in the future.
- In South Australia, farms may need to be accredited (or licensed), with the charge being approximately \$250/year. South Australia could restrict auditing of farms depending on the verification model adopted. It may be decided to rely on audits of the processors system to verify farm compliance or, alternatively, to audit where corrective action by the processor has been unsuccessful. The current rate for auditing is \$160/hr. The length of the audit would depend on the nature of the program and the level of compliance.
- Tasmania is not proposing to charge licence fees on farms. It proposes to enforce this requirement through the auditing of the poultry processor and if it is necessary to go back on farm, it would recoup the costs from the poultry processor. The audit fee would be approximately \$250/hr.

³⁴ PrimeSafe is the Victorian government authority responsible for the regulation of meat, poultry and seafood within this State.

The Northern Territory and the Australian Capital Territory do not have any farming operations growing poultry for sale for human consumption.

Table 2: Summary of proposed licensing/inspections costs for poultry growers by State enforcement agencies

State	Summary of proposed approach	Proposed licensing/ accreditation fees	Proposed auditing/inspection fees	Approx cost to poultry grower
NSW	Licence and audit at least yearly	\$323/annum	Cost of one audit included in licence fee. Additional costs apply if follow up audits needed.	\$323/annum if compliant
Qld	Accreditation of farms under a preferred supplier arrangement with an accredited processor.	None	None unless non-conformances require follow up audit at \$225/hr plus GST	None if fully compliant
Vic	Enforced through auditing of processors. Farms will be inspected if there are concerns.	None	None	None
WA	Enforced through auditing of processors. Farms will be inspected if there are concerns.	None	None	None
SA	May license each farm and audit if there are concerns.	\$250/annum	Audit farm where evidence of ongoing non-conformances at \$160/hr.	\$250/annum if compliant
Tas	Enforced through auditing of processors. Farms will be inspected if there are concerns at a cost to the processor.	None	None	None

4.4.1.3 Regulatory impact – consumers

The regulatory component of this option provides for greater public accountability and scrutiny than options 1 and 3 for poultry growers. In options 1 and 3, the degree to which poultry growers are meeting biosecurity measures is assessed by the poultry processor to which the grower is contracted to sell live poultry. The poultry processor owns the farms and the chickens but contracts the management of these farms. This contract includes an obligation to follow biosecurity measures. As argued under options 1 and 3, this industry arrangement may not provide enough incentive to poultry growers to continuously implement the biosecurity measures necessary to lower flock prevalence of *Salmonella* and *Campylobacter*. There are no immediate rewards or penalties within this system. Growers that meet contractual arrangements are more likely to obtain new contracts than those that do not. However, growers are normally contracted for 5 years to supply birds to processors.

This option introduces a legal obligation on the grower to implement biosecurity measures. The enforcement of this requirement will be the responsibility of government and the state enforcement agencies will need to be satisfied that these legal obligations are being met. If they are not being met, penalties will apply.

The combination of the legal obligation and penalties for non-compliance should provide more incentive than under options 1 and 3 for poultry growers to continuously implement the necessary biosecurity measures. Therefore, it is expected that this option has a greater potential to reduce the likelihood of poultry being infected with *Salmonella* and *Campylobacter* during the growing stage than options 1 to 3. If the likelihood of poultry being contaminated with *Salmonella* and *Campylobacter* is reduced, it follows that the incidence of food-borne illness occurring from these pathogens will also be reduced. This will directly benefit consumers.

Given that growers will experience higher costs when complying with a proposed Standard for poultry meat, and given that they will pass some part of these costs on to consumers in the form of higher prices, consumers could end up paying higher prices for their poultry meat products. This cost increase has already been reflected in the cost burden for industry and is therefore not repeated here. However, the benefit of safer poultry should compensate for any price rise.

4.4.2 Primary processing

For processing, the existing state and territory poultry meat safety requirements, embodied in AS4465-2005, would be implemented through a national outcome-based standard, which is not overly-prescriptive, incorporated into the Code.

The development of a national standard for poultry primary production and processing will enable the food safety hazards associated with the entire poultry meat supply chain (from the farm to the consumer) to be addressed within the one regulatory document i.e. the Code. The draft Standard for poultry meat will require a poultry processor to:

- examine all of its processing operations to identify potential hazards and implement control measures to address those hazards
- have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented
- verify that the control measures in place are effective.

A processor must operate according to a food safety management statement that sets out how the requirements of the Standard will be complied with. This is effectively a HACCP program, as currently required under State/Territory legislation. Other requirements have been included in the Standard for Poultry Meat in relation to:

- not processing poultry product that is, or may be, unsuitable
- controlling inputs
- waste disposal
- ensuring persons engaged in poultry processing have the necessary skills and knowledge in food safety and food hygiene
- traceability
- not selling poultry product that is, or may be, unsuitable.

These requirements are already included in AS4465-2005.

Given that processors are already required to control their processes through the application of a HACCP system, no new regulatory requirements are recommended at the primary processing stage.

4.4.2.1 Regulatory impact – industry (primary processors)

Under this option, no new costs are anticipated for primary processors as the regulatory requirements are essentially the same.

4.4.2.2 Regulatory impact – government

For primary processing, the enforcement costs are expected to be similar to option 1 as the regulatory requirements of the proposed Standard for Poultry Meat and AS4465 are essentially the same, with the main component being a HACCP-based system to control food safety hazards during processing.

4.4.2.3 Regulatory impact – consumers/community

There is no regulatory impact on consumers as the requirements on primary processors will essentially be the same.

4.4.3 Conclusion

The total cost to the community of food-borne illness associated with poultry contaminated with *Campylobacter* and *Salmonella* is estimated to be in the range of \$14 to \$74 m annually, with a median of \$44 m (see 4.1.5 above).

The adoption of Option 4 will impose additional costs on poultry growers as it introduces new regulatory requirements at the primary production stage of the poultry meat supply chain. It is estimated that industry will incur an initial cost of \$11.2 m in the first year and \$4.7 m each year thereafter (Data provided to FSANZ by the Australian Chicken Meat Federation in September 2009).

It is difficult to predict how much this option will lower flock prevalence with *Campylobacter* and *Salmonella*. Overseas examples do not provide a perfect predictive tool as there are many differences between countries with respect to the conditions under which poultry are grown such as climate which impact on the ability of poultry growers to maintain biosecurity. The interventions described in the countries above also do not perfectly parallel what is being recommended in Australia. However, all examples provided include improvements in biosecurity as part of the intervention.

As indicated in 4.4.1 above, if illness is reduced by 14.5% over five years or 13% over 10 years, the regulatory option will be cost effective.

4.5 Preferred option

The implementation of the Biosecurity Manual by poultry growers represents, on the best available scientific evidence, the most effective way to reduce flock infection with *Campylobacter* and *Salmonella*.

However, because consumers are not in a position to identify whether or not the poultry is contaminated due to the nature of the contamination, there is little incentive for poultry growers and producers to act. Therefore, an apparent market failure exists.

Option 4 is the preferred option to address this market failure as it is the most cost effective of the identified options for reducing the likelihood of food-borne illness occurring from the consumption of poultry. It provides a greater incentive to poultry growers to comply with biosecurity measures by legally obligating them to have these measures in place. It also introduces independent oversight by government and penalties for non-compliance. Poultry growers and transporters would be required to put in place measures to reduce flock infection with *Campylobacter* and *Salmonella*. This lowers the likelihood, and degree to which, raw poultry will be contaminated with *Campylobacter* and *Salmonella* and hence the likelihood that illness will occur.

It is uncertain what level of reduction of illness is likely to occur, but it is possible, given the calculations (see Attachment 4 for details), to identify the level of effectiveness this option needs to achieve in order to make it cost effective. Allowing for the fact that the benefits of initial infrastructure investments will be realised over a number of years, to achieve a positive net benefit over five years would require at least a 14.5% reduction in illness or 13% if considered over 10 years. International experience, while not directly comparable, would suggest that reductions in excess of these percentages might be achievable.

Option 1 (status quo) does not introduce any new measures to lower the likelihood of the community contracting food-borne illness from the consumption of poultry. Currently, it is estimated that consumption of contaminated chicken meat accounts for on average 83,100 cases of campylobacteriosis each year and 6480 cases of salmonellosis, at an annual cost to the community in the range of \$14 m to \$74 m.

Option 2 (consumer education) potentially lowers the likelihood of consumers contracting campylobacteriosis and salmonellosis through a targeted education campaign aimed at improving consumer handling and cooking of poultry. It is estimated that such a campaign would cost approximately \$3 m but could only reduce poultry-associated illness from *Campylobacter* and *Salmonella* by 3%, in financial terms a maximum of \$2.1 m, that is there would be a net cost. Applying sensitivity analysis using a margin of 0-5% effectiveness, the benefit could be in the range of \$0-\$3.4 m. Consequently, there would only be a net benefit if relatively extreme assumptions about the cost of illness and effectiveness of the option are applied. Using the mid-point estimate of cost of illness, this option would need to achieve at least a 6% reduction in illness over a period of 10 years before a positive net benefit is achieved. However, any benefit could be short lived as the impact of the education campaign is expected to lessen over time. As supported by the then ACA, it is recommended that any targeted education campaign be in conjunction with regulatory measures and not instead of them.

Option 3 (industry self-regulation), as per option 4, has the potential to reduce flock prevalence of poultry with *Campylobacter* and *Salmonella* over that possible under the *status quo*. This is achieved by encouraging poultry growers to have improved biosecurity systems in place and for industry to report to government on compliance levels. The benefits of this option are uncertain, but are not expected to be as high as those for option 4. Higher compliance levels are expected under option 4 because poultry growers are legally obligated to comply with biosecurity measures and penalties will apply for non-compliance.

5. A REVIEW OF TWO EXISTING REQUIREMENTS ON POULTRY IN THE CODE

As part of this Proposal, an evaluation of standards in the Code specifically related to poultry meat was undertaken. Requirements in two Standards, 1.6.2 – Processing Requirements and 2.2.1 – Meat and Meat Products, specific to poultry are being proposed for deletion.

The requirement in Standard 1.6.2 permits an eviscerated carcass to contain specified viscera and prohibits the freezing of uneviscerated poultry. The requirement in Standard 2.2.1 specifies the maximum amount of fluid that can be lost when frozen poultry is thawed.

5.1 Eviscerated poultry

5.1.1 Statement of the problem

Evisceration is the process of removing the crop, intestines and other internal organs from the poultry carcass. Some of these organs removed during the evisceration process can be highly contaminated. For example, the poultry digestive system i.e. the gizzard, and intestines, may contain *Campylobacter* and *Salmonella* that are pathogenic to humans.

The risk assessment concluded that evisceration could significantly contribute to carcass contamination. Because of the risk, it is undesirable for viscera to be attached to the poultry carcass. The significance of evisceration is recognised under State and Territory requirements where the processing of poultry must include evisceration. The Code, however, currently allows viscera to remain in the carcass. The Code also requires that uneviscerated poultry must not be frozen.

Clause 4 of Standard 1.6.2 states that:

- poultry in the form of an eviscerated carcass may include the gizzard, heart, liver, neck or a combination thereof; and
- uneviscerated poultry must not be frozen.

The clause applies in Australia only and does not apply in New Zealand.

5.1.2 Proposed amendment to the Code

5.1.2.1 Proposed amendment at Draft Assessment

AS 4465 requires the evisceration of poultry. The food safety elements of AS 4465 have been included in the draft standard and therefore it was proposed at Draft Assessment that clause 4 of Standard 1.6.2 be deleted. It was stated at Draft Assessment that deleting clause 4 would not impact on industry as it must currently comply with AS 4465 or impact on the jurisdictions as deletion brings the Code into alignment with requirements jurisdictions currently enforce.

No objections were received from stakeholders to this proposal and one submission supported the proposed deletion of clause 4.

5.1.2.2 *Proposed amendment at Final Assessment*

FSANZ has considered the approach proposed at Draft Assessment and approves the approach at Final Assessment.

The deletion of clause 4 of Standard 1.6.2 removes an inconsistency regarding eviscerated poultry between the current Code and the draft Standard and aligns the Code with the practice of the poultry processing sector and State and Territory requirements.

This amendment will have minimal economic implications for the poultry processing industry, the government and consumers because it reflects current industry practices.

5.2 **Limit on fluid loss from thawed poultry**

5.2.1 **Statement of the problem**

In poultry processing, water is used for scalding and washing carcasses and also for most businesses, chilling carcasses. This results in the absorption and uptake of water by the skin and muscle tissue of the poultry carcasses. When frozen poultry is thawed, a loss of fluid occurs, partly because of this absorption and uptake of water.

A limit on the amount of fluid that can be lost when frozen poultry is thawed is stipulated in clause 2 of Standard 2.2.1. This has the affect of limiting the amount of water that can be absorbed by poultry during processing and thereby preventing the selling of poultry that has been bulked with water. Clause 2 states that frozen poultry when thawed must yield no more than 60 g/kg of fluid as determined by the method prescribed in the schedule to Standard 2.2.1 and applies in Australia and New Zealand.

The limit of 60 g/kg (6%) of thawed poultry was set by the then Australia New Zealand Food Authority, predecessor of FSANZ, in 2000 to assist in preventing deceptive or misleading practices. Further background information about how the limit was established is available in section 9.2.1 of the Draft Assessment Report³⁵.

During the Draft Assessment stage of this Proposal, the Australian poultry industry raised concerns that it may not be feasible to consistently comply with the current fluid loss limit of 60 g/kg for thawed poultry. Several reasons were cited to support these concerns:

- The poultry industry has increased the number of washing steps used in poultry processing since the implementation of Hazard Analysis Critical Control Programs. This increase in washing steps is aimed at reducing microbial contamination, however, it also promotes increased water uptake. Therefore, the amount of water loss during thawing may exceed the limit of 60 g/kg.
- There was a belief that frozen poultry was being unfairly targeted because there is no such limit on water loss specified for frozen beef, pork, lamb or fresh poultry.

³⁵ http://www.foodstandards.gov.au/srcfiles/P282_Poultry_%20DAR_Attachments%20except_Attach3.pdf. Accessed 22 February 2010.

- The frozen poultry market has diminished to approximately 1% of the poultry currently sold, in comparison with 20 or 30 years ago when frozen poultry had a larger share of the poultry market.

FSANZ agreed to include this issue in this Proposal.

5.2.2 Statement of Options

5.2.2.1 Proposed options at draft assessment

FSANZ released a discussion paper entitled 'Limit on fluid loss from thawed poultry' for public consultation in October 2005. Fifteen submissions were received in response to the discussion paper. A summary of the submissions received has been presented in the Draft Assessment Report. Issues raised in these submissions were considered in the preparation of the Draft Assessment Report, and in the development of five options to address the issues raised about the limit on fluid loss in thawed poultry.

The five possible options and their regulatory impact analysis were presented in the Draft Assessment Report. Option 4 was the preferred option.

Option 1 – Maintain the *status quo*

Option 2 – Retain a limit but allow this limit to be calculated as an average over a number of birds

Option 3 – Delete the requirement and defer to Fair Trading /Food Act in case of offences

Option 4 – Delete the requirement and reinforce obligation to minimise water uptake under Standard 1.3.3 – Processing Aids

Option 5 – Require the percentage of water uptake to be declared on the label

5.2.2.2 Issues raised after the release of the Draft Assessment Report

Four submissions provided comment on the limit of fluid loss in thawed poultry. The details of these submissions are provided in Attachment 3 to this Report.

Of the four submissions, three supported the preferred option (option 4). One submission supported a combination of options 1 and 2, recommending the limit of 60 g/kg be retained and calculated as an average over a number of birds.

5.2.2.3 Proposed options at final assessment

FSANZ has considered the approach at Draft Assessment and has decided not to amend the options.

5.2.3 Impact analysis

The impact analysis was discussed in detail in the Draft Assessment Report. The main points are below.

5.2.3.1 *Option 1 – Maintain the status quo*

If the *status quo* was maintained the present limit of 60 g/kg, and the method of analysis, would be retained.

Maintaining the *status quo* has the greatest impact on poultry processors, particularly those that chill using water. The poultry industry has indicated that it is not always possible to meet this limit, due to increased use of water during processing to meet regulatory requirements. Therefore if the limit is retained, retailers could be penalised for selling non-complying frozen poultry. This has the effect of the retailers refusing to purchase non-complying frozen product from the processors and was threatened by the major supermarket chains when this issue arose. Processors that chill using air may then have an unfair advantage as they process poultry using less water and can therefore more easily comply with the limit.

Maintaining the *status quo* may impact on enforcement agencies. Increased enforcement may be necessary if it is suspected frozen poultry is not meeting the legal fluid loss limit.

Maintaining the *status quo* is not expected to have any impact on consumers.

5.2.3.2 *Option 2 – Retain a limit but allow this limit to be calculated over an average number of birds*

There is conflicting evidence as to whether a 60 g/kg or 80 g/kg limit is appropriate. The poultry processing industry favours applying the 80 g/kg limit, calculated as an average over 20 birds. However, there is evidence to suggest that poultry processors can meet the 60 g/kg limit.

If a limit was retained, that was calculated as an average over a number of birds, industry would be more able to comply with the specified limit as it would account for the variabilities that occur during processing. This benefits poultry processors, particularly those that chill using water, as they would have a greater chance of producing complying product that they can sell to retailers.

However, if a limit is retained for frozen birds, it only addresses the issue of water uptake in these birds. No limit would apply to fresh poultry, which also absorbs water during the slaughtering process. Fresh poultry also represents 99% of raw poultry sold. This unfairly targets frozen poultry.

This option is not expected to impact on enforcement agencies as a limit is still being maintained – only the way it is calculated is being changed. This option is also not expected to impact on consumers when compared to the *status quo* as a limit is still being maintained.

5.2.3.3 *Option 3 – Delete the requirement and defer to Fair Trading/Food Act offences*

Several jurisdictions in Australia supported deleting the fluid loss limit and deferring the matter to Fair Trading legislation. The Australian Competition and Consumer Commission advised that if the fluid loss limit were to be deleted, there is nothing specific in the State/Territory Fair Trading legislation that would stop excess water being added to poultry carcasses.

In the case that poultry was bulked with water, with no labelling that water had been added, consumers would be misled as they would be unknowingly paying for water instead of poultry.

Option 3 is the least costly for both industry and government, as there would be no requirement to comply with or enforce. However, it offers the least assurance to consumers.

5.2.3.4 Option 4 – Delete fluid loss limit and reinforce obligation to minimise water uptake in poultry processing under Standard 1.3.3 – Processing Aids

With this option the limit on fluid loss for thawed frozen poultry would be deleted. Poultry processors would then refer to the requirements of Standard 1.3.3 with respect to the use of water as a processing aid during poultry processing.

There is no regulatory impact for either industry or government with this option as it is a reinforcement of the current obligations. Poultry processors are permitted to use water for processing purposes provided it is used at the lowest level necessary to perform the processing function (see Standard 1.3.3). Where water is used in excess of what is necessary to meet the processing needs, it is no longer considered a ‘processing aid’ and would therefore need to be declared if it constitutes 5% or more of the final food (see Standard 1.2.4 – Labelling of Ingredients).

This option potentially benefits poultry processors as it ensures a level playing field for all processors, regardless of whether they chill using water or air – the same legal obligations apply.

Deleting the fluid loss option should have little impact on consumers. The frozen poultry market now represents <1% of current chicken production. The poultry market is now dominated by fresh chicken to which the current fluid loss requirement does not apply.

5.2.3.5 Option 5 – Require the percentage of water uptake to be declared on the label

Under this option, poultry processors would need to declare the amount of water that has been absorbed by poultry during processing. This would need to be declared as an average due to variation in the amount of water uptake by different types and sizes of poultry.

If an average were required to be included in the label, it is uncertain whether this would be effective in ensuring poultry processors minimise the amount of water absorbed by poultry during processing. It could provide an incentive to minimise water uptake, if a lower stated average percentage water pickup gave a poultry producer a competitive edge. For this to be effective, consumers would need to understand that the lower the stated percentage, the less retained water is present in the poultry and hence it represents better value for money.

This option could unduly penalise those poultry processors that exclusively use water for chilling as processors that use a combination of air and water or air only would have less water absorption occurring. The chicken meat industry has advised that approximately 75% of chicken carcasses are chilled using water only, with the remainder being chilled using a combination of water and air and a very small percentage air only.

Labelling of percentage water uptake is anticipated to be expensive to the poultry processing industry as it would have to calculate the average water uptake and print this value on the label.

There would also be costs associated with the enforcement of the requirement. State and Territory Governments would need to ensure the average percentage was stated on the label accurately.

This option could potentially benefit consumers if they were able to compare similarly processed poultry on the basis of the amount of water that is absorbed - the poultry with less absorbed water offering better value for money. However, industry has advised that similar percentages are likely to be specified on the label. The poultry industry is dominated by two major processors, supplying approximately 70% of the market.

5.2.3.6 Preferred option

Maintaining the *status quo* is not preferred as poultry processors who chill using water are unable to consistently meet the fluid loss limit, providing an unfair advantage to processors who air chill, thus using less water.

Option 2 overcomes the compliance difficulties of the *status quo*, by enabling the limit to be calculated as an average over a number of birds. However, it would still only apply to frozen poultry, which represents less than 1% of the raw poultry market.

Option 3 does not address the regulatory problem as there are no specific provisions in fair trading law to prevent excess water uptake during the processing of poultry.

Option 5 provides the same benefit as option 4 but at a higher cost.

Option 4 is the preferred option as it minimises the uptake of water during the processing of poultry at the least cost. Under this option, the current fluid loss limit for frozen poultry is deleted and processors of frozen poultry will need to ensure they meet the same obligations for the use of water during processing, as all other processors of poultry products. Water may be used for processing, provided it is used at the lowest level necessary to perform the processing function. Where water is used in excess of what is necessary to meet the processing needs, it is no longer considered a 'processing aid' and would therefore need to be declared if it constitutes 5% or more of the final food (see Standard 1.2.4).

To ensure the poultry industry is aware of their legal obligations under Standards 1.3.3 and 1.2.4, the following Editorial notes have been inserted into the draft Standard.

Editorial note:

See Standard 1.3.3 for requirements relating to the use of water as a processing aid.

See Standard 1.2.4 for labelling requirements where water is an ingredient in the final poultry product at a level of 5% or more.

6. COMMUNICATION AND CONSULTATION STRATEGY

6.1 Communication

The FSANZ process involves a consultative and transparent process that reaches the industry concerned, State and Territory Government agencies, as well as consumers. The SDC contributed a broad spectrum of knowledge and expertise covering industry, government, research and consumers. In addition, targeted consultations have been undertaken through on-site visits to glean, first hand, perspectives and information from poultry producers and processors.

FSANZ has reported on its progress on the Proposal on the FSANZ website, media releases and other communication channels to advise the community of opportunities to comment. Organisations and individuals have included their names on the 'interested parties list to receive information.

6.2 Consultation

Table 1 outlines the development of this Proposal in regard to the consideration by the FSANZ Board, the development and subsequent public release of assessment reports, the issues raised during public consultation and the formation and discussions of the SDC.

The development process relied on the advice received from the SDC which assisted FSANZ in resolving the scope, definition and proposed requirements for businesses covered under the proposed Standard for poultry meat.

Table 3: Outline of the development of P282 – Primary Production and Processing Standard for Poultry Meat.

	ASSESSMENT REPORTS	STANDARD DEVELOPMENT COMMITTEE	PUBLIC CONSULTATION
INITIAL ASSESSMENT	<p>The Initial Assessment Report detailed the regulatory framework for the development of PPP Standards and the current state of knowledge regarding the poultry meat industry and existing food safety management strategies.</p> <p>The Initial Assessment Report sought comment on:</p> <ul style="list-style-type: none"> the regulatory framework for the development of PPP Standards; the current operation of the poultry meat industry; the existing regulatory and non-regulatory food safety management strategies; the hazards potentially present in poultry meat that could result in food-borne illness; the stage of the poultry meat supply chain where hazards could be introduced; and poultry meat consumption and human disease in Australia. 	<p>An SDC was established to advise and assist FSANZ with this work.</p> <p>The 1st SDC meeting was held in February 2004 and involved discussion of the scope of the risk assessment and the proposed scope of the standard.</p> <p>The 2nd SDC meeting was convened by teleconference in August 2004 and discussed the issues raised during public consultation on the Initial Assessment Report.</p> <p>The 3rd SDC meeting was held in November 2004 discussed:</p> <ul style="list-style-type: none"> the risk assessment findings proposed risk management options development of an interpretive guide to the standard <p>The 4th SDC meeting was held in March 2005 discussed:</p> <ul style="list-style-type: none"> the peer review of the poultry meat risk assessment existing food safety management strategies proposed on-farm risk management options <p>The 5th SDC meeting in August 2005 discussed:</p> <ul style="list-style-type: none"> four options for managing food safety risks on-farm requirements for food safety programs for poultry processing issues surrounding the implementation of the standard (i.e. the interpretive guide) Communication strategy preparing the Draft Assessment Report 	<p>The Initial Assessment Report was released for public consultation for a 6-week period.</p> <p>Eleven submissions were received.</p> <p>The main issues raised in this round of public consultation were regarding:</p> <ul style="list-style-type: none"> the definition of poultry should include all avian species including ratites and wild-caught birds; the scope of the Standard and relationship with the activities covered by Chapter 3 standards; the responsibility of all sections of the poultry meat supply chain for reducing the pathogen load of poultry meat products; and the value of a consumer education program to accompany the standard. <p>The response to the issues raised in this round of public consultation was discussed in the Draft Assessment Report.</p>

	ASSESSMENT REPORTS	STANDARD DEVELOPMENT COMMITTEE	PUBLIC CONSULTATION
DRAFT ASSESSMENT	<p>The Draft Assessment Report proposed risk management options based on the scientific assessment and an assessment of the economic, social and political risks. The report included a brief overview of the poultry meat industry, the current food safety management strategies in place, and the findings of the risk assessment.</p>	<p>The 6th SDC meeting in March 2006 discussed issues raised during public consultation on the Draft Assessment Report, concerns with the draft standard, particularly the need for on-farm regulation, and the development of a code of practice to support the standard.</p> <p>The 7th SDC meeting in June 2007 consider proposed drafting changes to the Standard for Poultry Meat and proposed changes to the draft Code of Practice.</p> <p>The 8th SDC meeting in June 2008 considered:</p> <ul style="list-style-type: none"> • a further re-drafted poultry meat standard; • the development of the code of practice as a guidance document rather than under the FSANZ process involving a formal round of public consultation; and • the development of an explanatory memorandum for the standard as an attachment to the Final Assessment Report. 	<p>The Draft Assessment Report was released for public consultation for an 8-week period.</p> <p>The main issues raised in this round of public consultation were regarding:</p> <ul style="list-style-type: none"> • the definition of manufactured and fermented meats; • the proposed drafting of the standard; • the development of tools to aid the implementation of the standard (i.e. an interpretive guide); • the recognition of equivalence; • the scientific justification for mandating standard 3.2.1; • auditing; and • the potential impact of any standard on stakeholders. <p>The response to the issues raised in this round of public consultation is discussed in Attachment 3.</p>

6.2.1 Summary of submissions received

Seventeen submissions were received in response to the Draft Assessment Report mainly from the poultry industry, state enforcement agencies and commonwealth health and agriculture departments. For a full list of submitters, see Attachment 3.

Generally the submissions were in support of the proposed regulatory measures for the primary production and processing of poultry meat specified within the draft standard for poultry meat. Few comments were received with respect to the recommendations on fluid loss in poultry and partly eviscerated poultry. The main issues raised are summarised below. A full summary of the issues, and response to these issues, is at Attachment 3.

6.2.1.1 Primary production

- the use of guidelines, codes of practice and training for poultry growers should be considered instead of regulatory requirements
- given the high risk nature of poultry farms, some concerns with contractual arrangements between growers and processors being the key mechanism to ensure food safety practices are being followed and suggests ongoing and rigorous monitoring to assess adequacy of this arrangement
- queries whether it is necessary to regulate farming activities prior to the growing operations
- the Standard needs to be clear as to the legal responsibility (with respect to controlling hazards) between growers and processors
- concerns about costs for growers and processors to comply with the standards. Specific concerns raised in relation to costs for poultry growers, particularly cleaning out sheds between batches, minimising partial depopulation and building new sheds

6.2.1.2 Primary Processing

- the Standard should provide a level of detail regarding what is required by the poultry food business in order to enable it to comply with the Standard and ensure that the scope of activities covered within the documented food safety management system are consistent with AS 4465. Standard must also recognise equivalent measures to achieve the same outcomes.
- clause 6 of the draft Standard should also recognise a food safety program as set out in Standard 3.2.1 – Food Safety Programs as an equivalent means of complying with the Standard.
- a validated CCP is needed somewhere along the supply chain otherwise the Standard will have a limited impact on reducing food-borne illness.

6.2.1.3 *Implementation of Standard*

A uniform approach to legislation is essential to reduce compliance costs for industry. Industry must not be restricted into how the food safety outcomes are met. There must be flexibility to allow industry to adopt the best means to achieve safe food.

6.2.1.4 *Food Safety objectives, Acceptable Level of Protection, Performance Objectives and microbiological criteria*

- national pathogen targets should be set, based on agreed food safety objectives. The Standard should then require poultry to be tested for Salmonella and possibly Campylobacter (at a later stage) to assess whether these targets are being met, with results reported to the proper authority
- has an Acceptable Level of Protection been determined for consumers in respect of Campylobacter attributable to consumption of chicken meat?
- is it considered useful to set microbiological Performance Objectives for retail product for industry to meet over a prescribed period?

6.2.1.5 *Comments on Scientific Assessment*

New data from the NSW/SA retail poultry baselines study should be considered to enable recalculation of risk

6.2.1.6 *Consideration of additional management strategies*

Should there be a requirement for labelling of raw poultry products?

6.2.1.7 *Comments on risk management of other identified hazards*

Queries how risks from arsenic and fluoride have been managed.

6.2.1.8 *Limit on fluid loss in thawed poultry*

With respect to the limit on fluid loss, only four of the seventeen submissions received, provided comment on this issue. Of these four, three supported the deletion of the fluid loss limit and referring poultry processors to their legal obligations under Standard 1.3.3 – Processing Aids. The other submission, from the then Australian Consumers' Association supports retaining the limit but would accept allowing the limit to be measured (as an average) over a number of birds.

6.2.1.9 *Partly eviscerated poultry*

No issues were raised with respect to deleting the permission in clause 4 of Standard 1.6.2 to sell partly eviscerated poultry.

6.2.2 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

Australia notified the WTO of the draft standard on 19 December 2008 (G/SPS/N/AUS/228) with an initial comment period closing on 6 February 2009. The comment period was extended until 24 February 2009 (G/SPS/N/AUS/228/Add1) and no comment was received on the notification.

7. CONCLUSION

The main food-borne pathogens of concerns with poultry are *Campylobacter* and *Salmonella*. Raw poultry that is purchased by consumers is very likely to be heavily contaminated with *Campylobacter* and to a lesser extent, *Salmonella*. Poultry become infected with *Campylobacter* and *Salmonella* during the growing stage, on-farm. During slaughtering and processing, contamination from the infected poultry is transferred to the carcass and subsequently other raw poultry cuts and products. If consumers do not handle or cook this poultry correctly, illness can occur.

Campylobacteriosis is the most notified food-borne illness in Australia, followed by salmonellosis. It has been estimated that contaminated poultry is responsible for approximately 30% of all cases of campylobacteriosis (83,100 cases/year) and a lower percentage of salmonellosis.

To reduce illness occurring from contaminated raw poultry, it is recommended that measures be taken at the growing stage, to minimise the likelihood of poultry being infected with *Campylobacter* and *Salmonella*. The lower the prevalence and concentration of these two pathogens on poultry meat, the lower the likelihood of illness occurring.

While consumers have a part to play in ensuring they handle and cook poultry safely, this is made more difficult if the poultry is heavily contaminated, particularly with *Campylobacter*, as only relatively small numbers of this bacteria are needed for illness to occur.

Australia already has comprehensive regulatory requirements in place for the primary processing of poultry. Poultry processors are required to implement HACCP programs to control the hazards associated with the slaughter and processing of poultry.

At the primary production stage, there are no regulatory requirements. However, there are industry initiated measures in place. The majority of poultry growers are contracted to poultry processors and part of this contract of supply is compliance with biosecurity measures including having practices and procedures in place to minimise the likelihood of poultry being infected with *Campylobacter* and *Salmonella*.

The findings from both the FSANZ baseline survey and the retail study show that poultry are infected on-farm and this contamination is carried through to the processing plant and then to the retail product. Overseas studies show that steps can be taken to lower both the prevalence and concentration of *Salmonella* and *Campylobacter* on-farm and at primary processing.

This reduction has been achieved by measures including improving biosecurity measures on farm and, in particular, controls during processing.

To reduce the incidence of food-borne illness occurring from the consumption of poultry and poultry products, four options were considered:

1. *Status quo*
2. Consumer education
3. Industry self regulation
4. Through-chain food safety management consisting of regulatory elements on farm and on processors

Option 4 is the preferred option as it is the most cost effective of the identified options for reducing the likelihood of food-borne illness occurring from the consumption of poultry. This is achieved by legally obligating poultry growers and transporters to put in place measures to reduce flock infection with *Campylobacter* and *Salmonella*. This is expected to lower the likelihood, and degree to which, raw poultry will be contaminated with *Campylobacter* and *Salmonella* and hence the likelihood that illness will occur. The extent to which illness will be reduced is uncertain; however, a reduction of at least 14.5% a year over five years is needed to achieve a net benefit. This is thought to be achievable based on overseas experience, although this is not directly comparable.

It has also been recommended that two other amendments be made to existing requirements relating to poultry in the Code. These are:

- the deletion of clause 4 of Standard 1.6.2-Processing Requirements which permitted poultry to be sold that was not completely eviscerated - this requirement was not consistent with existing requirements in state and territory legislation and can be adequately covered under the proposed Standard for Poultry Meat; and
- the deletion of clause 2 of Standard 2.2.1-Meat and Meat Products, which specified a fluid loss limit for frozen poultry – this limit only applied to a small percentage of poultry products sold and can be adequately addressed by existing provisions in the code relating to the use of water as processing aid and the declaration of water as an ingredient.

Decision

To approve draft Standards 4.1.1 – Primary Production and Processing Standards Preliminary Provisions and 4.2.2 – Primary Production and Processing Standard for Poultry Meat and make consequential amendments to Standards 1.6.2 – Processing Requirements, 2.2.1 – Meat and Meat Products and 4.2.3 – Production and Processing Standard for Meat.

Reasons for Decision

At Final Assessment, FSANZ has approved draft variations to the Code. The amendments:

- address public health and safety concerns raised in the Scientific Assessment of the Public Health and Safety of Poultry Meat in Australia

- are consistent with the section 18 objectives of the FSANZ Act to protect public health and safety
- provide a nationally consistent legislative framework for a whole-of-chain approach to poultry and poultry product safety
- take into account existing state and territory requirements, providing a consolidated set of requirements based on scientific assessment
- provide measures that are outcome-based and would not impose any unwarranted overall additional costs to industry over existing requirements.

8. IMPLEMENTATION AND REVIEW

8.1 Implementation

Implementation is the responsibility of the states and territories. ISC is facilitating the consistent national implementation of the Standard. It is charged with the responsibility for overseeing cross-jurisdictional agreement on consistent approaches to implementing and ensuring compliance with food standards. ISC also has a major role in encouraging cost-effective approaches to compliance and enforcement.

ISC is currently developing an implementation package for the poultry primary production and processing standard. The intent is to ensure that information on implementation is available as early as possible during the implementation timeframe. As part of the implementation package ISC is considering the role of suitable reference materials such as templates, guidelines and codes of practice.

FSANZ had originally proposed to develop a separate document that provided guidance on the intent of the requirements and on means of compliance. FSANZ has prepared an Explanatory Memorandum which accompanies the draft standard to explain the intent of each clause (Attachment 2) but guidance on means of compliance is the role of the jurisdictions and within ISC's development of the implementation package. FSANZ is providing assistance to ISC in the development of the implementation package.

A two-year implementation timeframe has been recommended, from the date the Primary Production and Processing Standard for Poultry Meat is gazetted.

8.2 Review

FSANZ is committed to undertaking evaluation of the impact of implementing key new food regulatory measures and outlines the program for evaluation activities in its Evaluation Strategy documents available on the website. FSANZ is currently developing its evaluation strategy with the jurisdictions and will consider the Standard for Poultry Meat for inclusion.

FSANZ has already coordinated two baseline surveys on poultry, which provide data on the food safety practices in the poultry industry and the degree to which poultry was contaminated, prior to the introduction of the proposed Standard for Poultry Meat.

In 2005, FSANZ commissioned Colmar Brunton Social Research to undertake research on the knowledge and awareness of safe food handling of poultry meat within the poultry meat industry, enforcement officers and consumers (FSANZ, 2005).

FSANZ also coordinated a baseline survey on the prevalence and concentration of *Salmonella* and *Campylobacter* in chicken meat on-farm and at primary processing (FSANZ, 2010). This survey measured both the prevalence and where appropriate, concentration, of *Salmonella* and *Campylobacter* at three points along the poultry supply chain, on-farm, just prior to processing and at the end of primary processing. A summary of the results of this survey have been discussed in section 2.2 of this report.

FSANZ proposes that a follow up survey be undertaken, two to three years after the implementation of the Standard, to determine whether the Standard for poultry meat has been successful in lowering the amount of *Salmonella* and *Campylobacter* in poultry.

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ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Explanatory Memorandum
3. Summary of, and responses to, submissions received at Draft Assessment
4. Cost Benefit Scenarios

Attachment 1

Draft variations to the *Australia New Zealand Food Standards Code*

Standards or variations to standards are considered to be legislative instruments for the purposes of the Legislative Instruments Act 2003 and are not subject to disallowance or sunset.

To commence: 24 months from gazettal

[1] *Standard 1.6.2 of the Australia New Zealand Food Standards Code is varied by deleting clause 4, substituting –*

4 Deleted

[2] *Standard 2.2.1 of the Australia New Zealand Food Standards Code is varied by deleting clause 2, substituting –*

2 Deleted

[3] *Standard 2.2.1 of the Australia New Zealand Food Standards Code is varied by deleting the Schedule.*

[4] *The Australia New Zealand Food Standards Code is varied by inserting –*

STANDARD 4.1.1

PRIMARY PRODUCTION AND PROCESSING STANDARDS PRELIMINARY PROVISIONS

(Australia only)

Purpose and commentary

This Standard sets out preliminary provisions which apply to the Primary Production and Processing Standards contained in Chapter 4 of the Code.

Table of Provisions

- 1 Interpretation
- 2 Application

1 Interpretation

Unless the contrary intention appears, in this Chapter –

Authority means the State, Territory or Commonwealth agency or agencies having the legal authority to implement and enforce primary production and processing Standards.

control measure means a measure that prevents, eliminates or reduces to an acceptable level, a food safety hazard.

handling of food includes the producing (including growing, cultivation, picking, harvesting, or catching), collecting, extracting, processing, manufacturing, storing, transporting, delivering, preparing, treating, preserving, packing, cooking, thawing, serving or displaying of food.

hazard means a biological, chemical or physical agent in, or condition of, food that has the potential to cause an adverse health effect in humans.

inputs includes any feed, litter, water, chemicals or other substances used in, or in connection with the primary production or processing activity.

supply includes intra company transfer of produce.

verification means the application of methods, procedures, tests and other tools for evaluation to determine compliance with the relevant requirement.

2 Application

(1) Unless the contrary intention appears, this Standard applies to Primary Production and Processing Standards in Chapter 4 of this Code.

(2) Standards in Chapter 4 of this Code do not apply in New Zealand.

[5] *The Australia New Zealand Food Standards Code is varied by omitting Standard 4.2.2 substituting –*

STANDARD 4.2.2

PRIMARY PRODUCTION AND PROCESSING STANDARD FOR POULTRY MEAT

(Australia only)

Purpose and commentary

This Standard sets out a number of food safety requirements for the primary production and processing of poultry, and poultry carcasses and poultry meat for human consumption. At the primary production stage, businesses that produce poultry must implement measures to control the food safety hazards and must be able to trace their products. Businesses that process poultry must control their food safety hazards and must be able to trace their products.

It is the responsibility of these businesses not only to comply with this Standard but also to be able to demonstrate compliance. This Standard is, in part, intended to reduce the contamination of poultry, poultry carcasses and poultry meat by pathogenic *Campylobacter* and *Salmonella*.

Table of Provisions

Division 1 – Preliminary

- 1 Interpretation
- 2 Application

Division 2 – Primary production of poultry

- 3 General food safety management
- 4 Inputs
- 5 Waste disposal
- 6 Health and hygiene requirements
- 7 Skills and knowledge
- 8 Design, construction and maintenance of premises, equipment and transportation vehicles
- 9 Traceability
- 10 Sale or supply

Division 3 – Processing of poultry

- 11 Application
- 12 General food safety management
- 13 Receiving birds for processing
- 14 Inputs
- 15 Waste disposal
- 16 Skills and knowledge
- 17 Traceability
- 18 Sale or supply
- 19 Requirements for producers of ready-to-eat poultry meat

Clauses

Division 1 – Preliminary

1 Interpretation

- (1) Unless the contrary intention appears, and subject to Standard 4.1.1, the definitions in Chapter 3 of this Code apply in this Standard.
- (2) The definition of ‘condition’ in Standard 3.2.2 does not apply in this Standard.
- (3) In this Standard –

carcass means the whole dressed body of slaughtered poultry, but excludes any part that has been removed from the dressed body, for example, the head, feathers, viscera and blood.

food safety management statement means a statement, which at a minimum, has been approved or recognised by the relevant authority and subjected to ongoing verification activities by a poultry producer or poultry processor and the relevant authority.

Editorial note:

‘Authority’ is defined in draft Standard 4.1.1 as –

the State, Territory or Commonwealth agency or agencies having the legal authority to implement and enforce primary production and processing Standards.

poultry means chicken, turkey, duck, squab (pigeons), geese, pheasants, quail, guinea fowl, muttonbirds and other avian species (except ratites).

poultry handler means a person who handles or supervises the handling of poultry.

poultry meat means the parts of the poultry carcass intended for human consumption.

poultry producer means a business, enterprise or activity that involves –

- (a) growing; or
- (b) live transporting;

of poultry for human consumption.

poultry processor means a business, enterprise or activity that involves the processing or transporting of poultry product for human consumption.

poultry product means the carcass of poultry, poultry meat or poultry meat product, as the case may be.

premises means a poultry primary production or processing premises.

processing of poultry or poultry product includes the –

- (a) holding before stunning; or
- (b) stunning; or
- (c) bleeding; or
- (d) scalding; or
- (e) defeathering; or
- (f) removing of head or feet; or
- (g) processing of feet; or
- (h) removing of viscera; or
- (i) processing of offal; or
- (j) trimming; or
- (k) washing; or
- (l) chilling; or
- (m) spin chilling; or

- (n) freezing; or
- (o) thawing; or
- (p) deboning or portioning; or
- (q) mincing or dicing; or
- (r) marinating; or
- (s) injecting or massaging; or
- (t) partial cooking; or
- (u) crumbing; or
- (v) packaging; or
- (w) storage, associated with processing;

of poultry or poultry product, as the case may be, for human consumption.

unsuitable means unsuitable as defined in Standard 3.1.1, but includes poultry or poultry product that is in a condition, or contains a substance a person would ordinarily regard as making the poultry, after processing, or poultry product unfit for human consumption.

Editorial note:

‘Suitable’ are defined in Standard 3.1.1. Clause 2 of Standard 3.1.1 provides:

Food is not suitable if it –

- (a) is damaged, deteriorated or perished to an extent that affects its reasonable intended use; or
- (b) contains any damaged, deteriorated or perished substance that affects its reasonable intended use; or
- (c) is the product of a diseased animal or an animal that has died otherwise than by slaughter, and has not been declared by or under another Act to be safe for human consumption; or
- (d) contains a biological or chemical agent, or other matter or substance, that is foreign to the nature of the food.

However, food is not unsuitable for the purposes of the Food Safety Standards merely because –

- (a) it contains an agricultural or veterinary chemical in an amount that does not contravene the *Australia New Zealand Food Standards Code*; or
- (b) it contains a metal or non-metal contaminant (within the meaning of the *Australia New Zealand Food Standards Code*) in an amount that does not contravene the permitted level for the contaminant as specified in the *Australia New Zealand Food Standards Code*; or
- (c) it contains any matter or substance that is permitted by the *Australia New Zealand Food Standards Code*.

2 Application

This Standard does not apply to poultry retail sale activities or poultry product retail sale activities.

Division 2 – Primary production of poultry

3 General food safety management

- (1) A poultry producer must systematically examine all of its primary production operations to identify potential hazards and implement control measures to address those hazards.
- (2) A poultry producer must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.
- (3) A poultry producer must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.

4 Inputs

A poultry producer must take all reasonable measures to ensure inputs do not make the poultry unsuitable.

Editorial note:

See the definition of ‘inputs’ in Standard 4.1.1 which includes feed, litter, water and chemicals used in or in connection with the primary production activity.

5 Waste disposal

- (1) A poultry producer must store, handle or dispose of waste in a manner that will not make the poultry unsuitable.
- (2) For subclause 5(1), waste includes sewage, waste water, litter, dead poultry and garbage.

6 Health and hygiene requirements

- (1) A poultry handler must exercise personal hygiene and health practices that do not make the poultry unsuitable.
- (2) A poultry producer must take all reasonable measures to ensure that poultry handlers, personnel and visitors exercise personal hygiene and health practices that do not make the poultry unsuitable.

7 Skills and knowledge

A poultry producer must ensure that poultry handlers have –

- (a) skills in food safety and food hygiene; and
- (b) knowledge of food safety and food hygiene matters;

commensurate with their work.

8 Design, construction and maintenance of premises, equipment and transportation vehicles

A poultry producer must –

- (a) ensure that premises, equipment and transportation vehicles are designed and constructed in a way that minimises the contamination of poultry, allows for effective cleaning and sanitisation and minimises the harbourage of pests and vermin; and
- (b) keep premises, equipment and transportation vehicles effectively cleaned, sanitised and in good repair to ensure poultry is not made unsuitable.

9 Traceability

A poultry producer must be able to identify the immediate recipient of the poultry handled by the poultry producer.

10 Sale or supply of poultry

A poultry producer must not sell or supply poultry for human consumption if the producer ought reasonably know or ought reasonably suspect that the poultry is unsuitable.

Editorial note:

‘Supply’ is defined in Standard 4.1.1 as including intra company transfers of product.

Division 3 – Processing of poultry

11 Application

- (1) Subject to subclause (2), and to avoid doubt, Standards 3.2.2 and 3.2.3 apply to a poultry processor.
- (2) In areas where poultry is slaughtered –
 - (a) paragraph 17(1)(d) of Standard 3.2.2 does not apply; and
 - (b) paragraph 24(1)(a) of Standard 3.2.2 does not apply in relation to the poultry intended for slaughter.

12 General food safety management

- (1) A poultry processor must systematically examine all of its processing operations to identify potential hazards and implement control measures to address those hazards.
- (2) A poultry processor must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.
- (3) A poultry processor must verify the effectiveness of the control measures.

- (4) A poultry processor must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.

13 Receiving

A poultry processor must not process poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

14 Inputs

A poultry processor must take all reasonable measures to ensure inputs do not make the poultry product unsuitable.

Editorial note:

See Standard 4.1.1 for the definition of 'inputs'.

For guidance on what constitutes acceptable water in processing see the *Australian Drinking Water Guidelines 2004* of the National Health and Medical Research Council of Australia.

15 Waste disposal

- (1) A poultry processor must store, handle or dispose of waste in a manner that will not make the poultry product unsuitable.
- (2) For subclause 15(1), waste includes unsuitable poultry and unsuitable poultry product, sewage, waste water and garbage.

16 Skills and knowledge

A poultry processor must ensure that persons engaged in poultry processing have –

- (a) skills in food safety and food hygiene; and
- (b) knowledge of food safety and food hygiene matters; and
- (c) skills and knowledge to detect a condition that would render poultry or poultry product unsuitable;

commensurate with their work.

17 Traceability

A poultry processor must ensure that it can identify the immediate supplier and immediate recipient of poultry product handled by the poultry processing business.

18 Sale or supply

A poultry processor must not sell or supply poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

Editorial note:

See Standard 1.3.3 for requirements relating to the use of water as a processing aid.

See Standard 1.2.4 for labelling requirements where water is an ingredient in the final poultry product at a level of 5% or more.

19 Requirements for producers of ready-to-eat poultry meat

Division 3 of Standard 4.2.3 applies to the producers of ready-to-eat poultry meat.

Attachment 2

Explanatory Memorandum

September 2009

FOOD STANDARDS AUSTRALIA NEW ZEALAND

PRIMARY PRODUCTION AND PROCESSING STANDARD FOR POULTRY MEAT

EXPLANATORY MEMORANDUM

OUTLINE

Standard 4.1.1

Consistent with good drafting practice, Item 5 inserts a general application and interpretation Standard (Standard 4.1.1) at the beginning of Chapter 4. The application and interpretation provisions in new Standard 4.1.1 will apply to all primary production and processing standards (PPP standards) unless the individual standard states otherwise.

This drafting approach reflects the intent of Standard 3.1.1 in Chapter 3. Standard 3.1.1 provides for general application and interpretation provisions across the Chapter 3 Standards.

Standard 4.2.2

Standard 4.2.2 proposes to introduce through-chain measures in the poultry production chain with the aim of reducing the microbiological hazards associated with the production and processing of poultry and poultry meat products.

This standard applies to all businesses that produce and process poultry or poultry meat products intended for human consumption.

Standard 4.2.2 does not apply to New Zealand. While there is an agreement between Australia and New Zealand to establish one joint food standard-setting system for the two countries, the agreement specifically excludes food hygiene provisions (Chapter 3 and Chapter 4). New Zealand maintains and develops its own food safety regulatory measures.

Standard 4.2.2 has three Divisions. Division 1- Preliminary, contains definitions specific to the Standard; Division 2 sets out the requirements that a poultry primary production business must comply with to ensure suitability of the product. Further, Division 3 sets out the requirements that a poultry processing business must comply with to ensure suitability of the product.

In this Explanatory Memorandum:

- The text of the standard is included in bold Times New Roman type and clause, subclause and paragraph numbering and lettering are the same as those in the Standard.
- The meaning of the definitions used in the Standard are explained where it is thought that more explanation may be necessary.
- The intent behind every requirement in the Standard is explained.

The Explanatory Memorandum does not specify ways in which poultry producers or processors can comply with the requirements in the standard. When incorporated or adopted into law in the jurisdictions an implementation model may need to be developed to consistently implement Standard 4.2.2 across the jurisdictions.

To commence: 24 months from gazettal

The amendments in this instrument are to commence 24 months from gazettal to provide jurisdictions and industry with the ability to develop consistent implementation of the Standards.

[1] *Standard 1.6.2 of the Australia New Zealand Food Standards Code is varied by deleting clause 4, substituting –*

Deleted

Clause 4 of Standard 1.6.2 provides that eviscerated poultry may include gizzards and other parts of the bird and requires that uneviscerated poultry must not be frozen. Clause 4 is being deleted as it is considered to be no longer necessary. The food safety hazards are now addressed through general outcome based requirements in Division 3 of proposed Standard 4.2.2.

[2] *Standard 2.2.1 of the Australia New Zealand Food Standards Code is varied by deleting clause 2, substituting –*

Deleted

Clause 2 of Standard 2.2.1 provides a limit for fluid loss from thawed poultry. This provision is no longer considered necessary. However an editorial note at the end of proposed Standard 4.2.2 references Standard 1.3.3 as it is relevant to the use of water as a processing aid.

[3] *Standard 2.2.1 of the Australia New Zealand Food Standards Code is varied by deleting the Schedule*

The Schedule to Standard 2.2.1 provides the method for determining fluid loss. With the deletion of clause 2 of Standard 2.2.1, this Schedule is no longer necessary and is also being repealed.

[4] *The Australia New Zealand Food Standards Code is varied by inserting –*

STANDARD 4.1.1

***PRIMARY PRODUCTION AND PROCESSING STANDARDS
PRELIMINARY PROVISIONS***

(Australia only)

Purpose and commentary

This Standard sets out preliminary provisions which apply to the Primary Production and Processing Standards contained in Chapter 4 of the Code.

Table of Provisions

1 Interpretation

2 Application

1 Interpretation

Unless the contrary intention appears, in this Chapter -

Authority means the State, Territory or Commonwealth agency or agencies having the legal authority to implement and enforce primary production and processing Standards.

control measure means a measure that prevents, eliminates or reduces to an acceptable level, a food safety hazard.

handling of food includes the producing (including growing, cultivation, picking harvesting, or catching), collecting, extracting, processing, manufacturing, storing, transporting, delivering, preparing, treating, preserving, packing, cooking, thawing, serving or displaying of food.

The definition of ‘handling’ in Standard 3.1.1 has been expanded on for this Standard to clearly encompass all steps in the food supply chain including primary food production type activities – a concept which was considered by the Primary Production and Processing Working Group (PPPWG) when investigating the definition of ‘handling’ in the Model Food provisions.

hazard means a biological, chemical or physical agent in, or condition of, food that has the potential to cause an adverse health effect in humans.

inputs includes any feed, litter, water, chemicals or other substances used in, or in connection with the primary production or processing activity.

supply includes intra company transfer of produce.

verification means the application of methods, procedures, tests and other tools for evaluation to determine compliance with the relevant requirement.

The definitions proposed in clause 1 are used in Standard 4.2.2, but have also been used in other primary production and processing standards such as the seafood primary production and processing standard. These definitions are included as general definitions across Chapter 4 to avoid the need to repeat them in each vertical standard.

The term ‘verification’ has been introduced in Standard 4.2.2 and is defined in this general 4.1.1 standard as it is likely to be used in other primary production and processing standards.

2 Application

(1) Unless the contrary intention appears, this Standard applies to Primary Production and Processing Standards in Chapter 4 of this Code.

(2) Standards in Chapter 4 of this Code do not apply in New Zealand.

The inclusion of this application clause avoids the need to repeat the general application provision in each of the Chapter 4 standards.

[5] *The Australia New Zealand Food Standards Code is varied by omitting Standard 4.2.2 substituting –*

STANDARD 4.2.2

**PRIMARY PRODUCTION AND PROCESSING STANDARD FOR
POULTRY MEAT**

(Australia only)

Purpose and commentary

This Standard sets out a number of food safety requirements for the primary production and processing of poultry, and poultry carcasses and poultry meat for human consumption. At the primary production stage, businesses that produce poultry must implement measures to control the food safety hazards and must be able to trace their products. Businesses that process poultry must control their food safety hazards and must be able to trace their products. It is the responsibility of these businesses not only to comply with this Standard but also to be able to demonstrate compliance. This Standard is, in part, intended to reduce the contamination of poultry, poultry carcasses and poultry meat by pathogenic *Campylobacter* and *Salmonella*.

Table of Provisions

Division 1 – Preliminary

- 1 Interpretation**
- 2 Application**

Division 2 – Primary production of poultry

- 3 General food safety management**
- 4 Inputs**
- 5 Waste disposal**
- 6 Health and hygiene requirements**
- 7 Skills and knowledge**
- 8 Design, construction and maintenance of premises, equipment and transportation vehicles**
- 9 Traceability**
- 10 Sale or supply**

Division 3 – Processing of poultry

- 11 Application**
- 12 General food safety management**
- 13 Receiving birds for processing**

- 14 Inputs**
- 15 Waste disposal**
- 16 Skills and knowledge**
- 17 Traceability**
- 18 Sale or supply**
- 19 Requirements for producers of ready-to-eat poultry meat**

Clauses

Division 1 – Preliminary

1 Interpretation

- (1) Unless the contrary intention appears, and subject to Standard 4.1.1, the definitions in Chapter 3 of this Code apply in this Standard.**

This subclause carries over definitions from Chapter 3 standards, unless Standard 4.1.1 specifically defines the term.

- (2) The definition of ‘condition’ in Standard 3.2.2 does not apply in this Standard.**

Standard 3.2.2 has a specific definition of ‘condition’ as it relates to processing. The term ‘condition’ as used in Standard 4.2.2 should be read according to the ordinary dictionary meaning of the term.

- (3) In this Standard –**

carcass means the whole dressed body of slaughtered poultry, but excludes any part that has been removed from the dressed body, for example, the head, feathers, viscera and blood.

food safety management statement means a statement, which at a minimum, has been approved or recognised by the relevant authority and subjected to ongoing verification activities by a poultry producer or poultry processor and the relevant authority.

Editorial note:

‘Authority’ is defined in draft Standard 4.1.1 as –

the State, Territory or Commonwealth agency or agencies having the legal authority to implement and enforce primary production and processing Standards.

poultry means chicken, turkey, duck, squab (pigeons), geese, pheasants, quail, guinea fowl, muttonbirds and other avian species (except ratites).

poultry handler means a person who handles or supervises the handling of poultry.

poultry meat means the parts of the poultry carcass intended for human consumption.

a poultry producer means a business, enterprise or activity that involves –

- (a) growing; or**
- (b) live transporting;**

of poultry for human consumption.

a poultry processor means a business, enterprise or activity that involves the processing or transporting of poultry product for human consumption.

poultry product means the carcass of poultry, poultry meat or poultry meat product, as the case may be.

premises means a poultry primary production or processing premises.

processing of poultry or poultry product includes the –

- (a) holding before stunning; or**
- (b) stunning; or**
- (c) bleeding; or**
- (d) scalding; or**
- (e) defeathering; or**
- (f) removing of head or feet; or**
- (g) processing of feet; or**
- (h) removing of viscera; or**
- (i) processing of offal; or**
- (j) trimming; or**
- (k) washing; or**
- (l) chilling; or**
- (m) spin chilling; or**
- (n) freezing; or**
- (o) thawing; or**
- (p) deboning or portioning; or**
- (q) mincing or dicing; or**
- (r) marinating; or**
- (s) injecting or massaging; or**
- (t) partial cooking; or**
- (u) crumbing; or**
- (v) packaging; or**
- (w) storage, associated with processing;**

of poultry or poultry product, as the case may be, for human consumption.

unsuitable means unsuitable as defined in Standard 3.1.1, but includes poultry or poultry product that is in a condition, or contains a substance a person would ordinarily regard as making the poultry, after processing, or poultry product unfit for human consumption.

Editorial note:

‘Suitable’ are defined in Standard 3.1.1. Clause 2 of Standard 3.1.1 provides:

Food is not suitable if it –

- (a) is damaged, deteriorated or perished to an extent that affects its reasonable intended use; or**
- (b) contains any damaged, deteriorated or perished substance that affects its reasonable intended use; or**
- (c) is the product of a diseased animal or an animal that has died otherwise than by slaughter, and has not been declared by or under another Act to be safe for human consumption; or**
- (d) contains a biological or chemical agent, or other matter or substance, that is foreign to the nature of the food.**

However, food is not unsuitable for the purposes of the Food Safety Standards merely because –

- (a) it contains an agricultural or veterinary chemical in an amount that does not contravene the *Australia New Zealand Food Standards Code*; or**
- (b) it contains a metal or non-metal contaminant (within the meaning of the *Australia New Zealand Food Standards Code*) in an amount that does not contravene the permitted level for the contaminant as specified in the *Australia New Zealand Food Standards Code*; or**
- (c) it contains any matter or substance that is permitted by the *Australia New Zealand Food Standards Code*.**

Subclause 1(3) sets out definitions which are exclusively used in Standard 4.2.2 and introduces new concepts, namely, ‘food safety management statement’ as well as extending the definition of ‘unsuitable’ defined in Standard 3.1.1, by introducing the concept of ‘unfit’.

The definition of ‘food safety management statement’ has been added to provide clarity around the meaning of clauses 3 and 12 regarding general food safety management requirements.

The inclusion of ‘unsuitable’ (rather than reliance on the words ‘unsafe/unsuitable’ as defined in Standard 3.1.1) provides greater scope in the practical application for jurisdictions and industry in determining whether or not the product is unfit for human consumption. The concept of ‘unfit for human consumption’ has been used in other statutory instruments both in Australia and elsewhere and has been subject to judicial and parliamentary counsel scrutiny.

2 Application

This Standard does not apply to poultry retail sale activities or poultry product retail sale activities.

The scope of this Standard applies through chain up to the point of entry into the retail and service sector. Chapters 2 and 3 apply to these retail and service sectors.

Division 2 – Primary production of poultry

3 General food safety management

- (1) A poultry producer must systematically examine all of its primary production operations to identify potential hazards and implement control measures to address those hazards.**
- (2) A poultry producer must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.**
- (3) A poultry producer must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.**

Subclauses (1) and (2) set out the elements that a primary production business must develop and incorporate in a food safety management statement (subclause (3)). This statement becomes the vehicle whereby poultry producers demonstrate compliance with the elements of the standard as well as allowing the jurisdictions to monitor the businesses' compliance.

The poultry producer will need to prepare a food safety management statement setting out how the requirements of this Division are being complied with. This statement must be approved or endorsed by the state, territory or commonwealth agency which legally enforces or implements primary production and processing Standards.

4 Inputs

A poultry producer must take all reasonable measures to ensure inputs do not make the poultry unsuitable.

Editorial note:

See the definition of 'inputs' in Standard 4.1.1 which includes feed, litter, water and chemicals used in or in connection with the primary production activity.

When preparing the food safety management statement, producers are required to examine and show how they are managing the inputs into their production system, for example how they deal with water used in production of live poultry intended for poultry meat.

5 Waste disposal

- (1) A poultry producer must store, handle or dispose of waste in a manner that will not make the poultry unsuitable.**
- (2) For subclause 5(1), waste includes sewage, waste water, litter, dead poultry and garbage.**

6 Health and hygiene requirements

- (1) A poultry handler must exercise personal hygiene and health practices that do not make the poultry unsuitable.**
- (2) A poultry producer must take all reasonable measures to ensure that poultry handlers, personnel and visitors exercise personal hygiene and health practices that do not make the poultry unsuitable.**

7 Skills and knowledge

A poultry producer must ensure that poultry handlers have –

- (a) skills in food safety and food hygiene; and**
- (b) knowledge of food safety and food hygiene matters;**

commensurate with their work.

8 Design, construction and maintenance of premises, equipment and transportation vehicles

A poultry producer must –

- (a) ensure that premises, equipment and transportation vehicles are designed and constructed in a way that minimises the contamination of poultry, allows for effective cleaning and sanitisation and minimises the harbourage of pests and vermin; and**
- (b) keep premises, equipment and transportation vehicles effectively cleaned, sanitised and in good repair to ensure poultry is not made unsuitable.**

Clauses 5, 6, 7, and 8 are general requirements similar to those set out in Chapter 3 but have been tailored to on farm poultry production activities. These requirements, amongst others in this Standard, must be addressed by the production business when developing their management statement under clause 3.

9 Traceability

A poultry producer must be able to identify the immediate recipient of the poultry handled by the poultry producer.

This clause needs to be addressed in the management statement. Essentially producers need evidence to show to whom they have supplied their product for processing.

10 Sale or supply of poultry

A poultry producer must not sell or supply poultry for human consumption if the producer ought reasonably know or ought reasonably suspect that the poultry is unsuitable.

Editorial note:

‘Supply’ is defined in Standard 4.1.1 as including intra company transfers of product.

The intent of this clause is to prevent the transfer of product from the producer to the processor where the product is ‘unsuitable’ as defined in this Standard. This provision is complemented by clause 13 whereby the processor must not accept unsuitable poultry. The intent is to remove unsuitable product from the supply chain.

Division 3 – Processing of poultry

11 Application

- (1) Subject to subclause (2), and to avoid doubt, Standards 3.2.2 and 3.2.3 apply to a poultry processor.**
- (2) In areas where poultry is slaughtered –**
 - (a) paragraph 17(1)(d) of Standard 3.2.2 does not apply; and**
 - (b) paragraph 24(1)(a) of Standard 3.2.2 does not apply in relation to the poultry intended for slaughter.**

As a poultry processor is a ‘food business’ under Standard 3.1.1 Standards 3.2.2 and 3.2.3 automatically apply to the processor. However, the provisions in Standard 3.2.2 mentioned in paragraphs (2)(a) and (b) cannot practically be applied to areas where poultry processing is undertaken. Accordingly, poultry processing establishments have been exempted from those provisions.

12 General food safety management

- (1) A poultry processor must systematically examine all of its processing operations to identify potential hazards and implement control measures to address those hazards.**
- (2) A poultry processor must also have evidence to show that a systematic examination has been undertaken and that control measures for those identified hazards have been implemented.**
- (3) A poultry processor must verify the effectiveness of the control measures.**
- (4) A poultry processor must operate according to a food safety management statement that sets out how the requirements of this Division are to be or are being complied with.**

Subclauses (1), (2), and (3) set out the elements that a poultry processor must include in a food safety management statement (subclause (4)). This statement becomes the vehicle whereby poultry processors demonstrate compliance with the elements of the standard as well as allowing the jurisdictions to monitor the businesses’ compliance.

Subclause 12(3) introduces the concept of verification. This means that a processor must have verifiable evidence to show that their systems are operating in accordance with their management statement and in particular the control measures implemented are monitored regularly and are effective. One example of verifiable evidence that a control measure is effective in achieving the stated outcome is microbiological testing of specific pathogens and retention of the results for verification by all parties concerned.

The poultry processor must prepare a food safety management statement setting out how the requirements of this Division are being complied with and verified. This statement must be approved or endorsed by the State, Territory or Commonwealth agency which legally enforces or implements primary production and processing Standards.

13 Receiving

A poultry processor must not process poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

The intent of this clause is to prevent the transfer of product from the producer to the processor where the product is ‘unsuitable’ as defined in this Standard. This provision is complemented by clause 10 whereby the producer must not supply unsuitable poultry. The intent is to remove unsuitable product from the supply chain.

14 Inputs

A poultry processor must take all reasonable measures to ensure inputs do not make the poultry product unsuitable.

Editorial note:

See Standard 4.1.1 for the definition of ‘inputs’.

For guidance on what constitutes acceptable water in processing see the *Australian Drinking Water Guidelines 2004* of the National Health and Medical Research Council of Australia.

When preparing the food safety management statement, processors are required to examine and show how they are managing the inputs into their processing system, for example, how they deal with water used in processing of poultry product intended for human consumption.

15 Waste disposal

(1) A poultry processor must store, handle or dispose of waste in a manner that will not make the poultry product unsuitable.

(2) For subclause 15(1), waste includes unsuitable poultry and unsuitable poultry product, sewage, waste water and garbage.

16 Skills and knowledge

A poultry processor must ensure that persons engaged in poultry processing have –

- (a) skills in food safety and food hygiene; and**
- (b) knowledge of food safety and food hygiene matters; and**
- (c) skills and knowledge to detect a condition that would render poultry or poultry product unsuitable;**

commensurate with their work.

Clauses 15 and 16 are specific requirements similar to those set out in Chapter 3 but have been tailored to poultry processing activities. These requirements, amongst others in this Standard, must be addressed by the processing business when developing their management statement under clause 12.

As clauses 15 and 16 are specific provisions for poultry processing they would override any similar general provisions in Chapter 3 where there is an inconsistency between the specific and the general provisions.

17 Traceability

A poultry processor must ensure that it can identify the immediate supplier and immediate recipient of poultry product handled by the poultry processing business.

This clause needs to be addressed in the management statement. Essentially, processors need to have evidence (via a system) to show from whom they have received poultry and to whom they have supplied their poultry meat and poultry meat products.

18 Sale or supply

A poultry processor must not sell or supply poultry product for human consumption if the processor ought reasonably know or ought reasonably suspect that the poultry product is unsuitable.

The intent of this clause is to prevent the transfer of product from the processor to other parts of the supply chain, for example, retail sale or catering where the product is ‘unsuitable’ as defined in this Standard.

This clause, together with clauses 10 and 13 are designed to ensure that unsuitable product is not introduced into the human consumption chain. The intent is to remove unsuitable product from the supply chain.

Editorial notes:

See Standard 1.3.3 for requirements relating to the use of water as a processing aid.

See Standard 1.2.4 for labelling requirements where water is an ingredient in the final poultry product at a level of 5% or more.

19 Requirements for producers of ready-to-eat poultry meat

Division 3 of Standard 4.2.3 applies to the producers of ready-to-eat poultry meat.

Standard 4.2.3 (Primary Production and Processing of Meat) is currently a skeleton standard but contains Division 3 which provides requirements for the production of ready-to-eat meat. Clause 19 clarifies that Division 3 of Standard 4.2.3 also applies to producers of ready-to-eat poultry meat.

Attachment 3

Summary of, and responses to, submissions received at Draft Assessment

The following is a summary by issue of the submissions received in response to the release of the Draft Assessment Report and the draft Primary Production and Processing Standard for Poultry Meat provided in the Draft Assessment Report. FSANZ responses are in italics. The references to ‘options’ in the submissions are to the options as they were described in the Draft Assessment Report.

Seventeen submissions were received from:

1. Australian Chicken Growers Council Ltd (ACGC)
2. Australian Chicken Meat Federation Inc (ACMF)
3. Australian Consumers’ Association (ACA) (now CHOICE)
4. Australian Food and Grocery Council (AFGC)
5. Bartter Enterprises (Bartter)
6. Coles Myer Ltd (Coles)
7. Department of Agriculture, Fisheries and Forestry (DAFF)
8. Department of Health, WA (DoH, WA)
9. Department of Human Services, Victoria (DoH, Vic)
10. Food Technology Association of Victoria (FTA, Vic) (Now Food Technology Association of Australia)
11. NSW Farmers’ Association (Contract Poultry Group) (NSW Farmers’ Assoc Poultry Group)
12. NSW Food Authority (NSWFA)
13. New Zealand Food Safety Authority (NZFSA)
14. Poultry Industry Association of NZ (PIANZ)
15. Safe Food Queensland (SFQ)
16. SA Department of Health, Department of Primary Industries and Resources SA and the SA Research and Development Institute (DoH SA/PIRSA/SARDI)
17. WaterCulture

At Draft Assessment, four risk management options to reduce public health risks posed by contaminated poultry meat were proposed. The options were:

Option 1: maintain the *status quo*

Option 2: encourage compliance with a voluntary code-of-practice

Option 3: require poultry growers to control food safety hazards and obligate poultry processors to ensure growers supplying them are meeting this requirement

Option 4: require poultry growers to implement a documented HACCP based food safety management system.

Option 3 was the preferred option of FSANZ. The draft Standard required poultry growers to control food safety hazards and obligated poultry processors to ensure growers supplying them were meeting this requirement.

Summary by issue

General comments and support for a regulatory approach

The AFGC supported a through-chain, outcome-based approach which includes a standard at farm level where current management is not otherwise satisfactory. DAFF also supported the development of a standard as it would ensure a nationally consistent approach to poultry meat safety management in Australia. DAFF stated that the Standard should be based on minimum effective outcomes based regulation, should apply consistent regulation to import, export and domestic markets and be consistent with section 18 of the FSANZ Act. The Standard should also be consistent with the Codex *Code of Hygienic Practice for Meat* relevant to Australian conditions and consider the recommendations of the National Competition Policy review of Export legislation. The Standard should not duplicate any existing regulation within the Code.

The requirements proposed in the standard are consistent with the general principles of meat hygiene recommended by the Codex Code of Hygienic Practice for Meat. The proposed primary production and processing Standard for poultry meat does not duplicate other requirements in the Code.

There was support for a poultry primary production and processing standard from several organisations. The ACGC supported option 3 with the reservation that there does not appear to be a clear understanding in the proposed Standard of which factors in producing poultry that growers, processors and contractors have control over. This support was also conditional on the Standard being implemented consistently by the jurisdictions. Documented HACCP for poultry growers was not seen as viable either in terms of costs or outcomes. The ACA supported requirements for poultry growers to address their hazards either through option 3 or option 4. The ACA considered that documented HACCP-based food safety management systems for primary production of poultry would provide the greatest benefit for consumers with respect to lowering poultry contamination. The AFGC, Coles, DoH WA, DoH Vic, SFQ, the NZFSA and the FTA, Vic also supported the proposed draft standard.

The NSW Famers' Assoc Poultry Group supported a standard stating that there would be economic benefits for the industry by ensuring that poultry meat could be marketed as a quality product. Also, it reduced variability in chick and feed quality and the quality of the growing and transport environments which minimised fluctuations in costs and efficiency for processors and contracted growers. The NSWFA supported the Standard whereby the processors managed compliance by the individual growers as this enabled government to scrutinise arrangements and intervene only where necessary.

The proposed draft Standard identifies those factors which are the responsibility of growers and which are responsibilities of processors. Growers under contract may have to ensure these matters are addressed through their contracts.

Non-support for the proposed Standard.

DoH SA/PIRSA/SARDI, in a joint submission, did not support the proposed draft Standard; concerned that it would entrench current industry practice that currently resulted in frequent supply of contaminated poultry to consumers.

Support for a non-regulatory approach

The ACMF and Bartter supported a non-regulatory approach for the poultry production sector and considered that real progress on food safety outcomes with poultry meat could be achieved by strengthening critical controls during poultry processing phase, but not regulating the poultry production phase.

Issues on standard development, implementation and cost of compliance

The ACMF was concerned about costs to growers and processors to comply with the Standard and stated that it was crucial to ensure legislation did not impose duplications and restrict the operational means by which the industry could achieve the desirable food safety outcomes. Also, it stated that a uniform and outcome based approach to the implementation of the Standard would enable the compliance costs to be kept at a reasonable level

The ACGC commented (in response to evidence suggesting partial depopulation was associated with the spread of *Campylobacter* infection in poultry flocks) that a move to single age flocks would impose significant costs on growers and processors and significant logistical problems due to the size of the industry. There would be a major under utilisation of grow out facilities which could make farms unviable. The ACMF also considered that keeping partial depopulation to a minimum, suggested at Draft Assessment, could not be implemented at no or minimal cost to industry. Restricting partial depopulation would reduce production for a given production surface and lead to an increase in the cost of meat. Bartter supported the need for partial depopulation and the NSW Farmers' Assoc Poultry Group stated that the evidence that it increased contamination was not addressed in the risk management.

The ACGC stated that a fully equipped shed cost around \$12-15 per bird, with new sheds having a capacity of around 40,000 birds. The ACMF said that the cost of a standard new shed is substantially underestimated in the Draft Assessment Report; the cost of a small shed (24,000 birds) was around \$300,000, not \$60,000. The cost of poultry shed quoted in the Draft Assessment Report was misleading. Bartter stated that a tunnel ventilated controlled environment shed cost from \$500,000 to \$700,000.

FSANZ is liaising with the jurisdictions regarding implementation and information for the impact (cost:benefit) analysis and specific information from industry such as costs of sheds is very helpful. The specific reference to partial depopulation has been deleted in this Report.

Bartter supported the comments made by the ACMF. In addition, it stated that any bird management recommendations should be in the context of the poultry welfare code.

This is a matter for the implementation of the Standard and will be drawn to the attention of ISC.

The ACGC stated that growers implementing the National Biosecurity Manual requirements would probably not incur much additional cost unless there are significant changes. However, it noted that it is important to recognise that the Manual related only to matters that the grower had control over.

The NSW Farmers' Assoc Poultry Group stated that the auditing by third parties of processors activities in monitoring breach of contract by growers is the most cost-effective way of ensuring compliance of growers in the management of food safety. This Group also stated that the cost of production will increase and this is unlikely to be recouped from the consumer.

The impact analysis at Final Assessment will address the costs and benefits of the risk management options.

DAFF stated that the Standard should provide a level of detail regarding what was required by the poultry food business in order to enable it to comply with the Standard and ensure that the scope of activities covered within the documented food safety management system were consistent with AS 4465. It was recommended this detail be provided in a schedule to the Standard. Also, State regulations and codes of practice should be considered in developing the Standard to reduce impost on industry in complying.

Food safety requirements on poultry processing businesses in the proposed standard are consistent with those in AS 4465. Relevant State and Territory regulations and codes of practices have been considered in the development of the Standard.

Scientific assessment

DoH SA/PIRSA/SARDI suggested that new data from the NSW/SA retail poultry meat baseline study should be considered and the risk assessment conducted as part of the Draft Assessment Report should be updated to reflect the outcome of the retail survey. They also asked whether the scientific assessment had appropriately assessed chemical hazards like processing aids, food additives and leachate from packaging

Outcomes of the NSW/SA retail poultry meat survey, and later surveys, have been taken into account at Final Assessment. Processing aids, additive and leachate from packaging were specifically addressed in the Scientist Assessment of Public Health and Safety of Poultry Meat in Australia.

Food Safety Objectives, Acceptable Level of Protection, Performance Objectives and microbiological criteria

The NSWFA stated that a *Salmonella* testing requirement needed to be incorporated into the Standard with results reported to the proper authority. The possibility of testing for *Campylobacter* at a later stage should also be considered. Also, national pathogen targets should be set, based on agreed food safety objectives.

The proposed standard requires poultry processors to verify the effectiveness of their control measures.

DoH SA/PIRSA/SARDI asked whether an Acceptable Level of Protection had been determined for consumers in respect of *Campylobacter* attributable to consumption of chicken meat.

The Scientific Assessment concluded that any reduction in the prevalence and levels of Campylobacter and Salmonella on raw poultry meat is likely to reduce food-borne illness from these pathogens.

The South Australian joint submission also queried whether consideration had been given to:

- selecting a standard product form to use in a national program to monitor whether improvement are achieved by industry

This would be a matter for jurisdictions.

- setting microbiological performance objectives for retail products for industry to meet over a prescribed period?

The ISC-coordinated national survey on Campylobacter and Salmonella in poultry and poultry meat has provided baseline data to enable comparison and assessment of levels after the introduction of the Standard. This information would assist in the setting of target levels.

Clear delineation of responsibility

The ACGC stated that there must be a clear understanding in the Standard of what growers actually had control over and what was in the control of the processors or their other contractors. The NSW Farmers' Assoc Poultry Group also commented on the role of contractors stating that for some processors transport and feed milling was carried out by contractors; therefore a similar auditing mechanism for these contractors as for growers would be needed (auditing for breach of contract is suggested)

The NSWFA suggested the need for clarification of legal responsibility – records should separately indicate the farm inputs controlled by the processor and the grower.

DAFF raised some concerns with contractual arrangements between growers and processors being the key mechanism to ensure food safety practices were being followed and suggested ongoing and rigorous monitoring to assess adequacy of this arrangement.

The Standard places obligations on the various parties. The monitoring of compliance is a matter for the jurisdictions.

Consumer education and labelling product

The ACA stated it supported consumer education that referred specifically to poultry in conjunction with regulatory measures. This was needed to achieve further behaviour change among consumers. If consumer handling of poultry meat was considered to be contributing to food-borne illness, further 'generic' food safety messages would do little to address this. The PIANZ also made a comment regarding education; FSIC provided adequate advice to consumers on food safety. Control methods were the same for all meats. Singling out poultry might lead the consumer to have an irrational fear.

Education as an option to achieve the objective was one of the options assessed at Final Assessment and the above comments taken into account.

DoH SA/PIRSA/SARDI queried whether there should be a requirement for labelling of raw poultry products. For example, ‘this is a raw/partly cooked poultry meat product that may contain harmful organisms that must be handled carefully so as not to cross contaminate ready-to-eat foods and is required to be fully cooked before consumption’.

Standard 1.2.6 – Directions for Use and Storage already requires packaged food to include appropriate directions for the use and storage of food, where the food is of a nature as to warrant such directions for reasons of health and safety. This could apply to raw poultry, except where the poultry is ‘made and packaged on the premises from which it is sold’.

Drafting issues

Several issues were raised in respect of the requirements in the draft Standard included.

NZFSA sought to include muttonbirds in the definition of ‘poultry’.

Muttonbirds are now included in the definition of poultry in the Standard

NZFSA suggested the definition of ‘poultry primary production business’ needed clarification to avoid different interpretations.

The definition now reads:

a poultry producer means a business, enterprise or activity that involves –

- (a) growing; or*
- (b) live transporting;*

of poultry for human consumption.

DoH SA/PIRSA/SARDI suggested including ‘processing of offal and feet for human consumption’ and ‘mincing/dicing or altering the form of the meat’ in the definition of ‘processing of poultry’.

Processing of offal and mincing and dicing have been included.

NZFSA suggested

- more explicit coverage of extra vectors associated with a hatchery such as handling of dirty eggs, packaging material used for transportation of chicks etc
- an indication that chemical hazards from incorrect use of agricultural compounds and veterinary medicines are a safety hazard by adding another clause or include in guidance documents
- a clause be added to the effect that ‘only apparently visibly healthy birds are sent for processing’.

These issues are either no longer applicable because the proposed Standard has been substantially revised, or have been addressed in the revised Standard.

NZFSA sought clarification as to whether end-of-lay hens and end of production breeders that had not been subject to the requirements of the Standard can be accepted for processing.

The proposed Standard prohibits a poultry processing business processing poultry for human consumption if the business knows or ought reasonably suspects that the poultry is unacceptable’.

DoH SA/PIRSA/SARDI asked whether the requirements on poultry processing business applied to ‘custom processing’. (‘Custom processing’ refers to where people grow poultry for their own consumption and these poultry are slaughtered at processing plants).

The proposed Standard applies to poultry for sale for human consumption.

DAFF and SFQ suggested permitting compliance with a food safety program set out in Standard 3.2.1 to be one option for compliance. DAFF suggested providing a Schedule to cover the detailed requirements in a food safety management system.

The Standard requires an approved food safety management statement and does not specify details (other than it address the requirements of the standard) or means of compliance.

Deletion of the fluid loss limit

The AFGC and NZFSA supported deletion of fluid loss limit. Coles also supported the deletion of the limit, but supported water uptake guidance limits and suggested limits could be calculated over an average of 20 birds.

The ACA did not support the deletion of the fluid loss limit, nor raising the level of acceptable fluid loss to 8%. It supported its retention, but would accept allowing the limit to be measured (as an average) over a number of birds.

Deletion of requirement for eviscerated poultry

Coles supported the deletion of clause 4 of Standard 1.6.2.

Other issues

Several submitters mentioned specific issues in addition to those above. These have been taken into account in the final assessment.

The ACGC stated that mandating full cleanouts between batches was a problem as there were difficulties with obtaining new litter and disposal of spent litter. Past experience showed no benefit. In the USA where cleanout occurred only after 2 or 3 years or more, there were lower *Salmonella* and *Campylobacter* levels.

The draft Standard requires the producer to manage hazards from litter but does not prescribe full cleanouts.

WaterCulture described a water disinfection system which utilised electrochemical activation.

The PIANZ stated that traceability was inherently difficult in the poultry processing situation as there were many thousands of carcasses from each farm processed each day and inevitably there was some mixing

The revised Standard requires a poultry processing business to ensure that it can identify the immediate supplier and immediate recipient of poultry product handled.

The AFGC supported broadening processing aid permissions to give poultry processors greater flexibility to control bacterial contamination on poultry. It noted that the European Food Safety Authority considered that the treatment of poultry carcasses with trisodium phosphate, acidified sodium chlorite, chlorine dioxide, or peroxyacid solutions, under the described conditions of use, would be of no safety concern.

Chlorine dioxide is a generally permitted processing aid under the Code. The poultry industry can apply to FSANZ for approval to use these processing aids.

The NSW Farmers' Assoc Poultry Group stated that processor HACCP programs should include chick and feed quality, transport of chicks and pick up of marketable live poultry. These areas would also require third party auditing

The Standard requires the processor to address hazards associated with all of its processing activities – which may include the provision of feed and chicks to growers if this is part of their activities.

DoH SA/PIRSA/SARDI stated that a validated CCP was needed somewhere along the supply chain, otherwise the Standard would have a limited impact on reducing food-borne illness. The Standard should define what is meant by a CCP and preferably replace CCP by defined explicitly, non-critical control points and the principle of continuing quality management to constantly reduce hazards.

The Standard requires businesses to develop control measures for the hazards. Specific CCPs are not specified.

The PIANZ stated that The OzFoodNet unpublished data referred to in the Draft Assessment Report indicated the food service/retail sector was a significant problem of food-borne disease outbreaks. Rather than indicating this sector was adequately controlled, this pointed to that sector being a significant problem.

The food service/retail sector is already regulated under Chapter 3 of the Code and there are separate processes underway through FRSC examining risk management in these sectors. The Scientific Assessment concluded that reducing the levels of Campylobacter and Salmonella contamination on raw poultry would lead to reduction of human illness from these pathogens. Hence, if the food service/retail sector receives less contaminated poultry, there is less chance of this poultry causing illness.

DoH SA/PIRSA/SARDI commented that arsenic was likely to be present in poultry meat from the use of Roxarsone, an anti-coccidiosis treatment. However, as there was no residue limit specified in Standard 1.4.2 – Maximum Residue Limits for arsenic, the use of Roxarsone is in breach of the Code.

The APVMA has advised that an MRL is not required for the presence of arsenic in poultry from the use of Roxarsone. Arsenic levels are not expected to be above background if Roxarsone is used in accordance to the label instructions.

The same submission also raised that, as the presence of fluoride in mechanically separated meat (MSM) from poultry was identified as a potential public health safety issue for children in the Scientific Assessment, this risk needed to be managed. The submission suggested that use of MSM be prohibited in products predominantly eaten by children until information regarding safety is presented by industry.

This issue has been raised with the poultry industry. A more thorough assessment of the risk this fluoride may present to young children, having regard to other exposures, would need to be conducted before proposing a risk management strategy.

Attachment 10

UNITED STATES DEPARTMENT OF AGRICULTURE
FOOD SAFETY AND INSPECTION SERVICE
WASHINGTON, DC

FSIS DIRECTIVE

7120.1,
Revision 2

4/12/10

SAFE AND SUITABLE INGREDIENTS USED IN THE PRODUCTION OF MEAT, POULTRY, AND EGG PRODUCTS

I. PURPOSE

This directive provides inspection program personnel (IPP) with an up-to-date list of substances that may be used in the production of meat, poultry, and egg products. FSIS will continue to update this directive quarterly by issuing revisions to this directive as opposed to issuing amendments to the directive.

II. CANCELLATION

FSIS Directive 7120.1, Safe and Suitable Ingredients Used in The Production of Meat and Poultry Products, Revision 1, dated February 4, 2010.

III. REASON FOR ISSUANCE

This reissuance updates the list of substances that have been accepted by FSIS for use in the production of meat, poultry, and egg products from February 4, 2010 through March 31, 2010. The new additions are in **bold**.

IV. REFERENCES

9 CFR Chapter III

V. BACKGROUND

A. The Table of Safe and Suitable Ingredients identifies the food grade substances that have been approved in 21 Code of Federal Regulations (CFR) for use in meat, poultry, and egg products as food additives, generally recognized as safe (GRAS) notices and pre-market notifications, and approved in letters conveying acceptability determinations. Users of this table should be aware that some of the ingredient mixtures listed in the table may be considered to be proprietary even though the components are either approved food additives or GRAS. Substances added since the 02/04/2010 issuance of the directive are in **bold**. This information is also available on the USDA websites at:

[http://www.fsis.usda.gov/Regulations_& Policies/Ingredients_Guidance/index.asp](http://www.fsis.usda.gov/Regulations_&Policies/Ingredients_Guidance/index.asp)

[http://www.fsis.usda.gov/About FSIS/labeling_& consumer_protection/index.asp](http://www.fsis.usda.gov/About_Fsis/labeling_&consumer_protection/index.asp)

DISTRIBUTION: Electronic**OPI:** OPPD

NOTE: This directive does not include the use of substances in On-Line Reprocessing (OLR) operations that operate under an experimental exemption listed in 9 CFR 381.3(c). Establishments operating under this exemption should follow the conditions of use that are specific to their FSIS approved OLR protocol.

B. The questions and answers that follow the table address the use of antimicrobial agents in the production of meat, poultry, and egg products.

A handwritten signature in black ink, reading "Philip S. Neuffer". The signature is written in a cursive style with a large, stylized "P" and "N".

Assistant Administrator
Office of Policy and Program Development

Table of Safe and Suitable Ingredients

SUBSTANCE	PRODUCT	AMOUNT	REFERENCE	LABELING REQUIREMENTS
Acidifiers				
Ammonium hydroxide	pH control agent in brine solutions for meat products	Sufficient for purpose to achieve a brine solution with a pH of 11.6	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of acidic calcium sulfate	pH control agent in water used in meat and poultry processing	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (3)
An aqueous solution of hydrochloric and acetic acid	pH control agent in water used in poultry processing	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (3)
An aqueous solution of citric and hydrochloric acids	pH control agent in water used in poultry processing	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of citric acid, hydrochloric acid, and phosphoric acid	To adjust the pH in processing water in meat and poultry plants	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of sulfuric acid, citric acid, and phosphoric acid	To adjust the pH in poultry chiller water and the processing water in meat and poultry plants	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Sodium bisulfate	pH control agent in water used in meat and poultry processing	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Sodium bisulfate	pH control agent in meat and poultry soups	Not to exceed 0.8 percent of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Sodium bisulfate	Added to sauces used as separable components in the formulation of various meat products	Sufficient for purpose	GRAS Notice No. 000003	Listed by common or usual name in the ingredients statement (2)
Sulfuric acid	pH control agent in water used in poultry processing	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (3)
Anticoagulants				
Sodium tripolyphosphate	Sequestrant/anti-coagulant for use in recovered livestock blood which is subsequently used in	Not to exceed 0.5 percent of recovered blood	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

	food products			
Antimicrobials				
An aqueous solution of sodium diacetate (4%), lactic acid (4%), pectin (2%), and acetic acid (0.5%)	Cooked meat products	Not to exceed 0.5 percent of finished product formulation.	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
An aqueous solution of sodium octanoate or octanoic acid and either glycerin and/or propylene glycol and/or a Polysorbate surface active agent (quantity sufficient to achieve the intended technical effect of octanoic acid emulsification) adjusted to a final solution pH of 1.5 to 4.0 using sodium hydroxide, potassium hydroxide, or an acceptable GRAS acid	Various non-standardized RTE meat and poultry products and standardized meat and poultry products that permit the use of any safe and suitable antimicrobial agent	Applied to the surface of the product at a rate not to exceed 400 ppm octanoic acid by weight of the finished food product	Acceptability determination	None under the accepted conditions of use (3)
An aqueous solution of sodium octanoate, potassium octanoate, or octanoic acid and either glycerin and/or propylene glycol and/or a Polysorbate surface active agent (quantity sufficient to achieve the intended technical effect of octanoic acid emulsification) adjusted to a final solution pH of 1.5 to 6.0 using sodium hydroxide, potassium hydroxide, or an acceptable GRAS acid	Fresh meat primals and subprimals and cuts	Applied to the surface of the product at a rate not to exceed 400 ppm octanoic acid by weight of the final product	Acceptability determination	None under the accepted conditions of use (3)
A blend of citric acid and sorbic acid in a 2:1 ratio	To reduce the microbial load of purge trapped inside soaker pads in packages of raw whole muscle cuts of meat and poultry	Incorporated into soaker pads at a level not to exceed 1 to 3 grams per pad	Acceptability determination	None under the accepted conditions of use (1)
A blend of lactic acid (45-60%), citric acid (20-35%), and potassium hydroxide (>1%)	Beef carcasses, beef heads and beef organs	Applied as a spray. Cannot be used on livers. All other organ meats must be drained for 1-2 minutes before packaging. Tails and	Acceptability determination	None under the accepted conditions of use (1)

		tongues must be washed with potable water before packaging.		
A blend of salt, sodium acetate, lemon extract, and grapefruit extract	Ground beef, cooked, cured, comminuted sausages (e.g., bologna), and RTE whole muscle meat products	Not to exceed 0.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement for the RTE whole muscle meat products, and cooked, cured, comminuted sausages. Ground beef must be descriptively labeled (4)
A blend of salt, sodium acetate, lemon extract, and grapefruit extract	Beef steaks	Steaks that are sliced, scored and dipped in a solution containing 2.5% of the blend	Acceptability determination	Product must be descriptively labeled (4)
A blend of salt, lemon extract, and grapefruit extract	Ground beef	Not to exceed 0.5 percent of the product formulation	Acceptability determination	Product must be descriptively labeled (4)
A blend of salt, lactic acid, sodium diacetate, and mono- and diglycerides	Various non-standardized RTE meat and poultry products and standardized meat and poultry products that permit the use of any safe and suitable antimicrobial agent	Not to exceed 0.2 percent of product formulation	Acceptability determination	All ingredients, except for the mono- and diglycerides, must be listed by common or usual name in the ingredients statement (4)
A mixture of hops beta acids, egg white lysozyme, and cultured skim milk	In a salad dressing used in refrigerated meat and poultry deli salads	Not to exceed 1.5 percent of the finished salad	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
A mixture of maltodextrin (DE of 5 or greater), cultured dextrose, sodium diacetate, egg white lysozyme, and nisin preparation	In salads, sauces, and dressings to which fully cooked meat or poultry will be added	Not to exceed 1.5 percent by weight of the finished product	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Acidified sodium chlorite	Poultry carcasses and parts; meat carcasses, parts, and organs; processed, comminuted, or formed meat food products (including RTE)	500 to 1200 ppm in combination with any GRAS acid at a level sufficient to achieve a pH of 2.3 to 2.9 in accordance with 21 CFR 173.325 (<i>Note: The pH depends on the type of meat or</i>	21 CFR 173.325	None under the accepted conditions of use (3)

		<i>poultry product.)</i>		
Acidified sodium chlorite	Processed, comminuted or formed poultry products (including RTE)	500 to 1200 ppm in combination with any GRAS acid at a level sufficient to achieve a pH of 2.3 to 2.9 in accordance with 21 CFR 173.325 (<i>Note: The pH depends on the type of meat or poultry product.)</i>)	Acceptability determination	None under the accepted conditions of use (3)
Acidified sodium chlorite	Poultry carcasses, parts, trim, and organs	Mixing an aqueous solution of sodium chlorite with any GRAS acid to achieve a pH of 2.2 to 3.0 then further diluting this solution with a pH elevating agent (i.e., sodium bicarbonate, sodium carbonate, or an un-acidified sodium chlorite solution) to a final pH of 5.0 to 7.5. 500 to 1200 ppm when used in a spray or dip. 50 to 150 ppm when used in a pre-chiller or chiller solution. Per 21 CFR 173.325.	Food Contact Substance Notification No. FCN 739	None under the accepted conditions of use (6)
Acidified sodium chlorite	Red meat, red meat parts and organs, and on processed, comminuted, formed meat products (including RTE)	Applied as a spray or dip, the additive is produced by mixing an aqueous solution of sodium chlorite with any GRAS acid to achieve a pH in the range of 2.2 to 3.0, then further diluting this solution with a pH elevating agent such that the resultant sodium chlorite concentration does not exceed 1200 ppm, and the chlorine dioxide concentration does not exceed 30 ppm. The pH of the use solution is between 5.0 and 7.5	Food Contact Substance Notification No. FCN 450	None under the accepted conditions of use (6)

Ammonium hydroxide	Beef carcasses (in hot boxes and holding coolers) and boneless beef trimmings	In accordance with current industry standards of good manufacturing practice	Acceptability determination	None under the accepted conditions of use (1)
Anhydrous ammonia	Lean finely textured beef which is subsequently quick chilled to 28 degrees Fahrenheit and mechanically "stressed"	In accordance with current industry standards of good manufacturing practice	Acceptability determination	None under the accepted conditions of use (1)
Anhydrous ammonia	Ground beef	Followed with carbon dioxide treatment in accordance with current industry standards of good manufacturing practice	Acceptability determination	None under the accepted conditions of use (1)
Bacteriophage preparation (a mixture of equal proportions of six different individually purified lytic-type bacteriophages specific against <i>Listeria monocytogenes</i>)	Various RTE meat and poultry products	Applied as a spray at a level not to exceed 1 ml of the additive per 500 cm ² product surface area	21 CFR 172.785	Listed by common or usual name (i.e., bacteriophage preparation) in the ingredients statement of non-standardized meat and poultry products and standardized meat and poultry products that permit the use of any safe and suitable antimicrobial agent. Standardized meat and poultry products that do not permit the use of any safe and suitable antimicrobial agent must be descriptively labeled. (4)
Bacteriophage preparation	Various RTE meat and poultry products	Applied to the surface of the product to achieve a level of 1×10^7 to 1×10^9 plaque forming units (pfu) per gram of product	GRAS Notice No. 000218	Listed by common or usual name (i.e., bacteriophage preparation) in the ingredients statement of non-standardized meat and poultry products and standardized meat and poultry products that permit the use of any safe and suitable

				antimicrobial agent. Standardized meat and poultry products that do not permit the use of any safe and suitable antimicrobial agent must be descriptively labeled. (4)
Calcium hypochlorite	Red meat carcasses down to a quarter of a carcass	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	On whole or eviscerated poultry carcasses	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	In water used in meat processing	Not to exceed 5 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	In water used in poultry processing (except for product formulation)	Not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	Poultry chiller water	Not to exceed 50 ppm calculated as free available chlorine (measured in the incoming potable water)	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	Poultry chiller red water (i.e., poultry chiller water re-circulated, usually through heat exchangers, and reused back in the chiller)	Not to exceed 5 ppm calculated as free available chlorine (measured at influent to chiller)	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	Reprocessing contaminated poultry carcasses	20 ppm calculated as free available chlorine Note: Agency guidance has allowed the use of up to 50 ppm calculated as free available chlorine	9 CFR 381.91	None under the accepted conditions of use (1)
Calcium hypochlorite	On giblets (e.g., livers, hearts, gizzards, and necks) and salvage parts	Not to exceed 50 ppm calculated as free available chlorine in the influent to a container for chilling.	Acceptability determination	None under the accepted conditions of use (1)
Calcium hypochlorite	Beef primals	20 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
<i>Carnobacterium maltaromaticum</i> strain	Ready-to-eat comminuted meat	Applied as a spray to meat products at a	Gras Notice No. 000159	All ingredients of the <i>C. maltaromaticum</i>

CB1	products (e.g., hot dogs)	maximum concentration of at inoculation of 1×10^4 colony forming units per gram (cfu/g)		spray solution must be listed by common or usual name in the ingredients statement (2)
Cetylpyridinium chloride	To treat the surface of raw poultry carcasses prior to immersion in a chiller	Applied as a fine mist spray of an ambient temperature aqueous solution. The aqueous solution shall also contain propylene glycol complying with 21 CFR 184.1666 at a concentration of 1.5 times that of the cetylpyridinium chloride	21 CFR 173.375	None under the accepted conditions of use (3)
Cetylpyridinium chloride	To treat the surface of raw poultry carcasses either prior to or after chilling	Not to exceed 5 gallons of solution per carcass provided that the additive is used in systems that recapture at least 99 percent of the solution that is applied to the poultry carcasses. The concentration of cetylpyridinium chloride in the solution applied to the carcasses shall not exceed 0.8 percent by weight. When application of the additive is not followed by immersion in a chiller the treatment will be followed by a potable water rinse of the carcass	21 CFR 173.375	None under the accepted conditions of use (3)
Chlorine gas	Red meat carcasses down to a quarter of a carcass	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	On whole or eviscerated poultry carcasses	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	In water used in meat processing	Not to exceed 5 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	In water used in poultry processing (except for	Not to exceed 50 ppm calculated as free	Acceptability determination	None under the accepted conditions

	product formulation)	available chlorine		of use (1)
Chlorine gas	Poultry chiller water	Not to exceed 50 ppm calculated as free available chlorine (measured in the incoming potable water)	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	Poultry chiller red water (i.e., poultry chiller water re-circulated, usually through heat exchangers, and reused back in the chiller)	Not to exceed 5 ppm calculated as free available chlorine (measured at influent to chiller)	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	Reprocessing contaminated poultry carcasses	20 ppm calculated as free available chlorine Note: Agency guidance has allowed the use of up to 50 ppm calculated as free available chlorine	9 CFR 381.91	None under the accepted conditions of use (1)
Chlorine gas	On giblets (e.g., livers, hearts, gizzards, and necks) and salvage parts	Not to exceed 50 ppm calculated as free available chlorine in the influent to a container for chilling.	Acceptability determination	None under the accepted conditions of use (1)
Chlorine gas	Beef primals	20 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Citric acid	Bologna in an edible casing	Up to a 10 percent solution applied prior to slicing	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Citric acid	Bologna in an inedible casing	Up to a 10 percent solution applied prior to slicing	Acceptability determination	None under the accepted conditions of use (1)
Citric acid	Fully cooked meat and poultry products in impermeable casings.	Up to a 3 percent solution is applied to the casing just prior to removal.	Acceptability determination	None under the accepted conditions of use (1)
Citric acid	Separated beef heads and associated offal products (e.g., hearts, livers, tails, tongues)	A 2.5 percent solution applied as a spray prior to chilling	Acceptability determination	None under the accepted conditions of use (1)
Chlorine dioxide	In water used in poultry processing	Not to exceed 3 ppm residual chlorine dioxide as determined by Method 4500-ClO ₂ E in the "Standard Methods for the Examination of Water and Wastewater," 18 th	21 CFR 173.300	None under the accepted conditions of use (3)

		ed., 1992, or an equivalent method		
Chlorine dioxide	Red meat, red meat parts and organs; processed, comminuted, or formed meat food products	Applied as a spray or dip at a level not to exceed 3 ppm residual chlorine dioxide as determined by Method 4500-ClO ₂ E in the "Standard Methods for the Examination of Water and Wastewater," 18 th ed., 1992, or an equivalent method	Food Contact Substance Notification No. FCN 668	None under the accepted conditions of use (6)
Cultured Sugar (derived from corn, cane, or beets)	In enhanced meat and poultry products (e.g., beef or pork injected with a solution) and RTE meat and poultry products (e.g., hot dogs and cooked turkey breast)	At up to 4.8 percent of the product formula	GRAS Notice No. 000240	Cultured cane and beet sugar listed by common or usual name (e.g., "cultured cane sugar") or as "cultured sugar." Cultured corn sugar listed as "cultured corn sugar" or "cultured dextrose" (2)
DBDMH (1,3dibromo-5,5-dimethylhydantoin)	For use in poultry chiller water and in water applied to poultry via an Inside-Outside Bird Washer (IOBW) and in water used in poultry processing for poultry carcasses, parts, and organs	At a level not to exceed that needed to provide the equivalent of 100 ppm active bromine	Food Contact Substance Notification No. FCN 334 and FCN 453	None under the accepted conditions of use (6)
DBDMH (1,3dibromo-5,5-dimethylhydantoin)	For use in water supplied to ice machines to make ice intended for general use in poultry processing	At a level not to exceed that needed to provide the equivalent of 100 ppm of available bromine (corresponding to a maximum level of 90 mg DBDMH/kg water)	Food Contact Substance Notification No. FCN 775	None under the accepted conditions of use (6)
DBDMH (1,3dibromo-5,5-dimethylhydantoin)	For use in water applied to beef hides, carcasses, heads, trim, parts, and organs.	At a level not to exceed that needed to provide the equivalent of 300 ppm active bromine.	Food Contact Substance Notification No. FCN 792	None under the accepted conditions of use (6)
Egg white lysozyme	In casings and on cooked (RTE) meat and poultry products	2.5 mg per pound in the finished product when used in casings; 2.0 mg per pound on	GRAS Notice No. 000064	Listed by common or usual name in the ingredients statement (2)

		cooked meat and poultry products		
Electrolytically generated hypochlorous acid	Red meat carcasses down to a quarter of a carcass	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	On whole or eviscerated poultry carcasses	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	In water used in meat processing	Not to exceed 5 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	In water used in poultry processing (except for product formulation)	Not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	Poultry chiller water	Not to exceed 50 ppm calculated as free available chlorine (measured in the incoming potable water)	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	Poultry chiller red water (i.e., poultry chiller water re-circulated, usually through heat exchangers, and reused back in the chiller)	Not to exceed 5 ppm calculated as free available chlorine (measured at influent to chiller)	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	Reprocessing contaminated poultry carcasses	20 ppm calculated as free available chlorine Note: Agency guidance has allowed the use of up to 50 ppm calculated as free available chlorine	9 CFR 381.91	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	On giblets (e.g., livers, hearts, gizzards, and necks) and salvage parts	Not to exceed 50 ppm calculated as free available chlorine in the influent to a container for chilling.	Acceptability determination	None under the accepted conditions of use (1)
Electrolytically generated hypochlorous acid	Beef primals	20 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of citric and hydrochloric acids adjusted to a pH of 1.0 to 2.0	Poultry carcasses, parts, trim, and organs	Applied as a spray or dip with a minimum contact time of 2 to 5 seconds	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of citric and hydrochloric acids adjusted to a pH of 0.5 to 2.0	Meat carcasses, parts, trim, and organs	Applied as a spray or dip for a contact time of 2 to 5 seconds	Acceptability determination	None under the accepted conditions of use (1)
A blend of citric acid	Poultry carcasses	Applied as a spray	Acceptability	None under the

(1.87%), phosphoric acid (1.72%), and hydrochloric acid (0.8%)		with a minimum contact time of 1 to 2 seconds and allowed to drip from the carcasses for 30 seconds	determination	accepted conditions of use (1)
A blend of citric acid, hydrochloric acid, and phosphoric acid	To adjust the acidity in various meat and poultry products	Sufficient for purpose	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Hops beta acids	In casings and on cooked (RTE) meat and poultry products	2.5 mg per pound in the finished product when used in casings; 2.0 mg per pound on cooked meat and poultry products	GRAS Notice No. 000063	Listed by common or usual name in the ingredients statement (2)
Hypobromous acid	In water or ice used for processing meat and poultry products	Generated on-site from an aqueous mixture of hydrogen bromide and sodium, potassium, or calcium hypochlorite for use at a level not to exceed that needed to provide 300 ppm available bromine (or 133 ppm available chlorine*) in water or ice applied to meat products, and 200 ppm available bromine (or 89 ppm available chlorine*) in water or ice applied to poultry products. *(NOTE: Because there are a limited number of commercial test kits specific for bromine, chlorine kits may be used. The ppm levels between available bromine and chlorine is due to the difference in their molecular weight.)	Food Contact Substance Notification No. FCN 000944	None under the accepted conditions of use (6)
Lactic Acid	Livestock carcasses prior to fabrication (i.e., pre- and post-chill), offal, and variety meats	Up to a 5 percent lactic acid solution	Acceptability determination	None under the accepted conditions of use (1)
Lactic acid	Beef and pork sub-	2 percent to 5 percent	Acceptability	None under the

	primals and trimmings	solution of lactic acid not to exceed 55°C	determination	accepted conditions of use (1)
Lactic acid	Beef heads and tongues	A 2.0 to 2.8 percent solution applied to brushes in a washer cabinet system used to clean beef heads and tongues	Acceptability determination	None under the accepted conditions of use (1)
Lactic acid bacteria mixture consisting of <i>Lactobacillus acidophilus</i> (NP35, NP51), <i>Lactobacillus lactis</i> (NP7), and <i>Pediococcus acidilactici</i> (NP3)	RTE cooked sausages (e.g., frankfurters, bologna, etc.) and cooked, cured whole muscle products (e.g., ham)	Applied by dipping product into a solution containing 10 ⁷ colony forming units lactobacilli per ml	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Lactic acid bacteria mixture consisting of <i>Lactobacillus acidophilus</i> (NP35, NP51), <i>Lactobacillus lactis</i> (NP7), and <i>Pediococcus acidilactici</i> (NP3)	Poultry carcasses and fresh whole muscle cuts and chopped/ground poultry	10 ⁵ to 10 ⁶ colony forming units of lactobacilli per gram of product	Acceptability determination	Listed by common or usual name in the ingredients statement of non-standardized products. Single ingredient raw products must be descriptively labeled (2)
Lactic acid bacteria mixture consisting of <i>Lactobacillus acidophilus</i> (NP35, NP51), <i>Lactobacillus lactis</i> (NP7), and <i>Pediococcus acidilactici</i> (NP3)	Non-standardized comminuted meat products (e.g., beef patties), ground beef, and raw whole muscle beef cuts	10 ⁶ to 10 ⁸ colony forming units of lactobacilli per gram of product	GRAS Notice No. 000171	Listed by common or usual name in the ingredients statement of non-standardized comminuted meat products. Ground beef and raw whole muscle beef cuts must be descriptively labeled (2)
Lactoferrin	Beef carcasses and parts	At up to 2 percent of a water-based antimicrobial spray	GRAS Notice No. 000067	Listed by common or usual name in ingredients statement (2)
Lactoferrin	Beef carcasses	As part of an antimicrobial spray that would deliver 1 gram of lactoferrin per dressed beef carcass, followed by a wash with tempered water and rinse with lactic acid	GRAS Notice No. 000130	None under the accepted conditions of use (1)
Lauramide arginine ethyl ester (LAE), silicon dioxide, and	Non-standardized RTE comminuted meat products and	Not to exceed 200 ppm LAE by weight of the finished product	Acceptability determination	Listed by common or usual name (i.e., lauric arginate,

refined sea salt	standardized RTE comminuted meat products that permit the use of any safe and suitable antimicrobial agent			refined sea salt) in the ingredients statement (2)
Lauramide arginine ethyl ester (LAE), silicon dioxide, and refined sea salt	Fresh cuts of meat and poultry; and, non-standardized, non-comminuted RTE meat and poultry products and standardized, non-comminuted RTE meat and poultry products that permit the use of any safe and suitable antimicrobial agent	Not to exceed 200 ppm LAE, 67 ppm silicon dioxide, and 1640 ppm refined sea salt by weight of the finished product	Acceptability determination	Listed by common or usual name (i.e., lauric arginate, silicon dioxide, refined sea salt) in the ingredients statement (2) When applied to the surface of fresh cuts of meat and poultry none under the accepted conditions of use (1)
Lauramide arginine ethyl ester (LAE) dissolved at specified concentrations in either propylene glycol, glycerin, or water to which may be added a Polysorbate surface active agent (quantity sufficient to achieve the intended technical effect of LAE emulsification)	Non-standardized RTE comminuted meat products and standardized RTE comminuted meat products that permit the use of any safe and suitable antimicrobial agent	Not to exceed 200 ppm LAE by weight of the finished product	Acceptability determination	Listed by common or usual name (i.e., lauric arginate) in the ingredients statement (2)
Lauramide arginine ethyl ester (LAE) dissolved at specified concentrations in either propylene glycol, glycerin, or water to which may be added a Polysorbate surface active agent (quantity sufficient to achieve the intended technical effect of LAE emulsification)	Fresh cuts of meat and poultry and various non-standardized RTE meat and poultry products and standardized RTE meat and poultry products that permit the use of any safe and suitable antimicrobial agent	Applied to the surface of the product at a rate not to exceed 200 ppm LAE by weight of the finished food product	GRAS Notice No. 000164	When applied to the surface of RTE products listed by common or usual name (i.e., lauric arginate) in the ingredients statement (2) When applied to the surface of fresh cuts of meat and poultry none under the accepted conditions of use (1)
Lauramide arginine ethyl ester (LAE)	RTE meat and poultry products; raw pork sausage	Applied to the inside of the package via a process known as "Sprayed Lethality in Container" (SLIC) or similar process at up to 44 ppm (with a	Acceptability determination	None under the accepted conditions of use (1)

		process tolerance of 20 percent, allowing for an LAE concentration not to exceed 53 ppm) by weight of the finished food product		
Nisin preparation	Cooked, RTE meat and poultry products containing sauces	Not to exceed 600 ppm nisin preparation in the finished product	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Nisin preparation	Meat and poultry soups	Not to exceed 5 ppm of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Nisin preparation	In casings and on cooked (RTE) meat and poultry products	3.15 mg per pound in the finished product when used in casings; 2.5 mg per pound on cooked meat and poultry products	GRAS Notice No. 000065	Listed by common or usual name in the ingredients statement (2)
A blend of encapsulated nisin preparation (90.9 percent), rosemary extract (8.2 percent) and salt (0.9 percent)	Frankfurters and other similar cooked meat and poultry sausages	Not to exceed 550 ppm of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
A blend of nisin preparation, rosemary extract, salt, maltodextrin, and cultured dextrose	Cooked (RTE) meat and poultry sausages and cured meat products	Not to exceed 0.55 percent of product formulation in cooked (RTE) meat and poultry sausages and 0.7 percent of product formulation in cured meat products (where the nisin preparation will not exceed 250 ppm)	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
A blend of nisin preparation, rosemary extract, salt, and sodium diacetate	Cooked (RTE) meat and poultry sausages and cured meat products	Not to exceed 0.25 percent of product formulation (where the nisin preparation will not exceed 250 ppm)	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Organic Acids (i.e., lactic, acetic, and citric acid)	As part of a carcass wash applied pre-chill	At up to 2.5 percent of a solution	FSIS Notice 49-94	None under the accepted conditions of use (1)
Ozone	All meat and poultry products	In accordance with current industry standards of good manufacturing practice	21 CFR 173.368	None under the accepted conditions of use (3)
Peroxyacetic acid, octanoic acid, acetic acid, hydrogen	Meat and poultry carcasses, parts, trim and organs	Maximum concentrations for meat carcasses, parts,	21 CFR 173.370	None under the accepted conditions of use (3)

peroxide, peroxyoctanoic acid, and 1-hydroxyethylidene-1, 1-diphosphonic acid (HEDP)		and organs: Peroxyacetic acids 220 ppm, hydrogen peroxide 75 ppm; Maximum concentrations for poultry carcasses, parts, and organs: Peroxyacetic acids 220 ppm, hydrogen peroxide 110 ppm, HEDP 13 ppm		
A mixture of peroxyacetic acid, hydrogen peroxide, acetic acid, and 1-hydroxyethylidene-1, 1-diphosphonic acid (HEDP)	(1) Process water for washing, rinsing, cooling, or otherwise for processing meat carcasses, parts, trim, and organs; and (2) process water applied to poultry parts, organs, and carcasses as a spray, wash, rinse, dip, chiller water, or scald water	In either application, the level of peroxyacetic acid will not exceed 230 ppm, hydrogen peroxide will not exceed 165 ppm, and HEDP will not exceed 14.0 ppm	Food Contact Substance Notification No. FCN 000323	None under the accepted conditions of use (6)
An aqueous mixture of peroxyacetic acid, hydrogen peroxide, acetic acid, and 1-hydroxyethylidene-1, 1-diphosphonic acid (HEDP) and optionally sulfuric acid	(1) Water or ice for washing, rinsing, cooling, or otherwise processing whole or cut meat, including parts, trim, and organs; and, (2) water or ice applied to whole or cut poultry including parts, trim, and organs as a spray, wash, rinse, dip, chiller water or scald water	In either application, the level of peroxyacetic acid will not exceed 220 ppm, hydrogen peroxide will not exceed 85 ppm, and HEDP will not exceed 11 ppm.	Food Contact Substance Notification No. FCN 000887	None under the accepted conditions of use (6)
A mixture of Peroxyacetic acid and 1-hydroxyethylidene-1, 1-diphosphonic acid (HEDP)	Poultry finishing chillers and in process water applied to poultry parts, organs, and carcasses in low temperature (e.g., less than 40 degrees F) immersion baths	In either application, the level of Peroxyacetic acid will not exceed 2000 ppm and HEDP will not exceed 136 ppm	Food Contact Substance Notification No. FCN 000880	None under the accepted conditions of use (6)
Potassium diacetate	Various meat and poultry products which permit the addition of antimicrobial agents, e.g., hot dogs	Not to exceed 0.25 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
A solution of water, lactic acid, propionic acid, and acidic calcium sulfate (solution with a	Various RTE meat products, e.g., hot dogs.	Applied as a spray for 20-30 seconds of continual application just prior to packaging	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

pH range of 1.0-2.0)*		<i>*Propionic acid may be removed from the solution; sodium phosphate may be added to the solution as a buffering agent (the amount of sodium phosphate on the finished product must not exceed 5000ppm.</i>		
A solution of water, acidic calcium sulfate and 85-95,000 ppm of lactic acid (solution with a pH range of 0.35 to 0.55)	Raw comminuted beef.	To treat raw beef during grinding to lower the pH of the product.	Acceptability determination	Product must be descriptively labeled (2)
A solution of water, acidic calcium sulfate, lactic acid, and sodium phosphate (solution with a pH range of 1.45 to 1.55)	Raw whole muscle beef cuts and cooked roast beef and similar cooked beef products (e.g., corned beef, pastrami, etc.).	Spray applied for up to 30 seconds of continual application <i>*sodium phosphate on the finished product must not exceed 5000 ppm.</i>	Acceptability determination	Listed by common or usual name in the ingredients statement of multi-ingredient products. Single ingredient roast beef products and raw whole muscle beef cuts must be descriptively labeled (2)
A solution of water, acidic calcium sulfate, lactic acid, and sodium phosphate (solution with a pH of 1.45 to 1.6)	Cooked poultry carcasses and parts.	Spray applied for 20 to 40 seconds of continual application <i>* sodium phosphate on the finished product must not exceed 5000 ppm.</i>	Acceptability determination	Listed by common or usual name in the ingredients statement of multi-ingredient products. Single ingredient whole muscle cuts of poultry must be descriptively labeled (2)
A solution of water, acidic calcium sulfate, lactic acid, and disodium phosphate (solution with a pH of 1.0 to 2.0)	Beef jerky	Applied to the surface of the product with a contact time not to exceed 30 seconds	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Skim milk or dextrose cultured with <i>propionibacterium freudenreichii</i> subsp. <i>Shermanii</i>	Meat and poultry sausages including those with standards of identity which permit the use of antimicrobial agents	Not to exceed 2 percent by weight of the finished product	GRAS Notice No. 000128	Listed by common or usual name in the ingredients statement (2)
Sodium citrate buffered with citric acid to a pH of 5.6	Non-standardized and standardized comminuted meat and poultry products which permit ingredients of	Not to exceed 1.3 percent of the product formulation in accordance with 21 CFR 184.1751	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

	this type			
Sodium hypochlorite	Red meat carcasses down to a quarter of a carcass	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	On whole or eviscerated poultry carcasses	Applied as a spray at a level not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	In water used in meat processing	Not to exceed 5 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	In water used in poultry processing (except for product formulation)	Not to exceed 50 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	Poultry chiller water	Not to exceed 50 ppm calculated as free available chlorine (measured in the incoming potable water)	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	Poultry chiller red water (i.e., poultry chiller water re-circulated, usually through heat exchangers, and reused back in the chiller)	Not to exceed 5 ppm calculated as free available chlorine (measured at influent to chiller)	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	Reprocessing contaminated poultry carcasses	20 ppm calculated as free available chlorine Note: Agency guidance has allowed the use of up to 50 ppm calculated as free available chlorine	9 CFR 381.91	None under the accepted conditions of use (1)
Sodium hypochlorite	On giblets (e.g., livers, hearts, gizzards, and necks) and salvage parts	Not to exceed 50 ppm calculated as free available chlorine in the influent to a container for chilling.	Acceptability determination	None under the accepted conditions of use (1)
Sodium hypochlorite	Beef primals	20 ppm calculated as free available chlorine	Acceptability determination	None under the accepted conditions of use (1)
Sodium metasilicate	Component of marinades used for raw meat and poultry products	Not to exceed 2 percent by weight of the marinade	Acceptability determination	None under the accepted conditions of use (1)
Sodium metasilicate	Raw beef carcasses, subprimals, and trimmings	A 4 percent (plus or minus 2 percent) solution	Acceptability determination	None under the accepted conditions of use (1)
Sodium metasilicate	RTE meat products	Up to a 6 percent solution applied to the	Acceptability determination	None under the accepted condition

		surface of the product at a rate not to exceed 300 ppm of the finished product		of use (1)
Trisodium phosphate	Raw unchilled poultry carcasses and giblets	8-12 percent solution applied by spraying or dipping giblets for up to 30 seconds. 8-12 percent solution within a temperature range of 65° F to 85 ° F applied by spraying or dipping carcasses for up to 15 seconds	Acceptability determination (per 21 CFR 182.1778)	None under the accepted conditions of use (1)
Antioxidants				
BHA (butylated hydroxyanisole)	"Brown N Serve" sausages	0.02 percent in combination with other antioxidants for use in meat, based on fat content	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
BHT (butylated hydroxytoluene)	"Brown N Serve" sausages	0.02 percent in combination with other antioxidants for use in meat, based on fat content	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Binders				
A mixture of sodium alginate, calcium sulfate, glucono delta-lactone, and sodium pyrophosphate	Various meat and poultry products where binders are permitted	Mixture not to exceed 1.55 percent of product formulation with the sodium alginate not to exceed 1 percent of the product formulation and the sodium pyrophosphate not to exceed 0.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
A mixture of carrageenan, whey protein concentrate, and xanthan gum	Sausages where binders are permitted; cooked poultry products; beef and poultry patties; modified breakfast sausage, cooked sausages, and fermented sausages covered by FSIS Policy Memo 123; and modified substitute versions of fresh sausage, ground beef, or hamburger covered by FSIS Policy Memo	Not to exceed 3.5 percent by weight of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)

	121B.			
Beef collagen	Various meat and poultry products where binders are permitted	Not to exceed 3.5 percent of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Binders listed in 9 CFR 424.21(c) for use in cured pork products and poultry products	"Turkey ham and water products"	In accordance with 9 CFR 319.104(d) and 424.21(c)	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Carboxymethyl cellulose (cellulose gum)	Poultry franks	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Carboxymethyl cellulose	Cured pork products	Not to exceed 3 percent of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Carrot Fiber	Various comminuted meat and poultry products where binders are permitted	Not to exceed 3.5 percent of the product formulation	GRAS Notice No. 000116	List as "isolated carrot product" (2)
Cellulose, powdered conforming to the specifications in the Food Chemicals Codex 5 th Edition	Various comminuted poultry products where binders are permitted	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Guar powder, micronized	Various meat and poultry products where binders are permitted	Not to exceed 3.0 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Hydroxypropyl methylcellulose	Seasoning mixtures added to sauces and gravies produced under FDA jurisdiction that will be used in meat and poultry products	Sufficient for purpose	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Hydroxypropyl methylcellulose	Thickener in meat and poultry pot pie fillings, sauces, soups, and gravies	Not to exceed 1 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Inulin	Various meat and poultry products (e.g., frankfurters, sausage, patties, loaves, pates) where binders are permitted	2 to 5 percent of the product formulation	Acceptability determination and GRAS Notice No. 000118	Listed by common or usual name in the ingredients statement (2)
Konjac flour	Meat and poultry products in which starchy vegetable flours are permitted	No to exceed 3.5 percent of the product formulation individually or collectively with other binders	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

Methylcellulose	Various comminuted meat and poultry products where binders are permitted	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Methylcellulose	Thickener in meat and poultry pot pie fillings, sauces, soups, and gravies; a binder in poultry patties, loaves, and nuggets; a binder in meat patties, loaves, and nuggets; texturizer in Policy Memo 121B and 123 products.	Not to exceed 1 percent of the product formulation as a thickener in meat and poultry pot pie fillings, sauces, soups, and gravies; 1.6 percent as a binder in poultry patties, loaves, and nuggets; 0.25 percent as a binder in meat patties, loaves, and nuggets; 0.6 percent as a texturizer in Policy Memo 121B and 123 products	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Oat Hull Fiber	Various non-standardized comminuted meat products	Not to exceed 3.5 percent of the product formulation	GRAS Notice No. 000261	Listed as “isolated oat product” in the ingredients statement
Oat Fiber	Various meat products (e.g., frankfurters, sausage patties, loaves) where binders are permitted and whole muscle meat products	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed as “isolated oat product” or “modified oat product” in the ingredients statement. Whole muscle meat products must be descriptively labeled (4)
Orange pulp, dried	Non-standardized whole muscle meat and poultry products where binders are permitted and standardized whole muscle meat and poultry products where standards of identity permit the use of binders	Not to exceed 3.5 percent of the product formulation	Acceptability determination	List as “citrus flour” or “dried orange pulp” (2)
Orange pulp, dried and orange pulp, dried with guar gum	Various ground meat and poultry products where binders are permitted	Not to exceed 3.5 percent of the product formulation	GRAS Notice No. 000154	List as “citrus flour” or “dried orange pulp” (2)
Partially hydrolyzed proteins	Various meat and poultry products where binders are permitted.	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Pectin	Various meat and	Not to exceed 3	Acceptability	Listed by common or

	poultry products where binders are permitted	percent of the product formulation	determination	usual name in the ingredients statement (2)
Pork collagen	Various meat and poultry food products where binders are permitted	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Pork skin proteins	Various meat products where binders are permitted	Not to exceed 1.5 percent of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Rice bran	Various comminuted meat and poultry products where binders are permitted (e.g., hot dogs, meatballs, and chicken patties)	Not to exceed 3.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Rice starch	Cured pork products	Not to exceed 0.8 percent of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Sodium alginate	Various meat products where binders are permitted	Not to exceed 1 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Sodium alginate	Various poultry products where binders are permitted	Not to exceed 0.8 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
“(species) protein” (e.g., chicken protein)	Whole muscle poultry food products where binders are permitted provided the protein is used in products of the same kind (e.g., chicken protein in a marinade injected into whole muscle chicken food products)	Not to exceed 0.225 percent of the marinade solution	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
“(species) protein” (e.g., chicken protein, concentrated turkey protein)	Various poultry products where the protein solution is used in products of the same kind (e.g., chicken protein in a coating of a breaded chicken fritter)	As a coating applied to the product and/or as a portion of the batter. Not to exceed 0.8 percent of product formulation when applied as a protein coating only, 0.14 percent of product formulation when used in the batter only, and 0.89 percent of product formulation	GRAS Notice No. 000168	Listed by common or usual name in the ingredients statement (2)

		when used as both a coating and in the batter		
Transglutaminase enzyme	Texturizing agent in meat and poultry food products where texturizing agents and binders are permitted	Not to exceed 65 ppm of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Transglutaminase enzyme	Cross-linking agent in modified meat and poultry products addressed in Policy Memos 121B and 123.	Not to exceed 65 ppm of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Transglutaminase enzyme	Binding and cross-linking agent in uncooked restructured chicken breasts	Not to exceed 100 ppm of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Trehalose	Binding and purge control agent in various meat and poultry products where binders are permitted	Not to exceed 2 percent of the product formulation	GRAS Notice No. 000045	Listed by common or usual name in the ingredients statement (2)
Xanthan gum (purified by recovery with ethyl alcohol)	Various meat and poultry products where binders are permitted	Non-standardized meat and poultry products and products with a standard of identity which currently permit the use of xanthan gum listed in 9 CFR 424.21(c)	GRAS Notice No. 000121	Listed by common or usual name in the ingredients statement (4)
Coloring Agents				
Carmine (cochineal)	To color isolated soy protein for use in dry cured acidified sausages	0.2 to 0.4 percent of the hydrated protein gel. The protein gel must not exceed 30 percent of the meat food product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (5)
Curing Accelerators (must be used only in combination with curing agents)				
Potassium erythorbate	Cured pork and beef cuts; cured meat food products; cured comminuted poultry or poultry products	87.5 oz. to 100 gallons of pickle at 10 percent pump; 7/8 oz. to 100 lbs. Of meat, meat byproduct or poultry product; 10 percent to surfaces of cured meat cuts or poultry products prior to <i>packaging</i>	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

<i>Denuding agents (may be used in combination. Must be removed from tripe by rinsing with potable water.)</i>				
Calcium carbonate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Calcium citrate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Calcium hydroxide	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Potassium carbonate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Potassium citrate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Potassium hydroxide	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Tricalcium phosphate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Tripotassium phosphate	Denuding agent for washing tripe	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
<i>Film Forming Agents</i>				
A mixture of water, glycerin, carrageenan, and cornstarch	Used to aid in the release of elastic netting on cooked meat products that are cooked in elastic netting	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
A mixture of water, glycerin, carrageenan, cornstarch, and caramel	Used to aid in the release of elastic netting on cooked meat products that are cooked in elastic netting	Sufficient for purpose	Acceptability determination	"Caramel Color" listed as an ingredient and as a product name qualifier (2)
A mixture of water, glycerin, carrageenan, cornstarch, and smoke flavoring	Used to aid in the release of elastic netting on cooked meat products that are cooked in elastic netting	Sufficient for purpose	Acceptability determination	"Smoke Flavor" listed as an ingredient and as a product name qualifier (2)
A solution of sodium alginate, dextrose, isolated pea protein, sugar, and maltodextrin (DE of 6) used with a solution of calcium	Used to form a calcium alginate-based casing on pork and poultry sausages.	Quantity of the casing on the sausage ranges from 8 to 15 percent of total product formulation and calcium alginate	Acceptability determination	Listed by common or usual name in the ingredients statement (4)

chloride, powdered sugar, oleoresin black pepper, and isolated pea protein.		not to exceed 0.219 percent of the finished product formulation		
Gelatin spice sheets	To ensure even distribution of seasonings on cooked pork products	Sufficient for purpose	Acceptability determination	None under the accepted conditions of use (1)
Hydroxypropyl methylcellulose	Film-forming agent in glazes for meat and poultry products	Not to exceed 4 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Methylcellulose	Film-forming agent in glazes for meat and poultry products	Not to exceed 3 percent of the product formulation for poultry products, 3.5 percent of the product formulation for meat products	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Flavoring Agents				
Adenosine 5'-monophosphoric acid (AMP) and its monosodium and disodium salts	As a flavor enhancer for meat and poultry soups and soup mixes	Not to exceed 200 ppm of the product formulation	GRAS Notice No. 000144	Listed by common or usual name in the ingredients statement (2)
Lactic acid	As a flavor enhancer added to pork fatty tissue used in the production of dehydrated pork fatty tissue	Not to exceed 0.367 percent of the pork fatty tissue, prior to dehydration	Acceptability determination	Product must be descriptively labeled (4)
Laminaria japonica (brown algae)	As a flavor enhancer or flavoring agent in marinades for meat and poultry, meat and poultry soups, gravies, and seasonings	Not to exceed 0.08 percent of the product formulation	GRAS Notice No. 000123	Listed by common or usual name in the ingredients statement (2)
Potassium acetate	Various meat and poultry products	No to exceed 1.2 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (4)
Sucralose	Non-nutritive sweetener in various non-standardized meat and poultry products	Not to exceed 500 ppm in the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Trehalose	As a flavor enhancer in non-standardized RTE meat and poultry products	Not to exceed 2 percent by weight of product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Miscellaneous				
Alkyl polyglycosides	Hog scalding	Sufficient for purpose of increasing the	GRAS Notice No. 000237	None under the accepted conditions

		wetting ability of the caustic solution		of use (1)
Alkyl polyglycosides	Wash meat (i.e., beef carcasses after the hide has been removed to remove any extraneous hair, dirt, etc.) during butchering	Used at 2% active solution level followed by a potable water rinse	GRAS Notice No. 000237	None under the accepted conditions of use (1)
Ammonium hydroxide	To adjust the pH of brine solutions prior to injection into meat	Sufficient for purpose to achieve a brine solution with a pH of up to 11.6	Acceptability determination	None under the accepted conditions of use (1)
An aqueous solution of arginine, potassium hydroxide, salt, and water	pH control agent in brine solutions for beef subprimals or to make beef patties	Arginine is added to the salt and water brine solution at 0.2-0.6% by weight and the pH is maintained between 10.4 and 10.7. The potassium hydroxide is then added at 0.0528 – 0.0793% by weight to adjust the pH to 11.4 – 11.9	Acceptability determination L-arginine: GRAS Notice No. 000290	Salt and water must be listed by common or usual name on the ingredients statement
A 60/40 blend of sodium bicarbonate and citric acid	To generate carbon dioxide in packages of raw whole muscle cuts of meat and poultry	Incorporated into soaker pads at a level not to exceed 0.5 to 2 grams per pad	Acceptability determination	None under the accepted conditions of use (1)
A solution of water, dextrose, glycerin, maltose, and sodium phosphate	To aid in the removal of residual blood from beef and bison carcasses after the typical exsanguination process is completed	Sufficient for purpose	Acceptability determination	For all edible tissue none under the accepted conditions of use unless the Moisture Fat Free% (MFF%) analysis shows treated carcasses are not in compliance with retained water requirements. All edible tissue from treated carcasses not in compliance must be labeled in accordance with Policy Memo 066C. Organ meat from all treated carcasses must be descriptively labeled (1)
Algal oil derived from <i>Schizochytrium</i> sp.	For use as an alternative edible oil in the production of various meat and	Not to exceed 1.45 percent by weight of the product formulation for meat	GRAS Notice No. 000137	Listed by common or usual name in the ingredients statement (2)

	poultry products	products and 0.87 percent by weight of the product formulation for poultry products		
Cellulose (powdered)	To facilitate grinding and shredding in cheese	No to exceed 2 percent of the cheese	Acceptability determination	None under the accepted conditions of use (1)
Citroglycerides (citric acid esters of mono- and diglycerides)	To aid in the dispersion of lauric arginate (LAE)	Used in a 5:1 mixture with lauric arginate with the maximum amount in meat and poultry products not to exceed 1125 ppm	GRAS Notice No. 000222	Listed by common or usual name in the ingredients statement (2)
Cultured Sugar (derived from cane, corn, or beets)	In uncooked (raw) sausage meat	At up to 4.8 percent of the product formula	GRAS Notice No. 000240	Cultured cane and beet sugar listed by common or usual name (e.g., "cultured cane sugar") or as "cultured sugar." Cultured corn sugar listed as "cultured corn sugar" or "cultured dextrose" (2)
Diacylglycerol oil	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 11 percent of the meat or poultry product formula	GRAS Notice No. 000115	Listed by common or usual name in the ingredients statement (2)
Erythorbic Acid	To delay discoloration in ground beef and ground beef patties	Not to exceed 0.04 percent of the product formulation	Acceptability determination	Product must be descriptively labeled (2)
Fish oil concentrate	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 2.9 percent by weight of the product formulation for meat products and 1.7 percent by weight of the product formulation for poultry products	GRAS Notice No. 000105	Listed by common or usual name in the ingredients statement (2)
Fish oil (predominantly sardine, anchovy, and tuna)	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 3.3 percent by weight of the product formulation for meat products and 2.0 percent by weight of the product formulation for poultry products	GRAS Notice No. 000193	Listed by common or usual name in the ingredients statement (2)
Fish oil (predominantly	For use as an	Not to exceed 3.3	GRAS Notice	Listed by common or

anchovy)	alternative edible oil in the production of various meat and poultry products	percent by weight of the product formulation for meat products and 2.0 percent by weight of the product formulation for poultry products	No. 000138	usual name in the ingredients statement (2)
Fish oil (predominantly anchovy) microencapsulated	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 6.0 percent by weight of the product formulation for meat products and 3.6 percent by weight of the product formulation for poultry products	GRAS Notice No. 000138	Listed by common or usual name in the ingredients statement (2)
Glucose oxidase and catalase enzymes from <i>Aspergillus niger</i> with a dextrose energy source and sodium bicarbonate buffer	To maintain a low oxygen atmosphere in packages of raw whole muscle cuts of meat and poultry	Incorporated into soaker pads such that the enzymes do not exceed 0.03 percent by weight of the meat or poultry	Acceptability determination	None under the accepted conditions of use (1)
Glucose oxidase and catalase enzymes from <i>Aspergillus niger</i> with a dextrose energy source and sodium bicarbonate buffer	To maintain a low oxygen atmosphere in packages of shelf-stable, ready-to-eat, meat products	Applied to the surface of the product such that the enzymes do not exceed 0.03 percent by weight of the meat food product	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Glycerophospholipid cholesterol acyltransferase (GCAT) enzyme preparation from <i>Bacillus licheniformis</i> expressing a modified GCAT gene from <i>Aeromonas salmonicida</i> subsp. <i>salmonicida</i> (GCAT enzyme preparation)	For use as an emulsifier in comminuted meat products	Not to exceed 22.6 mg TOS/kg of total product formulation	GRAS Notice No. 000265	Listed by common or usual name in the ingredients statement (2)
Hydrogen peroxide	To minimize biofilm buildup on reverse osmosis and ultrafiltration membranes for processing beef plasma	Not to exceed 100 ppm added just prior to plasma entering membranes	Acceptability determination	None under the accepted conditions of use (1)
Hydrolyzed gelatin	To prevent moisture loss from fresh cuts of meat and poultry	A 13 percent aqueous solution of hydrolyzed gelatin sprayed on the surface not to exceed 2 percent hydrolyzed gelatin by weight of	Acceptability determination	Listed by common or usual name in the ingredients statement. Label must also bear a statement,

		the meat or poultry		contiguous to the product name, indicating product has been coated with hydrolyzed gelatin to prevent moisture loss. (4)
Medium and long chain triacylglycerol (tailored triglycerides containing approximately 12 percent medium chain fatty acids)	For use as a supplementary source of vegetable oil in the production of various meat and poultry products	Sufficient for purposes	GRAS Notice No. 000217	Listed by common or usual name in the ingredients statement (2)
Polyglycerol ester produced by transesterification of triglycerol with soybean oil	Added to fresh livestock blood during collection to eliminate foaming	Not to exceed 8.8 ppm in the fresh livestock blood	Acceptability determination	None under the accepted conditions of use (1)
Polyglycerol polyricinoleic acid (PGPR)	For use as an emulsifier in the formulation of color additives which are subsequently used in processed meat and poultry products for which colors are permitted	Sufficient for purpose using good manufacturing practices	GRAS Notice No. 000270	Listed by common or usual name in the ingredients statement (2)
Salmon oil	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 5.0 percent by weight of the product formulation for meat products and 3.0 percent by weight of the product formulation for poultry products	GRAS Notice No. 000146	Listed by common or usual name in the ingredients statement (2)
Small planktivorous pelagic fish oil	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 3.3 percent by weight of the product formulation for meat products and 2.0 percent by weight of the product formulation for poultry products	GRAS Notice No. 000102	Listed by common or usual name in the ingredients statement (2)
Sodium bicarbonate	Neutralize excess acidity (maintain pH) in fresh pork and beef cuts	In an injected solution, not to exceed 0.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Sodium bicarbonate	Maintain pH and reduce purge in fresh turkey products	In an injected solution, not to exceed 0.5 percent of the product formulation	Acceptability determination	Listed by common or usual name in the ingredients statement (2)

Sodium bicarbonate	To soak natural casings to ease stuffing	1.06 percent of an aqueous solution. Casings must be rinsed with potable water prior to stuffing	Acceptability determination	None under the accepted conditions of use (1)
Sodium hydroxide	For application to poultry carcasses immediately after removal of feathers and prior to evisceration to minimize fecal material from adhering to the carcass	0.05 percent solution	Acceptability determination	None under the conditions of use (1)
Sodium hydroxide and hydrochloric acid	To adjust the pH of (species) plasma during processing (in which it is exposed to heat) to prevent gelling	Sufficient for purpose to adjust pH	Acceptability determination	None under the accepted conditions of use (1)
Stearidonic acid (SDA) soybean oil	For use as an ingredient in meat and poultry products	Sufficient for purpose	GRAS Notice No. 000283	Listed by common or usual name in the ingredients statement (2)
Triple salt of magnesium, ammonium, and potassium chloride	For use as a substitute for a portion of the sodium chloride normally used in meat and poultry products.	Sufficient for purpose	GRAS Notice No. 000272	Listed by common or usual name in the ingredients statement (2)
Trisodium phosphate (as a component of phosphate blends, not to exceed 40 percent of the phosphate blend)	To decrease the amount of cooked out juices in meat food products except where otherwise prohibited by the meat inspection regulations and poultry food products except where otherwise prohibited by the poultry products inspection regulations	For meat food products, 5 percent of phosphate in pickle at 10 percent pump level; 0.5 percent of phosphate in meat food product (only clear solution may be injected into meat food product). For poultry food products, 0.5 percent of total product.	Acceptability determination	Listed by common or usual name in the ingredients statement (4) Note: Phosphates may be collectively designated as "sodium phosphates" or "potassium phosphates"
Tuna oil	For use as an alternative edible oil in the production of various meat and poultry products	Not to exceed 3.1 percent by weight of the product formulation for meat products and 1.8 percent by weight of the product formulation for poultry products	GRAS Notice No. 000109	Listed by common or usual name in the ingredients statement (2)
Xanthan gum	Suspending agent for carrageenan in a brine tank	Not to exceed 2 percent of the amount of carrageenan	Acceptability determination	None under the accepted conditions of use (1)

Packaging Systems				
Carbon monoxide gas as part of Cryovac's modified atmosphere packaging system (for use with 550P Tray/Lid and LID551P)	Packaging fresh cuts of case ready muscle meat and case ready ground meat to maintain wholesomeness, provide flexibility in distribution, and reduce shrinkage of the meat	The use of carbon monoxide (0.4 percent), carbon dioxide (30 percent) and nitrogen (69.6 percent) as part of the Cryovac low oxygen modified atmosphere packaging system used with 550P Tray /Lid	Acceptability Determination	None under the accepted conditions of use (2)
Carbon monoxide gas as part of Cryovac's modified atmosphere packaging system	Packaging fresh cuts of case ready muscle meat and case ready ground meat to maintain wholesomeness	The use of carbon monoxide (0.4 percent), carbon dioxide (30 percent) and nitrogen (69.6 percent) introduced directly into the package. System uses a barrier lid that only covers a highly permeable patch. The permeable patch is a one half inch hole in the lid film. Barrier lid removed prior to display for retail sale	Acceptability determination	None under the accepted conditions of use (2)
Carbon monoxide gas as part of the Pactiv modified atmosphere packaging system (ActiveTech 2001)	Packaging fresh cuts of case ready muscle meat and case ready ground meat to maintain wholesomeness	The use of carbon monoxide (0.4 percent), carbon dioxide (30 percent) and nitrogen (69.6 percent) as part of the Pactiv modified atmosphere packaging system	GRAS Notice No. 000083	None under the accepted conditions of use (2)
Carbon monoxide gas as part of a high oxygen modified atmosphere packaging system used in accordance with GRN 000083 (Cargill)	Packaging fresh cuts of case-ready muscle meat and ground meat to maintain wholesomeness	Not to exceed 0.4 percent of the modified atmosphere gas mixture	Acceptability determination	None under the accepted conditions of use (2)
Carbon monoxide gas as a part of Cargill's modified atmosphere packaging system introduced directly into the bulk or master container used for bulk transportation of fresh meat products. Meat	Packaging fresh cuts of muscle meat and ground meat to maintain wholesomeness	Not to exceed 0.4 percent of the modified atmosphere gas mixture	Acceptability determination	None under the accepted conditions of use (2)

products are subsequently repackaged in packages not containing a carbon monoxide modified atmosphere prior to retail sale (In accordance with GRN 000083)				
Carbon monoxide gas as part of the Precept modified atmosphere packaging system	Packaging case-ready fresh cuts of beef and pork as well as ground beef and pork to maintain wholesomeness	Carbon monoxide 0.4 percent (with a process tolerance of 20 percent, allowing for a carbon monoxide concentration up to 0.48 percent) in combination with carbon dioxide (20-100 percent) and nitrogen (0-80 percent)	GRAS Notice No. 000143	None under the accepted conditions of use (2) Products packaged in this MAP system must be coded with a "Use or Freeze by" date not to exceed 28 days after packaging for ground meat and 35 days for whole muscle cuts
Carbon monoxide gas as part of Precept's modified atmosphere packaging system	Packaging case-ready fresh cuts of poultry as well as ground poultry	Carbon monoxide 0.3 percent (with a process tolerance of 20 percent, allowing for a carbon monoxide concentration up to 0.36 percent), in combination with nitrogen (0-80 percent), and carbon dioxide (20-100 percent)	Acceptability determination	None under the accepted conditions of use (2) Products packaged in this MAP system must be coded with a "Use or Freeze by" date not to exceed 28 days after packaging for ground poultry and 35 days for whole muscle cuts of poultry
Carbon monoxide as a component of a modified atmosphere packaging system (Tyson Foods, Inc.)	Packaging case-ready fresh cuts of beef and pork as well as ground beef and pork	Carbon monoxide (at a level not to exceed 2.2 mg carbon monoxide per pound of packaged meat) in combination with carbon dioxide and nitrogen	GRAS Notice No. 000167	None under the accepted conditions of use (2) Products packaged in this MAP system must be coded with a "Use or Freeze by" date not to exceed 28 days after packaging for ground meat and 35 days for whole muscle cuts
<i>Poultry scald agents (must be removed by subsequent cleaning operations)</i>				
Alkyl polyglycosides	To remove feathers from poultry carcasses	Sufficient for purpose	GRAS Notice No. 000237	None under the conditions of use (1)
Calcium acid phosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)

Calcium acid pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium bicarbonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium carbonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium dodecylbenzene sulfonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium 2-ethylhexyl sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium hexametaphosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium hydroxide	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium lauryl sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium phosphate (mono-, di-, and tribasic)	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium sesquicarbonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Calcium tripolyphosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium acid phosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium acid pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium bicarbonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium carbonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium dodecylbenzene sulfonate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium 2-ethylhexyl sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium hexametaphosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium hydroxide	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium lauryl sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium phosphate (mono-, di-, and tribasic)	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium	To remove feathers	Sufficient for purpose	Acceptability	None under the

sesquicarbonate	from poultry carcasses		determination	conditions of use (1)
Potassium sulfate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Potassium tripolyphosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Tetracalcium pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Tetrapotassium pyrophosphate	To remove feathers from poultry carcasses	Sufficient for purpose	Acceptability determination	None under the conditions of use (1)
Tenderizing Agents				
Calcium gluconate	Raw meat products	Solutions applied or injected into raw meat shall not result in a gain of 3 percent above green weight	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Protease preparation derived from <i>Bacillus subtilis</i>	Raw meat products	Solutions applied or injected into raw meat shall not result in a gain of 3 percent above green weight	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Protease produced from <i>Bacillus subtilis</i> var. <i>amyloliquefaciens</i>	Raw meat products	Solutions applied or injected into raw meat shall not result in a gain of 3 percent above green weight	Acceptability determination	Listed by common or usual name in the ingredients statement (2)
Protease produced from <i>Aspergillus niger</i>	Raw meat cuts and raw poultry muscle tissue of hen, cock, mature turkey, mature duck, mature goose, and mature guinea	Solutions applied or injected into raw meat or poultry tissue shall not result in a gain of 3 percent above green weight	GRAS Notice No. 000089	Listed by common or usual name in the ingredients statement (2)

- 1) The use of the substance(s) is consistent with FDA's labeling definition of a processing aid.
- 2) Generally Recognized as Safe (GRAS)
- 3) Secondary Direct Food Additive
- 4) Direct Food Additive
- 5) Color Additive
- 6) Food Contact Substance

* Substances identified in bold print in the table are substances that have been added to the directive since it was last issued on December 17, 2002.

Questions and Answers on the Use of Antimicrobial Agents in the Production of Meat and Poultry Products

The following set of questions and answers provide information regarding the requirements for the use of antimicrobial agents in meat and poultry production.

References

- Final Rule, "Food Ingredients and Sources of Radiation Listed or Approved for Use in the Production of Meat and Poultry Products" (December 1999).
- MOU between FDA and FSIS for Ingredient Approval (January, 2000).
- FSIS Directive 7120.1, "Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products."
- Guidance document on "Ingredients and Sources of Radiation Used to Reduce Microorganisms on Carcass, Ground Beef and Beef Trimmings."
- Guidance Procedures for Notification and Protocol Submission of New Technology, February 2004
http://www.fsis.usda.gov/regulations_&_policies/New_Technology_Notification_&_Protocol_Submission/index.asp
- Federal Register* Notice, "FSIS Procedures for Notification of New Technology" (68 FR 6873) (February, 2003)
- 9 CFR Part 416.4
- [FSIS Directive 6355.1](#), "Use of Chlorine Dioxide in Poultry Chill Water."
- 9 CFR 424.21(c)
- FSIS Directive 6700.1 and [FSIS Directive 6700.1 Amendment 1 - Html](#) , "Retained Water in Raw Meat and Poultry Products."
- 21 CFR Part 172,173, 182, 184
- [21 CFR 101.100](#) (a)(3)(ii)(c)

1. Question: What is the definition of a New Technology?

Answer: According to the FSIS *Federal Register* Notice (68 FR 6873) entitled, "FSIS Procedures for Notification of New Technology," FSIS defines a "new technology" as new, or new applications of, equipment, substances, methods, processes or procedures affecting the slaughter of livestock and poultry or processing of meat, poultry, or egg products which could affect product safety, inspection procedures, inspection program personnel safety, or require a waiver of a regulation.

2. Question: What is the definition of a processing aid?

Answer: According to the Food and Drug Administration's (FDA) regulations (21 CFR 101.100 (a) (3) (ii)), the definition of a processing aid is:

- a. Substances that are added to a food during the processing of such food but are removed in some manner from the food before it is packaged in its finished form.
- b. Substances that are added to a food during processing, are converted into constituents normally present in the food, and do not significantly increase the amount of the constituents naturally found in food.
- c. Substances that are added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food.

An example of a processing aid is the use of organic acid(s) (e.g., lactic, acetic, or citric acid) as part of a livestock carcass wash applied pre-chill.

FSIS has posted guidelines on processing aids in regulating the labeling of meat and poultry products at:

http://www.fsis.usda.gov/PDF/Determination_of_Processing_Aids.pdf.

http://www.fsis.usda.gov/PDF/Prohibited_Substances_in_Fsis_Actions_on%20Use_of_Ingredients.pdf

3. Question: What are secondary direct food additives and direct food additives?

Answer: According to FDA's regulations (21 CFR Part 173), secondary direct food additives are substances whose functionality is required during the manufacture or processing of a food and are ordinarily removed from the final food. Although residuals might carry over to the final food, residuals must not exhibit any technical effects. Secondary direct food additives are consistent with FDA's definition of a processing aid so labeling is not required. Examples of secondary direct food additives are acidified sodium chlorite (21 CFR 173.325) and peroxyacids (21 CFR 173.370).

According to FDA's regulations (21 CFR Part 172), direct food additives are used to provide a technical effect in the final food. The antioxidants BHA and BHT are examples of substances that are approved as direct food additives.

4. Question: Do organic acid(s) (e.g., lactic, acetic, or citric acid) that are used as antimicrobial agents need to be declared on the label if they are applied to livestock carcasses after the chilling step?

Answer: Organic acid(s) are generally recognized as safe (GRAS) and are listed in FSIS regulations for use as an acidifier in various meat and poultry products at a level which is sufficient for purpose (9 CFR 424.21(c)). All ingredients, including organic acid(s), require labeling unless the use of a substance is consistent with FDA's definition of a processing aid or is a secondary direct food additive.

FSIS has recently stated no objection to the use of 5% hot lactic acid as an antimicrobial agent to treat beef carcasses prior to fabrication (i.e., pre and post-chill). Data was submitted to the Agency that demonstrated no lasting effect under the specified conditions of use. FSIS determined that the proposed use is consistent with the definition of a processing aid. Therefore, its use would not need

to be reflected on the labeling for treated carcasses or products produced from treated carcasses. This new use is listed in the table of this directive.

If a company is interested in using one or more of these organic acid(s) as an antimicrobial agent on livestock carcasses or trim in a manner other than which is currently approved, they must provide data to the Agency that show that the use complies with FDA's definition of a processing aid. The data must show that the organic acid has only a momentary technical effect, not a lasting effect on the meat, e.g., fresh color is not preserved, normal spoilage indicators (e.g. discoloration) are not masked; and there is no extension of shelf life as compared to products made with untreated trimmings. The data must also show that the nutrient composition is not affected by the treatment and the sensory characteristics of the product are not affected. (Note: the reference to "Guidance on Ingredients and Sources of Radiation used to Reduce Microorganisms on Carcasses, Ground Beef, and Beef Trim," can be accessed at [http: www.fsis.usda.gov/oppde/larc](http://www.fsis.usda.gov/oppde/larc) at the "ingredients" link)

5. Question: What is the maximum amount of organic acid(s) permitted to be applied to livestock carcasses pre-chill without having to declare the organic acid(s) on the label?

Answer: Historically, the maximum amount of organic acid(s) that can be used to treat livestock carcasses without labeling is up to 2.5 % of a solution applied pre-chill. Labeling is not required for this specific use of organic acid(s) (which the Agency has permitted for many years) because it is based on data that showed that this application is consistent with FDA's definition of a processing aid.

FSIS has recently stated no objection to the use of 5 % hot lactic acid as an antimicrobial agent on beef carcasses prior to fabrication (see question number four). This use was determined to be consistent with the definition of a processing aid. Therefore, its use would not need to be reflected on the labeling for treated carcasses or products produced from treated carcasses.

6. Question: Do organic acid(s) (e.g., lactic, acetic, or citric acid) that are used as antimicrobial agents need to be declared on the label if they are applied to livestock carcasses?

Answer: Unless the proposed use has been determined by FSIS to be consistent the definition of a processing aid (e.g., the application of acetic or citric acids at 2.5 % of a beef carcass wash solution applied pre-chill or the use of a 5% lactic acid solution to treat beef carcasses prior to fabrication either pre- or post-chill) the organic acid(s) would require labeling.

7. Question: Is the maximum amount of organic acid(s) allowed, without labeling the product, based on the concentration of the organic acid(s) applied to the carcass or the concentration of the organic acid(s) draining from the carcass?

Answer: The amount of organic acid(s) is based on the percentage of organic acid(s) in the carcass wash (aqueous solution) prior to application. It is not based on the residual level of organic acid(s) draining from a treated carcass during application.

8. Question: Do organic acid(s) (e.g. lactic, acetic, or citric acid) have to be declared on the label if they are applied to cut-up and ground meat and poultry?

Answer: Yes, all ingredients, including organic acid(s), require labeling unless the use of a substance is consistent with FDA's definition of a processing aid or is a secondary direct food additive. If an establishment is interested in using organic acid(s) to treat meat and poultry cuts and/or ground meat and poultry to momentarily reduce microorganisms, data must be submitted to FSIS to show that the proposed use of organic acid(s) is consistent with FDA's definition of a processing aid.

9. Question: Do organic acid(s) (e.g. lactic, acetic, or citric acid) have to be declared on the label if they are applied to livestock or poultry byproducts and giblets (e.g. livers, hearts, and gizzards)?

Answer: No, labeling is not required when organic acid(s) are applied pre-chill at up to 2.5% of an aqueous solution to treat livestock and poultry byproducts and giblets.

FSIS has recently stated no objection to the use of 5% lactic acid as an antimicrobial agent to treat beef carcasses prior to fabrication (i.e., pre and post-chill).

10. Question: Are organic acid(s) used as antimicrobial agents permitted to be used on poultry carcasses?

Answer: Yes, organic acid(s) are GRAS and are listed in FSIS regulations for use as an acidifier (which may have an antimicrobial effect) in various meat and poultry products at a level which is sufficient for purpose (9 CFR 424.21(c)). Organic acid(s) are permitted to be applied to poultry carcasses pre-chill at a concentration of up to 2.5 percent of a solution without labeling.

11. Question: If organic acid(s) (e.g., lactic, acetic, or citric acid) are used on ready-to-eat products as a spray or dip, must the application be followed by a potable water rinse?

Answer: No, the use of organic acid(s) on ready-to-eat products are not required to be followed by a potable water rinse. However, the organic acid(s) will be considered ingredients that require labeling unless data can be submitted to FSIS that show that their use is consistent with FDA's definition of a processing aid.

12. Question: Are organic acid(s) (e.g., lactic, acetic or citric acid) permitted to be used on a continuous basis on conveyor belts? What are the conditions for their use? When do the organic acids need to be declared on a product label?

Answer: FSIS has no objection to the use of organic acids on conveyor belts on a continuous basis. However, the process should not result in the organic acid(s) having a lasting technical effect on meat or poultry which comes into contact with the conveyor belts. Labeling is required if the organic acid(s) exhibit a lasting technical effect on meat or poultry which comes into contact with the treated conveyor belts.

13. Question: Are antimicrobial agents other than organic acid(s) permitted to be used on a continuous basis on conveyor belts if they are approved as an antimicrobial agent in the production of meat and poultry products? What are the conditions for their use? When do the antimicrobial agents have to be included on a product label?

Answer: Yes, antimicrobial agents approved for use in the production of meat and poultry products may be used on conveyor belts provided they are followed by a potable water rinse. Substances listed in 21 CFR 178.1010 may be used in sanitizing solutions on food contact surfaces with only adequate draining (no water rinse) before contact with food.

14. Question: Is trisodium phosphate (TSP) permitted to be used as an antimicrobial agent on livestock carcasses, viscera, and parts?

Answer: TSP may only be used on livestock carcasses according to interim Agency policy.

15. Question: Where is TSP allowed to be used as an antimicrobial agent on poultry?

Answer: FSIS regulations (9 CFR 424.21 (c)) permits the use of TSP on raw post-chill poultry carcasses. In addition, FSIS has permitted the application of TSP to raw poultry carcasses pre-chill by spraying or dipping the carcasses with an 8-12% solution maintained within a temperature range of 65° F to 85° F for up to 15 seconds. FSIS has permitted the use spraying or dipping of poultry giblets for up to 30 seconds with an 8-12% solution of TSP pre-chill.

TSP is also used in some on-line reprocessing operations. Establishments which use on-line reprocessing operate under an experimental exemption listed in 9 CFR 381.3(c). The conditions of use for TSP in on-line reprocessing are limited by the parameters listed in the FSIS approved on-line reprocessing protocol, not the conditions of use listed above.

16. Question: Is chlorine dioxide permitted to be used as an antimicrobial agent on livestock carcasses, viscera, and parts?

Answer: Chlorine dioxide may be used as an antimicrobial agent to treat red meat carcasses, parts, and organs. It is applied as a spray or dip at a level not to exceed 3 ppm residual chlorine dioxide.

17. Question: Is chlorine dioxide allowed to be used as an antimicrobial agent on poultry? What are the conditions for its use?

Answer: Chlorine dioxide may be used as an antimicrobial agent to treat water in poultry processing as prescribed in FDA's regulations (21 CFR 173.300). Residual chlorine dioxide must not exceed 3 ppm in the poultry processing water.

18. Question: Is hydrogen peroxide allowed to be used as an antimicrobial agent on meat and poultry products (e.g. carcasses, parts, processed products)?

Answer: No, hydrogen peroxide cannot be used as an antimicrobial when applied by itself. However, it can be used as an antimicrobial when used as a component of peroxyacids (21 CFR 173.370; FCN 000323; FCN 000880; FCN 000887). In addition, it is listed as GRAS in FDA regulations (21 CFR 184.1366) for use as a bleaching agent to treat beef feet and in FSIS regulations (9 CFR 424.21 (c)) as a bleaching agent to treat tripe (followed by a water rinse).

19. Question: Can any and all antimicrobial agents be used on poultry carcasses during on-line reprocessing?

Answer: No, on-line reprocessing operations function under an experimental exemption (9 CFR 381.3 (c)). The use of antimicrobial agents in on-line reprocessing are limited by the parameters of the FSIS approved on-line reprocessing protocol.

20. Question: Can antimicrobial agents be used (spray or dip) on the same carcasses or parts more than once, without labeling?

Answer: Yes, antimicrobial agents may be used more than once. However, the antimicrobial agents must be used in accordance with the approved or accepted conditions of use. Labeling is required unless the use of the substance is consistent with FDA's definition of a processing aid or is a secondary direct food additive.

21. Question: Do all uses of antimicrobial agents need to comply with the requirements of 9 CFR 441.10 for retained water? What are the requirements?

Answer: Yes, any establishment that uses a post-evisceration process that results in water retention in raw livestock or poultry carcasses or parts must maintain on file a written data collection protocol in accordance with 9 CFR 441.10 (c) (1). Any treatment in the chilling process such as antimicrobial treatments should be described in the protocol. An establishment does not have to maintain a protocol on file if it has data or information that clearly demonstrates that its products do not retain water as a result of the process, e.g., spraying boneless meat with antimicrobial agents where the end product does not retain water from the antimicrobial application [FSIS Directive 6700.1](#) and [6700.1 Amend 1](#)).

Attachment 11

Research Note

Effectiveness of 1,3-Dibromo-5,5 Dimethylhydantoin on Reduction of *Escherichia coli* O157:H7– and *Salmonella*-Inoculated Fresh Meat†

NORASAK KALCHAYANAND,* TERRANCE M. ARTHUR, JOSEPH M. BOSILEVAC, DAYNA M. BRICHTA-HARHAY, MICHAEL N. GUERINI, STEVEN D. SHACKELFORD, TOMMY L. WHEELER, AND MOHAMMAD KOOHMARATE‡

U.S. Department of Agriculture, Agricultural Research Service, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, Nebraska 68933-0166, USA

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ABSTRACT

1,3-Dibromo-5,5-dimethylhydantoin (DBDMH; 25°C) and hot water (85°C) spray treatments were evaluated for efficacy in decontamination of pathogenic bacteria attached to beef carcass surfaces represented by cutaneous trunci (CT) muscle sections and beef hearts. Treatments were evaluated using two different systems, a commercial carcass wash cabinet and a model carcass washer. The effects were measured immediately after treatment and again after 48 h of storage at 4°C. Sections of CT and beef hearts were inoculated with bovine fecal solution containing approximately 6 log CFU/cm² of *Escherichia coli* O157:H7 and *Salmonella*. After DBDMH or hot water spray treatments, bacterial populations were enumerated immediately and after storage for 48 h at 4°C. DBDMH treatments reduced aerobic plate counts, *Enterobacteriaceae*, *E. coli* O157:H7, and *Salmonella* by the same or slightly lower amounts relative to hot water treatment. DBDMH reduced aerobic plate counts and *Enterobacteriaceae* by 2.8 to 3.6 log CFU/cm², *E. coli* O157:H7 by 1.6 to 2.1 log CFU/cm², and *Salmonella* by 0.7 to 2.3 log CFU/cm² on CT sections and beef hearts. Hot water treatment reduced aerobic plate counts and *Enterobacteriaceae* by 3.0 to 4.1 log CFU/cm², *E. coli* O157:H7 by 1.8 to 2.3 log CFU/cm², and *Salmonella* by 2.5 to 2.8 log CFU/cm². After 48 h of storage, the reductions of organisms by DBDMH and hot water treatments were not different. This study demonstrated that DBDMH spray washing could be effective as an antimicrobial intervention for beef carcasses and variety meats.

Antimicrobial interventions are a crucial step for food industries to ensure that their products are safe before reaching consumers. Hot water treatment has been found to be effective against pathogens as well as spoilage bacteria (2, 7, 8, 9, 11, 16, 21), whereas the use of chlorinated water has shown little or no effect (6, 12, 24). The disadvantage of hot water treatment is the high-water-volume use and high cost of maintaining such a high temperature. 1,3-Dibromo-5,5-dimethylhydantoin (DBDMH; C₅H₆Br₂N₂O₂), or Bromitize, and other organohalamine derivatives have been widely used as disinfectants for water treatment and for treating industrial or commercial water-cooling systems (20, 22, 23). These halogenated hydantoin derivatives have shown considerable efficacy against several species of microorganisms (13, 15, 26). In aqueous solution, DBDMH hydrolyzes to hypobromous acid, an active antimicrobial agent, and dimethylhydantoin (22). In the poultry industry, DBDMH at a level of 100 ppm has been approved for use

as an antimicrobial in chiller water during processing (25). Although the use of DBDMH to decontaminate beef carcasses or variety meats has been recently approved, the use of bromine compounds for decontamination of red meat is very limited. The objective of this study was to evaluate the efficacy of DBDMH as an antimicrobial intervention in reducing aerobic bacteria, *Enterobacteriaceae*, *Escherichia coli* O157:H7, and *Salmonella* on inoculated fresh meat surfaces.

MATERIALS AND METHODS

Bacterial cultures. *E. coli* O157:H7 ATCC 43888 and ATCC 43895 were obtained from the American Type Culture Collection (Manassas, VA). *E. coli* O157:H7 FSIS EL50179, *E. coli* O157:H7 CO50, *E. coli* O157:H7 SSNE1040, *Salmonella* Newport 13324 POH2, *Salmonella* Newport 644AB2, *Salmonella* Typhimurium 11241 PRB1, and *Salmonella* Typhimurium 14218 PRH2 were obtained from the U.S. Meat Animal Research Center (USMARC; Clay Center, NE) culture collection. All strains were maintained in 25% glycerol at –70°C and were propagated individually in tryptic soy broth without dextrose, supplemented with 0.6% yeast extract (TSBY; Difco, Becton Dickinson, Sparks, MD) at 37°C for 18 h.

Feces screening and preparation of fecal solution. Fresh bovine fecal samples (10 g) were obtained from cattle at the US-MARC feedlot and then screened for the prevalence of *E. coli*

* Author for correspondence. Tel: 402-762-4224; Fax: 402-762-4149; E-mail: norasak.kalchayanand@ars.usda.gov.

† Mention of trade names or commercial products in this article is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture.

‡ Present address: IEH Laboratories & Consulting Group, 15300 Bothell Way N.E., Lake Forest Park, WA 98155, USA.

O157:H7 and *Salmonella* by methods described previously (1, 14). Only fecal samples that did not have both pathogens were combined and frozen at -20°C . The fecal solutions used for inoculation were prepared by thawing the screened feces in a refrigerator overnight. Two grams of feces was placed in a filtered stomacher bag (Whirl-Pak, Nasco, Ft. Atkinson, WI), mixed with 98 ml of phosphate buffered tryptic soy broth (Difco, Becton Dickinson), and hand massaged thoroughly.

Preparation of inoculums. All bacterial strains were grown in TSBY for 18 h at 37°C . For experiments utilizing the carcass wash cabinet, strain 43888 was used as it does not produce Shiga toxins (5), and the wash cabinet did not have containment facilities to prevent environmental release of pathogens. This *E. coli* culture was diluted 10-fold with fecal solution to achieve a final concentration of approximately 5×10^8 CFU/ml. For the experiments conducted in the model carcass washer installed in a biological containment hood, pathogenic bacteria were used. A four-strain mixture of pathogenic *E. coli* O157:H7 and a four-strain mixture of *Salmonella* were prepared separately by combining 1 ml of each strain into two 10-ml conical tubes. A cocktail mixture containing a combination of four strains of *E. coli* O157:H7 and four strains of *Salmonella* was then prepared by combining the *E. coli* O157:H7 and *Salmonella* mixtures in a 2:1 ratio. This ratio was empirically predetermined to ensure that nearly equal amounts of both pathogens were in the mixture. The cocktail was then diluted 10-fold with fecal solution to the concentration of approximately 5×10^8 CFU/ml. All inoculums were maintained on ice until used for inoculation onto fresh meats.

Fresh meat tissue preparation and inoculation. Fresh cutaneous trunci (CT) muscle and beef hearts from pre-rigor carcasses were obtained during online processing from a commercial processing plant, packed in insulated containers, and transported to the USMARC laboratory. Approximately 30 to 120 min elapsed between collection and use in the laboratory. Two replications were conducted, and each replication was composed of 24 CT sections and 48 beef hearts. For each CT section, 4 squares of 100 cm^2 were marked with edible ink and a template (10 by 10 cm). Each 100-cm^2 square was then divided into 4 25-cm^2 squares for a total of 16 25-cm^2 areas for each treatment. The hearts were cut lengthwise in half, and 2 100-cm^2 outlines on the outside surface of each half were marked and divided into 4 25-cm^2 areas for each heart. Therefore, two hearts were used to provide 16 25-cm^2 areas for each intervention treatment. A set of 12 CT sections and 24 beef hearts was inoculated with *E. coli* O157:H7 43888, and another set was inoculated with the pathogenic cocktail mixture. Two milliliters of each inoculum was applied over the marked areas (4 100-cm^2 areas) with either a disposable cell spreader or the back of a sterile plastic spoon. The inoculated CT sections and beef hearts were allowed to stand at room temperature for 15 min to allow bacterial attachment before applying any treatment.

Spray washing cabinets and washing procedures. Two spray wash cabinets were used to apply hot water or DBDMH in this study. A carcass wash cabinet was used for the *E. coli* O157:H7 43888 inoculation. The cabinet was a top half of a standard commercial beef carcass wash cabinet (Chad Co., Olathe, KS). Four nozzles (SS2510, Spraying Systems Co., Wheaton, IL) were positioned to spray from a 30° angle onto the tissue sample and were oscillated at 80 cycles per min, giving an up-and-down sweeping motion of the flat spray over the tissue sample. For the pathogenic-bacteria inoculation, a model carcass washer installed in a biological containment hood was used to apply treatments.

Three spray nozzles (SS2510; Spraying Systems) were oscillated at 60 cycles per minute. For both cabinets, all of the CT sections were spray washed either with hot water (85°C at nozzles) at 20 lb/in^2 , with a flow rate of 6.8 liters (1.8 gal) per min or DBDMH ($25 \pm 2^{\circ}\text{C}$) for 12 s at 35 lb/in^2 , while all of the beef hearts were spray washed for 28 s. The 12- and 28-s exposure times were based on carcass chain speed (300 head per hour) and the variety meat chain speed of a typical processing plant, respectively. The spraying pressure was based on the pressure for hot water and organic acid currently used in beef cattle processing plants. The pressure for hot water was 20 lb/in^2 in order to maintain the water temperature at 85°C . A higher pressure causes smaller droplets, which exchange temperature rapidly with the environment. The concentration of DBDMH (75, 175, or 270 ppm; Solution Bio-Sciences, Inc., Chatham, NJ) was determined with a bromine pocket colorimeter II test kit (Hach, Loveland, CO). With the carcass wash cabinet, each DBDMH concentration was applied through a vertical spray line via two fixed nozzles (SS9530, Spraying Systems) that delivered 9.8 liters (2.6 gal) per min at 35 lb/in^2 . With the model carcass washer, beef hearts and CT sections inoculated with a cocktail mixture of pathogens were sprayed with DBDMH at 35 lb/in^2 , with a flow rate of 7.6 liters (2.0 gal) per min. The pH values for DBDMH were 6.84, 6.76, and 6.71 for 75, 175, and 270 ppm, respectively. For all treatments, the excess liquid was allowed to drip off for 30 s before sampling for microbiological analyses.

Microbiological and statistical analyses. Samples from both tissues were collected before (controls) and after applying treatments. To avoid sampling bias, the four 25-cm^2 sections in each inoculation area were rotated clockwise during each collection. Before treatment, one of the four 25-cm^2 sections was aseptically excised and placed into a sterile filtered Whirl-Pak bag. After treatments, two additional 25-cm^2 sections were excised. One section was used for microbiological analyses on the same day. The other section was stored at 4°C for 48 h to determine the residual effect of the treatments. The time between spray treatment and microbiological analyses was approximately 15 min. A 50-ml aliquot of Dey-Engley neutralizing broth (Difco, Becton Dickinson) supplemented with 0.3% Soytone (Difco, Becton Dickinson) and 0.25% sodium chloride (Sigma, St. Louis, MO) was aseptically added into each tissue sample bag. Each bag was homogenized (540 rpm) for 1 min with a stomacher (InterScience, Markham, Ontario, Canada). An aliquot of 0.1 ml of each homogenate from the control bags was used to determine aerobic plate counts (APC) and *Enterobacteriaceae* counts (EBC) by using a Bactometer (bioMérieux, Hazelwood, MO), as described previously (3). Each homogenate from treated tissue samples was 10-fold serially diluted and appropriate dilutions were plated on Petrifilm Aerobic and *Enterobacteriaceae* Count Plates (3M Health Care, St. Paul, MN). The plates were incubated as recommended by the manufacture and counted with a Petrifilm plate reader (3M Health Care). The homogenates from both control and treated tissue samples also were enumerated on selective media for *E. coli* O157:H7 and *Salmonella*, as previously described (3) by using a spiral plater (Spiral Biotech, Inc., Norwood, MA) with the limit of detection 60 CFU/cm^2 . The bags from treated tissue samples were enriched by incubating at 25°C for 2 h, 42°C for 6 h, and stored at 4°C overnight in order to test for the recovery of viable but injured microorganisms. Tissue samples that showed no count on selective media were subjected to immunomagnetic separation. One milliliter from the enrichments was subjected to immunomagnetic separation for *E. coli* O157:H7 and *Salmonella* as described previously (1, 14). Three presumptive colonies of *E.*

TABLE 1. Effectiveness of DBDMH on APC, EBC, and *E. coli* O157:H7 43888 compared with hot water treatment of inoculated beef tissues using a commercial carcass wash cabinet

Tissue	Treatment ^a	Bacterial population, log CFU/cm ² (log reduction/cm ²)		
		APC	EBC	<i>E. coli</i> O157:H7
Cutaneous trunci ^b	Control	8.6 A	8.6 A	6.1 A
	Hot water	5.0 B (3.5 D) ^c	4.7 B (3.9 D)	4.3 B (1.8 D)
	Control	8.8 A	8.2 A	6.2 A
	DBDMH ^d , 75 ppm	5.7 B (3.0 E)	5.5 B (2.8 E)	4.5 B (1.6 D)
	Control	8.7 A	8.2 A	6.3 A
	DBDMH, 175 ppm	5.8 B (2.9 E)	5.5 B (2.8 E)	4.7 B (1.6 D)
	Control	9.0 A	8.6 A	6.4 A
	DBDMH, 270 ppm	5.7 B (3.3 DE)	5.5 B (3.1 E)	4.6 B (1.8 D)
Heart	Control	8.0 G	7.7 G	5.8 G
	Hot water	3.9 H (4.1 X)	3.6 H (4.1 X)	3.6 H (2.2 X)
	Control	8.0 G	7.6 G	6.0 G
	DBDMH, 75 ppm	4.5 H (3.5 Y)	4.3 H (3.3 Y)	4.2 H (1.7 Y)
	Control	8.0 G	7.4 G	5.8 G
	DBDMH, 175 ppm	4.5 H (3.6 XY)	4.2 H (3.2 Y)	4.2 H (1.7 Y)
	Control	7.9 G	7.6 G	6.1 G
	DBDMH, 270 ppm	4.3 H (3.6 XY)	4.2 H (3.4 Y)	4.1 H (2.1 X)

^a Hot water (85°C) was sprayed at 20 lb/in² for 12 s for CT sections and 28 s for beef heart. All DBDMH treatments (25 ± 2°C) were sprayed at 35 lb/in² for 12 s for CT sections and 28 s for beef hearts.

^b Representing carcass surface tissue.

^c A and B, and G and H (log CFU per square centimeter) denote means in the same column within the treatment group (control versus treatment), and tissue types bearing the common letter do not differ significantly at $P \leq 0.05$. D and E, and X and Y (log reduction per square centimeter) denote means in the same column within the column, and tissue types across treatments bearing the common letter do not differ significantly at $P \leq 0.05$.

^d DBDMH, 1,3-dibromo-5,5-dimethylhydantoin.

coli O157:H7 and *Salmonella* were confirmed by PCR (10, 17). Colony counts were transformed to values expressed in log CFU per centimeter squared from two experimental replications.

One-way statistical analysis of variance was performed using the General Linear Model procedure of SAS (SAS Institute, Inc., Cary, NC). Least-squares means were calculated, and pairwise comparisons of means were determined using Tukey-Kramer test method, with the probability level at $P \leq 0.05$.

RESULTS AND DISCUSSION

Spray treatments with a carcass wash cabinet. In this study, DBDMH was compared with hot water for its efficacy in reduction of inoculated CT sections and beef hearts. To demonstrate the effectiveness of these treatments on the target bacteria, high levels of organisms were inoculated on both tissues. The efficacy of hot water and DBDMH on APC, EBC, and *E. coli* O157:H7 43888 counts is presented in Table 1. Both hot water and DBDMH reduced ($P < 0.05$) all target bacteria on inoculated surfaces of CT sections and beef hearts. Hot water reduced APC and EBC on the CT sections by 3.5 and 3.9 log CFU/cm², respectively. Hot water treatment produced a 1.8-log reduction of *E. coli* O157:H7 43888-inoculated CT sections. Bosilevac et al. reported that hot water caused 2.7-log reductions of both APC and EBC (2). Hot water treatment also caused approximately 2.0-log reductions on *E. coli* O157:H7-inoculated bovine heads (11). Treatment with DBDMH at 270 ppm resulted in the same APC reduction as did treatment with hot water. Slightly lower ($P < 0.05$) reductions in APC were obtained with 75 and 175 ppm

DBDMH than with 270 ppm DBDMH. All levels of DBDMH had slightly lower ($P < 0.05$) reductions in EBC compared with hot water. DBDMH treatments on CT produced significant reductions in *E. coli* O157:H7 43888, which ranged between a 1.6- and a 1.8-log reduction compared with controls, which did not differ ($P > 0.05$) from reductions due to hot water treatment.

Increasing the concentration of DBDMH from 75 to 270 ppm did not increase the inactivation effect on APC, EBC, or *E. coli* O157:H7 ATCC 43888. This may be due to organic materials that could react with hypobromous acid. Hypobromous acid is a strong oxidant and is highly reactive with heme groups, amines, and amino acids (4). The nitrogen-bromine bond is relatively unstable (27) and can react further with other biological molecules (4). The pH values of DBDMH solution at 75, 175, and 270 ppm were 6.84, 6.76 and 6.71, respectively. The pH values of the solution dropped slightly as the concentration of DBDMH increased. The hydrolysis of DBDMH to hypobromous acid in water was critically dependent on its pH value (22). Because hypobromous acid is a very weak acid, the hydrolysis of DBDMH results in the slightly decreased pH (22). This suggests that a similar amount of hypobromous acid probably was generated, even though a higher concentration of DBDMH was used.

Hot water significantly reduced APC and EBC on beef hearts by 4.1 log CFU/cm², and reduced *E. coli* O157:H7 43888 by 2.2 log CFU/cm² compared with controls (Table 1). DBDMH caused reductions on hearts ranging between

TABLE 2. Effectiveness of DBDMH on APC, EBC, *E. coli* O157:H7, and *Salmonella* compared with hot water treatment of inoculated beef tissues, using a model carcass washer

Tissue	Treatment ^a	Bacterial population, log CFU/cm ² (log reduction/cm ²)			
		APC	EBC	<i>E. coli</i> O157	<i>Salmonella</i>
Cutaneous trunci ^b	Control	8.4 A	7.6 A	6.3 A	6.6 A
	Hot water	5.4 B (3.0 D) ^c	4.3 B (3.3 D)	3.9 B (2.3 D)	4.1 B (2.5 D)
	Control	8.5 A	7.7 A	6.3 A	6.6 A
	DBDMH, ^d 75 ppm	6.3 B (2.2 E)	5.9 B (1.8 E)	5.2 B (1.1 E)	5.9 B (0.7 E)
	Control	8.4 A	7.5 A	6.2 A	6.8 A
	DBDMH, 175 ppm	6.2 B (2.2 E)	5.8 B (1.8 E)	5.0 B (1.2 E)	5.7 B (1.1 EF)
	Control	8.5 A	7.8 A	6.3 A	6.8 A
	DBDMH, 270 ppm	6.0 B (2.5 E)	5.7 B (2.1 E)	4.8 B (1.5 F)	5.5 B (1.3 F)
Heart	Control	7.9 G	6.7 G	5.6 G	5.8 G
	Hot water	4.1 H (3.8 X)	3.3 H (3.4 X)	3.2 H (2.4 X)	3.0 H (2.8 X)
	Control	7.8 G	6.6 G	5.6 G	5.8 G
	DBDMH, 75 ppm	4.6 H (3.2 Y)	4.2 H (2.4 Z)	3.9 H (1.7 Y)	3.8 H (2.0 Z)
	Control	7.7 G	6.7 G	5.6 G	5.8 G
	DBDMH, 175 ppm	4.5 H (3.2 Y)	4.1 H (2.6 YZ)	3.8 H (1.8 Y)	3.6 H (2.2 YZ)
	Control	7.7 G	6.8 G	5.6 G	5.9 G
	DBDMH, 270 ppm	4.6 H (3.0 Y)	4.1 H (2.7 Y)	3.7 H (1.9 Y)	3.6 H (2.3 Y)

^a Hot water (85°C) was sprayed at 20 lb/in² for 12 s for CT sections and 28 s for beef heart. All DBDMH treatments (25 ± 2°C) were sprayed at 35 lb/in² for 12 s for CT sections and 28 s for beef hearts.

^b Representing carcass surface tissue.

^c A and B, and G and H (log CFU per square centimeter) denote means in the same column within the treatment group (control versus treatment), and tissue types bearing the common letter do not differ significantly at $P \leq 0.05$. D, E, and F and X, Y, and Z (log reduction per square centimeter) denote means in the same column within the column, and tissue types across treatments bearing the common letter do not differ significantly at $P \leq 0.05$.

^d DBDMH, 1,3-dibromo-5,5-dimethylhydantoin.

3.2 and 3.6 log cycles for APC and EBC, respectively, and reductions between 1.7 and 2.1 log cycles for *E. coli* O157:H7 43888. The larger reductions for APC, EBC, and *E. coli* O157:H7 43888 by DBDMH on beef hearts can be attributed to a longer exposure time than was used for CT (28 versus 12 s). DBDMH at 175 and 270 ppm provided a similar ($P > 0.05$) reduction in APC on hearts as did hot water. Hot water treatment reduced EBC on hearts more ($P < 0.05$) than did any level of DBDMH. Hot water and 270 ppm DBDMH reduced *E. coli* O157:H7 43888 on hearts more than did 75 and 175 ppm DBDMH. The slight advantage of using hot water is probably due to killing bacteria by denaturing of enzymes and damaging functional and structural components (18). Organic and other acids need to enter the bacterial cells through the membrane before killing bacterial cells (19).

Spray treatments with a model carcass washer. In this study, a cocktail of pathogenic bacteria, *E. coli* O157:H7 and *Salmonella*, was inoculated onto surfaces of CT sections and beef hearts. Spray treatments with hot water or DBDMH significantly reduced all target organisms on inoculated CT sections and beef hearts compared with untreated controls (Table 2). Hot water treatment of CT sections reduced APC, EBC, *E. coli* O157:H7, and *Salmonella* by 3.0, 3.3, 2.3, and 2.5 log, respectively. Log reductions on CT sections treated with DBDMH ranged from 1.8 to 2.5 for APC and EBC, and from 0.7 to 1.5 for *Salmonella* and *E. coli* O157:H7, respectively. Compared with hot water treatment, DBDMH treatments, regardless of level, re-

sulted in smaller ($P < 0.05$) reductions in all target organisms on surfaces of CT sections. Concentration of DBDMH did not alter ($P > 0.05$) its effectiveness against APC or EBC on CT. However, treatment with 270 ppm DBDMH reduced *E. coli* O157:H7 and *Salmonella* on CT more than did treatment with 75 ppm.

For beef hearts, APC, EBC, *E. coli* O157:H7, and *Salmonella* treated with hot water or DBDMH were significantly lower than untreated controls were (Table 2). Hot water treatment resulted in the reduction of all target organisms slightly more ($P < 0.05$) than did any level of DBDMH. Level of DBDMH did not affect ($P > 0.05$) the reduction of APC or *E. coli* O157:H7 on hearts. However, 270 ppm DBDMH reduced EBC and *Salmonella* on hearts more than did 75 ppm DBDMH. In both studies, hot water reduced more target bacteria than DBDMH did.

Effect of treatments after storage at 4°C. The third 25-cm² section of each inoculation was held at 4°C for 48 h to examine the residual activity of the treatments (Table 3). The differences in populations of APC, EBC, and *E. coli* O157:H7 43888 inoculations after DBDMH treatments of CT sections and beef hearts, which was followed by 48 h storage at 4°C, showed no further reduction ($P > 0.05$) compared with hot water treatment. For the CT sections inoculated with a mixture of pathogenic bacteria, DBDMH treatments caused a slightly greater decrease ($P < 0.05$) in APC (all levels) and *Salmonella* (175 ppm) after storage for 48 h at 4°C than did hot water treatment. For hearts inoculated with pathogenic bacteria, DBDMH treatment

TABLE 3. Reduction of microbiological populations on inoculated beef tissue storage for 48 h at 4°C^a

Tissue	Treatment ^c	Nonpathogenic inoculation					Pathogenic inoculation				
		Difference in population (log CFU/cm ²) ^b									
		APC	EBC	<i>E. coli</i> O157:H7 43888	APC	EBC	<i>E. coli</i> O157:H7	<i>Salmonella</i>			
Cutaneous tissue ^d	Hot water	0.14 ± 0.76 A ^e	0.11 ± 0.75 A	0.03 ± 0.75 A	-0.57 ± 0.72 A	0.22 ± 0.61 A	0.16 ± 0.71 A	0.18 ± 0.69 A			
	DBDMH, 75 ppm	0.15 ± 0.44 A	0.20 ± 0.46 A	0.04 ± 0.54 A	0.18 ± 0.31 B	0.32 ± 0.51 A	0.24 ± 0.49 A	0.43 ± 0.41 AB			
	DBDMH, 175 ppm	0.18 ± 0.45 A	0.27 ± 0.54 A	0.10 ± 0.45 A	0.24 ± 0.38 B	0.28 ± 0.55 A	0.23 ± 0.47 A	0.53 ± 0.46 B			
	DBDMH, 270 ppm	0.19 ± 0.58 A	0.19 ± 0.69 A	-0.03 ± 0.44 A	0.25 ± 0.44 B	0.31 ± 0.63 A	0.03 ± 0.68 A	0.47 ± 0.49 AB			
Heart	Hot water	0.07 ± 1.24 A	0.21 ± 1.04 A	0.24 ± 0.78 A	-0.17 ± 0.52 A	0.39 ± 0.83 A	-0.29 ± 0.65 A	-0.09 ± 0.69 A			
	DBDMH, 75 ppm	0.42 ± 1.19 A	0.35 ± 0.98 A	0.37 ± 0.76 A	0.52 ± 0.65 B	0.72 ± 0.64 A	0.63 ± 0.58 B	0.56 ± 0.72 B			
	DBDMH, 175 ppm	0.40 ± 0.83 A	0.46 ± 0.78 A	0.54 ± 0.78 A	0.28 ± 0.48 B	0.56 ± 0.53 A	0.58 ± 0.70 B	0.49 ± 0.62 AB			
	DBDMH, 270 ppm	-0.06 ± 0.69 A	0.38 ± 0.72 A	0.28 ± 0.72 A	0.44 ± 0.32 B	0.57 ± 0.62 A	0.46 ± 0.66 B	0.29 ± 0.62 AB			

^a Greater values indicate larger reductions in bacterial populations.^b The difference in population was calculated by subtracting the viable population after 48 h storage from 0 h.^c Hot water (85°C) was sprayed at 20 lb/in² for 12 s for CT sections and 28 s for beef heart. All DBDMH treatments (25 ± 2°C) were sprayed at 35 lb/in² for 12 s for CT sections and 28 s for beef hearts.^d Representing carcass surface tissue.^e A and B denote means in the same column within the treatment group, and tissue types bearing the common letter do not differ significantly at $P \leq 0.05$.^f DBDMH, 1,3-dibromo-5,5-dimethylhydantoin.

caused a slightly greater decrease ($P < 0.05$) in APC and *E. coli* O157:H7 (all levels) and *Salmonella* (75 ppm only) after 48 h storage at 4°C than did hot water. This is probably due to injured bacterial cells that could not be enumerated on selective media. Hypobromous acid has been shown to react with double bonds of unsaturated fatty acids of bacterial membranes, forming bromohydrins, which contribute to disruption of cell membranes (4). Thirty-six percent of hot water-treated and 43% of DBDMH-treated samples could not be enumerated for the pathogens (data not shown). These samples were enriched, immunomagnetic separated, and confirmed by PCR. Both pathogens were recovered from all of these samples. This indicated that hot water and DBDMH treatments reduced the number of uninjured or viable cells to a level below the limit of detection of our enumeration assay.

Although hot water treatment has been found to be effective for carcass decontamination, the disadvantage of this treatment is the high-water-volume use and high cost of maintaining such a high temperature. DBDMH requires no additional energy resources for treatment, and wastewater from the wash cabinet can be recirculated. This study demonstrated that spray treatments with the bromine compound DBDMH at 25°C could improve the microbiological safety of beef carcasses and variety meats by killing and inflicting injury to pathogenic bacteria.

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