FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

08/03
19 March 2003

FINAL ASSESSMENT REPORT

APPLICATION A438

GAMMA CYCLODEXTRIN AS A NOVEL FOOD INGREDIENT / FOOD ADDITIVE

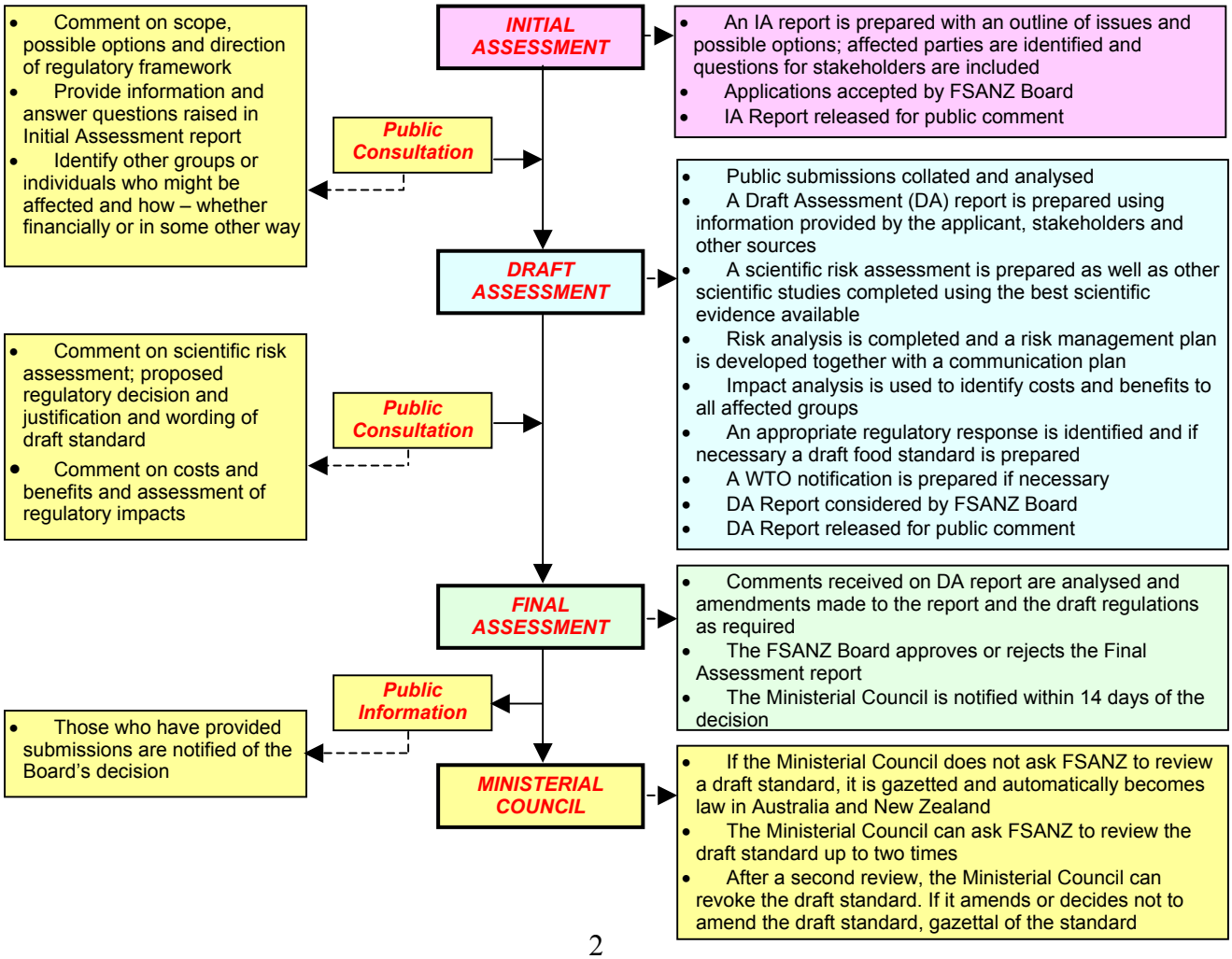
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

FSANZ's role is to protect the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply. FSANZ is a partnership between ten governments: the Commonwealth; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

FSANZ is responsible for developing, varying and reviewing standards and for developing codes of conduct with industry for food available in Australia and New Zealand covering labelling, composition and contaminants. In Australia FSANZ also develops food standards for microbiological safety, primary production and processing and a range of other functions including the coordination of national food surveillance and recall systems, conducting research and assessing policies about imported food.

The FSANZ Board approves new standards or variations to food standards in accordance with policy guidelines set by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) made up of Commonwealth, State and Territory and New Zealand Health Ministers as lead Ministers, with representation from other portfolios. Approved standards are then notified to the Ministerial Council. The Ministerial Council may then request that FSANZ review a proposed or existing standard. If the Ministerial Council does not request that FSANZ review the draft standard, or amends a draft standard, the standard is adopted by reference under the food laws of the Commonwealth, States, Territories and New Zealand. The Ministerial Council can, independently of a notification from FSANZ, request that FSANZ review a standard.

The process for amending the *Australia New Zealand Food Standards Code* is prescribed in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). The diagram below represents the different stages in the process including when periods of public consultation occur. This process varies for matters that are urgent or minor in significance or complexity.



Final Assessment Stage

The Authority has now completed two stages of the assessment process and held two rounds of public consultation as part of its assessment of this Application. This Final Assessment Report and its recommendations have been approved by the FSANZ Board and are now being reviewed by the Australia and New Zealand Food Regulation Ministerial Council (ANZFRMC).

If accepted by ANZFRMC, a change to the *Australia New Zealand Food Standards Code* is published in the *Commonwealth Gazette* and the *New Zealand Gazette* and adopted by reference and without amendment under Australian State and Territory food law.

In New Zealand, the New Zealand Minister of Health gazettes the food standard under the New Zealand Food Act. Following gazettal, the standard takes effect 28 days later.

Submissions

No submissions on this matter are sought as the Authority has completed its assessment and the matter is now with the Australia and New Zealand Food Regulation Ministerial Council for consideration.

Further Information

Further information on this application and the assessment process should be addressed to the Standards Liaison Officer at Food Standards Australia New Zealand at one of the following addresses:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2222
slo@foodstandards.gov.au

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
info@foodstandards.govt.nz

Assessment reports are available for viewing and downloading from the FSANZ website www.foodstandards.gov.au . Alternatively paper copies of reports can be requested from the Authority's Information Officer at either of the above addresses or by emailing info@foodstandards.gov.au including other general enquiries and requests for information.

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EXECUTIVE SUMMARY

The Australia New Zealand Food Authority (ANZFA - now Food Standards Australia New Zealand (FSANZ)) received an application from Wacker Chemie GmbH on 12 April 2001 seeking to amend Standard 1.5.1 of the *Australia New Zealand Food Standards Code* to permit the use of gamma cyclodextrin (γ-cyclodextrin) as a novel food ingredient.

Work on this application was commenced on 25 March 2002, as per the FSANZ Work plan.

Under the current food standards, novel foods are required to undergo a pre-market safety assessment, Standard 1.5.1 - Novel Foods. While γ-cyclodextrin has properties consistent with its use as either a food ingredient or a food additive under the provisions of the *Australia New Zealand Food Standards Code*, it is more appropriate to regulate γ-cyclodextrin as a food ingredient, albeit a novel food ingredient.

γ-Cyclodextrin is considered a novel food ingredient because it is a non-traditional food for which there is insufficient knowledge in the broad community to ensure safe use when incorporated into the Australian or New Zealand diet.

The objective of this assessment is to determine whether it is appropriate to amend the food regulations to permit the use of γ-cyclodextrin as a novel food ingredient. Such an amendment would need to be consistent with the section 10 objectives of the FSANZ Act.

A range of issues was considered during the assessment of the application; namely, the safety and nutritional impact of the use of γ-cyclodextrin. Other issues such as technological function and the level of dietary exposure were also addressed. γ-Cyclodextrin serves a variety of functions in food applications including stabilisations of emulsions, elimination of undesirable molecules, solubilisation of ingredients and protection from oxidation. It also serves as a carrier of nutrients and vitamins.

The available safety studies on γ-cyclodextrin indicate that there are no public health and safety concerns at the anticipated levels of dietary exposure. The estimated levels of dietary exposure are 3.6 g/day for Australia and 4.1 g/day (0.06 g/kg bw/day) for New Zealand. γ-Cyclodextrin consumption is not expected to affect the bioavailability of essential nutrients such as fat-soluble vitamins because of its rapid metabolism.

The only regulatory options identified were to approve or not approve the use of γ-cyclodextrin as a novel food ingredient. The impact analysis shows that the approval of γ-cyclodextrin satisfies the objectives of the assessment based on the outcome of the scientific risk assessment and the Regulatory Impact Statement (RIS). These issues included an assurance of the safety of γ-cyclodextrin, the provision of benefits to industry and Governments, in terms of enhanced market opportunities and trade (under Australia and New Zealand's requirements under the World Trade Organization), respectively, and in addition, the benefits to consumers in regard to possible greater choice of foods.

Two rounds of public consultations have been carried out. During the first round, six submissions were received in response to the public consultation. Two submitters supported the proposal to amend the *Australia New Zealand Food Standards Code* to permit γ-cyclodextrin.

One argued that γ-cyclodextrin is a traditional food and therefore should not be regulated, while another supported its permission to be used as a food additive but not as a novel food. Two were undecided. During the second round, two submissions were received, one for and one against the amendment to the *Australia New Zealand Food Standards Code*.

Statement of Reasons

FSANZ recommends the approval of the use of γ-cyclodextrin as a novel food ingredient in the listed food items for the following reasons:

- there is no evidence of any public health and safety concern associated with consumption of foods containing γ-cyclodextrin and there are no significant nutritional concerns at proposed levels of use;

- the proposed change to the *Australia New Zealand Food Standards Code* is consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of γ-cyclodextrin as a novel food ingredient, the benefits of the proposed amendment outweigh the costs.

The proposed drafting for amendments to Standard 1.5.1 is at **Attachment 1** of the Draft Assessment Report.

The Australia New Zealand Food Authority (ANZFA) to FSANZ transitional requirements for an application/proposal at preliminary (initial) stage provide that FSANZ is taken to have made an initial assessment of the Application. Any submissions received by FSANZ about an Application in response to a notice given under section 13A or 14 of the FSANZ Act, are taken to be submissions made to FSANZ about the application/proposal in response to a notice under section 13A or 14 under the FSANZ Act.

1. INTRODUCTION

An application has been received from Wacker Chemie GmbH on 12 April 2001 seeking to amend Standard 1.5.1 of the *Australia New Zealand Food Standards Code* to permit the use of gamma cyclodextrin (γ-cyclodextrin) as a novel food ingredient. After consultations with FSANZ regarding its use in food, the applicant agreed to amend the application title to include 'or food additive'; since at the time of application, it was considered that some of its uses might be in relation to technological functions of a food additive. This application is at the final assessment stage as detailed in the section 17 of the FSANZ Act.

1.1 Transitional Requirements

This Application reached Full (Draft) Assessment stage under the operation of the *Australia New Zealand Food Authority Act 1991*, and will be finalised in accordance with the provisions of the FSANZ Act.

FSANZ has therefore been required to:

1. give the Applicant the opportunity to (by 29 July 2002) request deferral of consideration of the application in order to provide any additional information;

2. give notice under section 14 of the FSANZ Act; and

3. review the Full (Draft) Assessment having regard to any new submissions received in response to the above notice as well as any written policy guidelines that have been notified by the Ministerial Council.

2. REGULATORY PROBLEM

Under the current food standards, both novel foods and food additives are required to undergo a pre-market safety assessment, as per Standard 1.5.1 – Novel Foods and Standard 1.3.1 – Food Additives. While food additives have always required a pre-market safety assessment, the pre-market assessment of novel foods commenced in 2001. The purpose of Standard 1.5.1 is to ensure that non-traditional foods that have features or characteristics, which raise safety concerns, will undergo a risk-based safety assessment before they are offered for retail for consumption in Australia or New Zealand.

Novel Food is defined in the Standard as:

> A non-traditional food for which there is insufficient knowledge in the broad community to enable safe use in the form or context in which it is presented, taking into account;
>
> (a) the composition or structure of the product; or
> (b) levels of undesirable substances in the product; or
> (c) known potential for adverse effects in humans; or
> (d) traditional preparation and cooking methods; or
> (e) patterns and levels of consumption of the product.

Non-traditional food means a food, which does not have a history of significant human consumption by the broad community in Australia or New Zealand.

2.1 Is γ-cyclodextrin a novel food or a food additive?

γ-Cyclodextrin has properties consistent with its classification in certain circumstances as either a food ingredient or as a food additive. When used in table spreads at levels up to 20%, it is more akin to being a food ingredient than a food additive. When used in this way, it is also comparable to other food ingredients, such as starch and maltodextrin, and is nutritionally equivalent to these carbohydrates. However, for certain uses, it appears to be acting as a food additive because its use is based on its functionality as a carrier of flavours, colours and sweeteners. The evaluation of γ-cyclodextrin carried out by the Joint FAO/WHO Expert Committee on Food Additives[1] (JECFA) was based on its use as a food additive. FSANZ initially considered assessing γ-cyclodextrin as both a food ingredient when used as carrier of vitamins and polyunsaturated fatty acids (PUFAs) because of high levels (up to 20%) of γ-cyclodextrin in these food items, and also as an additive when used for its functionality at low levels (< 5%). However, under Standard 1.3.1 – Food Additives, a carrier (complexant) is not one of the technological functions of a food additive. FSANZ therefore, has assessed γ-cyclodextrin as a food ingredient. Certain types of foods and food ingredients are used as food additives in some cases; examples are egg yolk (emulsifier) and starch (thickener).

γ–Cyclodextrin levels of use are more consistent with that of a food ingredient rather than an additive. Starch, maltodextrins and starch hydrolysates are considered as food ingredients in Australia and New Zealand.

2.2 γ-Cyclodextrin as a novel food ingredient

γ-Cyclodextrin is considered a non-traditional food ingredient because it does not have a history of significant human consumption in Australia or New Zealand. γ-Cyclodextrin is a new chemical that has not been used previously in food. Because of that, there is no knowledge in the broad community about the use of γ-cyclodextrin, since its safety has not yet been determined within the context of the Australian and New Zealand diet. In these circumstances, γ-cyclodextrin is considered to be a novel food ingredient and should be considered under Standard 1.5.1.

3. OBJECTIVE

The objective of this assessment is to determine whether it is appropriate to amend the *Australia New Zealand Food Standards Code* and permit the use of γ-cyclodextrin. Such an amendment to the Code will need to be consistent with the section 10 objectives of FSANZ Act.

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives, which are set out in section 10 of the FSANZ Act. These are:

[1] FAO/WHO (1999) Report of fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives, Evaluation of Certain Food Additives, γ-cyclodextrin, p43.

- the protection of public health and safety;
- 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 standards, 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.

4. BACKGROUND

4.1 Properties of γ-cyclodextrin

γ-Cyclodextrin is a cyclic polymer consisting of eight glucose units linked by γ-1,4 bonds. It is produced enzymatically from liquefied starch. Due to the steric arrangement of the glucose units, the torus-shaped molecule has a hydrophobic inner surface cavity, and a hydrophilic outer surface, which allows it to form inclusion complexes with various organic compounds. This property forms the basis of numerous applications of γ-cyclodextrin in foods.

The applicant claims that γ-cyclodextrin can form complexes with natural colours, flavours and vitamins allowing its use as a carrier and stabilizer for these additives. With PUFAs, it is also claimed that it can be used to protect them from oxidation. In baked foods it is claimed to act as a dough conditioner and as a stabilizer in oil/water emulsions in desserts. It is also claimed to act as a flavour modifier by suppressing undesirable characteristics.

4.2 Proposed uses

The substance is proposed to be used in the following foods for different applications:

1. Complexant for flavours, colours and sweeteners

- dry mixes for soups and beverages;
- dry mixes for dressings, gravies, and sauces;
- dry mixes for puddings, desserts, jellies and fillings
- instant coffees and teas;
- beverage whiteners;
- sugar confectionery, chewing gum, savoury snacks and biscuits;
- breakfast foods; and
- spices and seasonings

2. Complexant for vitamins- appropriate food uses

3. Complexant for PUFAs - appropriate food uses

4. Flavour modifier

- Soy milk products

5. Stabiliser

- table spreads (reduced fat);
- frozen dairy desserts;
- dairy desserts;
- baked foods;
- breads;
- fruit based fillings;
- fat based fillings; and
- processed cheese

4.3 Approval in other countries

γ-Cyclodextrin is available in the USA as a Generally Recognised As Safe (GRAS) dietary ingredient (GRAS Notice No. GRN 000046). γ-Cyclodextrin is being considered for approval under EU Novel Food regulations. It is considered to be a food in Japan and hence explicit approval is not required.

There are no Codex standards in relation to γ-cyclodextrin.

5. REGULATORY OPTIONS

FSANZ is required to consider the impact of various regulatory (and non-regulatory) options on all sectors of the community, which includes consumers, and the food industry and governments in both Australia and New Zealand. The benefits and costs associated with the proposed amendment to the *Australia New Zealand Food Standards Code* have been analysed in a Regulatory Impact Assessment.

Parties affected by the options listed below include:

- State, Territory and New Zealand Health Departments;

- manufacturers and producers of food products that use γ-cyclodextrin as a novel food ingredient; and

- consumers.

The regulatory options currently under consideration are:

Option 1. Not permit the use of γ-cyclodextrin as a novel food ingredient.

Option 2. Permit the use of γ-cyclodextrin as a novel food ingredient.

6. IMPACT ANALYSIS

The objective of regulatory impact analysis is to examine the impact of the permission to use γ-cyclodextrin, as a food ingredient/food additive in Standard 1.5.1. As the use of γ-cyclodextrin requires pre–market approval it is not appropriate to consider non–regulatory options to address this application. Novel food ingredients used in Australia and New Zealand are required to be listed in Standard 1.5.1- Novel Foods.

Option 1, which supports maintaining the *status quo* and not giving specific permission in the Code for the use of γ-cyclodextrin, provides no perceived benefits to the stakeholders, government, consumers and industry.

The parties who are disadvantaged by not permitting the use of γ-cyclodextrin are the applicant and the food industry.

Option 2, which supports the use of γ-cyclodextrin is the preferred option, as approval is of benefit to both producers and consumers. Approval of γ-cyclodextrin would promote international trade, while continuing to protect public health and safety.

7. CONSULTATION

7.1 Public Consultation

Two rounds of public consultations have been carried out. During the first round, six submissions were received in response to the public consultation. Two submitters supported the proposal to amend the Code to permit γ-cyclodextrin. One argued that γ-cyclodextrin is a traditional food and therefore should not be regulated, while another supported its permission to be used as a food additive but not as a novel food. Two were undecided on whether permission should be given or not because of insufficient information in the Initial Assessment Report. During the second round, two submissions were received, one for and one against the amendment to the Code. The names of submitters and issues raised in their submissions are provided in **Attachment 6**.

7.2 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 Government of Australia and the Government of New Zealand Concerning a Joint Food Standards System, FSANZ is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

As a member 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.

Amending the Code to allow foods to contain γ–cyclodextrin was not notified to the WTO under either the Technical Barrier to Trade (TBT) or Sanitary and Phytosanitary Measure (SPS) agreements as the permission is unlikely to significantly effect trade. The potential uses for γ–cyclodextrin as a carrier in food products is limited. Typically only very small amounts (<1%) will be used in the majority of food items and the market size and the range of potential suitable processed food products is limited. Suppliers of food products are not required to take up permissions granted through amendments to the *Code.*

8. ISSUES ADDRESSED DURING ASSESSMENT

8.1 Safety issues

In its safety assessment, FSANZ has made use of the recent evaluation conducted by Joint FAO/WHO Expert Committee on Food Additives (JECFA)[1,2] as well as reviewing more recent studies. Based on JECFA's safety assessment of γ-cyclodextrin for certain specified uses, γ- cyclodextrin was considered to be a substance of low toxicity which did not represent a hazard to human health. All of the studies considered by JECFA together with a carcinogenicity study in rats have been submitted to FSANZ. JECFA allocated Acceptable Daily Intake (ADI) of 'not specified' for γ-cyclodextrin.

FSANZ's toxicology report (**Attachment 2**) contains a summary of JECFA's evaluation as well as an assessment of the additional study on carcinogenicity study in rats. Based on the available toxicological data, FSANZ agrees with the JECFA allocation of an ADI 'not specified' and concluded that γ-cyclodextrin is safe for human consumption at the proposed levels.

8.2 Technological justification

The Food Technology Report (**Attachment 3**) concludes that γ–cyclodextrin is a starch product that as a food ingredient can provide specialised functions in place of some of the starches or maltodextrins in a food. Classifying γ–cyclodextrin as a food would neither restrict its use to perform a technological function in a food as a food additive nor its use as a processing aid since foods are generally permitted processing aids.

Under Standard 1.3.1 – Food Additives, a carrier (complexant) is not one of the technological functions of a food additive. At its 33rd Session in 2001, the Codex Committee on Food Additives and Contaminants (CCFAC) decided that carriers should be included in the General Standard for Food Additives (GSFA). The following definition of carrier which has been suggested in the discussion paper submitted by New Zealand is under consideration at CCFAC 34:

[1] FAO/WHO (1999) Report of fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives, Evaluation of Certain Food Additives, γ-cyclodextrin, p43.
[2] FAO/WHO (2000) Report of fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives, Specific Food Additives and Substances used in Food Fortification, γ-cyclodextrin, p26.

A carrier is a substance that is intended to serve as a vehicle for the introduction of, or to facilitate the delivery of another food additive, (or to stabilize another food additive), or to otherwise enhance the other food additive's intended functional effect in the final food

Thus it will be appropriate for FSANZ to consider amending the Standard 1.3.1 after a decision has been taken at the international level.

8.3 Dietary considerations

Based on the US Food consumption data (1989-1991), JECFA[1] has estimated that the mean estimated intake for γ- cyclodextrin from its use in food was approximately 4 grams per day. The estimated daily intake for the 90th percentile group was about 7.5 grams per day. These estimates are based on the use of γ-cyclodextrin in all foods and at the highest levels. Dietary intake would be much lower if estimated more accurately.

During the Draft Assessment dietary modelling was conducted by FSANZ to estimate the potential dietary intake of γ-cyclodextrin in Australia and New Zealand that may result from permitting its use in the foods specified in the application.

Dietary modelling by FSANZ shows that average daily intake of γ-cyclodextrin for the whole population, taking into account all the food items containing the substance, is 3.6 g/day (0.07 g/kg bw/day) for Australia and 4.1 g/day (0.06 g/kg bw/day) for New Zealand. For the 95th percentile average daily intake is 9.5g/ day for Australia and 10.8g/ day for New Zealand. The average daily intake is comparable to that reported for the US consumers (4.0 g/day) in the JECFA report. The full dietary modelling report is attached (**Attachment 4**).

Although γ-cyclodextrin levels in reduced fat table spreads could be up to 20%, estimates based on the use of γ-cyclodextrin in all foods and at the highest levels of predicted use indicate that, contribution from this source to the total daily intake of γ-cyclodextrin is only about 6% and 16% for the Australian and New Zealand populations respectively.

8.4 Nutritional considerations

γ-Cyclodextrin is hydrolysed by salivary and pancreatic amylases to glucose which is readily absorbed. Because starch and maltose are also converted to glucose after ingestion, γ-cyclodextrin can be considered to be nutritionally equivalent to these carbohydrates. From the Dietary Exposure Assessment Report (**Attachment 4**) the predicted mean exposure to γ-cyclodextrin for the total population in Australia and New Zealand is approximately 4 g/day (0.06 – 0.07 g/kg bw/day). The 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS reported mean daily intakes of total carbohydrate of 255 g/day (19 years and over) and 267 g/day (15 years and over) respectively. It can therefore be assumed that the quantity of γ-cyclodextrin expected to be consumed would not be significant compared to the expected overall daily carbohydrate intake.

Although children aged 2-6 years (Australia only) are estimated to have higher exposure than the total population on a g/kg bw/day basis (0.18 vs. 0.07), the mean dietary exposure for both groups are similar (3.3 g/day vs. 3.6g/day).

Further, these are likely to be overestimates as the dietary modelling assumes individual consumption of all food items containing γ-cyclodextrin at the proposed levels.

The impact of γ- cyclodextrin consumption on the bioavailability of certain essential nutrients such as fat-soluble vitamins was considered. The 51st JECFA Report (2000) states that *it is unlikely that interaction with lipophilic vitamins would impair their bioavailability because of the rapid metabolism of γ-cyclodextrin in vivo*. In addition the JECFA Report indicated that there is no evidence of vitamin deficiency in animals given high doses of γ-cyclodextrin.

It is therefore concluded that the proposed use of γ- cyclodextrin as a novel food ingredient will have minimal impact on nutrition when considered in the context of the overall diet.

8.5 Issues Raised In Public Submissions

8.5.1 Round One

Comment: Australian Food and Grocery Council argues that γ-cyclodextrin cannot be classified as a food additive because it is a polysaccharide and hence should be regarded as food (e.g.: egg yolk and starch).

Response: As discussed in section 2.1, γ-cyclodextrin is regarded as a food, albeit a novel food.

Comment: Brooke-Taylor & Co contends that γ-cyclodextrin cannot be classed as a novel food because its safety is well established based on JECFA report, GRAS Status in USA and is considered a food in Japan.

Response: γ-Cyclodextrin has not undergone a safety assessment in the context of the Australian and New Zealand diets. There is therefore insufficient knowledge in the broad community to ensure safe use in the form in which it is presented. Safety assessments from international bodies or other countries, while of assistance in the assessment process, cannot be used to replace an assessment of the safety of γ-cyclodextrin within the Australian and New Zealand context.

Comment: *Dietitians Association of Australia* is concerned that γ-cyclodextrin is a carbohydrate ingredient that potentially has a high glycaemic index and could contribute to an increased glycaemic load.

Response: Based on the dietary modelling, the level of consumption of γ-cyclodextrin from the proposed foodstuff (up to 4.1g/day) is not expected to significantly alter the glycaemic load of the diet based on the reported carbohydrate intake in Australia and New Zealand (average daily intake of approx. 250g/day).

8.5.2 *Round Two*

Comment: Australian Food and Grocery Council contends that γ-cyclodextrin cannot be classed as a novel food because 'there is sufficient knowledge to enable safe use' based on the Draft Assessment carried out by FSANZ which stated that γ-cyclodextrin is safe and raises no significant nutritional concerns.

Response: The object of the Novel Food Standard is to assess the safety of non-traditional food for which there is 'there is insufficient knowledge to enable safe use' in the broader community. Prior to the Application, γ-cyclodextrin had not undergone a safety assessment in the context of the Australian and New Zealand diets. There was therefore insufficient knowledge in the broad community to ensure safe use in the form in which it is presented. The safety of γ-cyclodextrin in the context of Australia and New Zealand, has been assessed by FSANZ as a consequence of γ-cyclodextrin being classified as a novel food. The safety assessment showed subsequently that γ-cyclodextrin is safe for human consumption, but without the due process required for novel food assessment, it would not have been possible for FSANZ to determine its safety.

Comment: Australian Food and Grocery Council argues that the proposed drafting should be revised to insert the provisions for the labelling of γ-cyclodextrin into the table to clause 4 of Standard 1.2.4.

Response: Table to Clause 4 in Standard 1.2.4 –Labelling of Ingredients, lists ingredients that use common, descriptive or generic names. FSANZ therefore considers it inappropriate to list a new chemical, γ-cyclodextrin, in this table.

Comment: *Australian Food and Grocery Council* suggests that FSANZ should consider allowing γ-cyclodextrin to be declared in the ingredient list as either 'γ-cyclodextrin' or 'cyclodextrin'.

Response: Because there are other forms of cyclodextrin that have not yet been assessed for safety by FSANZ, listing the full name of the chemical will ensure that the approved cyclodextrin has been used in the product.

9. CONCLUSION AND RECOMMENDATION

The conclusions from the Draft Assessment are as follows:

1. There is no evidence of any public health and safety concern associated with consumption of γ-cyclodextrin and there are no significant nutritional concerns at proposed levels of use;

2. The proposed change to the *Australia New Zealand Food Standards Code* is consistent with the section 10 objectives of the *Australia New Zealand Food Authority Act 1991*.

3. The Regulatory Impact Statement indicates that for the preferred option, namely, to approve the use of γ-cyclodextrin as a novel food ingredient in listed food items, the benefits of the proposed amendment outweigh the costs.

It is recommended that the application for the use of γ-cyclodextrin as a novel food ingredient be approved. The recommendations are based on the analysis of relevant scientific evidence that demonstrates that consumption of γ-cyclodextrin is safe and raises no significant nutrient concerns.

ATTACHMENTS

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Safety Assessment report
3. Food technology report
4. Dietary modelling report
5. Summary of public submissions

ATTACHMENT 1

DRAFT VARIATIONS TO THE *AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE*

To commence: On gazettal

[1] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in the Table to clause 2 -*

γ-cyclodextrin	The name 'gamma cyclodextrin' or 'γ-cyclodextrin' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4.

ATTACHMENT 2

FINAL SAFETY ASSESSMENT REPORT

GAMMA CYCLODEXTRIN AS A NOVEL FOOD INGREDIENT

BACKGROUND

γ- Cyclodextrin is a ring-shaped molecule made up of made up of eight glucose units linked by α-1,4-bonds. The circular structure of γ- cyclodextrin provides a hydrophobic cavity that allows incorporation and solubilisation of a variety of organic molecules, while the hydrophilic outer surface makes it water-soluble. γ- Cyclodextrin is proposed to be used as a carrier for flavours, sweeteners and colours. It is also proposed for use as a carrier for vitamins and polyunsaturated fatty acids and as a flavour modifier.

TOXICOLOGICAL ASSESSMENT

γ- Cyclodextrin was previously evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA)[1,2] and concluded that there were sufficient data to allocate an ADI 'not specified'. This conclusion was based on review of toxicological studies summarised below.

Summary of JECFA evaluation of γ-cyclodextrin

In metabolism studies carried out in rats, γ- cyclodextrin (at single oral doses of up to 1000 mg/kg of body weight) was metabolised to glucose, other low-molecular weight sugar metabolites and carbon dioxide by luminol and/or epithelial enzymes of the gastrointestinal tract. There was little involvement of the gut micro-flora. Only a fraction of the oral dose of γ- cyclodextrin was absorbed. This was mainly excreted in expired air while only very low levels could be detected in the urine. After intravenous injection, γ- cyclodextrin (at single doses of up to 600 mg/kg body weight) was rapidly cleared from the blood and the major route of excretion was the urine. γ- Cyclodextrin, unlike β- cyclodextrin, can be readily hydrolysed by human salivary and pancreatic amylases *in vitro*.

Acute toxicity studies of γ- cyclodextrin in mice and rats produced no deaths at the highest doses tested (oral dose up to 16000 mg/kg bw in mice and 8000 mg/kg bw in rats).

Short-term (28- and 90-day) toxicity studies indicated that γ- cyclodextrin had little toxicity when given intravenously or orally to rats or orally to dogs. After administration of a very high concentration (200g/kg or 20%) in the diet, caecal enlargement and associated changes were seen in both species. The effect is likely to result from the presence of a high concentration of an osmotically active substance in the large intestine. The result suggested that the metabolism of γ- cyclodextrin is less efficient at doses higher than those used in the studies of metabolism.. There were no gross pathological changes attributable to treatment with γ- cyclodextrin in either species.

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[1] FAO/WHO (1999) Report of fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives, Evaluation of Certain Food Additives, γ-cyclodextrin, p43.

[2] FAO/WHO (2000) Report of fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives, Specific Food Additives and Substances used in Food Fortification, γ-cyclodextrin, p26.

Microscopic examination in rats revealed increased mineralisation in the kidneys at low doses, which is believed to be common in rats, and not related to treatment with γ-cyclodextrin. The results of the studies in rats treated intravenously indicated that γ-cyclodextrin is well tolerated when given systemically.

In the 12-month rat study, four group of 20 male and 20 female Wistar rats were given γ-cyclodextrin at concentrations of up to 200g/kg of feed. No clinical signs of toxicity were seen during the study in any group. Slightly lowered body weight of females at the highest dose was not statistically significant. Some clinical parameters showed statistically significant treatment-related changes, but they were not progressive and occurred only in some animals. Small increase in the absolute and relative weights of caecum seen in males at the highest dose is probably a result of the presence of a large amount of an osmotically active substance in the large intestine. None of these changes were considered to be of any toxicological significance.

Studies conducted in rats and rabbits with γ- cyclodextrin at doses of up to 200g/kg (20%) in the diet did not indicate any teratogenic effects. Examination of the foetuses revealed no treatment-related increase in gross, skeletal, or visceral abnormalities in either species. An increase in the incidence of haemorrhagic fluid in rabbits was observed in the 5% and 20% γ-cyclodextrin groups and in the 20% lactose group, used as a control group. This was not considered to be treatment-related and is believed to be due to the method of preservation of the foetuses. Similarly, the results of a battery of genotoxicity studies were negative.

Ocular irritation and dermal sensitisation studies showed no adverse effects in animals when treated with γ- cyclodextrin. In *in vitro* studies, γ- cyclodextrin sequestered components of the membranes of erythrocytes, causing haemolysis. Furthermore, γ- cyclodextrin was not detected in blood after dietary administration of high doses to animals.

It was considered unlikely that interaction of γ- cyclodextrin with lipophilic vitamins would impair their bioavailability because of the rapid metabolism of γ- cyclodextrin *in vivo*. Also, there was no evidence that vitamin deficiency was induced in experimental animals given high doses of γ- cyclodextrin.

In a human tolerance study γ- cyclodextrin did not cause symptoms of gastrointestinal discomfort when ingested at levels of up to 8g per serving (equal to 0.11g/kg of body weight in males and 0.13g/kg body weight in females).

JECFA also considered studies on short-term toxicity and genotoxicity of the enzyme, cyclomaltodextrin glucanotransferase, used in the production of cyclodextrins, and of the complexant, γ- cyclohexadecen-1-one, used to optimise formation of γ- cyclodextrin. The toxicological data indicated that these substances are unlikely to be of toxicological concern in the final preparation of γ- cyclodextrin. JECFA also reviewed information on the genetic modification of the organism used to produce the enzyme, which did not raise any concerns.

On the basis of these results JECFA allocated an ADI 'not specified'[3] to γ- cyclodextrin.

[3] Defined by JECFA as follows: On the basis of available data (chemical, biochemical, toxicological and other), the total daily intake of the substance, arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not , in the opinion of the Committee, represent a hazard to health.

Toxicological evaluation of additional data

Carcinogenicity (2-year) study with γ-cyclodextrin in rats.
Report Number V 90.920 by Lina BAR Wijnands MVW. TNO Nutrition and Food research, The Netherlands, *January 1999.*

Test material:	γ- cyclodextrin
Control material	pregelatinised potato starch
Test Species:	Young (5-6 weeks old) Wistar albino rats (Crl:WI(WU)BR), 50 / sex / group dosed by administration in diet.
Dose:	0, 2.5, 5 or 10% w/w in diet for 24 months.
Guidelines:	USFDA 1982-Toxicological Guidelines, OECD Guideline for Testing of Chemicals 451, May 1981 and EC Guideline 88/302/EC.

Test article and control material

γ -Cyclodextrin was obtained as a crystalline white powder with > 98% purity. The control substance was a pregelatinised potato starch as a coarse white powder.

Study conduct

Four groups of rats (50/sex/group) were treated with γ-cyclodextrin in the diet at 0, 2.5, 5 or 10% (equivalent to 0, 0.9, 1.9 or 3.7 g/kg bw/day for males and 0, 1.1, 2.2 and 4.5 g/kg bw/day for females). The test substance was incorporated in the feed at the expense of 20% barley. The control, low-dose and mid-dose diets were compensated by adding respectively 20%, 17.5%, 15% and 10% pregelatinised potato starch.

Clinical observations were recorded daily and bodyweight were measured weekly for the first 13 weeks and subsequently once every month. From 6 months after the start of the study until the end of the study, the animals were palpated weekly to detect palpable masses. Food consumption was assessed on a cage basis, by weighing the feeders, over each 1-week period during the first 13 weeks and subsequently over 1-week periods every month. Blood samples for haematology were taken from the tip of the tail of all rats after 12, 18 and 24 months. At the end of the study, all animals were sacrificed and a complete necropsy performed (gross examination, organ weights and tissue sampling). Histopathology was performed on nearly all tissues and organs and on any lesions observed macroscopically.

Results

The highest average intake of the test substance was 3.7g/kg bw/day in males and 4.5 g/kg bw/day in females of the highest dose group. There were no dose related differences in appearance, general condition or behaviour among the groups. Although clinical signs such as sparsely haired skin and blepharitis (chronic inflammation of the eyelids) with discharge were observed, the frequency of occurrence was similar in test groups and controls, and hence did not represent any adverse effect of the test substance. The incidence of grossly visible or palpable masses was seen in both test groups and controls at a similar frequency and hence was not considered dose-related. Mortality rate was not affected by the test substance.

Mean body weights decreased slightly in males of all treatment. The decrease was statistically significant but there was no dose-response relationship. There were no noticeable differences in overall food intake.

Haematology showed no statistically significant changes in blood cell variables or thrombocyte counts Similarly no significant changes were observed in white blood cell counts in surviving rats.

The relative and absolute weights of the filled caecum showed statistically significant increase in high dose group. There were no significant changes in empty caecal weights. The relative weights of kidneys were increased in females of the low and high dose groups but there was no dose-response relationship.

The most frequent cause of death was fatal tumour, adenoma of the pituitary. Gross examination at autopsy did not reveal any treatment-related abnormalities. Microscopic examination at autopsy did not reveal any treatment-related histopathological changes. The observed changes are common in rats of this strain and age and were distributed evenly among the groups including controls.

Conclusions

Based on this 2-year study in which the rats were administered with γ-cyclodextrin in the diet for up to 10%, there was no evidence that the test substance is carcinogenic to these animals. Apart from slight changes in body weight and filled caecal weight in males, all other clinical and haematological parameters remained normal. Macroscopic and microscopic examinations did not reveal any treatment-related gross or histopathological changes. It is concluded that long-term exposure to γ-cyclodextrin does not lead to cancer risk in humans.

Overall Conclusions

There is no evidence of any public health and safety concern associated with consumption of γ-cyclodextrin. The ADI ‘not specified’ established by JECFA, is confirmed.

ATTACHMENT 3

FOOD TECHNOLOGY REPORT

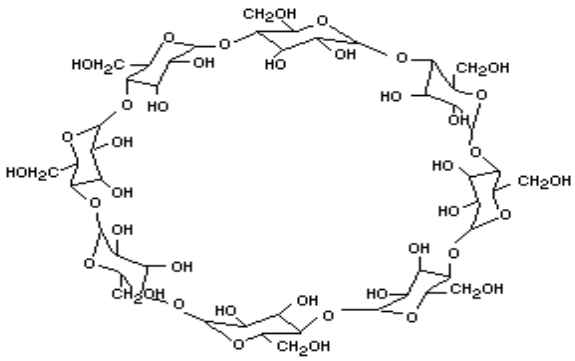
GAMMA CYCLODEXTRIN AS A NOVEL FOOD INGREDIENT

Introduction

Cyclodextrins are formed by converting linear starch chains into cyclic molecules by using an enzyme; cyclodextrin glucanotransferase. Cyclodextrin glucanotransferase reactions produce α-, β- and γ-cyclodextrins with six, seven, and eight units of glucose respectively, linked in α(1–4) .

The circular structure of γ-cyclodextrin (Figure 1) provides a hydrophobic cavity, which enables complexes to be formed with a variety of organic molecules, while the hydrophilic outer surface makes γ-cyclodextrin water-soluble. Because of these properties, γ - cyclodextrin can be used in a variety of ways in food, with a potential intake in the order of grams per person per day.

Figure 1. Chemical structure of γ-cyclodextrin



Manufacturing processes

For commercial production of cyclodextrins, two basic processes are used: the solvent and the non-solvent methods.

In a solvent method, a solvent directs the enzyme reaction to produce predominantly one type of cyclodextrin. Using this method, the reactor is filled with the starch substrate, the enzyme, and the solvent. The substrate is generally a partially hydrolysed starch with a dextrose equivalent of less than 10.

At the end of the reaction period, the reactor contains a mixture of an insoluble cyclodextrin complexed with the solvent. The cyclodextrin complex is separated from the other components by centrifugation or filtration. After removal of the chemical solvent from cyclodextrin, the soluble cyclodextrin is refined like any other soluble starch dried product and crystallized. The crystals are recovered and dried. Because the separation processes are highly efficient, the level of residual chemical solvent in the final product is less than 1 ppm.

In the non-solvent process, the reactor is filled with a starch hydrolysate and the enzyme. As no organic chemicals are present to prevent the growth of microorganisms, which could lead to contamination of the final product with microbial metabolites, aseptic or sterile conditions must be used. At the completion of the reaction, the cyclodextrin glucotransferase is inactivated by heat or acid. An alpha-amylase that is unable to hydrolyse the cyclodextrins is added to hydrolyse the non-cyclic dextrins.

The 3 cyclodextrins are sequentially crystallised from the solution by making use of the differences in their solubility (Table 1) via evaporation of water from the reaction mixture. β-Cyclodextrin, which is the least soluble cyclodextrin, crystallises most readily from the solution followed by α-cyclodextrin and finally γ-cyclodextrin. The crystals are collected by centrifugation or filtration, washed with a small amount of water, and dried.

In the past, cyclodextrins were expensive to produce and were available only in limited amounts as there was insufficient knowledge to produce them on an industrial scale. These barriers have been gradually removed so that use is now technologically possible in a variety of food applications.

Functional properties and applications

Cyclodextrins can function to dissolve other hydrophobic (water-disliking) substances. The advantage of cyclodextrins is that they offer a hydrophobic cavity of average size (1.5 nm x 0.7 nm x 0.8 nm) whereas the molecule is hydrophilic on the outside. Its torus shape allows stable inclusion complexes to form, with a wide diversity of organic substances and also with salts and halogens. Depending on their respective size, the 'guest' molecule is encapsulated fully or partially, with cyclodextrin acting as the 'host' molecule or receptor. In addition, the complex improves the stability of the 'guest' molecule not only in water but also in air in the case of dry products, as well as in relation to heat, oxidation and hydrolysis.

Some of the main functions of cyclodextrins are;

- stabilisation of volatile substances, emulsions, aromatic compounds, spices etc;
- elimination of undesirable molecules such as cholesterol or those that contribute to bitterness;
- modification of the chemical activity of a molecule by protecting some of its functional groups;
- increased solubility; and
- protection in terms of oxidation.

The most important parameter for complex formation with hydrophobic substances is their three-dimensional size (Table 1). γ–Cyclodextrins can for example accept bulky guests such as Vitamin D_2.

Table 1. Properties of Cyclodextrins

	Molecular Size (A^o)				Water solubility (g/100 ml; 25 °C
Type	**Glucose units**	**Inside diameter**	**Outside diameter**	**Height**	
α	6	5.7	13.7	7.0	14.50
B	7	7.8	15.3	7.0	1.85
γ	8	9.5	16.9	7.0	23.20

Cyclodextrins can stabilize emulsions of fats and oils, shielding them from oxidation and thus preventing rancidity. They can also be used to debitter citrus juices through removal of bitter components rather than masking them.

With respect to bioconversions and fermentations, cyclodextrins apparently possess an advantageous combination of properties. First, they enhance solubilisation of organic compounds. Second, they reduce toxicity since complexation of organic substrates and/or products may significantly reduce their concentrations. Third, they are biocompatible. Cyclodextrins are known to cause no damage either to free enzymes or to micro-organisms.

γ–Cyclodextrin use in food is not primarily as a food additive although it may perform some of the technological functions set out in Schedule 5 of Standard 1.3.1 - Food Additives, in the *Australia New Zealand Food Standards Code* such as a stabilizer and flavour modifier. γ–Cyclodextrin levels of use are more consistent with that of a food ingredient rather than an additive. Starch, maltodextrins and starch hydrolysates are considered as food ingredients in Australia and New Zealand.

As a food ingredient the labelling regulations would require the disclosure of the name in full on the food label. γ–Cyclodextrin can be used a carrier of other ingredients or flavours, and this use is consistent with other food ingredients such as starches or sugars that can be used as a carrier. The function of a carrier is not a technological function set out in Schedule 5, nor is the term currently included in the Codex General Standards for food additives.

Conclusions

The properties of starches can be modified by treatments, which result in products suitable for specific purposes in the food industry. γ–Cyclodextrin is a starch product that as a food ingredient can provide specialised functions in place of some of the starches or maltodextrins in a food.

Classifying γ–cyclodextrin as a food would neither restrict its use to perform a technological function in a food as a food additive nor its use as a processing aid since foods are generally permitted processing aids.

References

Guzman-Maldonado H. and Paredes-Lopez O. Amylolytic Enzymes and Products Derived from Starch: A Review. Crit. Rev Food Science Nutr. 35(5): 373-403 (1995).

Linden G and Lorient D. New ingredients in food processing. Biochemistry and agriculture. CRC Press 2000 Woodhead Publishing Ltd, Cambridge, England.

World Health Organization, Geneva, 1999. Food Additives Series: 42 Safety Evaluation Of Certain Food Additives. Prepared by the Fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). IPCS - International Programme on Chemical Safety of γ -cyclodextrin.

ATTACHMENT 4

DIETARY EXPOSURE ASSESSMENT REPORT

γ- CYCLODEXTRIN AS A NOVEL FOOD

An application was received by FSANZ requesting the approval of gamma cyclodextrin (γ-cyclodextrin) as a novel food. The applicant seeks to have γ-cyclodextrin approved for use in a variety of foods.

A dietary exposure assessment was deemed necessary in order to predict the potential exposures to γ-cyclodextrin in Australia and New Zealand if it were to be approved for use at the proposed levels of use in foods.

Background

γ -Cyclodextrin can be used as a complexant (or carrier), a flavour modifier and a stabiliser in a variety of foods. The Joint Expert Committee on Food Additives (JECFA) evaluated γ-cyclodextrin at its 51st and 53rd meetings, and concluded that an Acceptable Daily Intake (ADI) 'not specified' should be allocated. Such an ADI can be allocated to a food component with very low toxicity which, based on available data, will not represent a hazard to health (WHO, 2000).

Dietary Exposure Assessment provided by the applicant

The applicant provided details of estimated dietary exposure to γ-cyclodextrin in the United States (US) based on food consumption data from the 1989-91 Continuing Survey of Food Intakes by Individuals (CSFII). The CSFII surveyed each respondent over three subsequent one-day periods. The estimated mean dietary exposure to γ-cyclodextrin in the US, based on food consumption data from one-day, was 4.1 g/person/day. The 90th percentile estimate from one-day food consumption data was 8.8 g/person/day. The estimates of dietary exposure based on three days of food consumption data were 4.0 and 7.5 g/person/day for the mean and 90th percentile respectively. The greatest contributors to dietary exposure to γ-cyclodextrin were soy milk and dairy desserts.

Children aged 2-6 years had the highest estimated exposure on a per kilogram of body weight basis. The estimated dietary exposures to γ-cyclodextrin for this age group based on one-day food consumption data were 3.1 and 6.2 g/person/day for the mean and 90th percentile respectively (0.2 and 0.4 g/kg bw/day respectively). The estimates of dietary exposure based on three days of food consumption data were 3.0 and 5.3 g/person/day for the mean and 90th percentile respectively (0.2 and 0.3 g/kg bw/day respectively). Dairy desserts were the major contributor to total dietary exposure to γ-cyclodextrin.

The dietary exposure assessment provided by the applicant was based on US food consumption data. Therefore, FSANZ conducted a dietary exposure assessment to predict the potential dietary exposure to γ-cyclodextrin based on Australian and New Zealand food consumption data.

Dietary Modelling

The dietary exposure assessment was conducted using dietary modelling techniques that combine food consumption data with food chemical concentration data to predict the exposure to the food chemical from the diet. The dietary exposure assessment was conducted using ANZFA's dietary modelling computer program, DIAMOND.

The exposure was predicted by combining usual patterns of food consumption, as derived from national nutrition survey (NNS) data, with proposed levels of use of γ-cyclodextrin in foods.

Dietary exposure = food chemical concentration x food consumption

Dietary Survey Data

DIAMOND contains dietary survey data for both Australia and New Zealand; the 1995 National Nutrition Survey (NNS) from Australia that surveyed 13 858 people aged 2 years and above, and the 1997 New Zealand NNS that surveyed 4 636 people aged 15 years and above. Both of the NNSs used a 24-hour food recall methodology.

The dietary exposure assessment was conducted for both Australian and New Zealand populations. Modelling was conducted for the whole population, as well as for children aged 2-6 years for Australia only, as the New Zealand NNS did not include children of this age. An exposure assessment was conducted on children because children tend to have higher exposures on a per kilogram of body weight basis due to their smaller body weight and higher food consumption per kilogram of body weight compared to adults.

γ-Cyclodextrin concentration levels

The concentrations of γ-cyclodextrin in foods that were used in the dietary modelling were obtained from the application. The foods and proposed levels of addition of γ-cyclodextrin are shown below in Table 1. Dilution factors were applied to the concentration levels in the dietary modelling for dry mixes for beverages, soups, dressings, gravies, sauces, jellies and for instant coffee and tea to represent the levels of γ-cyclodextrin that would be present in these foods when made up or ready to consume. This was necessary as food consumption data in DIAMOND are in the 'ready to consume' state. The dilution factors used and the resulting concentration levels in 'ready to consume' foods are also shown in Table 1.

Table 1: Proposed uses of γ-cyclodextrin in foods and levels of use

Food Name	Proposed Concentration Level (g/kg)	Dilution factor	Level used in modelling (g/kg)
Dry mixes for beverages	10	10	* 1.0
Dry mixes for soups	10	20	* 0.5
Dry mixes for dressings, gravies and sauces	10	5	* 2.0
Dry mixes for puddings, desserts, jellies and fillings	10	6	* 1.7
Instant coffees and teas	10	80	* 0.125
Beverage whiteners	10	-	10
Sugar confectionery (compressed)	10	-	10
Chewing gum	10	-	10
Breakfast foods	20	-	20
Savoury snacks and biscuits	10	-	10

Soy milk products	20	-	20
Table spreads	200	-	200
Dairy desserts	30	-	30
Baked goods	20	-	20
Breads	10	-	10
Fruit based fillings	30	-	30
Fat based fillings	50	-	50
Processed cheese	30	-	30

* in the 'ready to consume' version of the food

γ-Cyclodextrin is also proposed to be used as a stabiliser in herbs and spices, as well as a complexant for vitamins and polyunsaturated fatty acids. DIAMOND does not contain the necessary food consumption data to include these uses of γ-cyclodextrin in the dietary modelling. It is assumed that these uses will not contribute substantially to the predicted dietary exposures.

How were the dietary exposures calculated?

The DIAMOND program allows γ-cyclodextrin concentrations to be assigned to food groups. The food groups included in dietary modelling are based on FSANZ's Australia New Zealand Food Classification System (ANZFCS). However, γ-cyclodextrin levels were assigned to specific foods only in some ANZFCS food groups and to the whole food group for other foods proposed to have γ-cyclodextrin added. Outlined below are examples of the application of γ-cyclodextrin concentration levels to foods for the purposes of dietary modelling:

- only reduced fat spreads;
- only dry mix varieties of beverages, such as dry mix cordials and drinking chocolate powder;
- only the instant varieties of coffee and tea;
- all soups;
- all dressings, gravies and sauces;
- all confectionery, including chewing gum, and;
- all biscuits, cakes and pastries (at 20 g/kg). This whole food group was included to incorporate baked goods, biscuits and the use of fruit and fat based fillings, none of which were assigned individual γ-cyclodextrin concentration levels.

The DIAMOND program multiplies the specified concentration of γ-cyclodextrin by the amount of food that an individual consumed from that group in order to predict the exposure to each food. Once this has been completed for all of the foods specified to contain γ-cyclodextrin, the total amount of γ-cyclodextrin consumed from all foods is summed for each individual. Population statistics (mean and high percentile exposures) are then derived from the individuals' ranked exposures.

Assumptions in the dietary modelling

Assumptions made in the dietary modelling include:

- all the foods within the group specified to contain γ-cyclodextrin contain γ-cyclodextrin at the proposed concentration levels;

- consumption of foods are actual amounts as recorded in the NNSs.

These assumptions are likely to lead to an overestimate of actual γ-cyclodextrin dietary exposure.

Limitations of the dietary modelling

A limitation of predicting dietary exposure is that only single 24-hour dietary survey data were available, and these tend to overestimate habitual food consumption amounts for high consumers. Therefore, predicted high percentile exposures are likely to be greater than actual high percentile exposures over a lifetime. The US estimates included in the application provided data on three-day exposure to γ-cyclodextrin. Food consumption amounts averaged over the three days will lower the high percentile estimated exposures. Therefore, the predicted high percentile exposures for Australia and New Zealand are also likely to be higher than the three-day US estimates included in the application.

Results

Predicted dietary exposure to γ-cyclodextrin

The number of consumers of γ-cyclodextrin represented over 99% of the total number of respondents for each population group in both Australia's and New Zealand's national nutrition surveys. As γ-cyclodextrin is proposed for use in such a wide variety of foods, most people in each survey consumed at least one of these γ-cyclodextrin containing foods. Therefore, only results for consumers are reported.

The predicted dietary exposure to γ-cyclodextrin for Australian and New Zealand populations is shown in Table 2. The mean predicted dietary exposures to γ-cyclodextrin in Australia and New Zealand are similar to those reported in the assessment on US data provided by the applicant (3.6 g/day and 4.1 g/day respectively). The predicted 95th percentile level of exposure was 9.5 g/day and 10.8 g/day for the total populations of Australia and New Zealand respectively. This is higher than the high percentile level reported from the US data, which was at the 90th percentile level.

Children aged 2-6 years (Australia only) had a higher exposure than the total population on a g/kg bw/day basis. Predicted mean dietary exposure for 2-6 year olds was 3.3 g/day or 0.18 g/kg bw/day, compared to 0.07 g/kg bw/day for the total population of Australia. Predicted 95th percentile exposure for 2-6 year olds was 8.7 g/day or 0.45 g/kg bw/day, compared to 0.20 g/kg bw/day for the total population of Australia.

The dietary modelling assumes that each food in a food group that may contain γ-cyclodextrin does actually contain γ-cyclodextrin at the proposed level of use. In reality, γ-cyclodextrin will not be used in every food in each food category. Therefore, predicted dietary exposures will be overestimates of actual dietary exposures.

Table 2: Predicted dietary exposures to γ-cyclodextrin for Australia and New Zealand

Country	Age group	Number of consumers of γ-cyclodextrin	Consumers as a % of total respondents[#]	Consumer intake		
				Units	Mean	95th percentile
Australia	All (2 years+)	13767	99.3	g/day	3.6	9.5
				g/kg bw/day	0.07	0.20
	2-6 years	986	99.7	g/day	3.3	8.7
				g/kg bw/day	0.18	0.45
New Zealand	All (15 years+)	4598	99.2	g/day	4.1	10.8
				g/kg bw/day	0.06	0.15

 # Total number of respondents for Australia: whole population = 13 858, 2-6 years = 989. New Zealand: whole population = 4 636.

Major contributing foods

Foods contributing to the predicted total exposures to γ-cyclodextrin are displayed in Table 3. The percent contributions are calculated by dividing the sum of consumers' exposures from a food group by the sum of all consumers' exposures from all foods, and multiplying this by 100. Breads as well as biscuits, cakes and pastries were the major contributing foods for each population group in both Australia and New Zealand. Ice cream and breakfast cereals contributed between 11% and 15% to γ-cyclodextrin exposures in Australia for the total population and for 2-6 year olds, while contributing 10% and 6% respectively for the New Zealand population. Reduced fat spreads contributed almost 16% to γ-cyclodextrin exposures for the total New Zealand population, and less than 6% for the total Australian population (less than 4% for 2-6 year olds). Dairy desserts and soymilk products also contributed above 5% to γ-cyclodextrin exposures for 2-6 year olds.

Table 3: Major contributors to mean γ-cyclodextrin dietary exposures for Australia and New Zealand

Country	Age group	Major Contributing foods and percent of total γ-cyclodextrin exposures
Australia	Whole population (2+ years)	Breads (30.5%) Biscuits, cakes & pastries (22.6%) Ice cream (14.6%) Breakfast cereals (11.6%) Reduced fat spreads (5.7%)
	2-6 years	Breads (22.4%) Biscuits, cakes & pastries (17.8%) Ice cream (14.7%) Breakfast cereals (14.4%) Dairy desserts (9.2%) Soy milk products (5.7%)

New Zealand	Whole population (15+ years)	Breads (30.5%) Biscuits, cakes & pastries (26.5%) Reduced fat spreads (15.8%) Ice cream (10.0%) Breakfast cereals (6.3%)

Conclusion

γ-Cyclodextrin is proposed for use in a variety of foods. The predicted mean exposures to γ-cyclodextrin for the total population in Australia and New Zealand are approximately 4 g/day (0.06-0.07 g/kg bw/day). The predicted 95th percentile γ-cyclodextrin exposures for the total populations of Australia and New Zealand are approximately 10 g/day (0.20 g/kg bw/day). Predicted mean and 95th percentile γ-cyclodextrin exposures for Australian children aged 2-6 years are double that of the total population on a g/kg bw/day basis. These are likely to be overestimates of actual dietary exposure to γ-cyclodextrin if it was approved for use in the foods and at the levels proposed in this application.

Reference

World Health Organisation (2000), *γ-Cyclodextrin*, in Safety evaluation of certain food additives, WHO Food Additives Series 44, WHO, Geneva.

ATTACHMENT 5

SUMMARY OF PUBLIC SUBMISSIONS

First Round

Brooke-Taylor & Co

- Considers that γ-cyclodextrin is a food additive and not novel food based on its use in the foodstuff primarily for its functionality.
- The Initial Assessment Report does not establish any risk to consumer safety arising from the storage, handling, preparation or consumption of foods containing γ-cyclodextrin.
- Considers that FSANZ is confusing the objective of the Novel Food standard. As a regulator, FSANZ, is not in a position to **ensure** the manner in which a product is used by the consumers other than by prohibiting it from the market place.

Food Technology Association, Victoria Inc

- Approve the use of γ-cyclodextrin.
- Request that they be maintained on the circulation lists for further changes to this application.

Dietitians Association of Australia

- DAA notes that γ-cyclodextrin is a carbohydrate with potential for a high glycaemic index. Recommends that dietary modelling takes into account the impact of such glycaemic load in the diet.

National Council of Women of Australia

- Considers that there is not sufficient information in the initial assessment report to support the application.
- Will await the nutritional and other considerations before deciding their position.

Australian Food And Grocery Council (AFGC)

- γ-cyclodextrin cannot be classified as a food additive because it is a polysaccharide and hence should be regarded as food.
- AFGC considers that, like Japan, γ-cyclodextrin to be a food.
- Internationally γ-cyclodextrin has been found to be safe and no limitations placed on its use.
- Its source, composition and metabolite fate leads to the conclusion that γ-cyclodextrin cannot be classified as novel and should be considered as a food in the same way as other polysaccharides.

Consumers Association of South Australia

- Supports the position taken by the National Council of Women of Australia.

Second Round

Food Technology Association, Victoria Inc

- Approve the use of γ-cyclodextrin.
- Request that they be maintained on the circulation lists for further changes to this application.

Australian Food And Grocery Council

- Supports FSANZ's proposal to permit unrestricted use of γ-cyclodextrin.
- However, contends that γ-cyclodextrin is not a novel food because 'there is sufficient knowledge to enable safe use' based on the Draft Assessment carried out by FSANZ.
- Recommends that the proposed drafting be revised to insert the provisions for the labelling of γ-cyclodextrin into the table to Clause 4 of Standard 1.2.4.
- Recommends that FSANZ should consider allowing γ-cyclodextrin to be declared in the ingredient list as either 'γ-cyclodextrin' or 'cyclodextrin'.