June 7, 2018

APPENDIX D: International and other National Standards

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Food enzymes are biological isolates of variable composition. Apart from the enzyme protein in question, microbial food enzymes will also contain some substances derived from the producing micro-organism and the fermentation medium. From a safety point of view, the similarity of the producing micro-organism is of higher importance than that of the enzyme protein in question. Therefore, sections below summarize not only authorized food enzymes with the same enzyme activity, but also authorized food enzymes from the same producing organism. As documented below, lactase from various micro-organisms (including genetically modified ones) are widely accepted and *Bacillus subtilis* - whether or not genetically modified - is widely accepted as a safe production organism for a broad range of enzymes.

1 Codex Standards

1.1 The enzyme

CB108 Lactase has not been evaluated by the Joint Expert Committee on Food Additives (JECFA).

1.2 Supporting evaluations

Alpha-Acetolactate decarboxylase, α-Amylase, Branching glycosyltransferase, Maltogenic amylase, Mixed carbohydrase and protease, and Xylanase from *B. subtilis* have been reviewed by the Joint Expert Committee on Food Additives (JECFA) of FAO/WHO and an acceptable daily intake (ADI) "not specified" has been set (Technical Report Series 733, 1986).

2 International Legislation

2.1 United States

2.1.1 The enzyme

CB108 Lactase has been determined to be GRAS as a food processing aid in producing lactose-reduced fresh dairy milk, and galacto-oligosaccharide (GOS) for addition to infant formula and other food/feed products by a panel of scientific experts in the USA (Appendix D1).

2.1.2 Supporting approvals

A practically identical lactase from *B. bifidum* produced in *B. subtilis* strain (BIF917) as *B. subtilis* CB108 Lactase with essentially the same expression system, the same IUBMB No. 3.2.1.23, received GRAS status (GRN 579) on Nov. 5th, 2015 (No questions letter, Appendix D2) for use in the production of galacto-oligosaccharide for infant formula and in the production of fresh dairy products, which are the same proposed uses for *B. subtilis* CB108 Lactase.

Carbohydrase (21CFR184.1250), Pectate lyase (GRN 114) from *B. subtilis* were affirmed as GRAS by U.S. FDA. Also, U.S. FDA has no questions to following GRAS Notices on enzymes derived from *B. subtilis*:

- Branching glycosyltransferase enzyme preparation from *Bacillus subtilis* expressing a branching glycosyltransferase gene from *Rhodothermus obamensis* (GRN 274)

- 1,4-α-glucan branching enzyme preparation from *Bacillus subtilis* strain 168 expressing the glucan branching enzyme gene from *Aquifex aeolicus* strain VF5 (GRN 406),
- Pullulanase enzyme preparation from *Bacillus subtilis* expressing the pullulanase gene from *B. acidopullulyticus* (GRN 205)
- Pullulanase derived from *Bacillus subtilis* carrying a gene encoding pullulanase from *Bacillus naganoensis* (GRN 20)

In addition, lactase from following production organisms have been granted GRAS status by U.S. FDA.

- Beta-galactosidase enzyme preparation (*E.coli*) (GRN 485)
- Acid lactase from *Aspergillus oryzae* expressed in *Aspergillus niger* (GRN 510)
- Lactase enzyme preparation from *Aspergillus niger* (GRN 132)
- Invertase enzyme preparation from *Saccharomyces cerevisiae* and lactase enzyme preparation from *Kluyveromyces marxianus* (GRN 88)

2.2 Europe

2.2.1 The enzyme

In Europe, most of the enzyme preparations used in food processing are considered processing aids, meaning that they have their technological function in the food-processing stage and not in the final food. They are excluded from the Food Additives Framework Directive. On 16 December 2008 the European Parliament and the Council adopted Regulation 1332/2008 EC on food enzymes which aims to harmonise authorisation and safety assessment procedures of enzymes used in food processing in the EU (Appendix D2). Several years will be needed for the new rules to become fully applicable across the EU. Until then, all national provisions on the use of food enzymes in individual EU Member States remain valid and applicable. Only France and Denmark have legislation covering all food-use enzymes. In Denmark and France, approval is needed prior to use. The information contained in the application dossier necessary for approval should follow the guidelines laid down by the SCF in 1992 or the EU Regulation 1332/2008. France has some additional national requirements specified in the Arrêté du 19 octobre 2006 relatif à l'emploi d'auxiliaires technologiques dans la fabrication de certaines denrées alimentaires as amended. In the other EU countries, enzyme preparation should be proved to be safe for use in food before being sold in EU according to the General EU Food Law. It is the producer's responsibility how to meet this requirement. DuPont IB uses the USA GRAS system as the backbone for this.

CB108 Lactase has been included in positive list in Freance (Arrêté du 19 Octobre 2006). Approval letter of CB108 Lactase in Denmark and its English translation is attached in Appendix D3.

2.2.2 Supporting approvals

B. subtilis, including genetically modified strains, has been approved for the production of xylanase, and beta-glucanase enzymes in the food industry in Denmark and in France. In France, it is also approved for the production of alpha acetolactate decarboxylase, alpha-amylase, glucotransferase, hemi-cellulase, protease and pullulanase (Arrêté du 19 Octobre 2006 as amended).

Lipase from *Bacillus circulans, Kluyveromyces lactis* and *Aspergillus oryzae* have been approved in France (Arrêté du 19 Octobre 2006)

2.3 Other countries

2.3.1 Supporting approvals

CB108 Lactase has passed the safety assessment in Canada, and Dupont IB has been informed that CB108 Lactase will be added to the positive list in Canada.

Appendix D1 : GRAS panel letter of CB108 Lactase

Michael W. Pariza Consulting LLC
7102 Valhalla Trail
Madison, WI 53719

Michael W. Pariza, Member

August 12, 2016

Vincent Sewalt, PhD
Senior Director, Product Stewardship & Regulatory
DuPont Industrial Biosciences
Danisco US, Inc.
925 Page Mill Road
Palo Alto, CA 94304

RE: GRAS opinion on the intended uses of DuPont's *Bifidobacterium bifidum* lactase preparation (designated *Milky Whey2*) derived from *Bacillus subtilis* CB108 (GICC03484)

Dear Dr. Sewalt,

I have reviewed the information you provided on DuPont's *Bifidobacterium bifidum* lactase enzyme preparation designated *Milky Whey2* which is expressed in *Bacillus subtilis* CB108 (GICC03484), an improved production strain that has been genetically modified to over express a synthetic analog of the native *Bifidobacterium bifidum* lactase gene. The intended uses of *Milky Whey2* are to produce lactose-reduced fresh dairy products, and galacto-oligosaccharide (GOS) for addition to infant formula, pet food, and production of animal feed. In these applications, the enzyme will be used as a processing aid where the enzyme protein is not present in the final food or present in negligible amounts with no function in the final food.

In evaluating the safety of *Milky Whey2*, I considered the biology of *Bacillus subtilis* and *Bifidobacterium bifidum*; information of *Milky Whey2* and the safety of lactase enzymes in food manufacture; information that you provided regarding the cloning methodology that was utilized; information pertaining to the safe strain lineage within which *B. subtilis* CB108 (GICC03484) was developed; and other relevant information available in the peer-reviewed scientific literature.

Bacillus subtilis is a ubiquitous gram positive spore-forming bacterium that is rarely associated with opportunistic infections or food poisoning outbreaks. Many non-pathogenic, non-toxigenic strains of this species are utilized by enzyme manufacturers worldwide to produce enzymes and other products for industrial applications, including human food and animal feed uses. Carbohydrase and protease enzyme preparations derived from *B. subtilis* have been affirmed as GRAS by the U.S. FDA per 21 CFR 184.1148 and 184.1150, respectively.

DuPont's safe lineage of non-pathogenic, non-toxigenic *B. subtilis* production strains, which includes *B. subtilis* CB108 (GICC03484), was developed from the wild-type *B. subtilis* 168 via a series of modifications that included classical mutagenesis, as well as rDNA and protein engineering utilizing techniques and reagents that are appropriate for the development of a safe lineage of food ingredient production microorganisms. The safety of the enzymes from these production strains have been evaluated with various *in vitro* genetic toxicity tests, as well as oral toxicity tests in rats (90-day, 28-day, or acute oral toxicity). Strains within this safe lineage are used to manufacture many food and feed enzymes, including proteases, arylesterase, maltotetraohydrolase, xylanase, cellulase, β-glucanase, and lactase designated *Milky Whey* (*Milky Whey2*, the subject of this opinion, has the identical lactase but lacks an esterase produced by the pUB110 gene.)

Published literature, government laws and regulations, and DuPont's unpublished safety studies, all support the conclusion that the lineage to which these production strains belong is safe and suitable for use in the development and manufacture of food-grade and feed-grade enzymes. Positive GRAS determination expert opinion letters were received for the following enzymes produced by other strains within this safe lineage: Multifect P300 protease for food and feed (Dr. Pariza to G. Mercer 18 May 1994, and to A. Caddow 1 October 1994), maltotetrahydrolases (SAS 1, 2, & 3 amylase; 27 May 2004, 17 October 2005, & 29 August 2006, respectively from Drs. Pariza, Borzelleca, and Blumenthal) from three strains for baking, xylanase for baking (Dr. Pariza to A. Caddow, 28 September 2006); BglS β-glucanase to facilitate hydrolysis of beta-glucans and related carbohydrates in brewing and potable alcohol manufacture (Dr. Pariza to V. Sewalt, 10 January 2013); and *Milky Whey* lactase for dairy applications and GOS manufacture (Dr. Pariza to V. Sewalt, 13 June 2014, updated 11 August 2016). GRAS Notices for BglS beta-glucanase and *Milky Whey* lactase were submitted to the US FDA, which responded with 'No Questions Letters' (GRN 592 and GRN 579, respectively).

Bifidobacterium spp. are Gram-positive, non-spore forming, anaerobic, pleomorphic bacilli that comprise dominant microbial residents of the colonic microbiota. The *Bifidobacterium* genus does not contain pathogenic or toxigenic species. *Bifidobacteria* were discovered in the feces of breast-fed infants and are regarded as a primary reason for the greater resistance of breast-fed infants to disease. *Bifidobacteria* and their metabolites also appear to play key positive roles in the intestinal health of humans throughout life. Accordingly, one may reasonably conclude that the intestinal tracts of

humans, beginning in infancy, typically contain lactase from *Bifidobacteria*, and that this exposure does not induce adverse events.

The synthetic lactase gene that codes for *Milky Whey2* and is expressed by *Bacillus subtilis* CB108 (GICC03484) is identical to the native lactase gene in *Bifidobacterium bifidum* DSM 20215, and was synthesized by using the published DNA sequence of the *Bifidobacterium bifidum* DSM 20215 lactase gene as a template. It is also identical to the synthetic lactase gene that is expressed by the *Bacillus subtilis* JL47 (GICC20006659) production strain, which I previously reviewed. The synthetic *Bifidobacterium bifidum* lactase gene was incorporated into *Bacillus subtilis* CB108 (GICC03484) by means of a pUB110 derived expression plasmid that was engineered to remove an esterase gene (*pnbA*) that caused undesired off flavors in dairy applications, using reagents/methods that are appropriate in the construction of production strains for food-grade ingredients. Accordingly, the lactase enzyme preparation from *Bacillus subtilis* CB108 (GICC03484) (*Milky Whey2*) is identical to the lactase enzyme preparation from *Bacillus subtilis* JL47 (GICC20006659) (*Milky Whey*), except for absence of the esterase produced by the pUB110 gene.

The synthetic *Bifidobacterium bifidum* lactase amino acid sequence was compared against databases of known allergenic and toxigenic proteins, and found to contain no matches. The *B. bifidum* lactase enzyme preparation from *Bacillus subtilis* JL47 (Milky Whey) was evaluated was evaluated with a battery of standard toxicological tests that included a sub-chronic (90-day) gavage study in male and female Crl:CD(SD) rats as well as an acute toxicity study in female Crl:CD(SD) rats, tests for dermal and eye irritation in rabbits, the induction of bacterial mutagenesis (Ames test), and the induction of chromosomal aberrations in human lymphocytes. No treatment-related adverse effects were observed. In the subchronic rat gavage study the NOAEL was highest dose tested, 1416.4 mg TOS/kg bw/day, corresponding to 1000 mg total protein/kg bw/day. Based on this finding the margins of safety for the proposed uses of *Milky Whey2* are as follows: from *Milky Whey2* use in dairy applications consumed by humans other than infants, 997; from the manufacture of GOS used in infant formulas, 757; from the manufacture of GOS used in pet food and production animal feed applications, 397 (dogs and cats), 530 (cattle), 353 (pigs), 244 (poultry).

The manufacturing process including the ingredients used for fermentation, extraction and concentration of *Milky Whey2*, and the specifications for *Milky Whey2*, are appropriate for a food ingredient.

Based on the foregoing, I concur with the evaluation made by DuPont that the *Bacillus subtilis* CB108 (GICC03484) production strain is safe and appropriate for use in the manufacture of food-grade *Milky Whey2* lactase. I further concur that based on scientific procedures, the synthetic *Bifidobacterium bifidum* lactase enzyme expressed by *Bacillus subtilis* CB108 (GICC03484) and designated *Milky Whey2*, manufactured in a manner that

is consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate food-grade specifications, is GRAS (Generally Recognized As Safe) for use as a processing aid to produce lactose-reduced fresh dairy products, and galacto-oligosaccharide (GOS) for addition to infant formula, pet food, and production of animal feed, where the enzyme protein is not present in the final food or present in negligible amounts with no function in the final food.

It is my professional opinion that other qualified experts would also concur in this conclusion.

Please note that this is a professional opinion directed at safety considerations only and not an endorsement, warranty, or recommendation regarding the possible use of the subject product by you or others.

Sincerely,

Michael W. Pariza, Ph.D.
Member, Michael W. Pariza Consulting, LLC
Professor Emeritus, Food Science
Director Emeritus, Food Research Institute
University of Wisconsin-Madison

Appendix D2 : US FDA GRAS Notice Number 579, "No Questions Letter" for *B. subtilis* Lactase enzyme preparation

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
College Park, MD 20740-3835

Dr. Vincent Sewalt
Danisco US, Inc.
(operating as DuPont Industrial Biosciences)
925 Page Mill Road
Palo Alto, CA 94304

Re: GRAS Notice No. GRN 000579

Dear Dr. Sewalt:

The Food and Drug Administration (FDA) is responding to the notice, dated April 30, 2015, that you submitted in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS); the GRAS proposal). FDA received the notice on May 4, 2015, filed it on May 21, 2015, and designated it as GRAS Notice No. GRN 000579.

The subject of the notice is lactase enzyme preparation from *Bacillus subtilis* carrying a synthetic lactase gene from *Bifidobacterium bifidum* (lactase enzyme preparation). The notice informs FDA of the view of Danisco US, Inc. (operating as DuPont Industrial Biosciences) that lactase enzyme preparation is GRAS, through scientific procedures, for use as an enzyme in the production of milk and milk products, at 1.1 milligrams total organic solids per gram (mg TOS/g) of milk, and as an enzyme in the production of galacto-oligosaccharide (GOS) at 1.3 mg TOS/g of GOS, for use in infant formula.

Commercial enzyme preparations that are used in food processing typically contain an enzyme component that catalyzes the chemical reaction as well as substances used as stabilizers, preservatives, or diluents. Enzyme preparations may also contain components derived from the production organism and components derived from the manufacturing process, e.g., constituents of the fermentation media or the residues of processing aids. DuPont's notice provides information about each of these components in the lactase enzyme preparation.

According to the classification system of enzymes established by the International Union of Biochemistry and Molecular Biology, lactase is identified by the Enzyme Commission Number 3.2.1.23. The accepted name for the enzyme is lactase; the systematic name is β-D-galactoside galactohydrolase. The CAS Registry Number for lactase is 9031-11-2. Other names include: β-galactosidase; β-lactosidase; β-D-lactosidase; lactozym; trilactase; β-D-galactanase. Lactase catalyzes the hydrolysis of terminal non-reducing β -D-galactose residues in β-D-galactosides. DuPont reported the primary amino acid sequence of the lactase enzyme to be 887.

DuPont states that the production strain, *B. subtilis* JL47, is obtained from the host strain *B. subtilis* BG3934 [1] via several classical mutagenesis and rDNA techniques. DuPont states that an intermediate strain in the construction of the host strain has been recognized as belonging to Risk Class 1, by Dutch

[1] *B. subtilis* BG3934 was modified by the deletion of several genes from the laboratory strain *B. subtilis* BG125. *B. subtilis* BG125 was obtained from *B. subtilis* strain 1A10, which has been deposited in the Bacillus Genetic Stock Center, Ohio State University, Columbus OH.

authorities. DuPont describes *B. subtilis* as a non-pathogenic and non-toxigenic source of industrial enzymes, with a history of safe use in their production.

DuPont describes the construction of *B. subtilis* JL47 production strain using a pUB110 derived expression plasmid containing the synthetic gene encoding a truncated wild-type lactase from *B. bifidum*, the endogenous alanine racemase gene as a selective marker, and the *B. subtilis* promoter and terminator elements. DuPont states that the truncated lactase gene was inserted multiple times into the genome of the host strain. DuPont also states that the entire genome of *B. subtilis* JL47 was sequenced to verify its construction, and that no antibiotic resistance genes were used in the construction of the production microorganism. DuPont confirms that the production strain remains stable for over sixty generations.

DuPont states that lactase enzyme is produced by the submerged fermentation of a pure culture of the production strain. The fermentation is carried out under controlled conditions and the culture is periodically tested to ensure production strain identity and purity, and enzyme-generating ability. After fermentation, the enzyme is recovered from the culture broth via cell separation followed by an ultrafiltration concentration step. The resulting liquid lactase enzyme concentrate is stabilized and formulated with maltodextrin and potassium sorbate. DuPont states that the entire process is performed in accordance with current good manufacturing practices using raw materials of food grade quality. DuPont states that the final lactase enzyme preparation does not contain any major food allergens from the fermentation medium.

DuPont has established food grade specifications and notes that the lactase enzyme preparation conforms to specifications established for enzyme preparations in the Food Chemicals Codex (FCC, 9th edition, 2014), and to the General Specifications and Considerations for Enzyme Preparations Used in Food Processing established by the FAO/WHO Joint Expert Committee on Food Additives (JECFA, 2006). DuPont confirms the absence of the production organism in the final enzyme preparation, as established by the set specifications. DuPont provides analytical data from three batches of lactase enzyme preparation to demonstrate consistency with the specifications.

DuPont intends to use lactase enzyme preparation to hydrolyze lactose to galactose and glucose in the production of milk and milk products at 1.1 mg TOS/g of milk. DuPont also proposes to use lactase enzyme preparation in the manufacture of GOS for use in infant formula at 1.3 mg TOS/g of GOS. To estimate dietary exposure to lactase enzyme preparation, DuPont assumes that the lactase enzyme preparation will be used at its maximum intended use levels, and that all of the enzyme preparation will remain in the final food. Based on these assumptions, DuPont estimates a dietary intake of lactase enzyme preparation from dairy products to be 1.4 mg TOS per kg body weight per day (mg TOS/kg bw/d), and from infant formula uses to be 1.9 mg/kg bw/d. DuPont states that the reaction products resulting from lactase enzyme activity are already part of the human diet.

DuPont summarizes unpublished toxicological studies using lactase liquid enzyme concentrate that corroborates the safety of the enzyme for the intended uses. Tests conducted using bacterial cells showed that lactase is not mutagenic. DuPont also demonstrates that the lactase enzyme is not clastogenic based on *in vitro* chromosomal aberration testing. DuPont uses a 13-week oral toxicity study conducted using rats to show that consumption of lactase enzyme concentrate does not cause any treatment-related adverse effects up to the highest dose tested, i.e., 1416 mg TOS/kg bw/d. DuPont calculates a margin of safety of 997 and 757, based on the highest dose tested in the 13-week study, and the estimated intakes of 1.4 mg TOS/kg bw/d and 19 mg TOS/kg bw/d from the intended uses of lactase enzyme preparation in dairy products and infant formula, respectively.

DuPont discusses potential food allergenicity of lactase enzyme. DuPont conducted an 80-amino acid sequence homology search for lactase enzyme against known allergens stored in the FARRP allergen protein database. DuPont states that there were no matches to known allergens by identity across 80

amino acids that exceeded 35 %. Additionally, Dupont did not observe any matches of contiguous stretches of eight amino acids of lactase with any oral allergenic protein. DuPont further cites the conclusions of several organizations and working groups about the low risk of allergenicity posed by enzymes due to their low use levels and extensive processing of the enzyme-containing foods during manufacturing. Based on the information available, DuPont concludes that it is unlikely that oral consumption of lactase enzyme will result in any allergenic responses.

Based on the data and information summarized above, DuPont concludes that lactase enzyme preparation is GRAS for its intended use.

Standards of Identity

In the notice, DuPont states its intention to use lactase enzyme preparation in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In its review of DuPont's notice that lactase enzyme preparation is GRAS for the intended uses, FDA did not consider whether section 301(ll) or any of its exemptions apply to foods containing lactase enzyme preparation. Accordingly, this response should not be construed to be a statement that foods containing lactase enzyme preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information provided by DuPont US Inc., as well as other information available to FDA, the agency has no questions at this time regarding DuPont US Inc.'s conclusion that lactase enzyme preparation is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of lactase enzyme preparation. As always, it is the continuing responsibility of DuPont US Inc. to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter responding to GRN 000579, as well as a copy of the information in this notice that conforms to the information in the GRAS exemption claim (proposed 21 CFR 170.36(c)(1)), is available for public review and copying at www.fda.gov/grasnoticeinventory.

Sincerely,

Michael A. Adams -S

Digitally signed by Michael A. Adams -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300042713, cn=Michael A. Adams -S
Date: 2015.11.05 16:00:25 -05'00'

Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Appendix D3. Denmark Authorization of Lactase from *B. bifidum* expressed in *B. subtilis* (Confidential Commercial information)

Please refer to Appendix D Confidential Attachment

Appendix D4 : EU Legislation on enzymes

Amfep/09/01 — Association of Manufacturers and Formulators of Enzyme Products — 18 January 2009

Amfep Statement on the EC Regulation 1332/2008 on Food Enzymes

On 16 December 2008 the European Parliament and the Council adopted Regulation 1332/2008 EC on food enzymes (OJ EU L 354/7, 31.12.2008).

The Association of Manufacturers and Formulators of Enzyme Products (Amfep) welcomes this EU legislation which is the first attempt ever to harmonise authorisation and safety assessment procedures of enzymes used in food processing in the EU. The Regulation is set to improve the functioning of the internal market by removing disparities among member states and bringing more legal certainty to the market.

Only authorised food enzymes will be allowed to be commercialised and/or used in foods sold in the EU – irrespective whether they are used as processing aids or ingredients. This also applies to imported foods. The European Food Safety Authority (EFSA) will play a pivotal role in the authorisation process of food enzymes. On the basis of EFSA's scientific advice, the EU Commission will grant authorisations after consulting member states and the EU Parliament.

The publication of the Regulation in the Official Journal of the European Union only marks the beginning of an extensive implementation process. In fact, several years will be needed for the new rules to become fully applicable across the EU. Until then, all national provisions on the use of food enzymes in individual EU Member States remain valid and applicable.

The European Commission, supported by EFSA, has until 2011 to specify what information is required to be submitted for a risk assessment of food enzymes. After that, the industry will have another two years (until 2013) to submit dossiers for evaluation and authorization of food enzymes presently used in food on the EU market. Only after the EU Commission and EFSA have completed the evaluation of all these dossiers will the first EU (positive) list of approved food enzymes be established. The Regulation 1332/2008 EC does not set a deadline by which this evaluation is to be completed.

Apart from the authorization requirements, Regulation 1332/2008 also lays down specific provisions on labelling of food enzymes, food enzyme preparations and food prepared with enzymes. The provisions on labelling of food enzymes and food enzyme preparations will enter into force on 20 January 2010, whereas the provisions on labelling of food prepared with enzymes enter into force on 20 January 2009. The latter do not increase the scope of the previous food labelling provisions, although some changes are introduced to the way the small number of food enzymes that are not used as processing aids are declared.

Amfep is working closely with relevant European Stakeholders to ensure a seamless implementation of the new EU legislation for the benefit of food enzyme manufacturers, their clients, and consumers.

NB: The proposal for a regulation on food enzymes is a part of a so-called Food Improvement Agents package (FIAP). While harmonising EU legislation for food enzymes, FIAP is also aiming at upgrading existing EU legislation on food additives (EC Regulation 1333/2008) and food flavourings (EC Regulation 1334/2008) and establishing a transversal authorisation procedure (EC Regulation 1331/2008) The EU Regulation on food additives will include a positive list of additives and carriers that will be allowed in food enzymes and food enzyme preparations. This list will come into force on 1 January 2011.

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