CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **CX/FA 17/49/13**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Forty-ninth Session

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PROPOSALS FOR ADDITIONS AND CHANGES TO THE PRIORITY LIST OF SUBSTANCES PROPOSED FOR EVALUATION BY JECFA
Replies to CL 2016/13-FA of European Union, CCC, EFEMA, ICBA, IOFI and NATCOL

European Union

The European Union and its Member States are proposing to add the following substances to the priority list of substances proposed for evaluation by JECFA:

1) Protease Aqualysin 1 from *Thermus aquaticus* produced by *B. subtilis*, strain LMGS 25520 - safety assessment and establishment of specifications

2) Inulinase from Aspergillus ficuum produced by *Aspergillus oryzae*, strain MUCL 44346 - safety assessment and establishment of specifications

3) Endo-1,4-β-xylanase from *Bacillus subtilis* produced by *B. subtilis* LMG S-28356 - safety assessment and establishment of specifications

4) Endo-1,4-β-xylanase from *Pseudoalteromonas haloplanktis* produced by *B. subtilis*, strain LMG S-24584 - safety assessment and establishment of specifications

5) Endo-1,4-β-xylanase from *Thermotoga maritima* produced by *B. subtilis*, strain LMG S-27588 - safety assessment and establishment of specifications

6) INS No 445(iii) glycerol ester of wood rosin – revision of specifications

Annex 1

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained

Name of Substance(s):	Protease Aqualysin 1 from *Thermus aquaticus* produced by *B. subtilis,* strain LMGS 25520
Question(s) to be answered by JECFA	Safety evaluation when used as a processing aid

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1. Proposal for inclusion submitted by:

The Belgian Federal Public Service Health, Food Chain Safety and Environment Place Victor Horta 40 box 10 1060 Brussels/Sint-Gillis Belgium

E-mail: apf.food@health.belgium.be

2. Name of substance; trade name(s); chemical name(s):

Name: Protease Aqualysin 1 from *T. aquaticus* produced by *B. subtilis,* strain LMGS 25520

IUBMB name: EC 3.4.21.111

Tradename: Premix X-220 (Main commercial name)

chemical names: Aqualysin 1, Caldolysin

3. Names and addresses of basic producers

Puratos NV- site Beldem Rue Bourrie 12 B-5300 Andenne Belgium

Tel. no: +32 8582 3250 Fax no: 32 8582 3260

4. Has the manufacturer made a commitment to provide data?

Puratos NV commits to provide data to support the proposal for the inclusion of Protease Aqualysin 1 in the list of substances to be evaluated by the JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Name: Puratos NV
Address: Industrialaan 25
Postal code and City: B-1702 Groot-Bijgaarden
Country: Belgium
Tel no.: +32 2481 4444
Fax no. +32 2466 2581
Contact Person: Bas Verhagen
Email: BVerhagen@puratos.com

6. Justification for use:

The food enzyme catalyses, i.e. accelerates, hydrolyses of the peptide bonds that link amino acids together in the polypeptide chains forming the proteins.

The addition of protease Aqualysin 1 provides the following benefits, of interest during the production of bakery products:

- Faster dough development upon mixing
- Better dough machinability
- Reduced dough rigidness which results in processing tolerance
- Improved dough's structure and extensibility during the shaping or moulding step
- Uniform shape of the bakery product
- Regular batter viscosity, beneficial in the production process for e.g. waffles, pancakes and biscuits
- Improved short-bite of certain products like hamburger breads.

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s)

The enzyme preparation is used as a processing aid during production of bakery products, it is therefore not added to the final food product. The food enzyme is denatured during the baking process. Therefore it cannot have any technological function anymore in final baked foods.

Food enzyme preparations are used by food manufacturers according to the *Quantum Satis* principle, which means that food manufacturers will typically fine-tune the enzyme dosage based on a dose range recommended by the enzyme supplier. The recommended dose ranges in baking processes is 2300 -12000 mU per kg raw material (flour).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

The use in food of the Protease Aqualysin 1 from T. aquaticus produced by B. subtilis, strain LMGS 25520 is officially approved in France, Canada and the US.

Moreover, the enzyme is legally traded and the use in food is legal in many countries worldwide, including in the EU.

Finally, a new dossier has also been submitted in the EU under Regulation (EC) No 1332/2008, and is currently under review by the EFSA.

9. List of data available (please check, if available)

Toxicological data

The *B. subtilis* production strain is from a safe lineage that has been tested according to the criteria laid out in Pariza and Johnson (2001[1]). The safety of *B. subtilis* as a production microorganism has been assessed by EFSA (2007[2]) and has been accorded Qualified Presumption of Safety (QPS) status. A review of the literature by the US EPA (1997[3]) failed to reveal the production of metabolites of toxicological concern by *B. subtilis.* Nonetheless, to comply with the various regulatory requirements in different countries, several toxicity experiments have been performed.

(i) Metabolic and pharmacokinetic studies Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

The food enzyme has been subjected to a standard package of toxicological tests in line with internationally accepted guidelines (OECD/EU), with the following results:

Ames test:	No mutagenic activity under the given test conditions
Chromosomal aberrations:	No clastogenic activity under the given test conditions
90-day oral toxicity on rats:	The No Observed Adverse Effect Level (NOAEL) is 606 mg

TOS/kg bw/day, which is the highest dose in the study.

Evaluating the safety of microbial enzyme preparations used in food processing: update for a new century. Regulatory Toxicology and Pharmacology 33:173-186.

Opinion of the Scientific Committee on a request from EFSA on the Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. The EFSA Journal 587, 1-16. https://www.epa.gov/sites/production/files/2015-09/documents/fra009.pdf.

In short, the food enzyme, object of the present dossier, was subjected to several toxicological studies to confirm its safety for consumers. The mutagenicity studies supported that the food enzyme does not have the potential to damage the genetic material of living organisms, including mammals. The oral toxicity study showed that the food enzyme does not exhibit signs of toxicity, up to doses that are several thousand times higher than those which are consumed via food.

(iii) Epidemiological and/or clinical studies and special considerations: Not applicable

(iv) Other data: None

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The food enzyme Auqualysin complies with the JECFA specifications for chemical and microbiological purity of food enzymes (FAO/WHO Monographs 3, 2006) and with the French purity criteria of enzymes (AR 19/10/2006). Neither the production strain nor antibiotic resistance genes are present in the final product. Moreover, no presence of biologically active DNA has been shown.

The Aqualysin 1 described in this dossier is manufactured in accordance with current Good Manufacturing Practice for Food (GMP) and the principals of Hazard Analysis of Critical Control Points (HACCP) and in line with Food Hygiene Regulation (EC) No 852/2004 and Regulation (EC) No 178/2002.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Aqualysin 1 from *B. subtilis* is a protein used at very low dosage. Therefore, it has no nutritional impact on the final baked products. The food enzyme is denatured during baking. As other food proteins, the enzyme may be hydrolyzed into its constitutive amino acids. Products of the protease hydrolysis are natural constituents of the cereals based foods and no anti nutritional effects could result of the degradation of proteins by the protease food enzyme. Use of Aqualysin 1 from *B. subtilis* in food (e.g. baking applications) doesn't alter the nutritional composition nor modify nutritional value of foodstuffs.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

The food enzyme object of this dossier is typically used in the manufacturing of bakery products such as, but not limited to, bread, biscuits, steamed bread, cakes, pancakes, tortillas, wafers and waffles.

Based on the maximum recommended use level for the enzyme per raw material (flour) and the average amount of flour used for baking, the maximum level of TOS in the final food will be 151.58 mg TOS/ kg food.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

The total Theoretical Maximum Daily Intake (TMDI) can be calculated on basis of the maximal values found in baked foods, multiplied by the maximum consumption of baked foods/kg body weight/day. Based on the recommended use levels, the amounts of the respective ingredients that end up in the final foods and the amount of produce consumed by the high end consumers, the TMDI of the food enzyme Aqualysin 1 from *B. subtilis* was calculated to be 622.9 pg TOS/kg body weight/day.

It should be stressed that this Total TMDI is based on conservative assumptions and represents a highly exaggerated value.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA.

As soon as required.

Annex 2

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Inulinase from *Aspergillus ficuum* produced by *Aspergillus oryzae,* strain MUCL 44346
Question(s) to be answered by JECFA	Safety evaluation when used as a processing aid

1. Proposal for inclusion submitted by:

The Belgian Federal Public Service for Health, Food Chain Safety and Environment Place Victor Horta 40 box 10 1060 Brussels/Sint-Gillis Belgium
E-mail: apf.food@health.belgium.be

2. Name of substance; trade name(s); chemical name(s):

Name: Inulinase from *Aspergillus ficuum* produced by *A. oryzae,* strain MUCL 44346

IUBMBname: EC3.2.1.7

Tradename: Oligofruct'ase (Main commercial name)

Chemical names: Inulase; indoinulinase; endo-inulinase; exoinulinase; 2,1-ß-D-fructan fructanohydrolase

3. Names and addresses of basic producers

Puratos NV- site Beldem Rue Bourrie 12 B-5300 Andenne Belgium

Tel. no: +32 8582 3250 Fax no: 32 8582 3260

4. Has the manufacturer made a commitment to provide data?

Puratos NV commits to provide data to support the proposal for the inclusion of Inulinase *from A. ficuum* produced by *A. oryzae* in the list of substances to be evaluated by the JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Name: Puratos NV
Address: Industrialaan 25
Postal code and City: B-1702 Groot-Bijgaarden
Country: Belgium
Tel no.: +32 2481 4444
Fax no. +32 2466 2581
Contact Person: Bas Verhagen
Email: BVerhagen@puratos.com

6. Justification for use:

The food enzyme catalyses the hydrolysis of inulin to produce fructo-oligosaccharides.

In principle, the enzymatic conversion of inulin with the help of inulinase may be used in the processing of all food raw materials which naturally contain inulin.

The food enzyme object of this dossier is typically used in the following food manufacturing processes:

- production of fructo-oligosaccharides

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s)

The enzyme preparation is used as a processing aid during production of fructo-oligosaccharides. The effect of the enzymatic conversion with the help of inulinase is the hydrolysis of (2^1)-ß-D- fructosidic linkages in inulin to produce fructo-oligosaccharides (FOS). This FOS is a quite pure product which can be used as sweetener to replace sucrose or as dietary fibre. The food enzyme is denatured during the FOS processing.

Food enzyme preparations are used by food manufacturers according to the *Quantum Satis* principle, which means that food manufacturers will typically fine-tune the enzyme dosage based on a dose range recommended by the enzyme supplier. The recommended dose ranges for this inulase is 1000-2750 IU per kg raw material (Inulin).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

The use in food of the inulinase from *A. ficuum* produced *A. oryzae* is officially approved in France and the USA.

Moreover, the enzyme is legally traded and the use in food is legal in many countries worldwide, including in the EU.

Finally, a new dossier has also been submitted in the EU under Regulation (EC) No 1332/2008, and is currently under review by the EFSA.

9. List of data available (please check, if available)

Toxicological data

A. oryzae is used since nearly 500 years in Japan to produce "Koji". The Koji is one of the basis of the traditional foods in this country. JECFA recommends testing food enzymes derived from fungal origin for the presence of the secondary metabolites. Based on the JECFA recommendations, already since decades a wide variety of food enzymes from *Aspergillus* sp. have been tested for their safety as well as presence of potential unsafe secondary metabolites. *A. oryzae* does not produce aflatoxins, as was confirmed by the absence of mycotoxins in production batches.

The US EPA has exempted *A. oryzae* from review by the Agency, due to its extensive history of safe use. Due to difficulty with the identification of *A. oryzae* and the possibility of some strains to produce certain mycotoxins, *A. oryzae* does not qualify for general QPS status by the EFSA. The EFSA does recognize that *A oryzae* has a long history of safe use, both in food outside Europe, and for enzyme / protein production.

(i) Metabolic and pharmacokinetic studies: Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

The food enzyme has been subjected to a standard package of toxicological tests in line with internationally accepted guidelines (OECD/EU), with the following results:

Ames test:	No mutagenic activity under the given test conditions
Chromosome aberration test:	No clastogenic activity under the given test conditions
90-day oral toxicity on rats:	The No Observed Adverse Effect Level (NOAEL) is 189.65 mg

TOS/kg bw/day, which is the highest dose in the study.

In short, the food enzyme object of the present dossier was subjected to several toxicological studies to confirm its safety for consumers. The mutagenicity studies supported that the food enzyme does not have the potential to damage the genetic material of living organisms, including mammals. The oral toxicity study showed that the food enzyme does not exhibit signs of toxicity, up to doses that are thousand times higher than those which are consumed via food.

(iii) Epidemiological and/or clinical studies and special considerations: Not applicable

(iv) Other data: None

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The food enzyme inulinase complies with the internationally accepted JECFA specifications for chemical and microbiological purity of food enzymes (FAO/WHO Monographs 3, 2006). Neither the production strain nor antibiotic resistance genes are present in the final product. Moreover, no presence of biologically active DNA has been shown.

The inulinase described in this dossier is manufactured in accordance with current Good Manufacturing Practice for Food (GMP) and the principals of Hazard Analysis of Critical Control Points (HACCP) and in line with Food Hygiene Regulation (EC) No 852/2004 and Regulation (EC) No 178/2002.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Inulinase from *A. oryzae* is a protein used at very low dosage. Therefore, it has no nutritional impact on final products. The food enzyme is denatured during processing. As other food proteins, the enzyme may be hydrolyzed into its constitutive amino acids. The reaction product of the hydrolysis of inulin with the help of endo-inulinase is a syrup of FOS. Like the substrate and the enzyme, the FOS also naturally occur in various organisms, including fruits. The use of inulinase from *A. oryzae* in the creation of FOS doesn't additionally alter the nutritional composition nor modify nutritional value of the final foods in which this FOS is used.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

The food enzyme object of this dossier is typically used in the production of fructo- oligosaccharides.

Based on the maximum recommended use level for the enzyme per raw material (inulin), the maximum level of TOS in the FOS will be 20.86 mg TOS/ kg food.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

The total Theoretical Maximum Daily Intake (TMDI) can be calculated on basis of the maximal values found in foods, multiplied by the maximum consumption of foods/kg body weight/day. Based on the recommended use levels, the amounts of the respective ingredients (FOS) that end up in the final foods (e.g. confectionary, fine bakery ware) and the amount of the wide range of possible foodstuffs with FOS consumed by the high end consumers, the TMDI of the food enzyme inulinase from *A. oryzae* was calculated to be 0.0069 mg TOS/kg body weight/day.

It should be stressed that this total TMDI is based on conservative assumptions and represents a highly exaggerated value.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA.

As soon as required.

Annex 3

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Endo-1,4-ß-xylanase from *Bacillus subtilis* produced by *B. subtilis* LMG S-28356
Question(s) to be answered by JECFA	Safety evaluation when used as a processing aid

1. Proposal for inclusion submitted by:

The Belgian Federal Public Service Health, Food Chain Safety and Environment Place Victor Horta 40 box 10 1060 Brussels/Sint-Gillis Belgium

E-mail: apf.food@health.belgium.be

2. Name of substance; trade name(s); chemical name(s):

Name: Endo-1,4-ß-xylanase from *B. subtilis* produced by *B. subtilis* strain LMG S-28356

IUBMB name: EC3.2.1.8

Tradename: Bel'Ase B210 / Premix X-600 (Main commercial names)

chemical names: 4-ß-D-xylan xylanohydrolase; endo-(1-4)-ß-xylan 4-xylanohydrolase; endo-(1^4)- β-xylan 4-xylanohydrolase; endo-1,4-xylanase; xylanase; ß-1,4-xylanase: endo-1,4- xylanase; endo-ß-1,4-xylanase; endo-1,4-ß-D-xylanase; 1,4-ß-xylan xylanohydrolase; β-xylanase; ß-1,4-xylan xylanohydrolase; endo-1,4-ß-xylanase; β-D-xylanase

3. Names and addresses of basic producers

Puratos NV- site Beldem Rue Bourrie 12 B-5300 Andenne Belgium

Tel. no: +32 8582 3250 Fax no: +32 8582 3260

4. Has the manufacturer made a commitment to provide data?

Puratos NV commits to provide data to support the proposal for the inclusion of Endo-1,4-ß-xylanase in the list of substances to be evaluated by the JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Name: Puratos NV
Address: Industrialaan 25
Postal code and City: B-1702 Groot-Bijgaarden
Country: Belgium
Tel no.: +32 2481 4444
Fax no. +32 2466 2581
Contact Person: Bas Verhagen
Email: BVerhagen@puratos.com

6. Justification for use:

The food enzyme catalyses, i.e. accelerates, the conversion of substrate arabinoxylan into products arabinoxylan oligosaccharides.

The transformation of substrate arabinoxylans provides the following benefits, of interest during the production of bakery products:

- Facilitate the handling of the dough
- Improve the dough's structure and behaviour during the baking step
- Ensure a uniform volume and an improved crumb structure of the bakery product
- Reduce batter viscosity
- reduce losses of dough (less stickiness of dough)

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s)

The enzyme preparation is used as a processing aid during production of bakery products. The food enzyme is denatured during the baking process. Therefore it cannot have any technological function anymore in final baked foods.

Food enzyme preparations are used by food manufacturers according to the *Quantum Satis* principle, which means that food manufacturers will typically fine-tune the enzyme dosage based on a dose range recommended by the enzyme supplier. The recommended dose ranges for this xylanase in baking processes is 2.1-31.5 IU per kg raw material (flour).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

The use in food of the Endo-1,4-ß-xylanase from *B. subtilis* produced by *B. subtilis* is officially approved in France; Canada; China; Brazil; Mexico; Australia; Japan.

Moreover, the enzyme is legally traded and the use in food is legal in many countries worldwide, including in the EU.

A new dossier has also been submitted in the EU under Regulation (EC) No 1332/2008, and is currently under review by the EFSA.

Finally, the enzyme endo-1,4-ß-xylanase from *B. subtilis* has also been approved in the EU for the use as feed additive under the trade name Belfeed B1100 MP/ML.

9. List of data available (please check, if available)

Toxicological data

This *B. subtilis* strains is from a safe lineage that has been tested according to the criteria laid out in Pariza and Johnson (2001[1]). The safety of *B. subtilis* as a production microorganism has been assessed by EFSA (2007[2]) and has been accorded Qualified Presumption of Safety (QPS) status. A review of the literature by the US EPA (1997[3]) failed to reveal the production of metabolites of toxicological concern by *B. subtilis.* Nonetheless, to comply with the various regulatory requirements in different countries, several toxicity experiments have been performed.

(i) Metabolic and pharmacokinetic studies: Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

The food enzyme has been subjected to a standard package of toxicological tests in line with internationally accepted guidelines (OECD/EU), with the following results:

Ames test: No mutagenic activity under the given test conditions

Chromosomal aberrations: No clastogenic activity under the given test conditions

Evaluating the safety of microbial enzyme preparations used in food processing: update for a new century. Regulatory Toxicology and Pharmacology 33:173-186.

Opinion of the Scientific Committee on a request from EFSA on the Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. The EFSA Journal 587, 1-16. https://www.epa.gov/sites/production/files/2015-09/documents/fra009.pdf.

Bone marrow micronucleus test: No cytogenetic adverse effects reported under the given

test conditions

90-day oral toxicity on rats: The No Observed Adverse Effect Level (NOAEL) is 140 mg

TOS/kg bw/day, which is the highest dose in the study.

In short, the food enzyme object of the present dossier was subjected to several toxicological studies to confirm its safety for consumers. The mutagenicity studies supported that the food enzyme does not have the potential to damage the genetic material of living organisms, including mammals. The oral toxicity study showed that the food enzyme does not exhibit signs of toxicity, up to doses that are thousand times higher than those which are consumed via food.

(iii) Epidemiological and/or clinical studies and special considerations: Not applicable

(iv) Other data: None

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The food enzyme xylanase complies with the internationally accepted JECFA specifications for chemical and microbiological purity of food enzymes (FAO/WHO Monographs 3, 2006) and with the French purity criteria of enzymes (AR 19/10/2006). Neither the production strain nor antibiotic resistance genes are present in the final product. Moreover, the no presence of biologically active DNA has been shown.

The endo-1,4-ß-xylanase described in this dossier is manufactured in accordance with current Good Manufacturing Practice for Food (GMP) and the principals of Hazard Analysis of Critical Control Points (HACCP) and in line with Food Hygiene Regulation (EC) No 852/2004 and Regulation (EC) No 178/2002.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Endo-1,4-ß-xylanase from *B. subtilis* is a protein used at very low dosage. Therefore, it has no nutritional impact on final baked products. The food enzyme is denatured during baking. As other food proteins, the enzyme may be hydrolyzed into its constitutive amino acids. Products of the xylanase hydrolysis are natural constituents of the cereals based foods and no anti nutritional effects could result of the degradation of (arabino)xylans by xylanase food enzyme. Use of endo- 1,4-ß-xylanase from *B. subtilis* in food (baking applications) doesn't alter the nutritional composition nor modify nutritional value of foodstuffs.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

The food enzyme object of this dossier is typically used in the manufacturing of bakery products such as, but not limited to, bread, biscuits, steamed bread, cakes, pancakes, tortillas, wafers and waffles.

Based on the maximum recommended use level for the enzyme per raw material (flour) and the average amount of flour used for baking, the maximum level of TOS in the final food will be 0.143 mg TOS/ kg food.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

The total Theoretical Maximum Daily Intake (TMDI) can be calculated on basis of the maximal values found in baked foods, multiplied by the maximum consumption of baked foods/kg body weight/day. Based on the recommended use levels, the amounts of the respective ingredients that end up in the final foods and the amount of produce consumed by the high end consumers, the TMDI of the food enzyme endo-1,4-ß-xylanase from *B. subtilis* was calculated to be 0.59 µg TOS/kg body weight/day.

It should be stressed that this total TMDI is based on conservative assumptions and represents a highly exaggerated value.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA.

As soon as required.

Annex 4

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Endo-1,4-ß-xylanase from *Pseudoalteromonas haloplanktis* produced by *B. subtilis,* strain LMG S-24584
Question(s) to be answered by JECFA	Safety evaluation when used as a processing aid

1. Proposal for inclusion submitted by:

The Belgian Federal Public Service for Health, Food Chain Safety and Environment Place Victor Horta 40 box 10 1060 Brussels/Sint-Gillis Belgium

E-mail: apf.food@health.belgium.be

2. Name of substance; trade name(s); chemical name(s):

Name: Endo-1,4-ß-xylanase from *P. haloplanktis* produced by *B. subtilis,* strain LMG S-24584

IUBMB name: EC3.2.1.8

Tradename: Bel'Ase B218 / Premix X-608 (Main commercial names)

chemical names: 4-ß-D-xylan xylanohydrolase; endo-(1-4)-ß-xylan 4-xylanohydrolase; endo-(1^4)- β- xylan 4-xylanohydrolase; endo-1,4-xylanase; xylanase; ß-1,4-xylanase: endo-1,4- xylanase; endo-ß-1,4-xylanase; endo-1,4-ß-D-xylanase; 1,4-ß-xylan xylanohydrolase; β-xylanase; ß-1,4-xylan xylanohydrolase; endo-1,4-ß-xylanase; β-D-xylanase

3. Names and addresses of basic producers

Puratos NV- site Beldem
Rue Bourrie 12 B-5300 Andenne Belgium
Tel. no: +32 8582 3250 Fax no: +32 8582 3260

4. Has the manufacturer made a commitment to provide data?

Puratos NV commits to provide data to support the proposal for the inclusion of Endo-1,4-ß-xylanase from *P. haloplanktis* produced by *B. subtilis,* strain LMG S-24584 in the list of substances to be evaluated by the JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Name: Puratos NV
Address: Industrialaan 25
Postal code and City: B-1702 Groot-Bijgaarden
Country: Belgium
Tel no.: +32 2481 4444
Fax no. +32 2466 2581
Contact Person: Bas Verhagen
Email: BVerhagen@puratos.com

6. Justification for use:

The food enzyme catalyses, i.e. accelerates, the conversion of substrate arabinoxylan into products arabinoxylan oligosaccharides.

The transformation of substrate arabinoxylans provides the following benefits, of interest during the production of bakery products. :

- Facilitate the handling of the dough
- Improve the dough's structure and behaviour during the baking step
- Ensure a uniform volume and an improved crumb structure of the bakery product
- Reduce batter viscosity

- reduce losses of dough (less stickiness of dough)

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s)

The enzyme preparation is used as a processing aid during production of bakery products. The food enzyme is denatured during the baking process. Therefore it cannot have any technological function anymore in final baked foods

Food enzyme preparations are used by food manufacturers according to the ***Quantum Satis*** principle, which means that food manufacturers will typically fine-tune the enzyme dosage based on a dose range recommended by the enzyme supplier. The recommended dose ranges in baking processes is 10-150 GDXU per kg raw material (flour).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

The use in food of the Endo-1,4-ß-xylanase from *P. haloplanktis* produced by *B. subtilis* is officially approved in France, Brazil, Canada and the USA.

Moreover, the enzyme is legally traded and the use in food is legal in many countries worldwide, including in the EU.

Finally, a new dossier has also been submitted in the EU under Regulation (EC) No 1332/2008, and is currently under review by the EFSA.

9. List of data available (please check, if available)

Toxicological data

The *B. subtilis* production strain is from a safe lineage that has been tested according to the criteria laid out in Pariza and Johnson (2001[1]). The safety of *B. subtilis* as a production microorganism has been assessed by EFSA (2007[2]) and has been accorded Qualified Presumption of Safety (QPS) status. A review of the literature by the US EPA (1997[3]) failed to reveal the production of metabolites of toxicological concern by *B. subtilis.* Nonetheless, to comply with the various regulatory requirements in different countries, several toxicity experiments have been performed.

(i) Metabolic and pharmacokinetic studies Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

The food enzyme has been subjected to a standard package of toxicological tests in line with internationally accepted guidelines (OECD/EU), with the following results:

Ames test: No mutagenic activity under the given test conditions

Chromosomal aberrations: No clastogenic activity under the given test conditions

Evaluating the safety of microbial enzyme preparations used in food processing: update for a new century. Regulatory Toxicology and Pharmacology 33:173-186.

Opinion of the Scientific Committee on a request from EFSA on the Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. The EFSA Journal 587, 1-16. https://www.epa.gov/sites/production/files/2015-09/documents/fra009.pdf.

90-day oral toxicity on rats: The No Observed Adverse Effect Level (NOAEL) is 13.94 mg

TOS/kg bw/day, which is the highest dose in the study.

In short, the food enzyme, object of the present dossier, was subjected to several toxicological studies to confirm its safety for consumers. The mutagenicity studies supported that the food enzyme does not have the potential to damage the genetic material of living organisms, including mammals. The oral toxicity study showed that the food enzyme does not exhibit signs of toxicity, up to doses that are several thousand times higher than those which are consumed via food.

(iii) Epidemiological and/or clinical studies and special considerations: Not applicable

(iv) Other data: None

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The food enzyme xylanase complies with the internationally accepted JECFA specifications for chemical and microbiological purity of food enzymes (FAO/WHO Monographs 3, 2006) and with the French purity criteria of enzymes (AR 19/10/2006). Neither the production strain nor antibiotic resistance genes are present in the final product. Moreover, no presence of biologically active DNA has been shown.

The endo-1,4-ß-xylanase described in this dossier is manufactured in accordance with current Good Manufacturing Practice for Food (GMP) and the principals of Hazard Analysis of Critical Control Points (HACCP) and in line with Food Hygiene Regulation (EC) No 852/2004 and Regulation (EC) No 178/2002.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Endo-1,4-ß-xylanase from *B. subtilis* is a protein used at very low dosage. Therefore, it has no nutritional impact on the final baked products. The food enzyme is denatured during baking. As other food proteins, the enzyme may be hydrolyzed into its constitutive amino acids. Products of the xylanase hydrolysis are natural constituents of the cereals based foods and no anti nutritional effects could result of the degradation of (arabino)xylans by xylanase food enzyme. Use of endo- 1,4-ß-xylanase from *B. subtilis* in food (baking applications) doesn't alter nutritional composition nor modify nutritional value of foodstuffs.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

The food enzyme object of this dossier is typically used in the manufacturing of bakery products such as, but not limited to, bread, biscuits, steamed bread, cakes, pancakes, tortillas, wafers and waffles.

Based on the maximum recommended use level for the enzyme per raw material (flour) and the average amount of flour used for baking, the maximum level of TOS in the final food will be 1.15 mg TOS/ kg food.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

The total Theoretical Maximum Daily Intake (TMDI) can be calculated on basis of the maximal values found in baked foods, multiplied by the maximum consumption of baked foods/kg body weight/day. Based on the recommended use levels, the amounts of the respective ingredients that end up in the final foods and the amount of produce consumed by the high end consumers, the TMDI of the food enzyme endo-1,4-ß-xylanase from *B. subtilis* was calculated to be 47 µ§ TOS/kg body weight/day.

It should be stressed that this Total TMDI is based on conservative assumptions and represents a highly exaggerated value.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA.

As soon as required.

Annex 5

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Endo-1,4-ß-xylanase from *Thermotoga maritima* produced by *B. subtilis,* strain LMG S-27588
Question(s) to be answered by JECFA	Safety evaluation when used as a processing aid

1. Proposal for inclusion submitted by:

The Belgian Federal Public Service Health, Food Chain Safety and Environment Place Victor Horta 40 box 10 1060 Brussels/Sint-Gillis Belgium

E-mail: apf.food@health.belgium.be

2. Name of substance; trade name(s); chemical name(s):

Name: Endo-1,4-ß-xylanase from *T. maritima* produced by *B. subtilis,* strain LMG S-27588

IUBMB name: EC3.2.1.8

Tradename: Anubis (Main commercial name)

chemical names: 4-ß-D-xylan xylanohydrolase; endo-(1-4)-ß-xylan 4-xylanohydrolase; endo-(1^4)- β-xylan 4-xylanohydrolase; endo-1,4-xylanase; xylanase; ß-1,4-xylanase: endo-1,4- xylanase; endo-ß-1,4-xylanase; endo-1,4-ß-D-xylanase; 1,4-ß-xylan xylanohydrolase; β-xylanase; ß-1,4-xylan xylanohydrolase; endo-1,4-ß-xylanase; β-D-xylanase

3. Names and addresses of basic producers

Puratos NV- site Beldem Rue Bourrie 12 B-5300 Andenne BelgiumTel. no: +32 8582 3250 Fax no: +32 8582 3260

4. Has the manufacturer made a commitment to provide data?

Puratos NV commits to provide data to support the proposal for the inclusion of Endo-1,4-ß-xylanase from *T. maritima* produced by *B. subtilis,* strain LMG S-27588 in the list of substances to be evaluated by the JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Name: Puratos NV
Address: Industrialaan 25
Postal code and City: B-1702 Groot-Bijgaarden
Country: Belgium
Tel no.: +32 2481 4444
Fax no. +32 2466 2581
Contact Person: Bas Verhagen
Email: BVerhagen@puratos.com

6. Justification for use:

The food enzyme catalyses, i.e. accelerates, the conversion of substrate arabinoxylan into products arabinoxylan oligosaccharides.

The transformation of substrate arabinoxylans provides the following benefits, of interest during the production of bakery products:

- Facilitate the handling of the dough
- Improve the dough's structure and behaviour during the baking step
- Ensure a uniform volume and an improved crumb structure of the bakery product
- Reduce batter viscosity
- Reduce losses of dough (less stickiness of dough)

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s)

The enzyme preparation is used as a processing aid during production of bakery products. The food enzyme is denatured during the baking process. Therefore it cannot have any technological function anymore in final baked foods.

Food enzyme preparations are used by food manufacturers according to the *Quantum Satis* principle, which means that food manufacturers will typically fine-tune the enzyme dosage based on a dose range recommended by the enzyme supplier. The recommended dose ranges for this xylanase in baking processes is 10 - 800 ADXU per kg raw material (flour).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

The use in food of the endo-1,4-ß-xylanase from *T. maritima* produced by B. subtilis is officially approved in France.

Moreover, the enzyme is legally traded and the use in food is legal in many countries worldwide, including in the EU.

Finally, a new dossier has also been submitted in the EU under Regulation (EC) No 1332/2008, and is currently under review by the EFSA.

The enzyme endo-1,4-ß-xylanase from *B. subtilis* is currently also being assessed by the EFSA as part of the approval request in the EU for the use as feed additive under the trade name Beltherm MP/ML.

9. List of data available (please check, if available)

Toxicological data

This *B. subtilis* strains is from a safe lineage that has been tested according to the criteria laid out in Pariza and Johnson (2001[1]). The safety of *B. subtilis* as a production microorganism has been assessed by EFSA (2007[2]) and has been accorded Qualified Presumption of Safety (QPS) status. A review of the literature by the US EPA (1997[3]) failed to reveal the production of metabolites of toxicological concern by *B. subtilis.* Nonetheless, to comply with the various regulatory requirements in different countries, several toxicity experiments have been performed.

(i) Metabolic and pharmacokinetic studies Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

Evaluating the safety of microbial enzyme preparations used in food processing: update for a new century. Regulatory Toxicology and Pharmacology 33:173-186.

Opinion of the Scientific Committee on a request from EFSA on the Introduction of a Qualified Presumption of Safety (QPS) approach for assessment ofselected microorganisms referredto EFSA. The EFSA Journal 587, 1-16. https://www.epa.gov/sites/production/files/2015-09/documents/fra009.pdf.

The food enzyme has been subjected to a standard package of toxicological tests in line with internationally accepted guidelines (OECD/EU), with the following results:

Ames test:	No mutagenic activity under the given test conditions
In vitro micronucleus test:	No clastogenic activity under the given test conditions
90-day oral toxicity on rats:	The No Observed Adverse Effect Level (NOAEL) is 139.38 mg

TOS/kg bw/day, which is the highest dose in the study.

In short, the food enzyme object of the present dossier was subjected to several toxicological studies to confirm its safety for consumers. The mutagenicity studies supported that the food enzyme does not have the potential to damage the genetic material of living organisms, including mammals. The oral toxicity study showed that the food enzyme does not exhibit signs of toxicity, up to doses that are thousand times higher than those which are consumed via food.

(iii) Epidemiological and/or clinical studies and special considerations: Not applicable

(iv) Other data: None

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The food enzyme xylanase complies with the JECFA specifications for chemical and microbiological purity of food enzymes (FAO/WHO Monographs 3, 2006). Neither the production strain nor antibiotic resistance genes are present in the final product. Moreover, no presence of biologically active DNA has been shown.

The endo-1,4-ß-xylanase described in this dossier is manufactured in accordance with current Good Manufacturing Practice for Food (GMP) and the principals of Hazard Analysis of Critical Control Points (HACCP) and in line with Food Hygiene Regulation (EC) No 852/2004 and Regulation (EC) No 178/2002.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Endo-1,4-ß-xylanase from *B. subtilis* is a protein used at very low dosage. Therefore, it has no nutritional impact on final baked products. The food enzyme is denatured during baking. As other food proteins, the enzyme may be hydrolyzed into its constitutive amino acids. Products of the xylanase hydrolysis are natural constituents of the cereals based foods and no anti nutritional effects could result of the degradation of (arabino)xylans by xylanase food enzyme. Use of endo- 1,4-ß-xylanase from *B. subtilis* in food (baking applications) doesn't alter the nutritional composition nor modify nutritional value of foodstuffs.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

The food enzyme object of this dossier is typically used in the manufacturing of bakery products such as, but not limited to, bread, biscuits, steamed bread, cakes, pancakes, tortillas, wafers and waffles.

Based on the maximum recommended use level for the enzyme per raw material (flour) and the average amount of flour used for baking, the maximum level of TOS in the final food will be 23.23 mg TOS/ kg food.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

The total Theoretical Maximum Daily Intake (TMDI) can be calculated on basis of the maximal values found in baked foods, multiplied by the maximum consumption of baked foods/kg body weight/day. Based on the recommended use levels, the amounts of the respective ingredients that end up in the final foods and the amount of produce consumed by the high end consumers, the TMDI of the food enzyme endo-1,4-ß-xylanase from *B. subtilis* was calculated to be 0.095 mg TOS/kg body weight/day.

It should be stressed that this total TMDI is based on conservative assumptions and represents a highly exaggerated value.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA.

As soon as required.

Annex 6

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	*INS 445iii, GLYCEROL ESTER OF WOOD ROSIN (GEWR)*
Question(s) to be answered by JECFA *(Provide a brief justification of the request in case of re-evaluations)*	Request for a revision of specifications for INS 445(iii) GEWR The purpose is to revise the applicable specifications which restrict the source material (aged pinus stump(s)) to only two pinus species (*Pinus palustris* and *Pinus elliottii*). Such restriction was not laid down in the definition of the specifications for GEWR prior to 2011 and it could be considered as trade restrictive taking into account that there are over 175 species of pine trees worldwide and that some others than *Pinus palustris* and *Pinus elliottii* are also suitable for rosin production (e.g. *Pinus halepensis*). The intention is to demonstrate a chemical equivalence between GEWR produced from *Pinus palustris* and *Pinus elliottii* and from other pinus species (Resinas 8WR).

1. Proposal for inclusion submitted by:

Hellenic Food Authority EFETL. Kifisias 124 & Iatridou 2

115 26 Athens, Greece

2. Name of substance; trade name(s); chemical name(s):

Substance : Glycerol Ester of Wood Rosin

Trade name : Resinas 8WR;

Chemical Name : Rosin acids; esters with glycerol

CAS 8050-30-4

3. Name and address of basic producer: (wood rosin feedstock producer)

Megara Resins- Anastasios Fanis S.A.38th km New National Road Athens-Corinth
191 00 Megara, Greece

Name and address of basic manufacturer: ("glycerol esters of wood rosins"-Resinas 8WR) Resinas Sinteticas León Tolstoi 18, suite 101, Col. Anzúres, Mexico City.

4. Has the manufacturer made a commitment to provide data?

Yes, Resinas Sinteticas (T&R Chemicals) commits to provide data to support its request.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Resinas Sinteticas León Tolstoi 18, suite 101, Col. Anzúres, Mexico City.
T&R Chemicals, Inc. 700 Celum Road Clint, Texas 79836 USA
Contact : Vasilios Fotopoulos (vasilios@trchemicals.com) 1-915-202-6783

6. Justification for use:

The request relates to the revision of specifications which does not have any impact on the justification for the use of INS 445(iii) as currently recognized. INS 445(iii) acts as an emulsifier and a stabilizer, e.g. by (i) increasing the density of non-alcoholic flavored beverages so as to maintain uniform suspension in the end products; (ii) adding desirable degree of cloudiness to finished beverages, and (iii) improving stability of finished non-alcoholic beverages.

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

The use of INS 445(iii) is in the GSFA recognized in the following categories:

04.1.1.2 Surface-treated fresh fruit at 110 mg/kg

04.2.1.2 Surface-treated fresh vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), seaweeds, and nuts and seeds at 110 mg/kg

14.1.4 Water-based flavoured drinks, including "sport," "energy," or "electrolyte" drinks and particulated drinks at 150 mg/kg

The request for the revision of specifications does not have any impact on the currently permitted uses.

8. Is the substance currently used in food that is legally traded in more than one country? or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

YES

Glycerol esters of wood rosins is a food additive authorized for use in the European Union (see Annex II to Regulation (EC) No 1333/2008) under the E-number 445. The applicable EU specifications (Regulation (EU) No 231/2012) refer to “aged pine stumps” without specifying any concrete species of pine trees as a source for wood rosin extraction.

E 445 is mainly used as an emulsifier and stabilizer in non-alcoholic flavored cloudy drinks. It can also be used as an emulsifier and stabilizer in cloudy spirit drinks and flavored cloudy alcoholic drinks containing less than 15% of alcohol (up to 100 mg/l). Other uses are for the surface treatment of citrus fruit (up to 50 mg/kg) and for printing on personalized and/or promotional hard-coated confectionery products (up to 320 mg/kg).

Glycerol esters of wood rosins are permitted for use also in other countries (to our knowledge e.g. in Canada, China, Mexico, South Africa and the USA).

9. List of data available:

Toxicological data

JECFA assessed GEWR (INS 445(iii)) in 2013 and allocated an ADI of 0-25 mg/kg bw.

Chemical equivalence is sought between Resins 8WR- glycerol esters of wood rosins derived from other pine species and GEWR (INS 445-iii) as specified in the current JECFA specification (2013) which restrict the source material to *Pinus palustris* (longleaf) and *Pinus elliottii* (slash) species.

Preliminary technical (IR Spectrum) tests conducted on JECFA specified (GEWR) and Resinas 8WR-“glycerol esters of wood rosins” indicate the “monograph” similarities between the two compounds.

Technological data

a. Submission of the certificate of analysis for wood rosin supplied by the Greek company ‘Megara Resins Anastasios Fanis SA’

b. Submission of the preliminary test (Technical Service Bulletin) of comparative analysis of Resina 8WR (GLYCEROL ESTERS WOOD ROSINS) to JECFA specified (GLYCEROL ESTER WOOD ROSIN).

10. Date on which data could be submitted to JECFA.

Final results of the chemical equivalency studies between the two test materials should be available by the date of the CCFA49 meeting.

Analytical Lab, conducting the chemical equivalence studies, is GLP and ISO 17025 certified.

Calorie Control Council (CCC)

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Steviol Glycosides
Question(s) to be answered by JECFA *(Provide a brief justification of the request in case of re-evaluations)*	To prepare a stand-alone JECFA specification monograph for rebaudioside M that is manufactured by fermentation using 2 nonpathogenic and nontoxigenic strains of yeast from the Saccharomycetaceae family or alternatively to broaden the current fermentation derived JECFA specification for rebaudioside A produced from Multiple gene donors expressed in *Yarrowia Lipolytica* (2016)

1. Proposal for inclusion submitted by:

The Calorie Control Council

2. Name of substance; trade name(s); chemical name(s):

Rebaudioside M (Chemical name:13-[(2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy]kaur-16-en-18-oic acid,2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-β-D-glucopyranosyl ester)

3. Names and addresses of basic producers:

Blue California
30111 Tomas
Rancho Santa Margarita, CA
U.S.A. 92688

4. Has the manufacturer made a commitment to provide data?

Yes

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Katharina Pueller
Project Manager
Blue California
30111 Tomas
Rancho Santa Margarita, CA
U.S.A. 92688

The Producer is represented by

Ashley Roberts, Ph.D.
Intertek Scientific & Regulatory Consultancy
www.intertek.com
E-mail: ashley.roberts@intertek.com
Tel: +1 905-542-2900; Fax: +1 905-542-1011
Skype: ashley.roberts.intertek
2233 Argentia Road, Suite 201
Mississauga, Ontario Canada L5N 2X7

6. Justification for use:

An amendment to the JECFA specification is justified based on the commercial availability of rebaudioside M, manufactured using a novel fermentation process. Rebaudioside M was included within the 2016 JECFA evaluation and incorporated within the 2016 JECFA specification.

Blue California's manufacturing process for its high purity Rebaudioside M preparation uses 2 nonpathogenic and nontoxigenic strains of yeast from the Saccharomycetaceae family. This strain was originally isolated from harvested plant material, cultured, and studied extensively by other groups. This microorganism is genetically modified to contain several enzymes that carry out multiple steps of glucose addition to naturally occurring steviol glycosides, eventually converting them to Rebaudioside M. These related genes are part of the yeast genome, so there are no vectors needed for this process. The microorganism is a unicellular yeast that is widely used in the biotechnology industry, it can be commonly found in nature, and can grow in a simple, inexpensive medium. Its morphological, physiological, and growth conditions have been widely studied and reported.

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

The existing provision of food products, food categories, and use levels previously adopted for steviol glycosides should apply as the proposal is to only amend the specification for steviol glycosides to include the genetically modified novel fermentation process. A few of these categories are highlighted below. For a complete listing of all food products, food categories and use levels, please see the GSFA for steviol glycosides.

Category	Maximum Use Level (as steviol equivalents)
Non-alcoholic, water-based flavored drinks	200 ppm
Confectionary, with no added sugar	700ppm
Jams, or jellies, energy reduced	360 ppm
Chewing gum	3,500 ppm
Sauces	350 ppm
Yogurt	0 m

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

In the United States, Reb M produced using a novel fermentation process is considered Generally Recognized as Safe (GRAS) and has been US FDA notified (GRN 667).

Rebaudioside M extracted from the stevia plant has undergone prior safety evaluations by JECFA, EFSA, FSANZ, Health Canada and the FDA and is currently marketed internationally.

9. List of data available (please check, if available)

Toxicological data

The toxicology data to support this application are available and can be provided upon request. Briefly, the data supporting the safety of steviol glycosides including Rebaudioside M are corroborated through a similar metabolism profile for all steviol glycosides and a thorough toxicological evaluation. The safety has previously been endorsed by the JECFA and other International regulatory agencies.

Technological data

Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce).

The current specification for steviol glycosides was prepared at the 82nd JECFA (2016) and published in FAO JECFA Monographs 19 (2016).

Technological and nutritional considerations relating to the manufacture and use of the listed substance.

The additive steviol glycosides are of principal interest for its sweetening properties. Steviol glycosides are known to have a solubility ranging between "freely to slightly soluble in water" rather than only "freely soluble in water". The sweetening potency of Rebaudioside M is approximately 350x sweeter than sucrose. Rebaudioside M is also thermally and hydrolytically stable for use in a variety of foods, including acidic beverages, under normal conditions of processing and storage.

Intake assessment data

(i) Levels of Rebaudioside M will be used in a range of foods based on technological function.

The proposed changes are for the specifications only. There are no changes to the food categories/use levels in the GSFA.

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

Since no changes in the categories or use levels for steviol glycosides are being requested, the dietary intake assessment outcome assessed in 2016 is still considered appropriate.

10. Date on which data could be submitted to JECFA.

December 2017.

The International Council of Beverages Associations (ICBA)

ICBA[1]/ has available substantial new evidence that warrants a JECFA re-review of benzoates. ICBA requests that the Codex Committee on Food Additives (CCFA) re-prioritize benzoates for JECFA re-review based upon actual brand-specific use level information, brand-specific market volume data allowing for quantitative market-weighted intake estimates reflective of actual consumer practices in key markets. In addition, a literature review of rodent and human clinical data is available that may support refinement of chemical-specific adjustment factors for benzoates leading to an adjustment to the ADI for benzoates.

The new data supplied by ICBA will allow JECFA to perform a highly refined intake assessment for benzoates in food category 14.1.4 based on the guidelines provided in Chapter 6 "Dietary Exposure Assessment of Chemicals in Food" of the WHO Principles and methods for the risk assessment of chemicals in food (EHC 240, 2009). The intake assessment performed by ICBA (along with the data) that will be included - and is currently available - was performed according to the guidance provided in EHC 240.

Name of Substance(s)	Benzoic Acid and Its Salts
Question(s) to be answered by JECFA *(Provide a brief justification of the request in case of re-evaluation)*	ICBA is seeking a JECFA re-review not only based on a refined exposure assessment reflective of actual consumer practices but also on toxicological considerations. The requested re-review for exposure is for food category 14.1.4. specifically. The new data consist of: • Highly refined intake assessment reflective of actual uses weighted according to market volume data to ensure quantitative representativeness for corresponding beverage types, and • Human clinical data on sodium benzoates demonstrating similar pharmacokinetics between humans and rats, supporting an adjustment to the chemical-specific adjustment factors for benzoates, and, consequently to the ADI. The refined intake assessment approach: • Leverages individual record data, which provide the most precise estimates of food consumption; • Assigns benzoate concentration levels only to the proportion of the beverage market in which that additive is used and not to consumption data for the whole food category; • Considers brand loyalty in the context of market share data; • Considered the 95th percentile "consumers only" in the brand-loyal scenario across subpopulations even though for chronic dietary exposure estimates - based on 1 or 2 days of food consumption data per individual - the 90th percentile of dietary exposure for "consumers only" often represents the high consumer; • Utilized the selected individual foods approach as dietary exposure to benzoates is predominantly influenced by water-based flavored drinks; • Ensures model accuracy which depends on food consumption data and food chemical concentration data being applied to the same food product(s); • Selected representative national populations as the "worst-case scenario" markets to ensure adequate consumer protection for the international situation.

1. Proposal for inclusion submitted by:

Katherine Loatman, Executive Director (1 202.321.3085)

International Council of Beverages Associations

[1]/ The International Council of Beverages Associations (ICBA) represents the interests of the worldwide non-alcoholic beverage industry. ICBA members include national and regional beverage associations and international beverage companies that operate in more than 200 countries and territories and produce, distribute and sell a variety of non-alcoholic sparkling (carbonated) and still (non-carbonated) beverages including soft drinks, sports drinks, energy drinks, bottled waters, flavored and/or enhanced waters, ready-to-drink teas and coffees, 100% fruit or vegetable juices, nectars and juice drinks, and dairy-based beverages.

E-mail: Kate@icba-net.org

2. Name of substance; trade name(s); chemical name(s):

Substance: Benzoic acid and its salts

Trade Name: N/A

Chemical Name(s):

Benzoic acid, benzenecarboxylic acid, phenylcarboxylic acid (CAS number 65-85-0)

Sodium benzoate, sodium salt of benzenecarboxylic acid, sodium salt of phenylcarboxylic acid (CAS number 532-32-1)

Potassium benzoate, potassium salt of benzenecarboxylic acid, potassium salt of phenylcarboxylic acid (CAS number 582-25-2 (anhydrous))

3. Names and addresses of basic producers:

Manufacturers may be contacted through Katherine Loatman of ICBA.

4. Has the manufacturer made a commitment to provide data?

The International Council of Beverages Associations (ICBA) on behalf of the beverage industry already has the detailed intake assessment data with confidential brand-specific use level information and quantitative brand-specific market volume data readily available for sharing. Moreover, the investigation into chemical-specific adjustment factors relative to the Acceptable Daily Intake (ADI) is complete and available.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Dietary Intake Assessment:

Ashley Roberts, Ph.D. (ashley.roberts@intertek.com, 905-542-2900)

Intertek Scientific & Regulatory Consultancy

2233 Argentia Road, Suite 201

Mississauga, Ontario, Canada

L5N 2X7

www.intertek.com

Chemical-Specific Adjustment Factors:

Julie E. Goodman, Ph.D., DABT, FACE, ATS, Principal (JGoodman@gradientcorp.com, 617-395-5525)

Gradient

20 University Road

Cambridge, MA 02138

6. Justification for use:

The use of benzoates is advantageous in beverage products and technologically justified to ensure preservation of beverage quality, enhanced beverage shelf-life and reduction in yeast, molds and bacterial growth.

Intrinsic, extrinsic and process-related factors affect susceptibility of water-based flavored drinks to microbial growth. In commercial practice, water-based flavored drinks may spoil and are rendered unappealing or unpalatable by the growth of various fungi and acid tolerant bacteria. Microbiological activity can occur in “still” and “sparkling” (carbonated) beverages, as well as in concentrates. In order to prevent undesirable microbiologically induced changes, manufacturers rely on sophisticated preservation systems including the appropriate use of antimicrobials such as benzoic acid or its salts (benzoates).

The need for benzoates is determined by beverage matrix, processing, packaging and storage conditions and the ubiquitous microflora of the environment, containers and ingredients. As pH increases, the active form of benzoates in beverages decreases resulting in higher minimum inhibitory concentrations (MIC) to have the same functionality. A beverage with pH 4.3 and 500 ppm of benzoic acid has approximately the same amount of undissociated benzoic acid (active form) as a beverage at pH 3.5 with 250 ppm of benzoic acid.

Sodium (and potassium) benzoates are usually preferred for use in beverages due to greater solubility than benzoic acid. When used, benzoates maintain the quality, stability and integrity of beverages as part of a multi-component multi-hurdle preservative system. Benzoates often are effective against organisms that are

otherwise somewhat tolerant to other antimicrobial agents and vice versa. For example, certain spoilage microorganisms of industrial significance (e.g., *Glocunobacter* spp. and certain *Aspergillus* spp.) are quite resistant to sorbate, thus limiting sorbates' value as a drop-in substitute preservative for benzoates.

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

14.1.4 Water-based flavoured drinks, including "sport," "energy," or "electrolyte" drinks and particulated drinks

14.1.4.3 Concentrates (liquid or solid) for water-based flavoured drinks

Maximum use of benzoates at a level of 250 mg/kg as benzoic acid as consumed in food category 14.1.4 with footnote Note 127 "On the served to the consumer basis" and an additional footnote that reads "Except for use in beverages with pH greater than 3.5 at 500 mg/kg as consumed".
Maximum use of benzoates at a level of 500 mg/kg as benzoic acid as consumed in food category 14.1.4.3 with footnote Note 127 "On the served to the consumer basis".

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies).

Australia, Brazil, Canada, China, European Union, India, Iran, Japan, Mexico, New Zealand, Philippines, South Africa, South Korea, Thailand, United States of America, etc.

9. List of data available (please check, if available) (Highlighted in Yellow)

Toxicological data

(i) Metabolic and pharmacokinetic studies – X - YES

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

(iii) Epidemiological and/or clinical studies and special considerations

(iv) Other data

X -Literature review of benzoate-related chemical specific adjustment factors

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

X (brand-specific for identified beverage types in Brazil, Canada, Mexico and U.S.A.)

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

X (based on WHO's individual food approach - please see ICBA comments in response to CCFA 49th Agenda Item 5(a) General Standard for Food Additives (GSFA): … provisions for benzoates in FC 14.1.4. … - CX/FA 17/49/7 Appendix 3.)

Other information (as necessary/identified)

X – Brand-specific market volume data to seek quantitative "representativeness" weighting for levels utilized in the assessment.

10. Date on which data could be submitted to JECFA.

Available now. March 20, 2017.

European Food Emulsifiers Manufacturers Association (EFEMA)

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Citric and Fatty Acid Esters of Glycerol (INS 472 c)
Question(s) to be answered by JECFA (Provide a brief justification of the request in case of re-evaluations)	Revision of the specifications (Change of neutralization agents in the definition)

1. Proposal for inclusion submitted by:

EFEMA, European Food Emulsifiers Manufacturers Association

2. Name of substance; trade name(s); chemical name(s):

Citric and Fatty Acid Esters of Glycerol (INS 472 c), also known as “CITREM”.

3. Names and addresses of basic producers:

BASF Personal Care and Nutrition GmbH
Robert-Hansen-Strasse 1
89257 Illertissen
Germany

DuPont Nutrition & Health
Danisco A/S | Edwin Rahrs Vej 38|
DK-8220 Brabrand
Denmark

Palsgaard
Palsgaardvej 10,
7130 Juelsminde
Denmark

4. Has the manufacturer made a commitment to provide data?

Yes

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

The EFEMA contact is Ms Caroline Rey, Secretary General
Avenue de Tervueren 13A
1040 Brussels
Belgium
Email : efema@ecco-eu.com

6. Justification for use:

The JECFA Monograph (2014) for INS 472 c defines this additive as *“Obtained by esterification of glycerol with citric acid and edible fatty acids, or by reaction of a mixture of mono- and diglycerides of edible fatty acid, with citric acid; consists of mixed esters of citric acid and edible fatty acids with glycerol; may contain minor parts of free fatty acids, free glycerol, free citric acid and mono- and diglycerides; may be wholly or partially neutralized with sodium hydroxide or potassium hydroxide (as declared on the label)”.*

Substances other than sodium hydroxide and potassium hydroxide have shown to be efficient for the purpose of the neutralisation of INS 472c. EFEMA therefore suggest updating the part of the JECFA definition dealing with the neutralization agents. In the addition of the listed bases, some milder salts of Sodium, Potassium and Calcium salts have shown to be efficient as neutralization agent. EFEMA therefore suggest to broaden the list of neutralizing agents to *“may be partially or wholly neutralised with sodium, potassium or calcium salts suitable for the purpose and recognized as food additives by Codex Standard 192-1995”.*

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

CITREM is listed as Antioxidant, Emulsifier, Flour treatment agent, Sequestrant and Stabilizer in Table 3 of the General Standard for Food Additives (GSFA) and as such may be used in a number of food categories under the conditions of good manufacturing practices (GMP) as outlined in the Preamble of the GSFA.

CITREM could also be used in heat-treated butter milk of food category 01.1.1 and spices of food category 12.2.1. It is acceptable in foods conforming to the following commodity standards: CS 117-1981.

Furthermore, CITREM can also be used in a number of categories that are mentioned in the Annex to Table 3 (see below):

GSFA Provisions for Citric and fatty acid esters of glycerol

Number	Food Category	Max Level	Notes
14.1.5	Coffee, coffee substitutes, tea, herbal infusions, and other hot cereal and grain beverages, excluding cocoa	GMP	Note 160
13.2	Complementary foods for infants and young children	5,000 mg/kg	Note 239 Note 268
09.2.4.1	Cooked fish and fish products	GMP	Note 241
01.2.1.2	Fermented milks (plain), heat-treated after fermentation	GMP	Note 234
04.2.2.7	Fermented vegetable (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera) and seaweed products, excluding fermented soybean products of food categories 06.8.6, 06.8.7, 12.9.1, 12.9.2.1 and 12.9.2.3	GMP	
08.1.2	Fresh meat, poultry, and game, comminuted	GMP	Note 281
08.1.1	Fresh meat, poultry, and game, whole pieces or cuts	GMP	Note 16 Note 326
09.1.2	Fresh mollusks, crustaceans, and echinoderms	GMP	Note 305 Note 304
06.4.1	Fresh pastas and noodles and like products	GMP	Note 211
09.2.4.3	Fried fish and fish products, including mollusks, crustaceans, and echinoderms	GMP	Note 41
09.2.2	Frozen battered fish, fish fillets, and fish products, including mollusks, crustaceans, and echinoderms	GMP	Note 16 Note 29
09.2.1	Frozen fish, fish fillets, and fish products, including mollusks, crustaceans, and echinoderms	GMP	Note 29
09.2.3	Frozen minced and creamed fish products, including mollusks, crustaceans, and echinoderms	GMP	Note 16
13.1	Infant formulae, follow-up formulae, and formulae for special medical purposes for infants	9,000 mg/kg	Note 381 Note 380
02.1.3	Lard, tallow, fish oil, and other animal fats	100 mg/kg	Note 322
11.4	Other sugars and syrups (e.g. xylose, maple syrup, sugar toppings)	GMP	Note 258
01.4.1	Pasteurized cream (plain)	GMP	Note 236
01.2.2	Renneted milk (plain)	GMP	
12.1.2	Salt Substitutes	GMP	
09.2.5	Smoked, dried, fermented, and/or salted fish and fish products, including mollusks, crustaceans, and echinoderms	GMP	Note 300
01.4.2	Sterilized and UHT creams, whipping and whipped creams, and reduced fat creams (plain)	GMP	
02.1.2	Vegetable oils and fats	100 mg/kg	Note 277

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

CITREM is legally used and traded in the European Union under the following E number: E 472 c.

9. List of data available (please check, if available)

Toxicological data

An ADI 'not limited' was established at the 17th JECFA (1973). The latest version of the JECFA specifications for CITREM is available at the following link: http://www.fao.org/fileadmin/user_upload/jecfa_additives/docs/monograph16/additive-136-m16.pdf

http://www.fao.org/documents/card/en/c/a6fe72dc-82fb-437c-81cc-bc4d739043a5/

(i) Metabolic and pharmacokinetic studies

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

(iii) Epidemiological and/or clinical studies and special considerations

(iv) Other data

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

The JECFA specifications for CITREM are available at the following link:
http://www.fao.org/documents/card/en/c/a6fe72dc-82fb-437c-81cc-bc4d739043a5/

Technological and nutritional considerations relating to the manufacture and use of the listed substance

EFEMA members would only use neutralizing salts that has obtained a positive JECFA evaluation.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

An ADI 'not limited' was established at the 17th JECFA (1973).

Other information (as necessary/identified)

EFEMA would also like to refer to the European Regulation 231/2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council[1], which describes Citric and Fatty Acid Esters of Glycerol as *"Esters of glycerol with citric acid and fatty acids occurring in food oils and fats. They may contain small amounts of free glycerol, free fatty acids, free citric acid and free glycerides. They may be partially or wholly neutralised with sodium, potassium or calcium salts suitable for the purpose and authorised as food additives according to this Regulation".*

10. Date on which data could be submitted to JECFA.

Immediately.

International Organization of the Flavor Industry (IOFI)

This is in response to the CL 2016/13-FA (May 2016): Request for information and comments on the priority list of substances proposed for evaluation by JECFA. On behalf of the International Organization of the Flavor Industry (IOFI), we provide the following comments for consideration at the forthcoming 49th Session of the Codex Committee on Food Additives.

IOFI respectfully requests the addition of 70 flavours to the JECFA Priority List, which include 3 new flavours, 27 flavors that were included on the JECFA Priority List at previous CCFA sessions, 1 material for re-evaluation due to substantial new data since its original evaluation and 39 flavors for which JECFA has requested additional information in order to complete its evaluation. The required information for the flavours as requested in Annex 2 of CL 2016/13-FA is attached as Annex2_2016CCFA49. The flavours in appendix II are sorted by Chemical Group and indicate whether they are new submissions, submissions from previous CCFA session (with session noted), or flavors that JECFA requested additional information to complete its safety evaluation by the Procedure.

Annex 2

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	See Appendix II for list of proposed substances
Question(s) to be answered by JECFA (Provide a brief justification of the request in case of re-evaluations)	Are these substances of no safety concern at the current levels of exposure?

1. Proposal for inclusion submitted by:

The International Organization of the Flavor Industry

2. Name of substance; trade name(s); chemical name(s):

List of 70 flavours (See Appendix II for list of chemical names)

[1] See http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:083:0001:0295:EN:PDF

3. Names and addresses of basic producers:

International Organization of the Flavor Industry (IOFI). Flavor producers are members of the International Organization of the Flavor Industry (IOFI). All contacts can be made through IOFI.

4. Has the manufacturer made a commitment to provide data?

Yes

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

International Organization of the Flavor Industry (IOFI)
Brussels, Belgium
Sean V. Taylor, Ph.D. (Science Director)
1101 17th Street NW
Suite 700
Washington, DC 20036
P: 202-293-5800
staylor@vertosolutions.net

6. Justification for use:

Flavouring ingredients in foods for human consumption

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

Natural occurrence, Food Categories and Use Levels to be submitted.

8. Is the substance currently used in food that is legally traded in more than one country (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

Yes (United Sates, European Union, Latin America and Japan)

9. List of data available (please check, if available)

Toxicological data

(i) Metabolic and pharmacokinetic studies Yes

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies Yes

(iii) Epidemiological and/or clinical studies and special considerations Yes

(iv) Other data Yes, where relevant.

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce) Yes

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance Yes, where relevant

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used Yes

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used. Yes

Other information (as necessary/identified)

10. Date on which data could be submitted to JECFA.

December 01, 2017

Appendix II

Appendix II - Priority list of 70 flavors proposed for inclusion on the JECFA Priority List to be considered at the 49th session of the Codex Committee on Food Additives

CCFA listing History	FEMA No	JECFA No	CAS	Principle Name	Group No	TRS No
	MISCELLANEOUS NITROGEN-CONTAINING SUBSTANCES				J56	TRS 934 TRS 952 TRS 974 TRS 990
Submitted at 48th CCFA	4798		902136-79-2	2-(((3-(2,3-Dimethoxyphenyl)-1*H*-1,2,4-triazol-5-yl)thio)methyl)pyridine		
Submitted at 48th CCFA	4802		1469426-64-9	(*S*)-1-(3-(((4-amino-2,2-dioxido-1*H*-benzo[c][1,2,6]thiadiazin-5-yl)oxy)methyl)piperidin-1-yl)-3-methylbutan-1-one		
Submitted at 48th CCFA	4809		1374760-95-8	2-(4-Methylphenoxy)-*N*-(1*H*-pyrazol-3-yl)-*N*-(thiophen-2-ylmethyl)acetamide		
	ALLYL ESTERS				J03	TRS 868
Submitted at 43rd CCFA	4074		6321-45-5	Allyl valerate		
Submitted at 43rd CCFA	4072		20474-93-5	Allyl crotonate		
	SATURATED ALIPHATIC ACYCLIC LINEAR PRIMARY ALCOHOLS, ALDEHYDES, AND ACIDS				J04	TRS 884
Submitted at 43rd CCFA	4432		591-11-7	(+/-) Acetaldehyde ethyl isopropyl acetal		
Submitted at 43rd CCFA	4335			Tridecanal		
Submitted at 43rd CCFA	4528		57743-63-2	Acetaldehyde ethyl isobutyl acetal		
Submitted at 43rd CCFA	4336		5617-64-1	Tridecanoic acid		
Submitted at 43rd CCFA	4527		851670-40-1	Acetaldehyde di-isobutylacetal		
Submitted at 45th CCFA	4688		851669-60-8	1-Dipropoxyethane		
Submitted at 43rd CCFA	4334		125187-30-6	Pentadecanoic acid		
Submitted at 43rd CCFA	4010		123-63-7	Paraldehyde		

	SATURATED ALIPHATIC ACYCLIC BRANCHED-CHAIN PRIMARY ALCOHOLS, ALDEHYDES, AND ACIDS				J05	TRS 884
Submitted at 48th CCFA	4795		127793-88-8	(±)-8-Methyldecanal		
Submitted at 48th CCFA	4803		3085-26-5	8-Methylnonanal		
	LINEAR AND BRANCHED-CHAIN ALIPHATIC, UNSATURATED, UNCONJUGATED ALCOHOLS, ALDEHYDES, ACIDS, AND RELATED ESTERS				J14	TRS 891
Submitted at 48th CCFA	4787		63196-63-4	*trans*-6-Octenal		
Submitted at 48th CCFA	4789		4234-93-9	2,6-Dimethyl-5-heptenol		
	CARVONE AND STRUCTURALLY RELATED SUBSTANCES				J16	TRS 891
Submitted at 43rd CCFA	4525		929116-08-5	Pinocarvyl isobutyrate		
Submitted at 43rd CCFA	4515		929222-96-8	Carvyl palmitate		
Submitted at 43rd CCFA	4523		51200-86-3	6-Hydroxycarvone		
	MENTHOL AND STRUCTURALLY RELATED SUBSTANCES				J19	TRS 891 TRS 952
Submitted at 43rd CCFA	4509		2230-90-2	Menthyl formate		
Submitted at 43rd CCFA	4510		86014-82-6	Menthyl propionate		
Submitted at 43rd CCFA	4524		68366-64-3	l-Menthyl butyrate		
Submitted at 45th CCFA	4729		3623-52-7	dl-Isomenthol		
Submitted at 43rd CCFA	4604		406179-71-3	Dimenthyl glutarate		
Submitted at 45th CCFA	4718		28804-53-7	(±)2-[(2-p-Menthoxy)ethoxy]ethanol		
	MALTOL AND RELATED SUBSTANCES				J52	TRS 934
Submitted at 43rd CCFA	4534		852997-28-5	Ethyl maltol isobutyrate		
	ALICYCLIC PRIMARY ALCOHOLS, ALDEHYDES, ACIDS AND RELATED ESTERS (RE-EVALUATION)				J32	TRS 913 TRS 960
New Submission	4783		1049017-63-1; 1049017-68-6	Mixture of 1-Vinyl-3-cyclohexenecarbaldehyde and 4-Vinyl-1-cyclohexenecarbaldehyde		

New Submission	4790		10138-32-6	(±)-Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, ethyl ester		
New Submission	4776		198404-98-7	(1-Methyl-2-(1,2,2-trimethylbicyclo[3.1.0]hex-3-ylmethyl)cyclopropyl)methanol		
Old	3557	973	2111-75-3	*p*-Mentha-1,8-dien-7-al (Perillaldehyde)		
	FURAN SUBSTITUTED ALIPHATIC HYDROCARBONS, ALCOHOLS, ALDEHYDES, KETONES, CARBOXYLIC ACIDS AND RELATED ESTERS, SULFIDES, DISULFIDES AND ETHERS.(RE-EVALUATION)				J53	TRS 934 TRS 952 TRS 974
Old	3317	1491	3777-69-3	2-Pentylfuran		
Old	3401	1492	3777-71-7	2-Heptylfuran		
Old	4090	1493	83469-85-6	2-Decylfuran		
Old	4174	1494	15186-51-3	3-Methyl-2-(3-methylbut-2-enyl)-furan		
Old	2494	1497	623-30-3	3-(2-Furyl)acrolein		
Old	4175	1499	5555-90-8	3-(5-Methyl-2-furyl)prop-2-enal		
Old	3163	1503	1192-62-7	2-Furyl methyl ketone		
Old	3609	1504	1193-79-9	2-Acetyl-5-methylfuran		
Old	4071	1505	22940-86-9	2-Acetyl-3,5-dimethylfuran		
Old	4083	1507	4208-57-5	2-Butyrylfuran		
Old	2496	1508	6975-60-6	(2-Furyl)-2-propanone		
Old	4192	1509	3194-17-0	2-Pentanoylfuran		
Old	4120	1510	699-17-2	1-(2-Furyl)butan-3-one		
Old	2495	1511	623-15-4	4-(2-Furyl)-3-buten-2-one		
Old	2435	1513	10031-90-0	Ethyl 3-(2-furyl)propanoate		
Old	2198	1514	105-01-1	Isobutyl 3-(2-furan)propionate		
Old	2071	1515	7779-67-1	Isoamyl 3-(2-furan)propionate		
Old	2070	1516	7779-66-0	Isoamyl 4-(2-furan)butyrate		
Old	2865	1517	7149-32-8	Phenethyl 2-furoate		
Old	3159	1520	13679-46-4	Furfuryl methyl ether		
Old	4114	1521	6270-56-0	Ethyl furfuryl ether		
Old	3337	1522	4437-22-3	Difurfuryl ether		
Old	4034	1523	55764-22-2	2,5-Dimethyl-3-furanthiol acetate		
Old	4119	1524	109537-55-5	Furfuryl 2-methyl-3-furyl disulfide		
Old	4056	1525	61295-44-1	3-[(2-Methyl-3-furyl)thio]-2-butanone		
Old	4043	1526	376595-42-5	*O*-Ethyl S-(2-furylmethyl)thiocarbonate		
Old	3535	1495	3782-00-1	2,3-Dimethylbenzofuran		
Old	4095	1496	64280-32-6	2,4-Difurfurylfuran		
Old	2704	1498	874-66-8	2-Methyl-3(2-furyl)acrolein		
Old	3307	1500	31704-80-0	3-(5-Methyl-2-furyl)-butanal		

Old	2492	1501	770-27-4	2-Furfurylidene-butyraldehyde		
Old	3586	1502	65545-81-5	2-Phenyl-3-(2-furyl)prop-2-enal		
Old	3391	1506	10599-70-9	3-Acetyl-2,5-dimethylfuran		
Old	3418	1512	14360-50-0	Pentyl 2-furyl ketone		
Old	2945	1518	623-22-3	Propyl 2-furanacrylate		
Old	3970	1519	114099-96-6	2,5-Dimethyl-3-oxo-(2H)-fur-4-yl butyrate		
Old	4541	2103	53282-12-5	(*E*)-Ethyl 3-(2-furyl)acrylate		
Old	4540	2104	1197-40-6	di-2-Furylmethane		
Old	4543	2105	4265-25-2	2-Methylbenzofuran		

Annex 3 - Priority list of compounds proposed for specifications modification by JECFA Priority List to be considered at the 49th session of the Codex Committee on Food Additives

History	FEMA No	JECFA No	CAS	Principle Name	Most recent Specification Evaluation	Status
Old	4709	2123	38837-70-60	Glutamyl-valyl-glycine	82nd JECFA	Full
Old	3748	433	59259-38-0	l-Menthyl lactate	55th JECFA	Full

Natural Food Colours Association (NATCOL)

FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	Lutein from *Tagetes erecta*
Question(s) to be answered by JECFA *(Provide a brief justification of the request in case of re-evaluations)*	Request I: JECFA is asked to consider extension of the acceptable daily intake (ADI) "*not specified*" for "Lutein esters from *Tagetes erecta*" to "Lutein from *Tagetes erecta*" Justification: "Lutein from *Tagetes erecta*" was evaluated by JECFA at the 63rd meeting (2004) and the Committee agreed on an ADI of 0 – 2 mg/kg bw which was also applicable to zeaxanthin (*WHO TRS 928*). Lutein esters from *Tagetes erecta* were evaluated by JECFA at the 79th meeting (2014) which established a temporary ADI "not specified" and considered establishing a group ADI "not specified" for lutein esters from *Tagetes erecta* that would include lutein from *Tagetes erecta* and synthetic zeaxanthin and related xanthophylls (*WHO TRS 990*). At its 82nd meeting (2016) the Committee removed the temporary designation from the ADI for "Lutein esters from *Tagetes erecta*" but was not able to consider this aspect in detail at this Committee session and recommended that this be taken up at a future meeting (*WHO TRS 1000*). As lutein and lutein esters are toxicologically equivalent and shall be listed in the same GSFA food categories at the same levels (when calculated as lutein), it is considered a matter of urgency that JECFA address this issue identified by the JECFA Committee itself with high priority. The Association and the basic producer are willing to support the process with a corresponding submission. Request II: JECFA is asked to revise the specification for "Lutein from *Tagetes erecta*" with respect to the item "Melting range" Justification: The current item "melting range" was derived from a limited number of batches in an early phase of product development and needs to be revised reflecting the commercial product. We note that JECFA in its 82nd meeting (2016, WHO TRS 1000) revised the specification for lutein esters and removed the "melting range" (see also FAO JECFA Monographs 19 Compendium of Food Additive Specifications (2016)).

1. Proposal for inclusion submitted by: NATCOL (Natural Food Colours Association)

2. Name of substance; trade name(s); chemical name(s): LUTEIN from TAGETES ERECTA

3. Names and addresses of basic producers:

DSM Nutritional Products Europe Ltd, PO Box 2676, 4002 Basel, Switzerland

4. Has the manufacturer made a commitment to provide data? Yes

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Dirk Cremer
DSM Nutritional Products Europe Ltd.
Wurmisweg 576, Building 242/2, 4303 Kaiseraugst, Switzerland

6. Justification for use:

Colour, nutrient supplement; no changes to previous evaluation by the 63rd JECFA in 2004.

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

See Appendix extracted from FA/48 INF/01 - Table One (pages 123-125).

8. Is the substance currently used in food that is legally traded in more than one country? (please identify the countries); or, has the substance been approved for use in food in one or more country? (please identify the country(ies))

According to our knowledge, lutein is presently used as both, nutrient and food colour. There is reported trade in lutein, among others, in the following countries:

USA, Canada, Mexico, Argentina, Columbia, Ecuador, Russia, Germany, UK, France, Netherlands, Bulgaria, Spain, Portugal, China, Japan, Philippines, Malaysia, Australia, New Zealand, India, South Africa.

Explicit regulatory information is available to the applicant which document that lutein is a permitted food/food supplement ingredient in USA, Canada, China, European Union Member States, Australia, and other jurisdictions.

9. List of data available (please check, if available)

Toxicological data

(i) Metabolic and pharmacokinetic studies

Not applicable

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

Not applicable

(iii) Epidemiological and/or clinical studies and special considerations

Not applicable

(iv) Other data

Expert report on a single group ADI “not specified” for “Lutein esters from *Tagetes erecta*” and “Lutein from *Tagetes erecta*”

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

Scientific/technical and analytical data as appropriate which discuss the relevance of the item “melting range” for the product characterization.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

Not applicable

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

Available (see also Appendix)

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

Available

Other information (as necessary/identified)

10. Date on which data could be submitted to JECFA.

December 2017

Appendix (FA/48 INF/01 - Table One (pages 123-125))

LUTEIN FROM TAGETES ERECTA

INS 161b(i) Lutein from Tagetes erecta Functional Class: Colour

FoodCatNo	FoodCategory	MaxLevel	Notes	Step	Year
01.1.2	Dairy-based drinks, flavoured and/or fermented (e.g., chocolate milk, cocoa, eggnog, drinking yoghurt, whey-based drinks)	100 mg/kg	52	4	
01.6.1	Unripened cheese	GMP		4	
01.6.2	Ripened cheese	GMP		4	
01.6.4.1	Plain processed cheese	GMP		4	
01.6.4.2	Flavoured processed cheese, including containing fruit, vegetables, meat, etc.	100 mg/kg		4	
01.6.5	Cheese analogues	GMP		4	
01.7	Dairy-based desserts (e.g., pudding, fruit or flavoured yoghurt)	150 mg/kg		4	
02.4	Fat-based desserts excluding dairy-based dessert products of food category 01.7	150 mg/kg		4	
03.0	Edible ices, including sherbet and sorbet	150 mg/kg		4	
04.1.2.5	Jams, jellies, marmelades	100 mg/kg		4	
04.1.2.7	Candied fruit	200 mg/kg		4	
04.1.2.9	Fruit-based desserts, including fruit-flavoured water-based desserts	150 mg/kg		4	
04.1.2.11	Fruit fillings for pastries	150 mg/kg		4	
04.2.2.7	Fermented vegetable (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera) and seaweed products, excluding fermented soybean products of food categories 06.8.6, 06.8.7, 12.9.1, 12.9.2.1 and 12.9.2.3	GMP		4	
05.2	Confectionery including hard and soft candy, nougats, etc. other than food categories 05.1, 05.3 and 05.4	300 mg/kg		4	
05.4	Decorations (e.g., for fine bakery wares), toppings (non-fruit) and sweet sauces	500 mg/kg		4	
06.5	Cereal and starch based desserts (e.g., rice pudding, tapioca pudding)	150 mg/kg		4	
07.2	Fine bakery wares (sweet, salty, savoury) and mixes	200 mg/kg		4	
08.1.2	Fresh meat, poultry, and game, comminuted	GMP	4 & 16	4	
08.3.1.1	Cured (including salted) non-heat treated processed comminuted meat, poultry, and game products	GMP		4	

08.4	Edible casings (e.g., sausage casings)	GMP		4
09.1.1	Fresh fish	300 mg/kg	4, 16 & 50	4
09.2.1	Frozen fish, fish fillets, and fish products, including mollusks, crustaceans, and echinoderms	500 mg/kg	95	4
09.2.4.2	Cooked mollusks, crustaceans, and echinoderms	250 mg/kg		4
09.2.5	Smoked, dried, fermented, and/or salted fish and fish products, including mollusks, crustaceans, and echinoderms	100 mg/kg	22	4
09.3.1	Fish and fish products, including mollusks, crustaceans, and echinoderms, marinated and/or in jelly	GMP		4
09.3.3	Salmon substitutes, caviar, and other fish roe products	500 mg/kg		4
10.2	Egg products	GMP		4
10.4	Egg-based desserts (e.g., custard)	150 mg/kg		4
12.2.2	Seasonings and condiments	500 mg/kg		4
12.4	Mustards	300 mg/kg		4
12.5	Soups and broths	50 mg/kg		4
12.6	Sauces and like products	500 mg/kg	92	4
13.3	Dietetic foods intended for special medical purposes (excluding products of food category 13.1)	50 mg/kg		4
13.4	Dietetic formulae for slimming purposes and weight reduction	50 mg/kg		4
13.5	Dietetic foods (e.g., supplementary foods for dietary use) excluding products of food categories 13.1 - 13.4 and 13.6	100 mg/kg		4
13.6	Food supplements	300 mg/kg		4
14.1.4	Water-based flavoured drinks, including "sport," "energy," or "electrolyte" drinks and particulated drinks	100 mg/kg		4
14.2.2	Cider and perry	200 mg/kg		4
14.2.4	Wines (other than grape)	200 mg/kg		4
14.2.7	Aromatized alcoholic beverages (e.g., beer, wine and spirituous cooler-type beverages, low alcoholic refreshers)	200 mg/kg		4
15.1	Snacks - potato, cereal, flour or starch based (from roots and tubers, pulses and legumes)	200 mg/kg		4
15.2	Processed nuts, including coated nuts and nut mixtures (with e.g., dried fruit)	100 mg/kg		4