codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 15 **CX/FAC 06/38/39**
March 2006

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES AND CONTAMINANTS

Thirty-eighth Session

The Hague, the Netherlands, 24 – 28 April 2006

PRIORITY LIST OF FOOD ADDITIVES, CONTAMINANTS AND NATURALLY OCCURRING TOXICANTS PROPOSED FOR EVALUATION BY JECFA

Comments submitted in response to Cl 2005/31-FAC by European Community, Switzerland, United States and IFAC

EUROPEAN COMMUNITY

CARRAGEENAN (INS 407)

In light of a recent opinion[1] of the European Scientific Committee on Food (SCF) the European Community and its Member States would like to request that carrageenan (INS 407) is added to the Priority List of Food Additives, Contaminants and Naturally Occurring Toxicants Proposed for Evaluation by JECFA.

In its opinion the SCF stated the following: 'In the absence of any further information on possible absorption of carrageenan by the immature gut in the very young infant, the Committee reaffirms its earlier view (SCF, 1998) that it remains inadvisable to use carrageenan in infant formula that are fed from birth, including those in the category of foods for special medical purposes. The Committee has no objection to the use of carrageenan in foods for older infants, such as follow-on milks (SCF, 1983) and weaning foods.'

This issue has been raised at meetings of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU), however this has not progressed as the list of additives in infant formula has not yet been finalised by the Committee. The European Community and its Member States consider that this it is appropriate that this issue is considered by JECFA before the Codex standard on infant formula can be revised.

SUNSET YELLOW (INS 110)

The European Community and its Member States has become aware that under certain circumstances Sudan I (1-phenylazo)-2-napthalenol) may be formed as an impurity during the production of Sunset Yellow. Sudan I is an unauthorised colour and undesired substance in food, therefore its presence in sunset yellow should be restricted. Manufacturers of sunset yellow have indicated that it is possible by varying the production conditions to restrict the formation of Sudan I to below the limit of detection (0.5 mg/kg). Within the The EC the specific purity criteria for sunset yellow is being revised to restrict the presence of this substance.

The European Community and its Member States are now formally requesting that JECFA consider amending the specifications for sunset yellow to address this issue.

[1] Opinion of the Scientific Committee on Food on Carrageenan (expressed on 5 March 2003)

SWITZERLAND

1) Switzerland has the honour to submit to you a request for the evaluation of **Cyclotetraose** by JECFA.

Please find below the information requested **in Annex II, Part A:**

1. Proposal submitted by:

   Switzerland

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

   Cyclotetraose, Cycloalternanotetraose, Cyclo ((-6)-alpha-D-glucopyranosyl-(1,3)-alpha-glucopyranosly-(1,6)-alpha-glucopyranosyl-(1,3)-alpha-glucopyranosyl-(1-))

3. Name and address of basic producer:

   Hayashibara Co. Ltd
   2-3 Shimoishii 1-Chome, 700-0907 Okayama, Japan

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

   Yes

5. Identification of the office that will be providing data (contact details):

   Bioresco Ltd.
   Food Scientific and Regulatory Services
   Bundesstrasse 29
   CH-4054 Basel, Switzerland

6. Justification for use:

   Carrier for flavours, carrier/stabiliser for PUFAs

7. Food products and food categories within the GSFA in which the compound is used, including use level(s):

   The compound is present in foods by carry-over from flavouring preparations; food supplements.

8. Has the compound been approved for use in 2 or more countries?

   May be used in Japan

9. List of data (toxicology, metabolism, specifications) available:

   Acute toxicity, Ames tests, 13-week toxicity study in rats, studies on digestibility and fermentability.

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

    31st December 2006

2) Switzerland has the honour to submit to you a request for the evaluation by JECFA of **Isoamylase from Pseudomonas amyloderamosa for use as an enzyme for starch processing**.

Please find below the information requested in **Annex II, Part A**:

1. Proposal for inclusion submitted by:

   Switzerland

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

   Isoamylase from Pseudomonas amyloderamosa

3. Name and address of basic producer:

   Hayashibara Co. Ltd, 2-3 Shimoishii 1-Chome, 700-0907 Okayama, Japan

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

Yes

5. Identification of the office that will be providing data (contact details):

   Bioresco Ltd.
   Food Scientific and Regulatory Services
   Bundesstrasse 29
   CH-4054 Basel, Switzerland

6. Justification for use:

   Debranching enzyme for use in the production of sugars and oligosaccharides from starch.

   Also used in the production process of trehalose (this use has already been evaluated by JECFA in connection with the safety assessment of trehalose).

7. Food products and food categories within the GSFA in which the compound is used, including use level(s):

   The enzyme is used as a processing aid.

8. Has the compound been approved for use in 2 or more countries?

   Yes. France and Japan

9. List of data (toxicology, metabolism, specifications) available:

   Acute toxicity, Ames tests, chromosome aberration test, 13-week toxicity study in rats.

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

    31st December 2006

3) Switzerland has the honour to submit to you a request for the **evaluation of Ligninsulfonate by JECFA**

Please find below the information requested in **Annex II, Part A**:

1. Proposal for inclusion submitted by:

   Switzerland

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

   Ligninsulfonate

3. Name and address of basic producers:

   DSM Nutritional Products Ltd, P.O. Box 3255, CH-4002 Basel, Switzerland

   Booregard Industries Ltd., N-1702 Sarpsborg P.O. Box 162, Norway

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

   Yes

5. Identification of the office that will be providing data (contact details):

   DSM Nutritional Products Ltd, Ms Karin Feltes
   Global Regulatory Affairs, Bldg 241/915
   P.O. Box 3255
   CH-4002 Basel, Switzerland

6. Justification for use:

   Use as a carrier for vitamins, carotenoids and other nutrient and additive formulations.

7. Food products and food categories within the GSFA in which the compound is used, including use level(s):

   The following list is not conclusive :

Fruit and soft drinks: 100ppm; ice-cream: 50ppm; dairy products: 150ppm;

Jelly baby: 50ppm; hard candies: 50ppm; other uses are also possible.

8. Has the compound been approved for use in 2 or more countries?

   Yes. United States of America, Bolivia (sold as an ingredient), Guatemala (sold as an ingredient), Venezuela (sold as an ingredient) and Taiwan (sold as an ingredient).

9. List of data (toxicology, metabolism, specifications) available:

   The applicant will provide a comprehensive set of data including product specification, ADME studies in rats, various safety studies (acute, sub-chronic, (28d and 90d rat oral toxicity study), genotox studies (AMES and chromosomal aberration), developmental toxicity study, sensibilisation (Local Lymph Node Assay).

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

    Monograph, intake assessment and CTA until December 2006.

4) Switzerland has the honour to submit to you a request for the **evaluation of by phytosterols/stanols and their esters JECFA**.

Please find below the information requested in **Annex II, Part A**:

1. Proposal for inclusion submitted by:

   Switzerland

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

   Phytosterols, phytostanols and their fatty acid esters.

3. Name and address of basic producers:

   Forbes Medi-Tech, Suite 200, 750 West Pender Street, Vancouver B.C, V6C 2T8, Canada

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

   Yes

5. Identification of the office that will be providing data (contact details):

   Bioresco AG, Bundesstrasse 29
   CH-4054 Basel, Switzerland

6. Justification for use:

   Nutritive substance added to food for the purpose of lowering cholesterol absorption.

7. Food products and food categories within the GSFA in which the compound is used, including use level(s):

   Use of phytosterols/phytostanols and their esters as nutritive substances to margarine-type spreads, fermented milk-type and yoghurt-type products, milk and fruit-based drinks.

8. Has the compound been approved for use in 2 or more countries?

   Yes. Switzerland, the European Union, the United States of America, Australia, New Zealand and others.

9. List of data (toxicology, metabolism, specifications) available:

   Specifications; mammalian microsome reverse mutation assay; gene mutation assay; chromosome aberration test; uterotrophic assay; sub-chronic feeding studies; double-blind, placebo-controlled human studies.

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

    31st December 2006.

UNITED STATES

1) This responds to CL 2005/31-FAC (July 2005) which requests additional comments for additions or amendments to the Priority List of Food Additives, Contaminants, and Naturally Occurring Toxicants Proposed for Evaluation by JECFA (ALINORM 05/28/12, paras. 223 and 225 and Appendix XXIX). The United States of America appreciates the opportunity to nominate Nisin to the Priority List for revision of specifications at the 38th session of the Codex Committee on Food Additives and Contaminants.

Nisin specifications published by JECFA in FNP 52 (1992) contain a definition that specifies the presence of non-fat milk solids:

> "Consists of several closely related polypeptide antibiotics produced by strains of *Streptococcus lactis*, Lancefield group N of which major component is shown below.
>
> Nisin concentrate contains not less than 900 units per mg. **In a mixture of non-fat milk solids** and a minimum sodium chloride content of 50%....."

Some nisin production processes involve the fermentation by nisin-producing strains of *Lactococcus lactis* subsp. *lactis* (formerly *Streptococcus lactis)* of hydrolyzed skimmed milk. The resulting product contains significant amounts of non-fat milk solids which can contain allergenic milk proteins.

New processes have been developed which involve fermentation by the same nisin-producing strains of *Lactococcus lactis* subsp. *lactis* on a starch- or sucrose-based medium. Milk is no longer used, so the potential presence of allergenic dairy protein is eliminated. Such products would not conform to the current JECFA specification. Accordingly, a revision of the JECFA definition for nisin will be proposed as follows:

> "Nisin concentrate contains not less than 900 units per mg in a mixture of a minimum sodium chloride content of 50% and **non-fat milk solids or other fermented solids."**

The attached Annex contains additional information for the additive as outlined in ANNEX II, Part A of the Circular Letter, the criteria of ANNEX I having been taken into account.

ANNEX

INFORMATION ON THE ADDITIVE TO BE EVALUATED BY JECFA

REVISION OF THE SPECIFICATION FOR NISIN

1. Proposal for inclusion submitted by:

   The United States of America

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

   Nisin – INS 234 (CAS RN 1414-45-5)

   Trade name - NISAPLIN

3. Names and addresses of basic producers:

   Mr J Delves-Broughton
   Danisco Beaminster Ltd
   15 North Street
   BEAMINSTER
   Dorset DT8 3DZ, UK
   Phone: +44 (0)1308 861552 Fax: +44 (0)1308 863320
   Email: joss.delves-broughton@danisco.com

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):

Pascale Parisot, Regulatory Affairs Manager
Danisco A/S
Langebrogade 1
PO Box 17
DK-1001 Copenhagen K, Denmark
Phone: +45 -32-66-22-61/ mob: +45-23-65-73-07
Fax: +45 -32-66-21-89
E mail: pascale.parisot@danisco.com

6. Justification for use:

Danisco has been the main EU manufacturer of the food preservative nisin (INS 234), sold under the name Nisaplin, for the past 50 years. Nisin is widely used to prevent food safety problems. But, use of milk-based fermentation media enables the presence of allergenic milk proteins. Production of Nisin by fermentation with other than milk solids will ensure a product free of allergenic milk proteins and make available a product more soluble than that obtained with the milk-based process. Such products, however, do not meet the current JECFA specifications. As nisin produced from milk-free fermentation media can be lawfully marketed in the United States, the proposed modification to JECFA specifications will also aid in international harmonization of food regulations.

7. Food products and food categories within the GSFA in which the additive is used, including use level(s):

NISIN (INS no. 234) Function: Preservative

(from the *Codex General Standard for Food Additives, Table 1,* for 38th CCFAC)

Food Cat. Number	**Food Category**	**Max Level (mg/kg)**	**Step**
01.0	Dairy products and analogues, excluding products of category 02.0	500	4
01.4.3	Clotted cream (plain)	10	7
01.6.1	Unripened cheese	12.5	7
01.6.2	Ripened cheese	12.5	7
01.6.3	Whey cheese	12.5	7
01.6.4	Processed cheese	250	7
01.6.5	Cheese analogues	12.5	7
01.6.6	Whey protein cheese	12.5	7
04.2.2.4	Canned or bottled (pasteurized) or retort pouch vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), and seaweeds	GMP	7
06.5	Cereal and starch based desserts (e.g., rice pudding, tapioca pudding)	3	7
07.2	Fine bakery wares (sweet, salty, savoury) and mixes	250	7
08.0	Meat and meat products, including poultry and game	500	4
10.2.1	Liquid egg products	GMP	4
12.5.1	Ready-to-eat soups and broths, including canned, bottled, and frozen	GMP	7
12.9.5	Other protein products	200	4

8. Has the compound been approved for use in 2 or more countries (please identify the countries)?

Nisin is authorized for use in the United States (21 CFR 184.1538 and GRN 000065). The specifications change also has been requested in the EU in December 2005.

9. List of data (toxicology, metabolism, specifications) available:

Data available showing that nisin from non-milk fermentation contains molecules that are already present in milk-based nisin, and has less impurities than the traditionally processed product will be provided. Consequently no new toxicology studies have been performed for the new process nisin.

JECFA specifications are available (see FAO Food and Nutrition Paper 52 (1992): Compendium of Food Additive specifications).

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

Data will be sent to JECFA once the call for data has been announced.

2) The United States of America appreciates the opportunity to nominate ethyl-N^{α}-lauroyl-L-arginate hydrochloride (Lauric arginate ethyl ester, LAE) to the Priority List for evaluation of safety and intake and elaboration of specifications at the 38th session of the Codex Committee on Food Additives and Contaminants.

The attached Annex contains additional information for the additive as outlined in ANNEX II, Part A of the Circular Letter, the criteria of ANNEX I having been taken into account.

ANNEX

INFORMATION ON THE ADDITIVE TO BE EVALUATED BY JECFA

1. Proposal for inclusion submitted by:

The United States of America

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

Chemical name: ethyl-N^{α}-lauroyl-L-arginate hydrochloride

Common and usual name: Lauric arginate

Other: Lauramide arginine ethyl ester (LAE)

3. Names and addresses of basic producers:

Laboratórios Miret, S.A. (LAMIRSA)
Polig. Industrial Can Parellada
Géminis, 4
08228 Terrassa
Barcelona, SPAIN

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):

Laboratórios Miret, S.A. (LAMIRSA)
Polig. Industrial Can Parellada
Géminis, 4
08228 Terrassa
Barcelona, SPAIN
Contact: Mr. Xavier Rocabayera
Telephone: +34 93 731 50 94
Facsimile: +34 93 783 58 87
E-mail: xrocabayera@vedeqsa.com

6. Justification for use:

Ethyl-N^{α}-lauroyl-L-arginate monohydrochloride is used in the United States as an antimicrobial preservative in a variety of foods, including meat and poultry products.

7. Food products and food categories within the GSFA in which the additive is used, including use level(s):

Ethyl-N$^{\alpha}$-lauroyl-L-arginate hydrochloride may be used in the following food products at a level of addition not to exceed 200 mg/kg:

GSFA Food Category No.	Food Description
01.6	Cheese and analogues
02.2	Fat emulsions mainly of type water-in-oil
04.1.2	Processed fruit
04.2.2	Processed vegetables
08.0	Meat and meat products
09.0	Fish and fish products
10.2	Egg products
10.4	Egg-based desserts
12.2	Herbs, spices, seasonings and condiments
12.5	Soups and broths
12.6	Sauces and like products
12.7	Salads and sandwich spreads
14.1	Non-alcoholic beverages

8. Has the compound been approved for use in 2 or more countries (please identify the countries)?

Ethyl-N$^{\alpha}$-lauroyl-L-arginate hydrochloride can be lawfully marketed and used in the U.S. as an antimicrobial preservative on a variety of foods, including meat and poultry products. The producer's agent has informed the U.S. that the additive has been approved by the Brazilian Ministry of Agriculture and is awaiting concurrence by Brazil's Ministry of Health.

9. List of data (toxicology, metabolism, specifications) available:

Specifications:

- Available for all starting materials
- Available for the article of commerce
- *In vitro* stability study

Metabolism:

- Metabolism study in the rat to determine absorption and excretion rates after a single oral dose of the additive
- Evaluation of biotransformation pathways of the additive in the rat
- Open-label metabolism study in humans after a single oral dose of the additive

Toxicology:

The additive can be used as a dry powder or dissolved in a suitable vehicle. "Mirenat-N," a solution of the additive in propylene glycol, was used in several toxicology studies.

Acute Oral Toxicity

- Acute oral toxicity of the additive in the rat

- Acute oral toxicity of Mirenat-N in the rat

Subchronic Toxicity

- 13-week dietary administration of the additive in the rat
- 13-week dietary administration of Mirenat-N in the rat

Chronic Toxicity

- 52-week dietary administration of the additive in the rat

Developmental and Reproductive Toxicity

- Embryo-fetal toxicity of the additive administered by oral gavage, in the rat
- Embryo-fetal toxicity of the additive administered by oral gavage, in the rabbit
- Two-generation reproductive performance study of the additive administered by diet, in the rat

Mutagenicity

- Bacterial mutation assay of the additive (Ames method)
- Mouse lymphoma assay of the additive
- *In vitro* mammalian chromosome aberration test of the additive using human lymphocytes
- Bacterial mutation assay of Mirenat-N (Ames method)
- Mammalian cell mutation assay of Mirenat-N
- Metaphase chromosome analysis of human lymphocytes cultured *in vitro* with Mirenat-N

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

The data are available now and can be submitted to JECFAimmediately upon request.

IFAC

The International Food Additives Council (IFAC) is an international association, representing companies who produce high quality substances used worldwide as food additives, including food grade phosphates. IFAC has Non Governmental Organization (NGO) status before Codex and is a regular participant in meetings of the Codex Committee on Food Additives and Contaminants (CCFAC).

The Summary Report for the 65th JECFA, states the specifications for Trisodium phosphate were withdrawn. We understand the Summary Report was in error and that Trisodium diphosphate is in fact the compound for which the Committee actually withdrew specifications. The JECFA Secretariat can correct the files and Trisodium Phosphate and its specifications will therefore be maintained.

On Trisodium diphosphate, anhydrous and monohydrate, tentative specifications were developed at the 61st JECFA (June 2003). The 65th JECFA report called for data by writing, reference Trisodium diphosphate, "On the method and level for loss on drying for the monohydrate is necessary in order to express the assay on the dry basis."

Since IFAC member companies have an interest in maintaining the status of TSPP, both anhydrous and the monohydrate, IFAC respectfully requests that JECFA add Trisodium diphosphate to its list Priority List, specifications only. IFAC asks that the tentative specifications developed by the 61st JECFA be reinstated and agrees to provide the information on Trisodium diphosphate as requested by the 65th JECFA and will do so, once Trisodium diphosphate is reintroduced to the JECFA Priority List and information is requested.

The final goal then is to establish specifications for Trisodium diphosphate, both the anhydrous and monohydrate, based on data already in JECFA's possession and on the monohydrate based on data to be provided by IFAC.