codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 12 **CX/FA 07/39/18-Add. 1**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Thirty-ninth Session

Beijing, China, 24-28 April 2007

PRIORITY LIST OF FOOD ADDITIVES PROPOSED FOR EVALUATION BY JECFA (IN RESPONSE TO CL 2006/41-FA)

The following comments have been received from the following Codex Members and observers: France

This document contains late submissions of comments received after the deadline, but those were submitted before 12 April 2007.

France

Proposal to include asparaginase from *Aspergillus niger* in the priority list of substances to be evaluated by JECFA

1. Proposal for inclusion submitted by:

Ministère de l'Economie, des Finances et de l'Industrie
Direction Générale de la Concurrence, de la Consommation et de la Répression des Fraudes (DGCCRF)
Bureau C2
59, Boulevard Vincent Auriol
75703 PARIS Cedex 13
FRANCE

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

Compound: *Aspergillus niger* asparaginase expressed in *Aspergillus niger*.

Trade name: Preventase™

Chemical name(s):

- Systematic name : L-asparagine amidohydrolase
- Common name : Asparaginase
- Other names : asparaginase II; L-asparaginase; colaspase; elspar; leunase; crasnitin; alpha-asparaginase
- Enzyme Commission No. : 3.5.1.1
- CAS number : 9015-68-3

3. Names and addresses of basic producers:

DSM Food Specialties
15 Rue des Comtesses
PO Box 50239
59472 SECLIN Cédex
FRANCE

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

DSM Food Specialties commits to provide data to support the proposal for inclusion of the asparaginase in the list of substances to be evaluated by JECFA.

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

DSM Food Specialties
15 Rue des Comtesses
PO Box 239
59472 Seclin Cédex
France

Attn.: Francois Strozyk
francois.strozyk@dsm.com
+33 320964514

6. Justification for use :

The asparaginase enzyme preparation is used as a processing aid during food production to convert asparagine to aspartic acid in order to reduce acrylamide formation.

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

The asparaginase enzyme preparation is intended to be used to reduce acrylamide formation during food production of L-asparagine- and carbohydrate-containing foods that are heated above 120°C, such as bread and other baked cereal-based products, baked or fried potato-based products and reaction flavors.

The commercial product, Preventase™, will be presented in two forms:

- one liquid standardized to an enzyme activity ranging from 2300 to 2600 ASPU/ml
- one granulated form standardized to an enzyme activity ranging from 9500 to 10500 ASPU/g

The dosage of Preventase™ in food production is typically less than 0.1%.

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

A US GRAS (Generally Recognized As Safe) Notification has been submitted in October 2006.

A submission of Preventase™ for approval in France has been submitted in January 2007.

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

The production organism is from a safe strain lineage as described in the article of P. van Dijck et al[1] and the decision tree in Pariza and Johnson[2]. Nevertheless, to comply with various approval requirements in different countries world-wide, a full safety program as described in the SCF Guidelines[3] has been performed:

- 14-day dose range-finding/ feasibility study with an enzyme preparation of *Aspergillus niger* containing asparaginase activity in rats.

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[1] Dijck, P.W.M. van, Selten, G.C.M., Hempenius, R.A., *On the safety of a new generation of DSM Aspergillus niger enzyme production strains*, Regulat. Toxicol. Pharmacol. 38:27-35 (2003)

[2] Pariza, M.W. and Johnson, E.A., *Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century*, Regulat. Toxicol. Pharmacol. 33:173–186 (2001)

[3] Guidelines for the presentation of data on food enzymes – *Opinion expressed on 11 April 1991* – Reports of the Scientific Committee for Food (27th series), 1992

- Repeated-dose (13-week) oral toxicity study with an enzyme preparation of *Aspergillus niger* containing asparaginase activity in rats

- Oral prenatal developmental toxicity study with an enzyme preparation of *Aspergillus niger* containing asparaginase activity in rats

- Bacterial reverse mutation test with enzyme preparation of *Aspergillus niger*.

- Chromosomal aberration test with an enzyme preparation of *Aspergillus niger* in cultured human lymphocytes.

The conclusion of the safety studies can be summarized as follows:

The enzyme preparation showed to be not mutagenic in a bacterial mutation assay (AMES test) or clastogenic in the chromosomal aberration assay with human lymphocytes in vitro. In addition the test item was evaluated in two studies with Wistar rats: a subchronic (90-day) feeding study and a prenatal developmental toxicity study. No adverse effects were observed at any level in these studies resulting in an overall No Observed Adverse Effect Level (NOAEL) of 1157 mg/kg body weight/day. This corresponds to a Margin of Safety (NOAEL/estimated daily intake) in the range of 648 - 30772.

The test material used in these studies originates from one batch which was produced by the procedure used for the commercial preparation. After the purification step, the batch was spray dried to produce the final, non-stabilised test item.

The above mentioned safety studies were all performed on a liquid asparaginase enzyme concentrate, obtained in accordance with an ordinary production procedure, omitting stabilization and standardization. Preventase™ complies with the purity criteria recommended for enzyme preparations as described in the Food Chemical Codex, 4th edition, 3rd supplement, 2001, as well as with the General Specifications and Considerations for Enzyme Preparations Used in Food Processing as laid down by the Joint FAO/WHO Expert Committee on Food Additives in 2006 (http://www.fao.org/ag/agn/jecfa-additives/search.html?lang=en)

Furthermore, it is documented that the production strain lacks the ability to produce relevant mycotoxins.

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

Before December 2007.