INFORMATION ON THE SUBSTANCE TO BE EVALUATED BY JECFA

1. ***Proposal for inclusion submitted by:***

Danish Veterinary and Food Administration.

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

Substance: Lactase from *Bifidobacterium bifidum* expressed in *Bacillus licheniformis*

Chemical name: Beta-galactosidase; CAS 9031-11-2, EC 3.2.1.23

3. ***Names and addresses of basic producers:***

Novozymes A/S
Krogshøjvej 36
DK-2880 Bagsværd
Denmark

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

Novozymes A/S commits to provide data to support the proposal for inclusion of the lactase in the list of substances to be evaluated by JECFA.

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

Novozymes A/S
Krogshøjvej 36
DK-2880 Bagsværd
Denmark

Attn.: Peter Hvass
phva@novozymes.com
+45 4446 3610

6. ***Justification for use:***

The lactase enzyme preparation is used as a processing aid during food manufacture for hydrolysis of lactose during processing of milk and other lactose containing dairy products, e.g. in order to obtain lactose-reduced milk products for lactose-intolerant individuals as well as dairy products with better consistency and increased sweetness due hydrolysis of lactose to form glucose and galactose.

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

The enzyme preparation is not added to final foodstuffs but used as a processing aid during food manufacturing. The lactase is used in processing of milk and other lactose containing food products.

The lactase is used at the minimum dosage necessary to achieve the desired enzymatic reaction. The range of dosage recommended for the lactase is up to 3500 LAU(B) per kg milk.

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

A US GRAS (Generally Recognized As Safe) notification was submitted to FDA and the agency did not question Novozymes' conclusion that the lactase enzyme preparation is GRAS under the intended conditions of use. The enzyme was approved under the trade name NS46086 in Denmark in 2015. Novozymes has also applied for approval of the enzyme in France, Mexico and Brazil. The approvals are expected in 2016.

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

Toxicological data

(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

The following food toxicity program according to the EFSA Guideline[i] has been performed:

- Test for mutagenic activity (Ames Test)
- *In vitro* micronucleus
- 13 weeks oral toxicity study in rats

The main conclusions of the safety studies can be summarized as follows:
The lactase preparation showed no mutagenic activity by testing in a bacterial reverse mutation assay (Ames Test) and did not induce micronuclei in cultured human peripheral blood lymphocytes *in vitro*.

The lactase preparation did not result in treatment-related adverse effects when administered to rats for 13 weeks, and the overall No Observed Adverse Effect Level (NOAEL) is considered to be the highest administered dose, corresponding to 672 mg TOS/kg body weight/day.

The safety studies described above were all performed on liquid lactase enzyme concentrate produced in accordance with ordinary production procedure, omitting stabilization and standardization.

Bacillus licheniformis is generally considered to be a safe production organism with a long history of safe use for food ingredients.

Technological data

(i) Specifications for the identity and purity of the listed compounds (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 compound

The lactase enzyme preparation complies with the purity criteria recommended for enzyme preparations by Food Chemicals Codex (VIII online edition, 2012). In addition to this, the enzyme preparation also conforms to the General Specifications and Considerations for Enzyme Preparations Used in Food Processing (2006) as proposed by the Joint FAO/WHO Expert Committee on Food Additives in Combined Compendium of Food Additive Specifications.

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

Method used for the dietary exposure assessment

Using EFSA Comprehensive European Food Consumption Database, the maximum average intake over 17 countries and all age groups, except infants, is 40.5 g “Milk and dairy products”/kg body weight/day.

Overall, the human exposure to the lactase will be negligible because the enzyme preparation is used as a processing aid and in low dosages. It is also supposed that the totality of the food enzyme will end up in the final food. This assumption is exaggerated since the enzyme protein and the other substances resulting from the fermentation are diluted or removed in certain processing steps.

Therefore the safety margin calculation derived from this method is highly conservative.

Theoretical Maximum Daily Intake (TMDI) calculation

The highest lactase dosage is 3500 LAU(B) per kg milk. 3500 LAU(B) correspond to 33.0 mg TOS. Based on this 40.5 g milk will maximally contain 1.34 mg TOS.

The theoretical maximum daily intake (TMDI) of the enzyme by consumers is therefore 1.34 mg TOS/kg body weight/day.

Other information as necessary

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

August 2016

[i] Guidance of EFSA prepared by the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids on the Submission of a Dossier on Food Enzymes. The EFSA Journal (2009) 1305, 1-26