

Safety Assessment of Yestimun[®] Beta-Glucans

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Novel Food Classification: *Article 1.2(d)*

Introduction

An application for the authorisation of insoluble yeast beta-glucans was submitted to the Food Safety Authority of Ireland (FSAI) by Leiber GmbH of Germany in accordance with *Article 4* of the novel food Regulation (EC) No. 258/97. The application was accepted by the FSAI on April 19th, 2016.

Beta-glucans are β -D-glucose polysaccharides that occur naturally in the cell wall of cereals, yeast, bacteria and fungi. The novel beta-glucans is derived from the cell wall of the yeast *Saccharomyces cerevisiae*, which has a long history of safe use in the production of beer and bread, and is commonly referred to as bakers' or brewers' yeast. Approximately half of the yeast cell wall mass is attributed to beta-glucans. Yestimun[®] beta-glucans is the same as the insoluble fraction of yeast beta-glucans authorised for the EU market through Commission Implementing Decision 2011/762/EU. However, because the applicant wishes to extend the possible food uses of this food ingredient, a full novel food application is required.

The novel ingredient falls under *Article 1.2(d)* of the novel food Regulation (EC) No 258/97: "Foods and food ingredients consisting of or isolated from micro-organisms, fungi or algae". In order to assess wholesomeness, the application dossier was prepared pursuant to Class 2 of Commission Recommendation 97/618/EC; "*Complex NF from non-GM source*", and subclass (1); "*the source of the NF has a history of food use in the Community*".

I. Specification of the novel food

The novel beta-glucans consists of a backbone of β -1-3-linked glucose residues which are branched by β -1-6-linkages. The applicant has provided product specifications which are very similar to those for the same product authorised by Commission Implementing Decision 2011/762/EU. The novel ingredient is a light beige fine powder with a moderately higher beta glucan content specification than the authorised comparator, as well as having relatively

lower fat and protein content. Specifications are also provided for undesirable substances including microorganisms and heavy metals.

The stability of the novel ingredient was established at 36 months under normal storage conditions.

II. Effect of the production process applied to the novel food

The manufacturing facility in Germany is certified to FSSC 22000 and IFS standards, which incorporate GMP standards and HACCP principles. Food grade brewers' yeast (specifications provided) is firstly subjected to autolysis. The cell wall fraction containing the insoluble beta-glucan is collected for subsequent alkali extractions, followed by acid neutralisation. The extraction and purification process is described in detail and summarised in a process flow. The novel ingredient can be consistently produced to the applicant's specifications.

III. History of the organism used for the novel food

Yeast beta-glucans are isolated from the cell walls of brewer's yeast (*Saccharomyces cerevisiae*) which has a significant history of safe use in the production of beer.

IX. Anticipated intake/extent of use of the novel food

The applicant wishes to extend the use of Yestimun[®] beta-glucans to a broader range of food categories compared to the yeast beta-glucan already authorised by Commission Implementing Decision 2011/762/EU. The additional food categories are breads, grain milling products and pasta, as well as jams, marmalades and other fruit spreads. The applicant also intends to increase the daily dose of yeast beta-glucan up to 1.275 g/day in dietary supplements and foods for particular nutritional uses (compared to 0.375 g/day and 0.6 g/day respectively for the authorised ingredient) and ≤ 0.85 g/day in other foods. The applicant clarified that the proposed increase in use levels is associated with the doses purported to achieve the immune-function health benefit linked with beta-glucans consumption. Authorisation of a health claim may be sought under separate EU legislation but is not addressed in this safety assessment.

The applicant calculated potential intake levels of the novel ingredient using consumption data from the UK National Diet and Nutrition Survey (NDNS) extracted from the EFSA Comprehensive European Food Consumption Database. The potential intake of Yestimun[®]

beta-glucans was estimated based on mean consumption of the relevant food categories by the total population.

Table 1: Beta-glucan intake for all population groups

Population class	Yeast beta-glucan intake g/day	Yeast beta-glucan intake mg/kg BW/day
Toddlers	1.9	158
Other children	2.3	98
Adolescents	2.7	55
Adults	2.8	40
Elderly	2.8	40
Very elderly	2.7	39

The applicant intends marketing the novel ingredient as a premium product based on the health benefits linked to beta-glucans consumption. Therefore, it will not be a generic ingredient, nor will it be added to infant formula or follow-on formula. The combined intake of different fortified foods was calculated using the “worst-case scenario” proposed by EFSA for food additives (FAIM European Food Safety Authority, 2014) and the results are summarised for all population classes in Table 1. The anticipated daily intake/kg of body weight for toddlers and older children is relatively high in comparison to other population classes. To counter this, the applicant proposes a separate fortified food category which would have reduced recommended daily intakes more appropriate for children up to 14 years of age.

- Toddlers" (12 months - 35 months): ≤ 100 mg/day
- Supplements for older children (36 month - 14 years): ≤ 750 mg/day
- Fortified food for older children (36 month - 14 years): ≤ 500 mg/day

X. Information from previous human exposure to the novel food or its source

Saccharomyces cerevisiae, has a long history of safe use in the production of beer and bread, and is commonly referred to as bakers’ or brewers’ yeast. Insoluble yeast beta-glucan derived from *Saccharomyces cerevisiae* was authorised for the European market through Commission

Implementing Decision 2011/762/EU. Exposure of the EU population to yeast beta-glucan was estimated by the applicant, with beer and bread found to be significant contributors.

XI. Nutritional information on the novel food

Yestimun[®] beta-glucans is a high molecular mass ingredient and is primarily a source of indigestible carbohydrate, with very low proportions of protein and fat making up the remaining nutritional content. Absorption of *beta*-glucans from the gastrointestinal tract is extremely limited, with most being fermented by intestinal microorganisms prior to excretion in the faeces.

XII. Microbiological information on the novel food

Microbiological specifications are set for the product in relation to *Salmonella*, total plate counts (CFUs), total coliforms, *Escherichia coli*, *Enterobacteriaceae*, *Bacillus cereus*, *Staphylococcus aureus*, yeasts and moulds. Microbial quality of four representative batches was provided, demonstrating compliance with the proposed specifications. The applicant states that routine microbial analysis will be performed within the quality assessment system.

XIII. Toxicological information on the novel food

Metabolic fate

In the human digestive system, beta-glucans reach the colon largely undigested where they may be subjected to fermentation by intestinal microorganisms. Based on an evaluation of published literature, the applicant contends that no significant systemic exposure is to be expected upon consumption of insoluble yeast beta-glucans. The applicant does not anticipate any differences in the metabolic fate of Yestimun[®] beta-glucans compared to the authorised yeast beta-glucans.

Toxicological Studies

The applicant has provided an overview of acute and short-term toxicity studies on soluble and insoluble yeast beta-glucans. Studies cited include parenteral administrations of up to 1,000 mg/kg bw in mice, rats, rabbits and guinea pigs. However, those studies did not involve the novel ingredient *per se* and therefore toxicological relevance to the current application could be considered limited.

In the safety evaluation of the authorised yeast beta-glucans, EFSA concluded that yeast beta-glucans are safe for human consumption if used in the same manner as the reference product. A NOAEL for yeast beta-glucans was not established, but a sub-chronic oral toxicity study

conducted by Biothera in 2009 did not reveal adverse effects at a dose of 2.5 g/kg bw/day (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011b).

Human Safety Data

The safety of insoluble *Saccharomyces cerevisiae* beta-glucans has already been evaluated by EFSA in 2011. Human clinical trials conducted with the novel ingredient are included in the dossier. The purpose of these studies was to clarify the effects of Yestimun[®] beta-glucan on the defence against pathogens. The product was well tolerated in general, with adverse effects likely relating to previously unidentified hypersensitivities.

Allergenicity

The applicant performed an assessment which did not reveal process-related risks for allergenicity. The principle raw material (liquid yeast) is obtained from breweries. The culture medium for the brewing process includes hops and malt. The gluten content of the final product is monitored and controlled to below detection limits. The manufacturer has an allergen management program in place which the applicant claims guarantees that Yestimun[®] beta-glucans does not contain any of the allergens listed in *Annex II* of Regulation (EU) No 1169/2011.

In order to inform consumers, the designation of the novel ingredient in foods containing it should be consistent with that set out in *Article 2* of Commission Implementing Decision 2011/762/EU: “yeast (*Saccharomyces cerevisiae*) beta-glucans”.

Conclusions

The applicant is seeking authorisation to extend the use and use levels of Yestimun[®] beta-glucans. For this assessment, a “worst-case scenario” as proposed by EFSA for food additives was applied. The analysis suggests that fortifying conventional foods with Yestimun[®] beta-glucans could substantially increase the intake of yeast beta-glucans in specific groups, compared to the background intake of beta-glucans from other dietary sources. However, considering the conservative nature of intake estimates, and supplementary data from human and animal studies, specific safety concerns related to the extension of use have not been identified. The applicant intends marketing the product as a premium product for the health benefit linked to beta-glucans consumption, and proposes a separate fortified food category with lower recommended daily intake values to cater for children up to 14 years of age.

Recommendation

The Food Safety Authority of Ireland has not identified any safety concerns associated with the consumption of Yestimun[®] beta-glucans at the proposed use levels in foods or food supplements containing the novel ingredient.

Therefore the FSAI is of the opinion that Yestimun[®] beta-glucans meets the criteria for novel food set out in *Article 3.1.* of the novel food Regulation (EC) No 258/97.