Meeting

Cellobiose Additional Information Discussion Paper

Committee Paper for Discussion - ACNFP/162/02

Advisory Committee for Novel Foods and Processes

Application for Authorisation as a Novel Food for Cellobiose - Additional Information from applicant for review

Application number RP1109

Issue

The Committee reviewed this application for the first time at the February 2023 meeting and further information was identified as being needed on production process, proposed uses and ADME for the assessment of the novel food to be completed. Members are invited to consider the response from the applicant and whether it addresses the requests for information satisfactorily or if further information is required.

In parallel, the Committee requested that the Secretariat draft an assessment output for this novel food for consideration, subject to the applicant’s response to the request for information addressing outstanding questions. Comments are sought on the draft Committee Advice Document.

Background

1. On May 12th 2021, the FSA received the submission for Cellobiose, a sugar replacement ingredient. The novel food ingredient is a disaccharide consisting of two glucose units linked by a β-1-4 glycosidic bond obtained from two-step enzymic conversion of sucrose into cellobiose. The applicant intends to use the novel food as an ingredient in various food categories to partially replace sugars such as sucrose or lactose.

2. The Committee reviewed this dossier at a ACNFP meeting on 8th February 2023, where they identified areas requiring further clarification to assess the safety of the novel food and its proposed use. Information was requested on the:

- Production Process
- Proposed use levels and anticipated intake
- ADME

3. The applicant has provided a response and the Committee is asked whether this addresses the outstanding questions on the dossier. To inform the discussion and further development of an opinion, the FSA's requested further information (Annex B), the applicant's response (Annex C) and supporting documents (Annex D)are provided. In parallel a draft Committee Advice Document (Annex A) has been prepared and the Committee is invited to comment on the draft with a view to it being finalised.

Applicant's response to request for further information

Production Process

4. The Committee noted the information on the enzymes used in the production process that was provided in the dossier. However, they requested further information on the purity of the enzymes and the parameters used to ensure the reaction was effectively managed to minimise variability and unsure a consistent product was produced.

5. The applicant has responded by stating that the novel food ingredient is manufactured using 2 enzymes, sucrose phosphorylase and cellobiose phosphorylase, both of which are under review with EFSA. Currently in the UK food production enzymes are not subject to an authorised list and as such there is no parallel process occurring in the UK at this time. They further explain activity of each incoming enzyme is tested in-house as the primary quality assurance step. In their response they comment that enzyme activity is determined by the efficient transformation of the starting material to the end product. They do not consider it necessary for additional purity criteria within the production process and do not have additional measures for controlling the process and managing product quality.

Proposed use levels and anticipated intake

6. The Committee queried on the limits of cellobiose in the food categories listed. They also noted the adverse effect identified at high doses was diarrhoea. Given the nature of the novel food and the adverse effect observed it was suggested that consideration of the impact of a number of lower dose intakes rather than cumulative exposure may be more informative. Consequently, they requested additional information to understand the likely exposure in a mock diet/meal based approach to better illustrate a worse-case scenario and explore likely effects of intolerance to the novel food.

7. The applicant has responded by stating that the human tolerance study demonstrated the intake of 1 x 20 g cellobiose (0.29 g/kg bw/day) or 2 x 15 g cellobiose (30 g in total, corresponding to 0.43 g/kg bw/day) was well tolerated and have adjusted the proposed maximum intake as such.

8. The full list of uses for cellobiose is outlined in table 1 and 2 of the RFI responses. This also details the maximum use levels in recipes. The applicant has adjusted the proposed uses of cellobiose to be certain meat products and meat analogues where sugars are permitted to be added, as a table top sweetener and as a substitute for sucrose/lactose in food supplements for the general population, excluding infants and young children below three years., as well as foods for children’s growth for toddlers and young children older than 1 year.

9. To address the request to provide a meal scenario analysis of exposure, the applicant recalculated the anticipated intake using DietEx tool which cumulates chronic intake data from all participating members on all reporting days and consuming days. From the data collected and taking account of the proposed uses (excluding food supplements), they state the resulting anticipated intake in the 95th percentile by all age groups in the whole population is below the conservative reference level for a single dose of 0.29 g/kg bw/day that was determined in the human tolerance study.

Annex C: RFI Table 3-9 outlines the results and anticipated intake of cellobiose by the various age groups in the meal scenario. The applicant concludes that with the revised proposed uses and use levels consumption of cellobiose is safe.

Absorption, Distribution, Metabolism, Excretion (ADME)

10. The Committee noted that the data presented in the studies available in literature suggest that cellobiose is not absorbed in the human intestine in significant quantities with a slight increase in absorption in those with coeliac disease. Following this, further information was sought on the digestibility of cellobiose. It was also suggested that the pH study while providing initial results did not simulate digestion and in particular the potential for fermentation of cellobiose in the gut.

11. The applicant refers back to the data in their application (Section 2.8.1) and a further additional document of a recently finalised human study Annex C (Section 2.8.04) concluding that the results are in line with human data by Nakamura et al. (2004) with findings that cellobiose is not absorbed in the GI tract, nor after hydrolysis, but is metabolized by the colonic microbiota.

12. Various studies (Section 2.8.1) provided in the dossier conclude cellobiose is not significantly hydrolysed at the brush border and is not absorbed through the intestinal barrier. As a result it is expected that cellobiose remains intact and can be further metabolized by the intestinal microflora.

Committee Action Required

- The Committee is asked whether the response from the applicant is sufficient to clarify the concerns discussed at the last meeting.
- If not, the Committee is asked to indicate what further data is required and the feedback that should be given to the applicant
- The Committee is also asked to review and comment on the draft output for the assessment of this novel food.

ACNFP Secretariat

September 2023

Annexes

Annex A – Draft Output for Cellobiose

Annex B – Request for Information

Annex C – Applicant’s Response to Request for Information

Annex D – Supporting Documents