

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

D-RIBOSE

Issue

Members are invited to consider the response provided by Bioenergy, Inc. to the comments raised at their June meeting, and whether this provides sufficient information for the Committee to conclude its evaluation of this novel food application.

Background

1. At the June meeting, Members requested further information on an application for the authorisation of D-Ribose as a novel food ingredient (NI), under the novel foods regulation (EC) 258/97 (ACNFP 88/4).
2. A letter detailing the ACNFP's comments from the June meeting was sent to the applicant on 6 June (**Annex A**) and sought additional information on a number of points:
 - (i) whether preliminary range finding studies had been conducted prior to selecting ribose doses used in developmental studies as certain effects from these studies (incomplete bone ossification and delayed growth) seemed to indicate that the maximum tolerated dose was exceeded. The relevance of the results was questioned due to nutritional imbalance of the dams;
 - (ii) clarification that the observed changes in blood glucose concentration following consumption of the NI did not occur as a result of increased insulin secretion;
 - (iii) anticipated intake - the practicality of applying the same target dose of the NI irrespective of serving size, the possibility of consumers expecting larger volumes of drinks to contain larger amounts of the NI and the fact that old NDNS data used do not account for the possibility that present day consumption patterns of energy drinks may have changed;
 - (iv) increased plasma/serum uric acid levels and the lack of experimental data on patients with hyperuracaemia;
 - (v) additional heavy metal analyses were requested which had not been provided; and
 - (vi) data were requested to confirm that the production strain was actually *Bacillus subtilis* (*B.subtilis*).
3. Bioenergy, Inc. responded to these comments on 8 August (**Annex B**). The Secretariat wishes to highlight the following points:

(i): doses of the NI used in developmental studies

4. the applicant clarified that a preliminary dose range-finding study was conducted in non-pregnant animals at the doses outlined in the developmental study and no adverse effects were reported which is why the selected doses were used in the 90 day and developmental studies. As might be anticipated, the intakes in the developmental study were later found to exceed those in non-pregnant animals.
5. The applicant highlighted that no malformations were reported even at doses at least 100 times the likely exposure in adult women and considered the observed effects to be transient and reversible. The applicant provided reassurance that conclusions have been accepted by the scientific community at large, as the report has been published in the peer reviewed literature and Professor Nigel Brown from whom the applicant previously obtained advice on this issue shared the same views.

(ii): decreased blood glucose levels as a result of increased insulin secretion

6. The applicant has presented relevant data from the dossier more clearly by drawing out specific studies which demonstrate the lack of correlation between decreased glucose and increased insulin levels. Only one study reported significant increases in plasma insulin which corresponded to significant decreases in blood glucose after consumption of the NI.
7. The applicant has also provided other explanations for decreased blood glucose levels (these explanations are already in the dossier). The applicant concludes that while the NI likely causes a change in insulin secretion, this is not the major contributory factor to decreased blood glucose levels.

(iii): anticipated intake

8. The applicant accepts it would not be practical for soft drinks manufacturers to change drinks recipes to provide the same dose of ribose in different volumes but states that as this will be a new soft drink product, it is likely that it will be marketed initially in a single product format :
9. the applicant proposes that if drinks containing ribose were to prove successful and warrant a change in serving size, labelling the product to indicate the amount of ribose it contains may be a method to ensure that consumers are not misled into expectation that larger volumes of drinks contain greater amounts of ribose.

10. The applicant has evaluated the 2008 UK soft drinks report and states that sports and energy drink production has increased around 100% since 2001 when the last intake survey was carried out. The applicant proposes the increase in energy drink production since 2001 is likely due to an increase in the number of people consuming these products rather than change in individual intakes of these products. A detailed account of the applicant's response is provided in **Annex B**.

(iv): increased plasma/serum uric acid levels

11. The applicant's response draws out key studies described in the dossier concerning this issue. There were four studies where blood uric acid levels increased significantly following consumption of the NI. The applicant concludes that the daily doses in three of these studies were much higher than the estimated intake of the NI from the proposed food uses. Regarding the remaining study, the applicant concludes (with explanations) that the findings are neither biologically or clinically significant. Reference is also made to a study in the dossier which revealed no significant increase in blood uric acid levels of healthy individuals who received 58-87g of the NI over ten hours.
12. The applicant also highlights that individuals suffering from gout are usually men in their 50s and 60s who are diabetic or obese. The applicant's view is that these individuals and individuals with hyperuracaemia are unlikely to be consumers of energy drinks, in addition to which, individuals with hyperuracaemia are also advised to monitor their diet carefully .

(v): heavy metal analyses data for all heavy metals analysed

13. The applicant has provided results from heavy metal analyses, which can be found in **Annex C**.

(vi): confirmation that the production strain is *B. subtilis*

14. The applicant's response highlighted that bacterial strains commonly used to produce ribose are all of the genus *Bacillus* and species *subtilis* or *pumilus* and that other fermentation organisms are unable to produce commercial yields of ribose. The applicant explains that lack of transketolase activity is a requirement for ribose production and *B.subtilis* and *B.pumilus* are the only transketolase negative bacteria used in fermentation. The applicant has stated that they have carried out an AOAC Gram staining method to identify the species, but have not as yet provided data. The applicant intends to carry out the necessary analyses to confirm the identity of the production strain.

Committee Action required

15. The Committee is asked whether the applicant's responses provide sufficient information and adequately address the questions raised at the June meeting.
16. If so, the Secretariat proposes to draft an opinion incorporating the ACNFP's comments on Bioenergy's application which will be discussed at the Committee meeting in November.
17. If not, the Committee is asked to indicate what additional information would be required.

**Secretariat
August 2008**

Annexes attached

- ANNEX A** Letter of 6 June 2008 to the applicant with the Committee's comments
- ANNEX B** Response from the applicant of 8 May 2008 (including revised response to serving sizes)
- ANNEX C** Heavy metal analyses