

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

D-RIBOSE

Issue

Members are invited to consider the comments provided by Bioenergy, Inc. in response to the Committee's request for further reproductive toxicity studies to be carried out on this proposed novel ingredient, and to advise whether these data are still required.

Background

1. Bioenergy's application for the authorisation of D-ribose as a novel ingredient was discussed on a number of occasions during 2008 (ACNFP/87/4, ACNFP/88/4 and ACNFP 90/3). During the most recent discussion in September 2008, the Committee discussed the request for additional reproductive toxicity data: The relevant section of the minutes records the discussion as follows:

"The Committee remained concerned that the maximum tolerated dose was exceeded in the developmental study and that the data were therefore of limited value. The Committee also noted that ribose consumption alters glucose and insulin levels but the mechanism for this effect is unclear. The Committee recalled the important role of glucose during pregnancy and development and remained concerned that ribose consumption could interfere with this, noting that young active women may be particularly attracted to products containing this ingredient. It therefore advised that developmental studies be repeated at lower doses to address this gap in the available data. "
2. This conclusion was relayed to the applicant, who has considered what additional information an additional study would provide, over and above the existing study, in relation to the risk assessment of D-ribose. Their response is attached at **Annex 1** and it considers the following points:
 - whether the Maximum Tolerated Dose was exceeded in the existing study
 - the significance of skeletal variations seen in the existing study
 - the rationale for a possible link between D-ribose intake, blood glucose and birth defects.
3. Their detailed analysis notes that the "wavy ribs" and incomplete ossification observed in rat studies are non-permanent effects that are related to a physiological response to maternal stress. Such changes are not linked mechanistically to malformations and they are not unusual findings in studies

where the maximum dose is set, in accordance with regulatory guidelines, at a level that causes small (up to 10%) reductions in body weight and/or increases in caecal weights.

4. The skeletal variations observed in the existing study are summarised on page 7 of the Annex. The changes were dose dependent and a clear No Observable Effect Level was established at a dietary inclusion level of 5%, equivalent to a daily dose of 4.25 grams/kg bw/day. If a new study were to be conducted at lower levels of inclusion, it is unlikely that additional information regarding the risk assessment would be obtained.
5. The applicant accepts that the risk of birth defects is increased in women whose diabetes is poorly controlled, especially in the first trimester. Although large bolus doses of D-ribose have been found to cause a transient reduction in blood glucose in fasting individuals, they suggest that it is highly unlikely that D-ribose consumption, at levels resulting from its proposed use as a novel food ingredient, would lower blood glucose.

Committee Action required

6. The Committee is asked whether the applicant's responses provide sufficient information and adequately address the concern arising from the interpretation of the existing reproductive toxicity study.

**Secretariat
June 2009**

Annexes attached

ANNEX A Bioenergy letter of 2 April to the Secretariat.