

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

GLUCOSAMINE FROM *ASPERGILLUS NIGER***Issue**

The Committee is invited to consider the response provided by Cargill (Incorporated) to the comments raised at the September meeting and indicate whether this provides sufficient information for the Committee to conclude its evaluation of this novel food ingredient.

Background

1. Members considered an application from Cargill for the approval of glucosamine from *Aspergillus niger* as a novel food ingredient at the September 2006 meeting (ACNFP/79/4).
2. A letter detailing the ACNFP's comments on this application was sent to the applicant on 16 October (see **Annex A**) and these are summarised below:
 - I. **Diabetics:** The Committee was concerned that the safety of the NI for diabetics had not been adequately demonstrated. The single human study cited was considered insufficient as only a limited number of Type II diabetics were studied (38 individuals), and no information was provided on Type I diabetics. Members also drew attention to a recent article which concludes that the long term effects of glucosamine in patients with diabetes has yet to be established in well controlled trials (Stumpf J.L. & Lin S.W., 2006: *Annals of Pharmacology*, **40**, 694-698).
 - II. **Intakes:** The Committee was unsure what the applicant considered to be a safe level of glucosamine intake and how they would ensure that it would not be exceeded, for example if people were to consume both supplements and the NI (see also the comment under toxicology below). Also the Committee noted that a number of the products would be attractive to young children and asked how the issue of consumption by children would be addressed.
 - III. **Protein:** The Committee commented that the use of SDS-PAGE gels was not the most sensitive way to measure protein levels in the novel ingredient. The Committee accepted that nitrogen-based methods could not be used but suggested that the applicant should use an alternative method such as Mass Spectrometry.
 - IV. **Toxicological studies:** The Committee requested a justification for dismissing the results of the adverse effects study by Nguyen et al, as this was an *in vivo* study to which greater weight would normally be given than many of the other studies quoted. The Committee also requested an assessment of the safe maximum intake for glucosamine, noting that of the

human studies referred to, only 2 or 3 used high enough glucosamine levels to give meaningful results. Also, the Committee would like to see the primary data from the animal toxicity studies that might be used to establish a safety factor for glucosamine intake.

- V. **Labelling:** The Committee suggested that the label should retain the reference to 'fungus' as consumers would not be familiar with the name *Aspergillus*.
3. The applicant responded to these comments on 2 November (see **Annex B**). The Secretariat wishes to highlight the following points:
- I. **Diabetics:** The applicant has addressed the issue of the safety of glucosamine for diabetics by emphasising the lack of a demonstrated effect of glucosamine on parameters that affect diabetes such as glucose metabolism and blood sugar levels. However, they concede the statement attributed to Stumpf and Lin (2006) that there have been limited controlled studies of diabetics. The expert clinician who has advised the applicant concludes that "Based on the weight of scientific evidence, there seems to be no reason to restrict the use of glucosamine for individuals at risk for diabetes or for diabetic individuals."
 - II. **Intakes:** The applicant points to the widespread consumption of glucosamine supplements at levels of 1500mg per day and the number of human clinical trials at this level of consumption. It is claimed that labelling will prevent overconsumption above this level and that products will be marketed for adult joint health and not directly targeted at children. Cargill has also proposed a simplified list of food applications (see Annex B).
 - III. **Protein:** The applicant refers to the previous advice of the Committee in August 2004 in relation to the same question when the Committee considered the NI under substantial equivalence and concluded that the gel analysis was adequate to demonstrate the absence of protein. Furthermore, the applicant reports that there have been no reports of allergic reactions to the NI, which is already on the market in the form of food supplements.
 - IV. **Toxicological studies:** The applicant has provided a more detailed explanation of their reasoning in relation to the study by Nguyen et al. and the type and severity of the adverse events encountered.

The applicant has also explained their approach to an assessment of the safe upper limit for glucosamine intake, citing a number of reasons why they consider 1500mg/day to be well within safe levels and deriving safe upper limits/ADI's from published studies that have used doses above the suggested intake of 1500mg/day. They have also offered to provide primary data for any studies carried out by Cargill of relevance to the Committee.

- V. **Labelling** – The applicant proposes that the product should simply be labelled as "glucosamine hydrochloride". The Secretariat notes that this proposed labelling differs from that proposed by the applicant in 2004 when requesting an opinion on the substantial equivalence of the NI with shellfish

derived glucosamine. At the time members accepted a proposal from the applicant to label the product as, “non-shellfish glucosamine hydrochloride”, with a footnote referring to its source from, “from the fungus *Aspergillus niger*.” However, the applicant is of the view that the new simplified label is in line with the approach taken by the Commission for highly purified materials from microbial sources and points out that *Aspergillus* species are used to make other food ingredients such as soy sauce and citric acid, which are not labelled to indicate the method of manufacture.

Committee Action Required

4. The Committee is asked whether the applicant’s response provides sufficient information and adequately addresses its concerns.
5. If so, the Secretariat proposes that an opinion be drafted incorporating the ACNFP’s comments on Cargill’s application to be discussed at the next Committee meeting in March.
6. If not, the Committee is asked to indicate what additional information would be required.

**Secretariat
January 2007**

Annexes attached:

ANNEX A Letter of 17/10/06 to the applicant with the Committee’s comments

ANNEX B Response from the applicant of 01/11/06

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Letter to the applicant with the Committee's comments (16 October 2006)

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Response from the applicant (1 November 2006)