

Mr Brent Rogers
Cargill Acidulants
Cargill Drive
Eddyville
IA 52553
USA

5 August 2004

Reference: NFU 486

Dear Mr Rogers,

**OPINION ON THE SUBSTANTIAL EQUIVALENCE OF GLUCOSAMINE HCl
DERIVED FROM *Aspergillus niger***

The Advisory Committee on Novel Foods and Processes (ACNFP) has now completed your request for an opinion on the substantial equivalence of your glucosamine hydrochloride (HCl) derived from *Aspergillus niger* with the existing glucosamine HCl derived from shellfish.

I am pleased to inform you that, in view of the positive opinion given by the ACNFP, the Food Standards Agency, UK Competent Authority for all novel food issues, is content that your fungal glucosamine HCl meets the criteria for equivalence, as defined in Article 3(4) of regulation (EC) 258/97.

This opinion is issued on the basis that your fungal glucosamine HCl ingredient is to be used in the same way as glucosamine HCl derived from shellfish, namely in food supplements and PARNUTS products, in accordance with the Directives 2002/46/EC and 89/398/EEC.

Please note that, in accordance with Article 5 of (EC) 258/97, you should notify the European Commission when you intend to market your fungal glucosamine HCl ingredients when they are first marketed. You should send this to Mr Andreas Klepsch at the following address:

European Commission
DG SANCO
Rue de la Loi 200
B-1049
Brussels
Belgium

If you have any other queries, please do not hesitate to contact my colleague, Dr Chris Jones (Tel: 00 44 (0) 207 276 8572) or myself.

Yours sincerely,

Annie-Laure Robin
Novel Foods Division

Enc.: ACNFP opinion

ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES

OPINION ON SUBSTANTIAL EQUIVALENCE OF GLUCOSAMINE HCl (ASPERGILLUS NIGER) CONSIDERED UNDER ARTICLE 5 OF THE NOVEL FOODS REGULATION

Applicant Cargill Acidulants
Cargill Drive
Eddyville
IA 52553
USA

Responsible Person Brent Rogers

Introduction

1. A request was received by the UK Competent Authority for an opinion on the equivalence of glucosamine HCl derived from *Aspergillus niger* compared with the existing glucosamine HCl obtained from shellfish.
2. According to Article 3(4) of (EC) 258/97, the notification procedure applies to “foods or food ingredients... which on the basis of scientific evidence available and generally recognised or on the basis of an opinion delivered by one of the competent bodies... are substantially equivalent to existing foods or food ingredients as regards their:
 - Composition
 - Nutritional value
 - Metabolism
 - Intended use
 - Level of undesirable substances contained therein”.

Composition

3. Glucosamine is a naturally occurring amino sugar, found largely in cartilage that is thought to play a role in the health and resilience of joints.
4. After acid hydrolysis of the non-GM *A. niger* biomass at high temperature, glucosamine HCl is extracted using the same process used for the production of shellfish glucosamine HCl. In both cases, the product is a crystalline product of high chemical purity (98%).
5. By means of infrared absorption, HPLC and specific rotation, Cargill Acidulants has demonstrated that glucosamine HCl obtained from *A. niger* is chemically identical to its shellfish counterpart.

Discussion. *The Committee accepted that the chemical composition of the fungal derived glucosamine is equivalent to the existing product.*

Nutritional value and metabolism

6. In view of the chemical analyses described above, the applicant states that the bioactivity of the fungal glucosamine HCl is not thought to vary from the bioactivity of shellfish derived glucosamine HCl.

Discussion. *The Committee was content that the alternative source of glucosamine HCl would have no impact on its nutritional value.*

Intended Use

7. Glucosamine HCl from *A.niger* will be used as an ingredient in food supplements¹ and foodstuffs intended for particular nutritional uses (PARNUTS)² in the same way that shellfish-derived glucosamine HCl is currently marketed in the EU. The applicant has highlighted that although the recommended daily intakes for glucosamine HCl vary, the most widely recommended intake is up to

¹ As defined in Directive 2002/46/EC of 10 June 2002 on the approximation of the laws of the Members States relating to food supplements

² As defined in Directive 89/398/EEC of 3 May 1989 on the approximation of the laws of the Member States relating to foodstuffs intended for particular nutritional uses

1500 mg of glucosamine HCl per day. The fungal product would be used in the same way as its existing counterpart and at the same doses.

Discussion: *The Committee agreed that the intended use of the fungal derived glucosamine HCl did not differ from the existing product.*

Levels of undesirable substances

8. Cargill Acidulants has implemented a quality control system and uses good manufacturing practice for the production of its fungal glucosamine HCl. These include routine checks to ensure the absence of bacterial and fungal contamination (including bacterial and fungal spores).
9. Regarding the potential allergenicity of fungal glucosamine, the applicant provided an expert's opinion that states that this product should not be considered as potentially allergenic. The applicant has also provided data showing the absence of protein in its products. As typical methods for quantifying low levels of proteins cannot be applied to the product due to the interference by the amino group of glucosamine, the applicant has used an alternative SDS-PAGE method. As this analysis was not capable of identifying low molecular weight proteins, the applicant was asked to carry out further analysis of its product using a gel with a greater resolving power to detect proteins of a molecular weight of 5-20 KDa. The results obtained demonstrate the absence of low molecular weight protein and therefore the absence of potentially allergenic compounds in their ingredient.
10. The fungal source, *A.niger*, is non-pathogenic and non-toxic for humans and is currently used for production of citric acid, enzymes and a range of other food ingredients. Although some strains of *A.niger* can produce ochratoxin A, the applicant has stated that none was detected in the production strain. This mycotoxin was also not detected in a sample of fungal glucosamine, at the limit of detection (LOD) of the analytical method used. Similar results were obtained on the detection of aflatoxin in fungal glucosamine HCl. The applicant will conduct routine tests for the presence of ochratoxin A, in accordance with Good Manufacturing Practice.

11.No pesticide was found in glucosamine HCl from *A.niger*, at the LOD of the analytical methods used.

Discussion. *Members accepted that the product was free from microbiological contamination and did not contain detectable levels of proteins and mycotoxins.*

Additional information- Labelling

12.The applicant intends to label the product as “Non-Shellfish Glucosamine Hydrochloride” with a footnote referring to its source “from the fungus *Aspergillus niger*”.

13.Glucosamine HCl from *A. niger* products could also carry a certificate to indicate the product was Kosher.

Discussion *The Committee accepted the proposed labelling noting that it contained sufficient information for individuals who wished to avoid consumption of products derived from fungal sources.*

Conclusion

14.The Committee is content that Cargill’s approach to demonstrate the equivalence of their product, glucosamine HCl from *A. niger* with the existing product derived from shellfish is consistent with the criteria set out in Article 3(4) of the Novel Foods Regulation (EC) 258/97. The glucosamine is shown to be chemically equivalent to the existing product and the new and existing products are to be used in the same way. The source and manufacturing process do not give rise to concerns over the presence of undesirable compounds, compared with the existing product.

15.Therefore the glucosamine HCl produced by Cargill can be considered substantially equivalent to the existing glucosamine HCl obtained from shellfish.

August 2004