Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to a notification from AIIBP and FAIBP on acid hydrolysed vegetable protein from soy pursuant to Article 6 paragraph 11 of Directive 2000/13/EC

(Request N° EFSA-Q-2004-125)

(adopted on 22 February 2005)

SUMMARY

Soy is a common dietary constituent and allergic reactions to soy proteins are well described. Soy allergy prevalence studies are lacking. Estimated prevalences are about 0.5% in the general population with about 3-6% of children being allergic to soy proteins. Clinical reactions are similar to those observed with other major food allergens, such as milk, egg or peanut. Soy allergy can affect all common allergy target organs such as the gastrointestinal tract, respiratory tract and the skin and can also cause systemic anaphylaxis.

The applicant provides information on acid hydrolysed vegetable proteins prepared from soy and on potential effects in soy allergy. It is stated that acid hydrolysed vegetable protein is not likely to trigger adverse reactions. This statement is based on the manufacturing process. The evidence of non-allergenicity of acid hydrolysed vegetable protein includes a literature review. Analytical data provided regarding residual proteins are incomplete. Finally, a planned clinical study is outlined in individuals suffering from soy allergy.

Acid hydrolysed vegetable (soy) protein may contain low levels of known and novel allergenic proteins and peptides. It is not known at which levels of intake soy protein-based acid hydrolysed vegetable protein would cause allergic reactions in soy allergic individuals. The scientific data provided by the applicant are insufficient to predict the likelihood of adverse reactions in soy allergic individuals. Nevertheless, taking into account the levels of soy proteins reported that cause allergic reactions in severely allergic individuals, the Panel considers that this product could trigger an allergic reaction. Clinical information is needed with regard to the effects of soy protein-based acid hydrolysed vegetable proteins in soy allergic individuals. Appropriate clinical studies applying best clinical and laboratory practice should be carried out.

KEY WORDS

Acid hydrolysed vegetable protein (soy), soy allergy, food allergy.

BACKGROUND

In November 2003, the European Parliament and the Council adopted Directive 2003/89/EC[1] amending Directive 2000/13/EC, as regards indication of the ingredients present in foodstuffs.

Annex IIIa of the Directive specifies a list of ingredients that are known to trigger allergic reactions or intolerances for which no labelling exemptions are allowed. Whenever the listed ingredients or their derivatives are used in the production of foodstuffs, they must be labelled.

Article 1, paragraph 11 of the Directive establishes a procedure allowing for temporary labelling exemption of derivatives from ingredients listed in Annex IIIa for which it has been scientifically established that it is not possible for them to cause adverse reactions. In accordance with this provision, submissions of request for temporary labelling exemption were notified to the Commission before 25 August 2004. The Commission shall, not later than 25 November 2004, and after consultation with the European Food Safety Authority, adopt a list of those ingredients which shall be temporarily excluded from Annex IIIa, pending the final results of the notified studies, or at the latest until 25 November 2007. Therefore, the European Food Safety Authority is asked to provide scientific opinions on the submissions in accordance with the present terms of reference.

TERMS OF REFERENCE

In accordance with Article 29 (1) (a) of Regulation (EC) N° 178/2002, the European Commission requests the European Food Safety Authority to evaluate the scientific data submitted by Association Internationale de l'Industrie des Bouillons et Potages (AIIBP), Fédération des Associations de l'Industrie des Bouillons et Potages de la CEE (FAIBP) in the framework of the procedure laid down for temporary labelling exemptions in Article 6 paragraph 11 of Directive 2000/13/EC. On the basis of that evaluation, EFSA is requested to issue an opinion on the information provided, and particularly, pending the final results of the studies undertaken, to consider the likelihood of adverse reactions triggered in susceptible individuals by the consumption of the following ingredients/substances used under the conditions specified by the applicant: acid hydrolysed vegetable protein from soy.

ASSESSMENT

Since soy is relevant as a source of protein epitopes known to elicit soy allergy (NDA, 2004), it is appropriate to assess soy products, in this case acid hydrolysed vegetable protein (from soy among other sources), for their potential to trigger adverse reactions in soy allergic individuals.

The applicant comes to the conclusion that, based on their history of safe use and on the available analytical data, no "clinical evidence for adverse reactions caused by such products exists". Furthermore, the applicant lists a planned scientific study including *in vitro* and *in vivo* approaches.

The following evidence is presented by the applicant in support of the statement given above.

[1] Directive 2003/89/EC of the European Parliament and of the Council amending Directive 2000/13/EC as regards indication of the ingredients present in foodstuffs. OJ L 308. 25.11.2003, p. 15.

1. Manufacturing process and characterisation of the product

The data provided show that in the preparation of acid hydrolysed vegetable protein (hydrolysis, neutralisation, filtration, ripening), a code of practice issued by the applicant is observed. Manufacturing includes acid hydrolysis (6-8 hours, temperature 110-140 ºC, maximum pressure 4 bar). After neutralisation several filtration cycles and active carbon treatment is following. Thus residual crude material of the protein source is removed. Analytical data submitted shows that the residual soy protein content of the final product is estimated to be below 1-5 mg/kg.

2. Exposure assessment

The opinion focuses on acid hydrolysed vegetable protein produced from soy. It is in widespread use as an ingredient in soups and various convenience foods. An exposure scenario given by the applicant results in a daily intake of 70 mg of unmodified soy protein. The applicant's exposure scenario leading to a daily intake of 70 mg of unmodified soy protein appears to be theoretical. The Panel was unable to follow the derivation of this daily intake calculation.

3. Evidence of non-allergenicity

3.1 History of non-allergenicity of the product

The literature review gives information on soy allergy. However, the given threshold levels for amounts of soy protein causing allergy are not generally accepted. The levels at which soy protein hydrolysates would cause allergic reactions in soy allergic individuals are not known.

The applicant correctly states that there are no case reports of allergic reactions to soy-based acid hydrolysed vegetable protein. However, in view of the lack of labelling requirements, under-reporting is likely. In principle, hydrolysed proteins or protein isolates are able to trigger allergic reactions. In support of this assumption, Leduc *et al*. (2004) reports an anaphylactic reaction to a wheat isolate.

3.2 Laboratory-based tests

Analytical data are reported from two producers. Soy protein analysis of different samples by a non-specified ELISA method showed values below 1 mg/kg or not detectable. In view of the difficult methodology of soy protein analysis by ELISA, a better description of the method used would have been helpful.

SDS-PAGE of acid hydrolysed vegetable (soy) protein did not show bands in the molecular weight range over 7 kDa. Original data are not shown. HPLC amino assay chromatograms of different products do not add relevant information as to the presence of allergens and epitopes related to soy protein.

In summary, analytical data provided by the applicant are incomplete.

3.2.1 IgE-binding studies

To further determine the allergenicity of soy derived products, the applicant reviews relevant reports from the literature (Businco *et al*., 1993; Cordle, 1991; Niggemann, 1999; Hill *et al*., 1995; Businco *et al*., 1994; Herian, 1993; Shreffler, 2001) addressing allergenicity of hydrolysed and fermented food products.

Herian (1993) performed IgE immuno blotting studies with 8 sera from soy allergic patients and reported the absence of binding of soy protein after fermentation.

Further RAST inhibition studies investigated the potential of acid hydrolysed soy proteins to inhibit IgE-binding to crude soy in patients with a positive skin test to soy. A 1000 fold reduction of IgE-binding activities after acid hydrolysis is reported. It must be noted however that IgE-binding does not necessarily correspond to biological activity and the degree of hydrolysis was not reported. According to the applicant, a hydrolysis of around 80% of the starting material is usually achieved.

3.2.2 Clinical studies

The applicant reports preliminary results from the EU-funded FAREDAT Project (Food Allergy Risk Evaluation based on improved Diagnosis, Allergens and Test methods), where 14 soy allergic (DBPCFC confirmed) patients aged 14-41 years were challenged with increasing doses of soy proteins. Threshold levels or levels at which acid hydrolysed soy proteins trigger allergic reactions in soy allergic individuals have not been established.

3.3 Proposed studies

3.3.1 In vitro studies

The description of future studies planned by the applicant is related to improvement of analytical methods, *in vitro* IgE-binding, biological and clinical exposure studies in well characterised, DBPCFC confirmed individuals.

3.3.2 Clinical studies

A proposed study outline on a research project relating to the "evaluation of allergenic activity of soy bean acid hydrolysed vegetable protein" is given including *in vitro* and *in vivo* methods. Clinical investigations intended include *in vitro* serology of patients with food allergy, skin prick tests and double-blind placebo-controlled oral provocations. Further specifications are not given detailing the number of patients, power estimations and a specific test protocol.

CONCLUSIONS AND RECOMMENDATIONS

Soy protein-based acid hydrolysed proteins may contain low levels of known and novel allergenic proteins and peptides. It is not known at which levels of intake soy protein based acid hydrolysed proteins would cause allergic reactions in soy allergic individuals. The scientific data provided by the applicant are insufficient to predict the likelihood of adverse reactions in soy allergic individuals. Nevertheless, taking into account the levels of soy

proteins reported that cause allergic reactions in severe allergic individuals, the Panel considers that this product could trigger an allergic reaction. Clinical information is needed with regard to the effects of soy protein-based acid hydrolysed proteins in soy allergic individuals. Appropriate clinical studies applying best clinical and laboratory practice should be carried out.

DOCUMENTATION PROVIDED TO EFSA

Dossier submitted by Association Internationale de l'Industrie des Bouillons et Potages (AIIBP), Fédération des Associations de l'Industrie des Bouillons et Potages de la CEE (FAIBP) to the European Commission pursuant to Article 6 paragraph 11 of Directive 2000/13/EC as amended by Directive 2003/89/EC, 24 August 2004.

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