Guidance on Novel Foods

Allergenicity Assessment

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NDA Panel (2006-2015)

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OUTLINE

- The Guidance
- Comments made at the public consultation
- Causes for requests for additional information
- Examples of previous opinions and advice to applicants

GUIDANCE: 2.11. ALLERGENICITY (1)

- Food allergens are mostly **proteins**, and thus the allergenic potential of a Novel Food (NF) is linked to the presence of proteins: a NF **containing no protein** (or peptides) has a very **low** allergenic potential (if any).

- The default assumption for **NF containing** proteins is that such NF **have** allergenic potential.

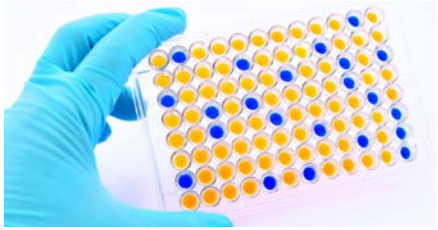
- **Methods of analysis for protein** (including the LOD, LOQ) and the results should be provided.

2.11. ALLERGENICITY (2)

- Allergenicity should be explored by considering the NF **composition, particularly its protein(s), its source** (including taxonomic relationships), **the production process, and available experimental and human data,** including information on **cross-reactivity**.
- It is necessary therefore to perform a **comprehensive literature review** in order to retrieve available information on sensitisation, case reports of allergic reactions and/or allergenicity studies (*in vitro*, in animals, in humans) of the NF and/or its source(s).

2.11. ALLERGENICITY (3)

Information on **appropriate methods** to further investigate the potential allergenicity of foods is provided by the **NDA Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes (EFSA, 2014)**. Such methods include:



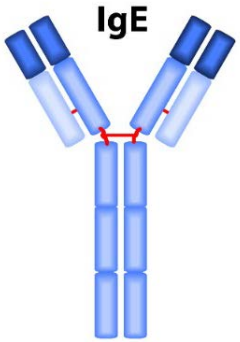
2.11.1. Protein analysis

- protein content of the NF
- molecular weight of potentially allergenic protein, heat stability, sensitivity to pH, digestibility by gastrointestinal proteases
- degree of sequence homology with known allergens
- immunological tests (e.g. Western blotting).

2.11. ALLERGENICITY (4)

2.11.2. Human testing

- Detection of specific IgE antibodies
- Skin prick testing
- Double blind placebo controlled food challenge studies



2.11. ALLERGENICITY (4)

- If an applicant wishes **to demonstrate that the NF is unlikely to trigger adverse reactions in sensitive individuals**, he/she should follow the approach outlined in the **EFSA Guidance** on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive **2000/13/EC, as amended (EFSA, 2013).**

- Applicants for **NF which potentially contain allergens listed in Annex II of Regulation (EU) No 1169/2011,** and who seek exemption from mandatory labelling, are advised to file an application pursuant to Article 21 paragraph 2 of Regulation 1169/2011 (previously Article 6 Paragraph 11 of Directive 2000/13/EC) by using the afore-mentioned **Guidance document (EFSA, 2013).**

PUBLIC CONSULTATION (1)

- *To which extent **history of use** may be appreciated as an indicator of allergenic safety in the assessment, i.e. the conditions under which this type of information could be used to demonstrate safety?*

Absence of reported allergenicity ≠ evidence for its absence

Evidence on allergenicity (including cross-reactivity and sensitisation) provided in the literature review would be mentioned in the EFSA output to inform risk managers.

Reports on allergenicity usually do not result in a conclusion that a food is unsafe.

PUBLIC CONSULTATION (2)

- *It was noted that the botanical relatedness of plants, fruits and vegetables should be considered regarding **cross-reactivity**.*
- *There were comments that the issue of **de novo sensitization** requires further consideration in the guidance and that de novo sensitization **is difficult to predict** and may be better addressed with risk management activities such as post market monitoring.*

The "taxonomic relationship" of the source of the novel food should be considered together with cross-reactivity.

De novo sensitisation is difficult, if not impossible, to predict, therefore the default assumption is that NFs with proteins have allergenic potential.

EFSA REQUESTS FOR ADDITIONAL INFORMATION WHEN:

- No information on the content of protein, its identity and/or the source (e.g. from raw material, enzymes, substrate used in the production).
- No information on the applied method of analysis for protein.
- No limit of detection for protein content **(LOD/LOQ).**
- No considerations on whether the applied production process may increase/decrease allergenicity (if information is available from the literature).
- No or insufficient literature review on existing evidence on cross-reactivity of the NF and/or its source.
- Insufficient information on the test material used in the provided studies.

EXAMPLES FROM PAST OPINIONS (1)

- **Synthetic chewing gum base:** no protein in starting materials or production process used; Panel: no concerns.
- **Lycopene from tomato oleoresin**: Panel: extraction process does not enrich the protein fraction (containing profilin), therefore potential allergenicity is, at most, similar to that observed for tomatoes
- **Cold water dispersible synthetic lycopene**: no tomato source, but Panel noted the **added** fish gelatine.
- **Rapeseed protein:** same family *(Brassicacae)* as mustard, high homology of the protein, few reports on rapeseed sensitisation/cross-reactivity in the literature, no studies with the NF. Panel: risk of sensitisation to rapeseed cannot be excluded; it is likely that rapeseed can trigger allergic reactions in mustard allergic subjects.

EXAMPLES FROM THE PAST (2)

- **UV-treated bakers yeast, milk, bread:** Limited data available on the effect of UV on proteins. Panel: risk of allergic reactions to the NF is not dissimilar to that associated with conventional yeasts, milk, and bread.
- **Soy-derived Novel Foods** (fermented soy bean extract). Panel: the risk of allergic reactions to the NF is not dissimilar to that associated with other soy-derived products (allergenicity of the source).
- **Chia seeds:** Panel (2005): Cross-reactivity of Chia seeds with food allergens cannot be ruled out. Limited data on cross-reactivity, uncertainties expressed by EFSA. Panel (2009) noted the cross-reactivity of sera from patients known to be allergic to peanuts and sesame, and reiterates its previous opinion that it is not possible to predict the potential allergenicity of Chia.

EFSA OPINION ON RISK PROFILE OF INSECTS (1)

- **Reported cases of allergic reaction and anaphylactic shock in humans**
- **Insects may cause allergic reactions either by *de novo* sensitization or by cross-reactivity**

Allergic reactions may occur through:

- elicitation of an allergic reaction in individuals already sensitised to the insect
- or to a cross-reacting allergen
- and/or de novo sensitisation of individuals

EFSA OPINION ON RISK PROFILE OF INSECTS (2)

The allergenicity assessment by the Applicant should consider:

- The composition of the food (protein content),
- Information on the applied method of analysis,
- Comprehensive literature review on the concerned and closely related species,
- Information on allergenic properties of insects,
- Specific immunological tests with sera of people with confirmed allergy to that insect,
- Sequence homology with pan-allergens (i.e. tropomyosin), inducing cross-reactivity with crustaceans, molluscs,…
- Considerations on possible impact of the production process applied.

Thank you for your attention !