Food and Agriculture Organization of the United Nations

World Health Organization

Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens

Part 4: Review and establish exemptions for the food allergens

FAO HQ, Rome, Italy: 14 - 18 November 2022

SUMMARY AND CONCLUSIONS

Issued in January 2023

The main purpose of the fourth meeting of the ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens was to develop a process for the consideration of future exemptions of highly refined foods and ingredients derived from or containing a priority allergen food.

Dr Simon Brooke-Taylor served as Chairperson.

Dr Joseph Baumert served as rapporteur.

An Expert Committee, comprising scientists, regulators, physicians, clinicians and risk managers from academia, government and the food industry were selected to participate in the series of meetings of the FAO/WHO Expert Consultation on Risk Assessment of Food Allergens (FAO and WHO, 2020a).

This document summarizes the conclusions of this meeting and is made available to facilitate the deliberations of the Codex Committee on Food Labelling (CCFL) and Codex Committee on Food Hygiene (CCFH). The full report of the meeting will be published as part of the Food Safety and Quality Series and will describe the scientific evidence available to the Expert Committee and its deliberations during the meeting.

The meeting participants are listed in Annex 1 of this summary report.

More information on this work is available at:

http://www.fao.org/food-safety/en/

and

https://www.who.int/foodsafety/en/

Background and objective

At its 45th session in May 2019, the CCFL requested FAO and WHO to provide scientific advice to validate, and if necessary, update the list of foods and ingredients in section 4.2.1.4 of GSLPF (General standard for the labelling of prepackaged foods) (FAO and WHO, 2019). In December 2020, the first meeting of the ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens, addressed the request by firstly identifying and agreeing upon the criteria for assessing additions and exclusions to the priority food allergen list, then evaluating the available evidence for foods of concern (FAO and WHO, 2020b & 2022).

The CCFH has developed a code of practice (CoP) to provide guidance to food business operators and competent authorities on managing allergens in food production, including controls to prevent allergen cross-contact (FAO and WHO, 2020c). In relation to this CoP, the 50th session of CCFH requested FAO and WHO to provide scientific advice with respect to the list of priority allergens and the use of allergen threshold levels to inform allergen risk management for foods (FAO and WHO, 2018). In March 2021, the Expert Consultation reconvened to establish threshold levels for priority allergenic foods and recommend analytical methods for detection in food and food processing environments. This second meeting addressed a part of the CCFH request by establishing recommended reference doses, based on health-based guidance values (FAO and WHO, 2021a).

The CCFL is also developing guidance on the use of precautionary allergen or advisory labelling (PAL) (FAO and WHO, 2021b). In October 2021, FAO and WHO convened the Expert Consultation for a third meeting to review and evaluate the evidence in support of precautionary allergen labelling (FAO and WHO, 2021c) to support the ongoing work of the CCFL.

This report summarizes the fourth meeting of the ad hoc expert committee and addresses the remaining request from Codex on whether certain foods and ingredients, such as highly refined foods and ingredients, that are derived from any of the foods on the list of priority allergenic foods could be exempted from mandatory declaration. The purpose of this fourth meeting was to further elaborate on the recommendations from the 1st meeting on derivatives of food allergens and to establish a framework for evaluating labelling exemptions for derivatives of priority allergenic foods (Annex 2).

Conclusions

A pro forma process (i.e. a flow-chart, Annex 3) has been developed and tested against allergen derivatives previously granted exemptions in various countries or regions and found to be effective for consideration of future exemption decisions.

After a succinct description of the derivative, including its source and composition (especially regarding protein from the allergenic source food), other key elements of the flow-chart include the documentation of existing uses of the derivative, its safety and any reported adverse reactions, other compositional features, past exposure routes and amounts, and method of manufacture. The information should include a specification for the derivative. The intended uses of the derivative and predicted exposure, expressed in mg total protein from the allergenic source, resulting from these uses should also be included.

The proposal for the exemption should assess the equivalence of any new derivative and its uses to any existing ingredient(s) of a similar type from similar sources, taking into account species of origin, total protein content, other critical compositional features, safety and any reported adverse reactions, and methods of manufacture.

For total protein quantification (flow-chart Annex 3, box 3), it is recommended to use more than one test method, each based on different principles, that are fit for purpose and may include total amino acid analysis as appropriate. Methods employing extraction should include assessments of recovery and precision. The choice of an appropriate calibrant is important, as well as using appropriate sampling and sample preparation procedures.

Assessments of potential alterations in the allergenicity of the protein(s) in the derivative (flow-chart Annex 3, box 8) can be established using a weight of evidence approach based on data from:

- Allergen profiling assays, e.g. mass spectrometry or allergen molecule specific assays. These approaches could provide additional information to show how the allergen profile has been modified by the process used to manufacture a derivative. Also, protein/peptide size distribution through size exclusion chromatography or mass spectrometry or a combination thereof to assess if larger peptide fragments (e.g. with 15 amino acids or more) exist may be used; and
- IgE binding studies using sera from relevant food allergic subjects with a clinically confirmed food allergy using appropriate methods such as IgE-immunoblotting, IgE immunoassay (including inhibition assays) and effector cell assays.

Clinical evaluation (flow-chart Annex 3, box 10), when necessary, may require an oral food challenge study. Oral food challenge study design and assessment criteria should be determined on a case-by-case basis in consultation with relevant parties.

Exposure assessment based on safety assessment principles is an essential component of the process.

Inputs needed for the exposure assessment are:

- Intended use levels of the derivative for relevant food product categories;
- Consumption values for intended food product categories and relevant consumer groups on a per eating occasion basis; and
- Analytical data or calculated equivalent of concentration of total protein or total protein from the priority allergenic source.

The above inputs are combined into an estimation/calculation of exposure doses, and if applicable, of exposures from a combination of multiple food categories consumed on a single eating occasion.

Existing dossiers and recommendations have typically estimated exposures using:

- Food consumption data based on the 90th, 95th or 97.5th percentile of consumers (a p90, p95 or p97.5 quantity of a single eating occasion), which may vary regionally; and
- Maximum levels of intended uses of the derivative(s).

Protein concentrations have typically been presented as ranges. Estimation/calculation of exposure doses typically are presented using either the means or maximum concentrations. This may vary depending on the applicant or the regulatory body doing the assessment.

The expert committee concluded that:

- For the current accepted exemptions, there is an established history of safe consumption.

- The exposure estimates in reasonable worst-case consumption scenarios, based on the scientific data considered for the exemptions approved to date (in EU, ANZ and USA), lead to values around the relevant Reference Doses (RfD) established by the 2nd meeting divided by 30 (RfD/30). Consequently, the RfD/30 appears to provide an adequate margin of exposure (MoE) for derivative safety assessment.
- Suitable methods of analysis are available for protein levels based on the RfD/30.
- A derivative that undergoes the weight of evidence risk assessment as outlined in this report and meets the criterion (RfD/30) may not require clinical studies to establish safety.

Based on these conclusions, the expert committee recommends that the process outlined in the flow-chart (Annex 3) be used to guide any future development and evaluation of derivative exemptions. Establishment of safety based upon this weight of evidence approach is dependent upon consideration of data quality, outcome of the exposure assessment for all intended ingredient uses (specified for exemption) and review by Competent Authorities (as needed). When safety is established, exemption can be justified.

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Annex 1. List of participants

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RESOURCE PERSONS

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SECRETARIAT

Akio Hasegawa, WHO, Switzerland

Christine Kopko, FAO, Italy

Jeffrey LeJeune, FAO, Italy

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Annex 2. Meeting plan of the Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens

Meeting 1: Review and validation of Codex priority allergen list through risk assessment (November – December 2020)

I. Whether the published criteria for assessing additions and exclusions to the list is still current and appropriate.
II. Subject to the advice on the criteria above:
    - Whether there are foods and ingredients that should be added to or deleted from the list.
    - Clarification of the groupings of foods and ingredients in the list.

Meeting 2: Review and establish threshold levels in foods of the priority allergens (March – April 2021)

I. What are the threshold levels for the priority allergens below which the majority of allergic consumers would not suffer an adverse reaction?
II. For the priority allergens, what are appropriate analytical methods for testing food and surfaces?
III. What should be the minimum performance criteria for these different analytical methods?

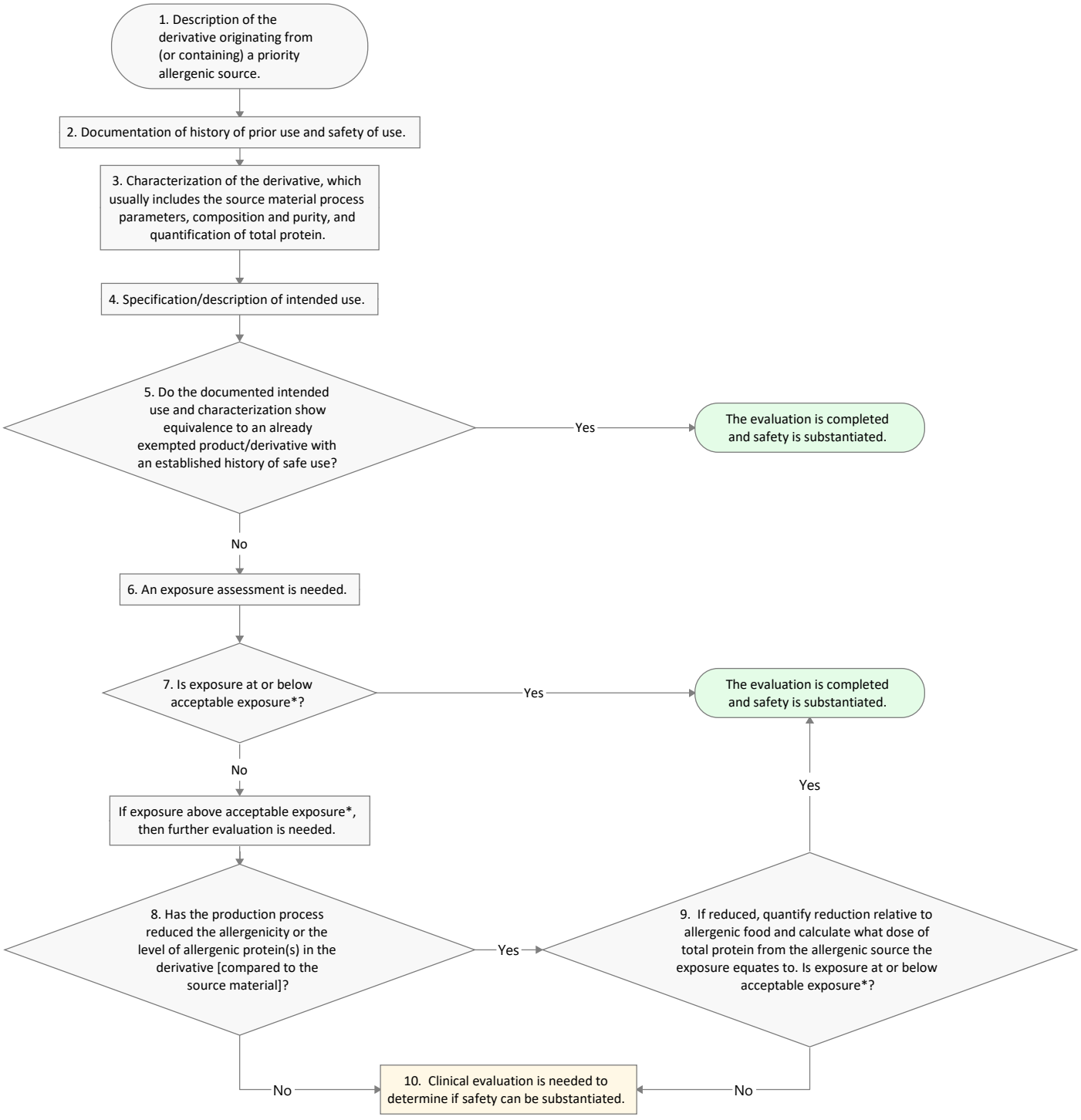
Meeting 3: Review and evaluate the evidence in support of precautionary labelling (October 2021)

I. What methods/tools are available for FBOs to determine:
    - whether allergen cross-contact is reasonably likely to occur in a food after a cleaning procedure;
    - whether allergen cross-contact is reasonably likely to occur from equipment used for foods with different allergen profiles; and
    - the level of allergen in a food resulting from cross-contact?
II. Guidance on precautionary labelling.
    - The use of scientifically based threshold levels to evaluate risk for consumers with food allergies.
    - Determine the conditions for using the precautionary allergen labelling.
III. How can thresholds be used by FBOs to determine:
    - the extent to which a cleaning procedure removes an allergen to a level that prevents or minimises the risk to the majority of allergic consumers from allergen cross-contact; and
    - whether an ingredient that contains a low level of an allergen (e.g. an ingredient with a precautionary allergen label) warrants control of its use to prevent or minimise allergen cross-contact?

Meeting 4: Review and establish exemptions for the food allergens (November 2022)

I. Whether certain foods and ingredients, such as highly refined foods and ingredients, that are derived from the list of foods known to cause hypersensitivity can be exempted from mandatory declaration.

Annex 3. Outline of the process for consideration of labelling exemptions for foods and ingredients derived from priority allergenic sources



* acceptable exposure in the context of assessing an exemption application can be derived by applying a Margin of Exposure (MoE) to the Reference Dose (RfD) proposed in the 2nd meeting of this expert consultation (i.e. RfD divided by MoE; RfD/MoE). The RfD/30 appears to provide an adequate MoE for derivative safety assessment. For comparison with the acceptable exposure, exposure should be calculated into and expressed as the equivalent of dose of total protein from the priority allergenic source.

NOTE: Establishment of safety based upon this weight of evidence approach is dependent upon consideration of data quality, outcome of the exposure assessment and review by competent authorities (as needed). When safety is established, a labeling exemption can be granted.