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Scientific and technical guidance for the preparation and presentation of applications
pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended**

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SCIENTIFIC OPINION

Scientific and technical guidance for the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on Scientific and technical guidance for the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended. This guidance applies to food ingredients or substances with known allergenic potential listed in Annex IIIa of 2003/89/EC (as amended) or products thereof, and aims to assist applicants in the preparation and presentation of well-structured applications for exemption from labelling. It presents a common format for the organisation of the information to be provided and outlines the information and scientific data which must be included in the application, the hierarchy of different types of data and study designs, reflecting the relative strength of evidence which may be obtained from different study types, and the key issues which must be addressed in the application in order to assess the likelihood of a food allergen-derived preparation/foodstuff(s) triggering adverse reactions in sensitive individuals under the proposed conditions of use. This draft guidance document was endorsed by the NDA Panel on 11 July 2013, and was released for public consultation from 26 July 2013 to 13 September 2013.

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KEY WORDS

food allergens, allergenicity, foodstuff, exemption, labelling, application, guidance document

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² Panel members: Carlo Agostoni, Roberto Berni Canani, Susan Fairweather-Tait, Marina Heinonen, Hannu Korhonen, Sébastien La Vieille, Rosangela Marchelli, Ambroise Martin, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Sean (J.J.) Strain, Inge Tetens, Daniel Tomé, Dominique Turck and Hans Verhagen. Correspondence: nda@efsa.europa.eu

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SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on Scientific and technical guidance for the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC.

This guidance applies to food ingredients or substances with known allergenic potential listed in Annex IIIa of 2003/89/EC (as amended) or products thereof, hereafter referred to as food allergens. Food allergen-derived preparation refers to a product derived from a food allergen, and for which an exemption from labelling is requested. In this guidance, foods or beverages manufactured using (i.e. intentionally adding) food allergen-derived preparations, and for which an exemption from labelling is requested, are referred to as food allergen-derived foodstuffs.

The purpose of this guidance is to update the Commission guidelines in view of assisting applicants in the preparation and presentation of well-structured applications for exemption from labelling pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC. It presents a common format for the organisation of the information to be provided and outlines the information and scientific data which must be included in the application, the hierarchy of different types of data and study designs, reflecting the relative strength of evidence which may be obtained from different study types, and the key issues which should be addressed in the application in order to assess the likelihood of a food allergen-derived preparation/foodstuff(s) triggering adverse reactions in sensitive individuals under the proposed conditions of use. This format will also help the NDA Panel to deliver its scientific advice in an effective and consistent way.

To allow a scientific evaluation by the NDA Panel of the likelihood that the food allergen-derived preparation/foodstuff(s) for which an exemption is requested triggers adverse reactions in sensitive individuals under the proposed conditions of use, the application must contain:

a) information on the characteristics of the food allergen-derived preparation for which the labelling exemption is requested. If the food allergen-derived preparation is intended for use in the manufacturing of foodstuff(s), information on the characteristics of the foodstuff(s) as consumed must be provided in the application. Where applicable, this information should contain aspects considered pertinent to the allergenic potential of the food allergen-derived preparation/foodstuff(s) for which an exemption is requested, such as the composition, physical and chemical characteristics, detailed description of the manufacturing process, stability, intended use, and an assessment of the residual allergenic proteins contained in the food allergen-derived preparation/foodstuff(s).

b) all pertinent scientific data which form the basis for the scientific evaluation of the allergenicity of the food allergen-derived preparation/foodstuff(s) for which an exemption from labelling is requested. Pertinent data means all human and non-human studies, published or unpublished, in favour and not in favour of the non-allergenicity of the food allergen-derived preparation/foodstuff(s) for the proposed use.

In cases where any of the required data are not relevant for a particular application, reasons/justification must be given for the absence of such data in the application.

Pertinent published human data should be identified through a comprehensive review which addresses the allergenicity of the food allergen-derived preparation/foodstuff(s) for the proposed conditions of use in a transparent manner. Data from food challenge studies in humans addressing the presence/absence of adverse reactions in susceptible (food allergic) individuals while consuming the food-allergen derived preparation/foodstuff(s) may provide important information regarding its allergenicity. Double-blind placebo controlled food challenges (DBPCFC) are less subject to bias

than single-blind challenges or open challenges. Sufficient characterisation of the study population regarding the diagnosis of food allergy is important. The selected sample size should be adequately justified within the context of each application. Because of the scientific uncertainties in extrapolating non-human data to humans, data from studies in animals or other model systems alone cannot substitute for human data as evidence of non-allergenicity, but may be included as supporting evidence.

It is intended that the guidance will be kept under review and will be further amended and updated as appropriate in the light of experience gained from the evaluation of applications for exemption from labelling.

This draft guidance document was endorsed by the NDA Panel on 11 July 2013, and was released for public consultation from 26 July 2013 to 13 September 2013.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC, establishes the cases and conditions for amending Annex IIIa to that Directive, which includes a list of food ingredients or substances known as likely to trigger adverse reactions in sensitive individuals. These products must always appear in the list of ingredients on food labels.

The same Directive also sets up a procedure for exempting from labelling, under certain conditions, derivatives of these ingredients or substances. Applicants who are seeking the exclusion of a given product from Annex IIIa (i.e. exemption from labelling) have to submit a request supported by the results of relevant scientific studies.

The legislation, however, does not specify the content of such requests. Therefore, the Commission services established in 2005, in close cooperation with EFSA, an administrative guidance document specifying in a very succinct way what type of information the application should contain.

In the light of the experience gained with the evaluation of applications for exemption from labelling, and to further assist applicants in preparing and submitting their applications, the Commission deems it important to update the above-mentioned guidance document. In particular, in relation to the technical dossiers to be submitted, it appears useful to provide guidance as to which type of scientific data and information could be expected to substantiate the unlikelihood of adverse reactions triggered in susceptible individuals by the consumption of food ingredients or substances with known allergenic potential under the conditions of use specified by the applicants.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

On the basis of Article 29 of Regulation (EC) No 178/2002, EFSA is requested to advise on the scientific data and information expected to be provided by the applicants, in view of improving and updating by the Commission the guidelines for the submission and preparation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC.

OBJECTIVES

The guidance presented in this document is for updating the Commission guidelines in view of assisting applicants in the preparation and presentation of well-structured applications for exemption from labelling pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC.

It presents a common format for the organisation of the information to be provided and outlines:

- the information and scientific data which must be included in the application,
- the hierarchy of different types of data and study designs, reflecting the relative strength of evidence which may be obtained from different study types,
- the key issues which should be addressed in the application in order to assess the likelihood of a food ingredient or substance triggering adverse reactions in sensitive individuals under the proposed conditions of use.

It is intended that the guidance will be kept under review and will be further amended and updated as appropriate in the light of experience gained from the evaluation of applications for exemption from labelling.

SCOPE

The guidance presented in this document is to assist applicants in preparing and presenting applications for exemption from labelling pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC, which foresees that the list of ingredients in Annex IIIa shall be systematically re-examined and, where necessary, updated on the basis of the most recent scientific knowledge. This guidance is not intended for requesting other type of updates of Annex IIIa (e.g. addition of new ingredients).

GENERAL PRINCIPLES

This document should be read in conjunction with Directive 2003/89/EC⁴ (amending Directive 2000/13/EC) of the European Parliament and of the Council as regards indication of the ingredients present in foodstuffs, other administrative guidance⁵, and current and future⁶ Community guidelines and Regulations. This document should also be read in conjunction with the scientific opinion of the NDA Panel on the evaluation of allergenic foods for labelling purposes⁷, which is currently under revision and is expected to be released for public consultation in the first quarter of 2014.

⁴ 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.

⁵ Second administrative guidance from the Commission's services for the application of Article 6 Paragraph 11 of Directive 2000/13/EC http://ec.europa.eu/food/food/labellingnutrition/foodlabelling/2nd_guid_art6_11_200013ec_en.pdf

⁶ Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004. OJ L 304. 22.11.2011, p.18. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32011R1169:EN:NOT>

⁷ NDA (Scientific Panel on Dietetic Products, Nutrition and Allergies) (2004). Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission relating to the evaluation of allergenic foods for labelling purposes. The EFSA Journal 32, 1-197. <http://www.efsa.europa.eu/en/efsajournal/pub/32.htm>

1. This guidance applies to food ingredients or substances with known allergenic potential listed in Annex IIIa of Directive 2003/89/EC (as amended) or products thereof. The term **food allergen** will be used for all substances listed under Annex IIIa, being aware that lactose and sulphites are not food allergens, and that gluten may induce both food allergy and coeliac disease.

Food allergen-derived preparation (e.g. potassium caseinate), for which an exemption from labelling is requested, means a product derived from a **food allergen** (e.g. milk).

Foods or beverages (e.g. white wine) for which an exemption from labelling is requested that are manufactured using (i.e. intentionally adding) the **food allergen-derived preparation** (e.g. potassium caseinate) are referred to as **food allergen-derived foodstuffs** in this guidance.

Allergenicity refers to the capacity of the **food allergen-derived preparation/foodstuff(s)** to trigger adverse reactions in susceptible (food allergic) individuals when consumed orally under the specified conditions of use.

Allergenic protein refers to proteins or peptides (e.g. ovalbumin and lysozyme) responsible for the allergenicity of **food allergens** (e.g. egg).

2. The term **application** hereafter means a stand-alone dossier containing the information and the scientific data submitted for exemption from labelling of a food allergen-derived preparation/foodstuff(s) under the proposed conditions of use.
3. This guidance presents a common format for the organisation of the information in order to assist applicants in the preparation of a well-structured application. Adherence to this format will also facilitate access to the information by the NDA Panel in order to conduct the evaluation and deliver scientific advice in an effective and consistent way.
4. The NDA Panel evaluates the likelihood of adverse reactions in sensitive individuals after oral consumption of the food allergen-derived preparation/foodstuff(s) for which the labelling exemption is requested according to the nature and quality of the totality of the evidence provided. This includes information about the characteristics of the food allergen-derived preparation/foodstuff(s), its intended use, and the residual allergenic proteins it contains, as well as information on its residual allergenicity. There is no pre-established formula as to how much or what type of information is required to conclude on the non-allergenicity of the food allergen-derived preparation/foodstuff(s) for which the labelling exemption is requested. Scientific requirements are considered by the NDA Panel on a case-by-case basis and are to be found in published opinions relative to previous applications for exemption.
5. It is the duty of the applicant to provide all pertinent scientific data in the application (published and unpublished, data in favour and not in favour) relative to the assessment of the likelihood of adverse reactions being triggered in sensitive individuals by the oral consumption of the food allergen-derived preparation/foodstuff(s) under the proposed conditions of use.
6. Not all the information and data specified in this guidance will be required for each application. However, reasons/justification must be given for the absence of such data in the application.
7. The application must contain information on the characteristics of the food allergen-derived preparation for which an exemption from labelling is requested. If the food allergen-derived preparation is intended for use in the manufacturing of a foodstuff(s), information on the

characteristics of the food allergen-derived foodstuff(s) must be provided. Where applicable, this information should contain aspects such as the composition, physical and chemical characteristics, manufacturing process, and stability.

Measurements should be performed in a competent laboratory. Whenever a quality system is in place for performance/control/documentation (e.g. good manufacturing practice (GMP), good laboratory practice (GLP), applicable ISO standard), the particular system should be indicated.

8. The application must contain a detailed description of the conditions under which the food allergen-derived preparation/foodstuff(s) is intended to be used, including the corresponding use levels and exposure data (amount consumed on a single occasion).
9. The application must contain a detailed description of the manufacturing process of the food allergen-derived preparation and, if appropriate, of the food allergen-derived foodstuff(s) which has been manufactured from it, as consumed, including any steps introduced in the process to reduce the quantity of allergenic proteins in the food allergen preparation/foodstuff(s), or their allergenicity.
10. The application should contain an analysis of all residual major⁸ allergenic proteins contained in the food allergen-derived preparation and, if appropriate, of all residual major allergenic proteins in the food allergen-derived foodstuff(s) which has been manufactured from it, as consumed. The protocol used to obtain the samples for analysis and the analytical methods used for the detection of allergenic proteins should be adequately described. Analytical methods need to be standardised and validated to ensure quality and consistency of the data. If no allergenic proteins are detected, this information on its own does not necessarily imply the non-allergenicity of the food allergen-derived preparation/foodstuff(s).
11. Data from food challenge studies in humans addressing the presence/absence of adverse reactions in susceptible (food allergic) individuals while ingesting the food allergen-derived preparation or foodstuff(s), whichever is intended for human consumption, may provide important information regarding its allergenicity. Double-blind placebo controlled food challenges (DBPCFC) are less subject to bias than single-blind challenges or open challenges. Sufficient characterisation of the study population regarding the diagnosis of food allergy/intolerance is important. The reasons for selecting a particular sample size in the context of each application should be indicated. Other human studies which do not entail oral consumption of the food allergen-derived preparation/foodstuff(s) (e.g. skin-prick testing studies) can be used as supportive evidence of non-allergenicity. Observational studies (e.g. case-reports) in humans consuming the food allergen-derived preparation/foodstuff(s), if available, should also be provided.

It is not within the scope of this guidance to provide details on how food challenges should be performed, or on which clinical outcomes should be considered. For this, the NDA Panel considers what is generally accepted in the research field and consults experts in the discipline, as appropriate.

Because of the scientific uncertainties in extrapolating non-human data to humans, data from studies in animals or other model systems alone cannot substitute for human data as evidence of non-allergenicity, but may be included as supporting evidence.

⁸ For example, for the food allergen-derived preparation egg white, the major allergenic proteins ovomucoid, ovalbumin, conalbumin and lysozyme should be measured.

Whenever a quality system has been used in the conduct of the studies (e.g. good clinical practice (GCP), good laboratory practice (GLP), applicable ISO standard), the particular system used should be indicated.

12. A comprehensive review of published human studies reporting on adverse reactions to the food allergen under the proposed use is required. The review should be performed in a transparent manner in order to demonstrate that the application adequately reflects all the evidence available.

Data from studies in humans should be organised according to a hierarchy of study designs, and should reflect the relative strength of evidence which may be obtained from different types of studies.

13. The application in itself cannot be confidential. Sections considered as confidential by the applicant should be kept to a minimum and clearly identified.
14. One application should be prepared for each individual food allergen-derived preparation. In this context, if several preparations of the food allergen exist, only one can be the subject of each application. However, multiple foodstuffs manufactured using the same food allergen-derived preparation can be proposed by the applicant in the same application as candidates for labelling exemption, provided that the scientific evidence is valid for all proposed food allergen-derived foodstuffs⁹.

ORGANISATION AND CONTENT OF THE APPLICATION

The following information should be provided in the application, and the structure should follow a common format, i.e. order and numbering system of different parts, headings and sub-headings. Data provided in the application should be organised into **four Parts**.

Part 1 contains the specific requirements for the administrative and technical data, such as the application form, and information related to the applicant and the application specifications, including conditions of use and exposure data.

Part 2 contains information specific to the food allergen-derived preparation, and to the food allergen-derived foodstuff(s) if applicable, for which an exemption is requested regarding the characteristics (such as the composition, physical and chemical characteristics, manufacturing process, and stability) and allergenic protein content.

Part 3 contains all scientific data (published and unpublished, in favour and not in favour) relative to the residual allergenicity of the food allergen-derived preparation, and of the food allergen-derived foodstuff(s) if applicable, under the proposed conditions of use.

Part 4 comprises the glossary or abbreviation of terms quoted throughout the different Parts, copies/reprints of publications, and full study reports of unpublished data.

Where some of the data that are required as described in this guidance document do not apply to a particular application, reasons/justification must be given for the absence of such data in the application.

⁹ For example, if multiple milk-derived preparations exist (e.g. potassium caseinate, skimmed milk) for the same use (e.g. manufacture of wine), only one (e.g. either potassium caseinate or skimmed milk) can be the subject of an application. However, different types of wine (e.g. white and red) manufactured using the same preparation (e.g. same potassium caseinate preparation) under the proposed conditions of use can be proposed in the same application for labelling exemption.

1. PART 1: ADMINISTRATIVE AND TECHNICAL DATA

1.1. Comprehensive table of contents of the application

1.2. Application form

Please use the application form provided in the **Appendix**.

1.3. Applicant

1.3.1. Company/organisation

Provide the name and address of the company or organisation¹⁰.

1.3.2. Contact person

Indicate the contact person authorised to communicate with EFSA on behalf of the applicant¹¹.

1.4. Specifications

1.4.1. Confidential data

State whether it includes confidential data yes no

If yes, please specify the related Part in the application, stating section and page number, and providing (a) verifiable justification(s)/declaration(s).

1.4.2. Food allergen-derived preparation

Specify the food allergen-derived preparation for which an exemption from labelling is requested. If the name of the food allergen-derived preparation differs from those listed in Annex IIIa as amended, the food allergen as listed in Annex IIIa should also be specified¹².

1.4.3. Conditions of use

Specify whether the food allergen-derived preparation will be consumed as such and/or will be used in the manufacturing of foodstuff(s). In the latter case, specify the foodstuff(s) that will be manufactured using the food allergen-derived preparation.

1.4.4. Anticipated intake/exposure

Specify the expected quantity and pattern of consumption of the food allergen-derived preparation. If applicable, specify the expected quantity and pattern of consumption of the food allergen-derived foodstuff(s) for which an exemption from labelling is requested.

¹⁰ In case more than one company or organisation submits an application, provide their names and addresses. EFSA requires that **only one contact person be authorised to communicate with EFSA**.

¹¹ To facilitate communication, EFSA requires that there be only **one contact person per application**.

¹² For example, if exemption from labelling is requested for potassium caseinate, milk should be specified as the food allergen listed in Annex IIIa.

Information on the expected quantity of consumption per single occasion, on the pattern of consumption (e.g. times per day, time span in which a certain amount is consumed), and on particular conditions in which the food allergen-derived preparation/foodstuff(s) is meant to be consumed (e.g. before/during/after intense physical exercise) should be specified on an individual basis in different age groups.

1.5. References

References quoted under Part 1 should be given here (alphabetical order of first authors).

2. PART 2: CHARACTERISTICS OF THE FOOD ALLERGEN-DERIVED PREPARATION/FOODSTUFF(S)

2.1. Food allergen-derived preparation

The food allergen-derived preparation for which an exemption is requested should be characterised. If several preparations derived from the food allergen exist, please clarify the specific preparation of the food allergen that is the subject of this application.

Please note that one application should be prepared for each individual food allergen-derived preparation¹³.

2.1.1. General specifications

The source and specifications (e.g. physical and chemical properties, composition, and where applicable, microbiological constituents) of the food allergen-derived preparation for which an exemption is requested should be provided.

Analytical methods applied should be scientifically sound, standardised and validated to ensure quality and consistency of the data.

Measurements should be performed in a competent laboratory. Whenever a quality system is in place for control/documentation (e.g. GLP and ISO17025) the particular system should be indicated.

2.1.2. Manufacturing process

Where applicable, a detailed description of the manufacturing process should be provided. If the production follows a quality process (e.g. GMP) the particular system should be indicated. Please specify whether the manufacturing process is mandatory or refers to a voluntary code.

Any steps introduced in the process which could reduce the quantity of allergenic proteins or their allergenicity in the food allergen-derived preparation should be described in detail.

2.1.3. Allergen specifications

An assessment of all major residual allergenic proteins contained in the food allergen-derived preparation should be provided. Data/a rationale for the selection of the allergenic proteins to be measured should be provided.

¹³ For example, if multiple milk-derived preparations exist (e.g. potassium caseinate, skim milk) for the same use (e.g. manufacture of wine), only one (e.g. either potassium caseinate or skim milk) can be the subject of an application.

Analytical methods applied should be scientifically sound, standardised and validated to ensure quality and consistency of the data for detection of residual allergenic proteins.

Details on the protein extraction method used and the conditions applied should be described. Attention should be paid to whether the extraction methods used are appropriate for the matrix of interest.

Details on the performance of the method used for detecting allergenic proteins should be provided in terms of accuracy, precision, limit of detection (LOD), recovery, and limit of quantification (LOQ) whenever possible (e.g. whenever certified reference materials are available). Cross-reactivity should be considered.

2.1.4. Stability

Where applicable, a brief summary of the studies undertaken to assess the stability of the food allergen-derived preparation (e.g. conditions, batches and analytical procedures) should be provided. Conclusions with respect to storage conditions and shelf-life should be given. Batch-to-batch variability should be addressed.

2.2. Food allergen-derived foodstuff(s)

If the food allergen-derived preparation for which an exemption is requested is intended for use in the manufacturing of a foodstuff(s), information on the characteristics of the food allergen-derived foodstuff(s) as consumed should be provided in the application.

If multiple foodstuffs manufactured using the same food allergen-derived preparation are proposed as candidates for labelling exemption, please provide the information below for each of the proposed food allergen-derived foodstuffs.

2.2.1. General specifications

The source and specifications (e.g. physical and chemical properties, composition, and where applicable microbiological constituents) of the food allergen-derived foodstuff(s) for which an exemption is requested should be provided.

Analytical methods applied should be scientifically sound, standardised and validated to ensure quality and consistency of the data.

Measurements should be performed in a competent laboratory. Whenever a quality system is in place for control/documentation (e.g. GLP and ISO17025) the particular system should be indicated.

2.2.2. Manufacturing process

Where applicable, a detailed description of the manufacturing process should be provided. If the production follows a quality process (e.g. GMP), the particular system should be indicated. Please specify whether the manufacturing process is mandatory or refers to a voluntary code.

Any steps introduced in the process (e.g. heating, high pressure, ultrasound, fermentation, digestion, and filtration) which could affect the quantity of allergenic proteins or their allergenicity in the food allergen-derived foodstuff(s) should be described in detail.

2.2.3. Allergen specifications

An assessment of all major residual allergenic proteins contained in the food allergen-derived foodstuff(s) should be provided by using direct methods for allergen detection whenever possible (e.g. ELISA, and mass spectrometry). Data/a rationale for the selection of the allergenic proteins to be detected should also be provided. Indirect methods for allergen detection (i.e. for DNA analysis, e.g. PCR) may be used in addition, or whenever direct methods are not available (e.g. celery) or not suitable (e.g. extensive heat treatments) for allergen detection.

Analytical methods applied should be scientifically sound, standardised and validated to ensure quality and consistency of the data for detection of residual allergens. A rationale for the selection of the methods of detection used in the context of a particular application should be provided.

Details on the protein/DNA extraction method used and the conditions applied should be described. Attention should be paid to whether the extraction methods used are appropriate for the matrix of interest.

Details on the performance of the detection method(s) should be provided in terms of accuracy, precision, limit of detection (LOD), recovery, and limit of quantification (LOQ) whenever possible (e.g. whenever certified reference materials are available). Cross-reactivity should be considered.

2.2.4. Stability

Where applicable, a brief summary of the studies undertaken to assess the stability of allergenic proteins in the food allergen-derived foodstuff(s) (e.g. conditions, batches and analytical procedures) should be provided. Conclusions with respect to storage conditions and shelf-life should be given. Batch-to-batch variability should be addressed.

2.3. References

References quoted under **Part 2** should be given here (alphabetical order of first authors).

3. PART 3: SCIENTIFIC DATA ON ALLERGENICITY

Part 3 contains all pertinent scientific data relative to the allergenicity of the food allergen-derived preparation/foodstuff(s) for which an exemption is requested. Pertinent data means all human and non-human studies, published or unpublished, in favour and not in favour of the non-allergenicity of the food allergen-derived preparation/foodstuff(s) for the proposed use.

Reporting of primary data should be transparent, complete, and unambiguous, in order to allow for a full scientific evaluation. In this context, journal abstracts and articles published in newspapers, magazines, newsletters or handouts that have not been peer-reviewed, books or chapters of books for consumers or the general public, and posters or abstracts of conference proceedings **do not generally meet** the reporting standards required for a scientific evaluation and should not be quoted.

3.1. Identification of pertinent data

3.1.1. Identification of published human data

Published human data should be identified through a comprehensive review which addresses the allergenicity of the food allergen-derived preparation/foodstuff(s) for the proposed use in a transparent manner.

The following information on the comprehensive review should be provided, as appropriate:

3.1.1.1. Authorship

The name, affiliation, declaration of interests in relation to the subject covered by the review, and signature of the reviewer(s) responsible for the comprehensive review should be indicated.

3.1.1.2. Background

The suitability (strengths and limitations) of the proposed search strategy to retrieve all available information on the allergenicity of the food allergen-derived preparation/foodstuff(s) for the proposed use should be discussed here.

3.1.1.3. Exclusion and inclusion criteria

Exclusion and inclusion criteria that have been applied by the applicant in order to select the pertinent publications.

3.1.1.4. Literature search

The databases that have been searched should be listed, and details about the search strategy (including the terms used, limits used such as dates of publication, publication types, languages, population subgroups or default tags) should be provided. Other sources of data should be acknowledged (web sites, hand searching, etc.).

A list of references (but not copies/reprints) of the publications considered as NOT PERTINENT to the application and therefore **excluded** should be provided here (alphabetical order of first authors).

For pertinent published human data identified, please go to Section 3.2.

3.1.2. Identification of unpublished human data

The strategy followed to identify unpublished human studies that are considered as pertinent to the application should be depicted.

For pertinent unpublished human data identified, please go to Section 3.2.

3.1.3. Identification of published and unpublished non-human data

The strategy followed to identify published and unpublished non-human studies that are considered as pertinent to the application should be depicted, and the reasons for selecting them as supporting evidence should be stated.

For pertinent published and unpublished non-human data identified, please go to Section 3.2.

3.2. Pertinent scientific data identified

A list of references of the pertinent published and unpublished studies (by alphabetical order of first authors, clearly indicating the publication status) should be provided in the sections below in accordance with the hierarchy of study design and publication type.

Copies/reprints of pertinent publications and full study reports of unpublished studies should be provided in **Part 4**.

3.2.1. Human intervention studies

3.2.1.1. Food challenge studies

- Double-blind placebo controlled food challenges
- Single-blind placebo controlled food challenges
- Open label food challenges

3.2.1.2. Skin prick testing studies

3.2.1.3. Other

3.2.2. Human observational studies

3.2.2.1. Case reports

3.2.2.2. Retrospective or recall studies

3.2.3. Animal studies

3.2.4. *In vitro* studies

3.2.4.1. IgE-binding capacity analysed by inhibition studies

3.2.4.2. Other

3.2.5. Review publications

4. PART 4: ANNEXES TO THE APPLICATION

4.1. Glossary and Abbreviations

To be presented in alphabetical order

4.2. Copies/reprints of pertinent published data

To be presented in alphabetical order of first authors

4.3. Full study reports of pertinent unpublished data

To be presented in alphabetical order of first authors

APPENDIX

A. APPLICATION FORM

APPLICATION FORM



The application form should be used for an application submitted for exemption from mandatory labelling pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended by Directive 2003/89/EC¹⁴, to the European Commission, and for scientific evaluation by the European Food Safety Authority (EFSA).

A separate application for each preparation of the food allergen under the conditions of use specified by the applicant is required.

DECLARATION and SIGNATURE

Food allergen-derived preparation:

Food allergen-derived foodstuff(s)¹⁵:

Food allergen as listed in Annex IIIa:

Proposed use:

Applicant's¹⁶ (Company) name:

Address:

Country:

Contact person's¹⁷ name:

Address:

Country:

Telephone:

Fax:

e-mail:

It is hereby confirmed, to our best knowledge, that all existing data which are relevant to the application for exemption from mandatory labelling have been supplied in the application, as appropriate.

On behalf of the applicant:

Signature

Name

Function

Place and date (yyyy-mm-dd)

¹⁴ 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.

¹⁵ If applicable.

¹⁶ If the application is being submitted by more than one company or organisation, names and addresses of all applicants should be provided.

¹⁷ To facilitate communication, EFSA requires that there be only one contact person per application.

GLOSSARY AND ABBREVIATIONS

Note: The definitions given in this glossary are valid only for the purpose of this guidance document.

Allergenicity	The capacity of a food allergen to trigger adverse reactions in susceptible (food allergic) individuals when consumed orally under the specified conditions of use.
Allergenic protein	Proteins or peptides responsible for the allergenicity of food ingredients or substances listed in Annex IIIa of Directive 2003/89/EC (as amended).
Applicant	Refers to the natural or legal person responsible for the submission and content of the application, and for the interaction with regulatory authorities in the course of the evaluation.
Application	Stand-alone dossier containing the information and scientific data submitted for exemption from labelling pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended, of a food allergen-derived preparation/foodstuff(s) under the proposed conditions of use.
DNA	Deoxyribonucleic acid
ELISA	Enzyme-linked immunosorbent assay
Food allergens	Food ingredients or substances with known allergenic potential listed in Annex IIIa of Directive 2003/89/EC (as amended) or products thereof.
Food allergen-derived foodstuffs	Foods or beverages that are manufactured using (intentionally adding) food allergen-derived preparations, and for which an exemption from labelling is requested.
Food allergen-derived preparation	Product derived from a food allergen, and for which an exemption from labelling is requested
GCP	Good clinical practice
GLP	Good laboratory practice
GMP	Good manufacturing practice
LOD	Limit of detection
LOQ	Limit of quantification
PCR	Polymerase chain reaction