European Food Safety Authority

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SCIENTIFIC OPINION

Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1)[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The scientific and technical guidance of the EFSA Panel on Dietetic Products, Nutrition and Allergies for the preparation and presentation of an application for authorisation of a health claim presents a common format for the organisation of information for the preparation of a well-structured application for authorisation of health claims which fall under Article 14 (referring to children's development and health, and to disease risk reduction claims), or 13(5) (which are based on newly developed scientific evidence and/or which include a request for the protection of proprietary data), or for the modification of an existing authorisation in accordance with Article 19 of Regulation (EC) No 1924/2006 on nutrition and health claims made on foods. This guidance 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 types of studies) and the key issues which should be addressed in the application to substantiate the health claim.

KEY WORDS

Health claims, Regulation, food, substantiation, human data, comprehensive review, application, guidance.

[1] On request from the European Commission, Question No EFSA-Q-2007-066, adopted on 06 July 2007. Revision on request from EFSA, Question No EFSA-Q-2011-00215, adopted on 13 May 2011.

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SUMMARY

The European Commission has requested the European Food Safety Authority (EFSA) to issue an opinion on a scientific and technical guidance for applications for authorisation of health claims under Regulation (EC) No 1924/2006 on nutrition and health claims made on foods.

The Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) prepared a draft opinion which was published for public consultation. After considering all comments received, the Panel adopted its opinion on 06 July 2007. In 2011, the NDA Panel was requested by EFSA to revise the opinion with regard to the forms to be used for the submission of an application for authorisation of health claims pursuant to Article 13(5) and 14, and for the modification of an existing authorisation in accordance with Article 19 of Regulation (EC) No 1924/2006. The revision of the guidance, adopted by the NDA Panel on 13 May 2011, was of a purely administrative nature and concerned Parts 1 to 4, as well as the Appendices, of the guidance in order to simplify the presentation of an application.

This guidance applies to health claims related to the consumption of a food category, a food, or its constituents (including a nutrient or other substance, or a combination of nutrients/other substances); hereafter referred to as food/constituent.

The purpose of this guidance is to assist applicants in preparing and presenting their applications for authorisation of health claims which fall under Article 14 (referring to children's development and health, and to disease risk reduction claims) or 13(5) (which are based on newly developed scientific evidence and/or which include a request for the protection of proprietary data), of for modification of an existing authorisation in accordance with Article 19 of the Regulation. 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 health claim applications.

The guidance presents a common format to assist the applicant in the preparation of a well-structured application. This format will also help the NDA Panel to deliver its scientific advice in an effective and consistent way.

In accordance with the requirements of the Regulation, the application must contain:

(a) information on the characteristics of the food/constituent for which a health claim is made. Where applicable, this information should contain aspects considered pertinent to the claim, such as the composition, physical and chemical characteristics, manufacturing process, stability, and bioavailability.

(b) a proposal for the wording of the health claim, including, as appropriate, the specific conditions of use. The following should be specified, with a rationale: the target population for the intended health claim; where appropriate, a statement addressed to persons who should avoid using the food/constituent for which the health claim is made; the quantity of the food/constituent and pattern of consumption required to obtain the claimed effect, and whether this quantity could reasonably be consumed as part of a balanced diet; a warning for any food/constituent that is likely to present a health risk if consumed to excess; any other restrictions of use; directions for preparation and/or use.

The application must also contain all pertinent scientific data (published and unpublished, data in favour and not in favour) which form the basis for substantiation of the health claim. Data from studies in humans addressing the relationship between the consumption of the food/constituent and the claimed effect will be required for substantiation of a health claim. Because of the scientific uncertainties in extrapolating non-human data to humans, data from studies in animals or model systems may be included only as supporting evidence, for example to provide evidence of the

mechanisms by which the food/constituent could exert the claimed effect, and of the biological plausibility of the specific claim.

A comprehensive review of the data from human studies addressing the specific relationship between the food/constituent and the claimed effect is required. This review, and the identification of data considered pertinent to the claim, should be performed in a systematic and transparent manner in order to demonstrate that the application adequately reflects the balance of all the evidence available.

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.

As specified in the Regulation, health claims should be substantiated by taking into account the totality of the available scientific data and by weighing the evidence, subject to the specific conditions of use. In particular, the evidence should demonstrate the extent to which:

(a) the claimed effect of the food/constituent is relevant for human health,

(b) a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food/constituent and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

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BACKGROUND

Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods[3] (hereafter "the Regulation") entered into force on 19 January 2007. In relation to applications for authorisation of health claims, Article 15, paragraph 4 of the Regulation provides the following provision:

"The Commission, having first consulted EFSA, shall establish in accordance with the procedure referred to in Article 25(2) (comitology procedure) implementing rules for application of this Article, including rules concerning the preparation and presentation of the application."

The Commission made available administrative guidance for the preparation and presentation of the application. This guidance needed to be complemented with scientific and technical guidance regarding the content of the application for health claim authorisation.

Therefore, the Commission requested EFSA to provide scientific guidance for the preparation and presentation of applications for health claim authorisation.

TERMS OF REFERENCE

In accordance with Article 31 of Regulation (EC) No 178/2002[4], the European Commission requested the European Food Safety Authority (EFSA) to issue an opinion on scientific and technical guidance for applications for authorisation of health claims. This opinion was adopted on 06 July 2007.

In 2011, the NDA Panel was requested by EFSA to revise the opinion related to this scientific and technical guidance with regard to the forms to be used for the submission of an application for authorisation of health claims pursuant to Article 13(5) and 14 and for modification of an existing authorisation in accordance with Article 19 of Regulation (EC) No 1924/2006.

The NDA Panel is requested to ensure that all revisions are in line with the provisions laid down in Commission Regulation (EC) No 353/2008[5] and reflect the experience gained so far with the evaluation of applications for authorisation of health claims pursuant to Article 13(5) and 14 of Regulation (EC) No 1924/2006, and in the framework of consultations held with applicants. The revision should be of a general administrative nature and not affect the scientific content of the scientific and technical guidance.

The revised opinion related to the scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim should be finalised by June 2011.

[3] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

[4] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

[5] Commission Regulation (EC) No 353/2008 of 18 April 2008 establishing implementing rules for applications for authorisation of health claims as provided for in Article 15 of Regulation (EC) No 1924/2006 of the European Parliament and of the Council. OJ L 109, 19.4.2008, p. 11–16.

OBJECTIVES

Without prejudice to Commission Regulation (EC) No 353/2008, this guidance is intended to assist applicants in preparing and presenting their applications for authorisation of health claims. It presents a common format for the organisation of the information to be presented to assist applicants in the preparation of a well-structured application.

This guidance 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 types of studies,
- the key issues which should be addressed in the application to substantiate the health claim.

SCOPE

The guidance presented in this document is for preparing and presenting applications for authorisation of health claims which fall under Article 14 of the Regulation, i.e. reduction of disease risk claims and claims referring to children's development and health.

- "Reduction of disease risk claim" means any health claim that states, suggests or implies that the consumption of a food category, a food or its constituents significantly reduces a risk factor in the development of a human disease (as defined in the Regulation).
- "For children's claims", there is no definition given in the Regulation. Therefore the proposed health claims referring to children's development and health will be considered on a case by case basis (see also Commission guidance on the implementation of Regulation (EC) No 1924/2006).

The guidance is also applicable to applications for authorisation of health claims which fall under Article 13(5) of the Regulation, i.e. which are based on newly developed scientific evidence and/or which include a request for the protection of proprietary data.

Applications for the modification of existing authorisations of health claims in accordance with Article 19 of the Regulation shall also be presented, as appropriate, in the format outlined in this document.

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 health claim applications.

GENERAL PRINCIPLES

This document should be read in conjunction with Regulation (EC) No 1924/2006 of the European Parliament and of the Council on nutrition and health claims made on foods, other administrative and scientific guidance[6, 7], and current and future Community guidelines and Regulations.

1. This guidance applies to health claims related to the consumption of a food category, a food, or its constituents (including a nutrient or other substance, or a combination of nutrients/other substances); hereafter referred to as **food/constituent**.

2. The term **application** hereafter means a stand-alone dossier containing the information and the scientific data submitted for authorisation of the health claim in question.

3. It is the duty of the applicant to provide all of the available scientific data (including data in favour and not in favour) which are pertinent to the health claim in order to demonstrate that the health claim is substantiated by the totality of the scientific data and by weighing the evidence. The Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA Panel) should not be required to consider other data that are not part of the application, to undertake any additional literature reviews, or to assemble, or process, data in order to evaluate the application. As such, the application substantiating a proposed health claim should be comprehensive and complete. Each application will be considered on a case by case basis.

4. This guidance presents a common format for the organisation of the information in order to assist the applicant in the preparation of a well-structured application. Adherence to this format will also facilitate easy access to information and scientific data in applications to help the NDA Panel to carry out its evaluation and to deliver its scientific advice in an effective and consistent way.

5. **It is emphasised that not all the information and data specified in this guidance will be required for each application. In cases where some of the data which are required according to this guidance do not apply to a particular application, reasons/justification must be given for the absence of such data in the application**.

6. The application must contain information on the characteristics of the food/constituent for which a claim is made. Where applicable, this information should contain aspects such as the composition, physical and chemical characteristics, manufacturing process, stability, and bioavailability. Measurements should be performed in a competent laboratory which can certify the data. Whenever a quality system is in place for control/documentation (e.g. good manufacturing practice (GMP), good laboratory practice (GLP), applicable ISO standard), the particular system should be indicated.

7. The application must contain a proposal for the wording of the health claim, including, as appropriate, the specific conditions of use. The following should be specified, with a rationale: the target population for the intended health claim; where appropriate, a statement addressed to persons who should avoid using the food/constituent for which the health claim is made; the quantity of the food/constituent and pattern of consumption required to obtain the claimed

[6] For example:
- EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.
- EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. Guidance on the scientific requirements for health claims related to gut and immune function. EFSA Journal 2011, 9(4):1984, 12 pp.

[7] All health claim related guidance documents of EFSA and the NDA Panel are available from: http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm

effect, and whether this quantity could reasonably be consumed as part of a balanced diet; a warning for any food/constituent that is likely to present a health risk if consumed to excess; any other restrictions of use; directions for preparation and/or use.

8. The application must contain all pertinent scientific data (published and unpublished, data in favour and not in favour) which form the basis for substantiation of the health claim. Data from studies in humans addressing the relationship between the consumption of the food/constituent and the claimed effect will be required for the substantiation of a health claim. 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 to substantiate the health claim, but may be included only as supporting evidence, for example to provide evidence of the mechanisms by which the food/constituent could exert the claimed effect, and of the biological plausibility of the specific claim.

9. A comprehensive review of the data from human studies addressing the specific relationship between the food/constituent and the claimed effect is required. This review, and the identification of data considered pertinent to the health claim, should be performed in a systematic and transparent manner in order to demonstrate that the application adequately reflects the balance of all the evidence available.

10. The data from intervention and observational 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.

11. Data provided to substantiate a health claim should be of the quality expected from a peer-reviewed Journal. Whenever a quality system has been used/reported in the conduct of the studies (e.g. GLP, good clinical practice (GCP), as relevant), the particular system should be indicated.

12. As specified in the Regulation, health claims should be substantiated by taking into account the totality of the available scientific data and by weighing the evidence, subject to the specific conditions of use. In particular, the evidence should demonstrate the extent to which:

    (a) the claimed effect of the food/constituent is relevant for human health,

    (b) a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

    (c) the quantity of the food/constituent and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

    (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

13. The application in itself cannot be confidential. Sections considered as confidential by the applicant should be kept to a minimum and clearly identified. As defined in the Regulation, EFSA will make public the summary of the application when received and as provided by the applicant. EFSA will also make public, once adopted, its scientific opinion on the data and information included in the application, excluding the information considered as confidential.

14. One application should be prepared for each individual health claim; this means that only a relationship between a food/constituent and **a single claimed effect can be the object of each application**. However, multiple formulations of a food/constituent can be proposed by the

applicant in the same application as candidates to bear the health claim, provided the scientific evidence is valid for all proposed formulations of a food/constituent bearing that same health claim.

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 (particularly for the Parts, their main heading and first and second sub-headings)**. Data provided in the application should be organised into **five Parts** (see **Figure 1**).

Part 1 contains the specific requirements for the administrative and technical data, such as the application form, information related to the applicant and the nature of the application (including the national and international regulatory status of the health claim), health claim particulars, and the summary of the application.

Part 2 contains information specific to the food/constituent and its characteristics (such as the composition, physical and chemical characteristics, manufacturing process, stability, and bioavailability data).

Part 3 contains summaries (tabulated summaries of all pertinent studies identified, and written summaries of data from pertinent human and non-human studies) and overall conclusions, which follow the scope and the outline of the body of scientific data identified under Part 4.

Part 4 contains all identified pertinent scientific data (published and unpublished, data in favour and not in favour) which form the basis for substantiation of the health claim.

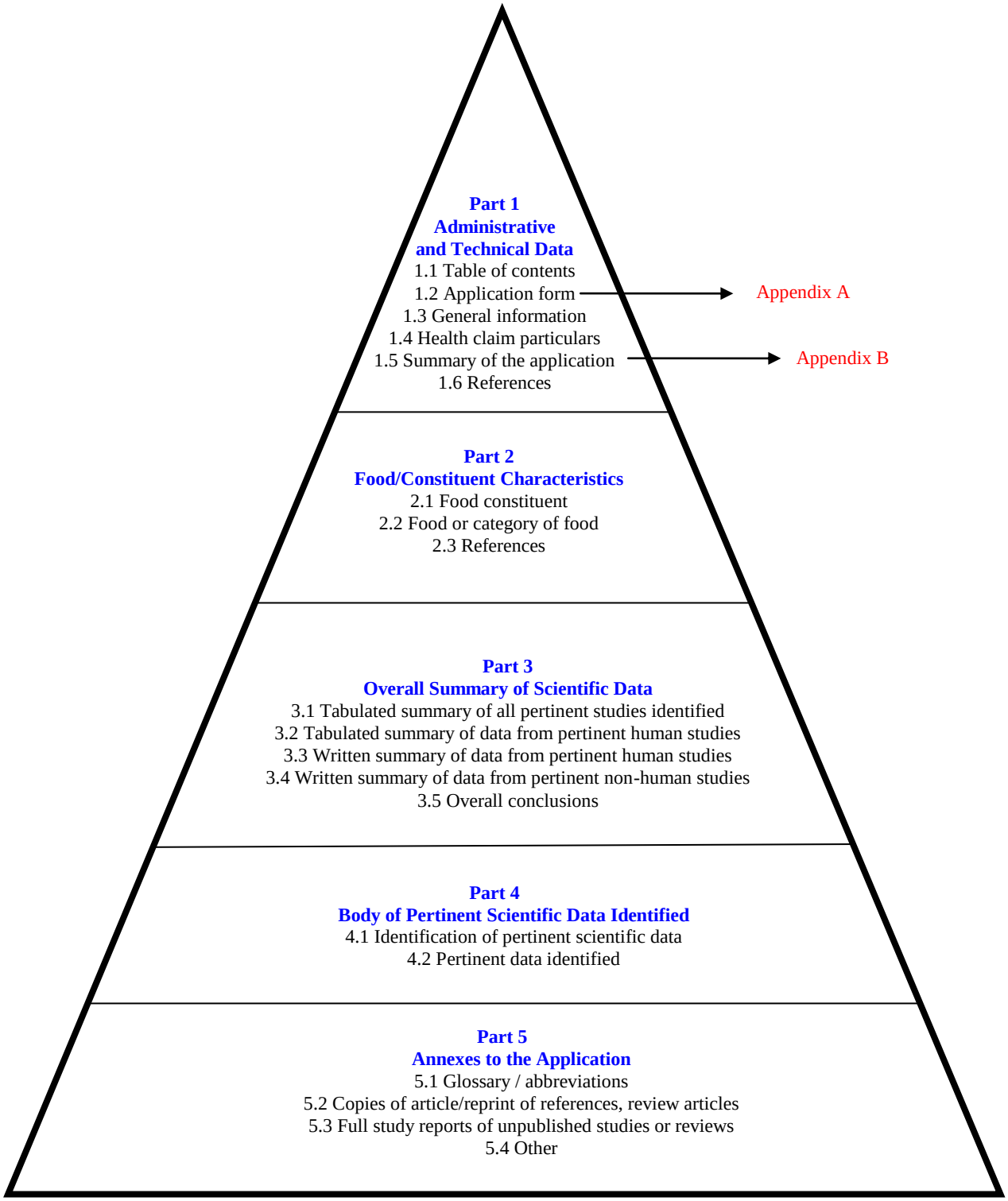
Part 5 comprises the glossary or abbreviation of terms quoted throughout the different Parts, copies/reprints of pertinent publications identified, full study reports of unpublished pertinent data, and scientific opinions of national/international regulatory bodies.

Where some of the data that are required as described below 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.

If a study appears under different Parts, cross-references should be given.

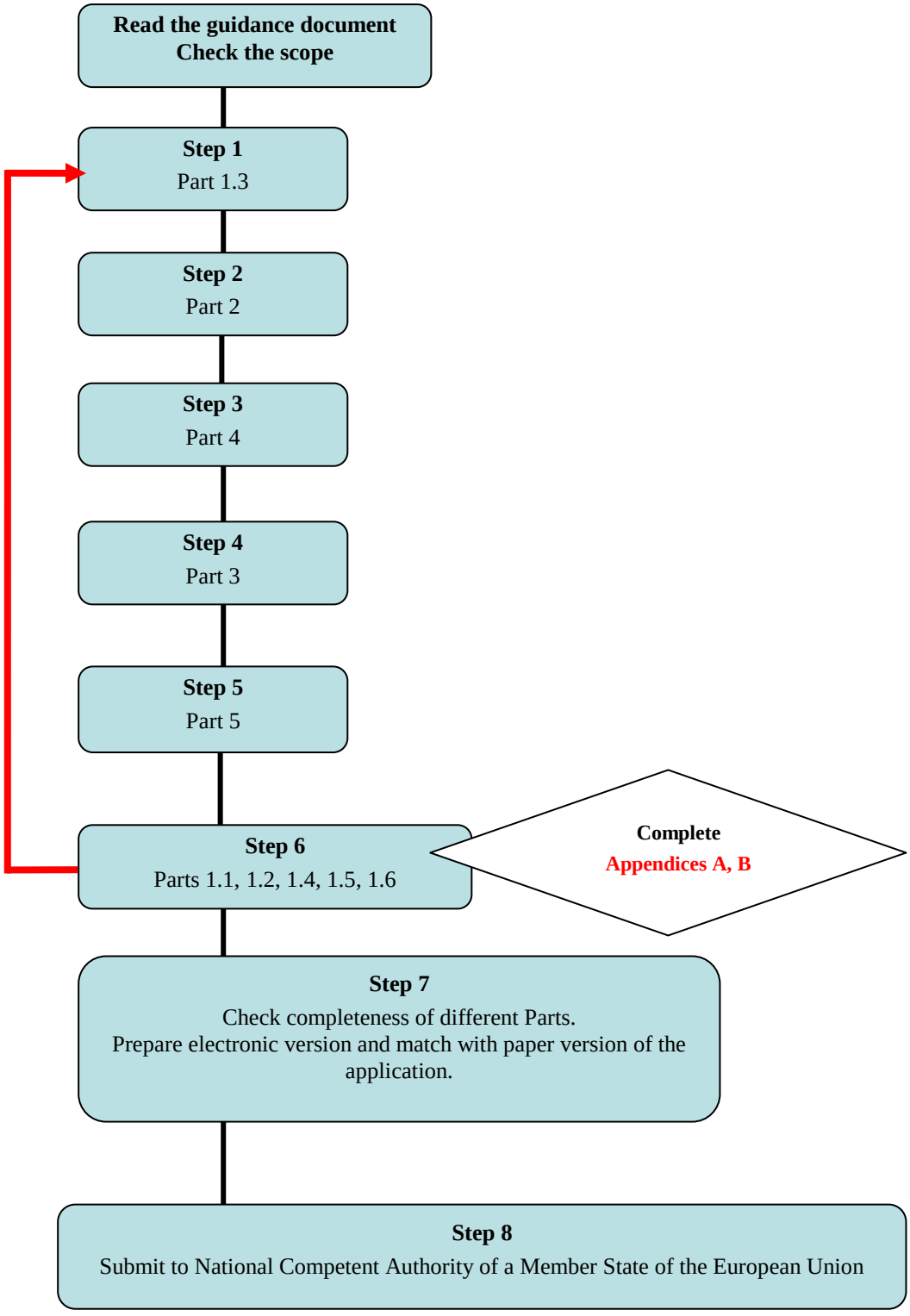
Suggested steps for the preparation of the application are given in **Figure 2**.

Figure 1: Representation of the organisation of the application[8]



[8] Appendices corresponding to the related Parts/Sections of the guidance document are also indicated.

Figure 2: Suggested steps for the preparation of the application



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 **Appendix A**.

1.3. General information

1.3.1. Applicant[9]

1.3.1.1. Provide the name and address of the company or organisation

1.3.1.2. Indicate the contact person[10] authorised to communicate with EFSA on behalf of the applicant

1.3.2. Nature of the application

1.3.2.1. Application for authorisation of a health claim pursuant to Article 14 of the Regulation

Indicate whether it is a disease risk reduction claim ☐ yes

If yes, please specify the health claim:

Indicate whether it is a claim referring to children's development and health ☐ yes

If yes, please specify the health claim:

State whether it includes proprietary data ☐ yes

If yes, please specify the related Part in the application, stating section and page number:

[9] 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**.

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

Please provide verifiable justification/declaration:

State whether it includes confidential data ☐ yes

If yes, please specify the related Part in the application, stating section and page number:

Please provide verifiable justification/declaration:

1.3.2.2. Application for authorisation of a health claim pursuant to Article 13(5) of the Regulation

Indicate whether it is based on newly developed scientific evidence ☐ yes

If yes, please specify the health claim:

State whether it includes a request for the protection of proprietary data ☐ yes

If yes, please specify the health claim and the related Part in the application, stating section and page number:

Please provide verifiable justification/declaration:

State whether it includes confidential data ☐ yes

If yes, please specify the related Part in the application, stating section and page number:

Please provide verifiable justification/declaration:

1.3.2.3. Application for a modification of an existing authorisation of a health claim in accordance with Article 19 of the Regulation

Indicate whether the modification of authorisation relates to an Article 14 health claim

☐ yes

Indicate whether the modification of authorisation relates to an Article 13(5) health claim

☐ yes

Please specify the Commission Regulation under which the claim has been authorised

Please specify the part of the authorisation which should be modified

State whether it includes proprietary data ☐ yes

If yes, please specify the related Part in the application, stating section and page number:

Please provide verifiable justification/declaration:

State whether it includes confidential data ☐ yes

If yes, please specify and locate the related Part in the application, section and page number:

Please provide verifiable justification/declaration:

1.3.3. National and international regulatory status

Indicate whether this health claim or a similar one has been scientifically evaluated, either within or outside the European Union. If so, provide a copy of the scientific evaluation.

If this health claim or a similar one has been submitted by the applicant to any regulatory body for a health claim authorisation, either within or outside the European Union, please indicate the status of the evaluation of such health claim by each regulatory body (if more than one), as appropriate:

☐ Under consideration

Provide the wording of the claim submitted, the date of submission, and the formulation, and specify the food/constituent for which the claim has been submitted. Indicate the name of the regulatory body which dealing with the application for authorisation of the health claim.

☐ Approved

Provide the wording of the claim approved, the date of approval, and the formulation, and specify the food/constituent for which the claim has been approved. Indicate the name of the regulatory body which approved the health claim.

If available, provide a copy of the scientific opinion of the regulatory body which authorised the health claim (in **Part 5,** Section 5.4).

☐ Rejected

Provide the wording of the claim which was rejected, the date of rejection and the reasons for rejection. Indicate the name of the regulatory body which rejected the health claim.

If available, provide a copy of the scientific opinion of the regulatory body which rejected the health claim (in **Part 5,** Section 5.4).

☐ Withdrawn

Provide the wording of the claim which was withdrawn, the date of submission, the date of withdrawal, and the reason for withdrawal. Indicate the name of the regulatory body at the time of withdrawal.

1.4. Health claim particulars

1.4.1. Specify the food/constituent for which a health claim is made

1.4.2. Describe the relationship between the food/constituent and the claimed effect, including the outcome measure(s) used to assess the claimed effect in humans

1.4.3. If known, describe the mechanism(s) by which the food/constituent exerts the claimed effect

1.4.4. Provide a proposal for the wording of the health claim for which authorisation is sought

The proposed wording should be in English (regarding language requirement, please refer to the available administrative guidance[11]).

[11] EFSA Pre-submission guidance for applicants intending to submit applications for authorisation of health claims http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm

1.4.5. Specific conditions of use

1.4.5.1. Specify the target population for the intended health claim and provide a rationale

Cross references should be given for the scientific data provided in Parts 3 and 4 (i.e. Have the human studies been carried out in a study group which is representative of the population group for which the claim is intended? Can the results obtained in the studied population be extrapolated to the target population?)

1.4.5.2. Indicate the quantity of the food/constituent and pattern of consumption required to obtain the claimed effect, and whether this quantity could reasonably be consumed as part of a balanced diet.

Provide a rationale, with cross-referencing to the scientific data provided in Parts 3 and 4 (i.e. the claimed effect observed with the amount of food/constituent and pattern of consumption proposed).

1.4.5.3. Provide, where appropriate, a statement addressed to the category(ies) of the population who should avoid using the food/constituent for which the health claim is made, and include the rationale.

1.4.5.4. Specify, where applicable, the warning for any food/constituent that is likely to present a health risk if consumed to excess, and provide a rationale.

1.4.5.5. Specify, where applicable, other restrictions of use, and provide a rationale.

1.4.5.6. Specify, where applicable, directions for preparation and/or use.

1.5. Summary of the application

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

1.6. References

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

2. Part 2: Food/Constituent characteristics

2.1. Food constituent

The food constituent (e.g. the nutrient or other substance, or a combination of nutrients/other substances) for which the health claim is made should be characterised. For a food or category of food, go directly to **Part 2**, Section 2.2.

2.1.1. Name and characteristics

The source and specifications (e.g. physical and chemical properties, composition, and where applicable microbiological constituents) of the food constituent for which the health claim is made should be provided.

The variability from batch to batch should be addressed.

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

Measurements should be performed in a competent laboratory that can certify the data. 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 brief overview should be provided, and if the production follows a quality system (e.g. GMP) the particular system should be indicated.

2.1.3. Stability information

Where applicable, a brief summary of the studies undertaken (e.g. conditions, batches and analytical procedures), and of the results and conclusions of the stability studies, should be provided. Conclusions with respect to storage conditions and shelf-life should be given.

2.1.4. Bioavailability data

Where applicable, the relevant data and rationale that the constituent for which the health claim is made is in a form that is available to be used by the human body (e.g. absorption studies) should be provided.

If absorption is not necessary to produce the claimed effect (e.g. plant sterols, fibres and lactic acid bacteria), the relevant data and rationale that the constituent reaches the target site should be provided.

If available, data on any factors (e.g. formulation and processing) that could affect the absorption or utilisation in the body of the constituent for which the health claim is made should be provided.

2.2. Food or category of food

The food or category of food for which the health claim is made should be described.

2.2.1. Name and composition

A brief description of the food or food category, including characterisation of the food matrix and the overall composition (including the nutrient content of the food), should be provided.

The source and specifications of the food or food category for which the health claim is made should be provided, and in particular the content of the constituent(s) related to the health claim.

The variability from batch to batch should be addressed.

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

Measurements should be performed in a competent laboratory that can certify the data. 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 brief overview should be provided, and if the production follows a quality system (e.g. GMP) the particular system should be indicated.

2.2.3. Stability information

Where applicable, a brief summary of the studies undertaken (e.g. conditions, batches and analytical procedures), and of the results and conclusions of the stability studies, should be provided. Conclusions with respect to storage conditions and shelf-life should be given.

2.2.4. Bioavailability data

Where applicable, the relevant data and rationale that the constituent for which the health claim is made is in a form that is available to be used by the human body (e.g. absorption studies) should be provided.

If absorption is not necessary to produce the claimed effect (e.g. plant sterols, fibres and lactic acid bacteria), the relevant data and rationale that the constituent reaches the target site should be provided.

If available, data on any factors (e.g. formulation and processing) that could affect the absorption or utilisation in the body of the constituent for which the health claim is made should be provided.

2.3. References

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

3. Part 3: Overall summary of pertinent scientific data

The overall summary follows the scope and the outline of the body of scientific data identified in **Part 4**. Provide the information in the following order:

3.1. Tabulated summary of all pertinent studies identified

All pertinent studies identified should be included (published and unpublished); individual studies included in any review publication should be counted separately.

Study type	**Number of pertinent studies (published)**	**Number of pertinent studies (unpublished)**
1. Human studies[1]		
2. Animal studies[2]		
3. *In vitro* studies[3]		
4. Other		
Total		

[1] Human intervention and observational studies dealing with the relationship between the consumption of the food/constituent and the claimed effect, including human studies dealing with the mechanisms by which the food/constituent could be responsible for the claimed effect (mechanistic studies), or studies on bioavailability.
[2] Animal studies dealing for example with the mechanisms by which the food/constituent could be responsible for the claimed effect (mechanistic studies).
[3] *In vitro* studies based on either human or animal biological samples.

3.2. Tabulated summary of data from pertinent human studies

3.2.1. Human intervention studies

All human intervention studies dealing with the relationship between the consumption of the food/constituent and the claimed effect (i.e. including appropriate outcome measures for the assessment of the claimed effect) should be included; individual studies included in any review publication should be counted separately.

Study type	**Number of pertinent studies (published)**	**Number of pertinent studies (unpublished)**
1. Experimental intervention studies		
a. RCT (full randomisation[1])		
b. RCT (concealed allocation)		
c. RT (non-controlled)		
2. Quasi-experimental intervention studies		
a. Non-randomised, controlled		
b. Non-randomised, non-controlled		
Total		

RCT = Randomised controlled trial
RT = Randomised trial

[1] Method of randomisation reported as coin toss, computer generated numbers, random number tables or similar.

3.2.2. Human observational and mechanistic studies

All human observational studies dealing with the relationship between the consumption of the food/constituent and the claimed effect (i.e. including appropriate outcome measures for the assessment of the claimed effect), and human studies dealing with the mechanisms by which the food/constituent could be responsible for the claimed effect should be included; individual studies included in any review publication should be counted separately.

Study type	Number of pertinent studies (published)	Number of pertinent studies (unpublished)
1. Observational studies		
a. Cohort studies		
b. Case-control studies		
c. Cross-sectional studies		
d. Other (e.g. case reports)		
2. Other[1]		
Total		

[1] Human studies dealing with the mechanisms by which the food/constituent could be responsible for the claimed effect (mechanistic studies), or studies on bioavailability.

3.3. Written summary of data from pertinent human studies

The scope of this section is to clarify the extent to which the relationship between the food/constituent and the claimed effect is supported by the totality of human data identified as pertinent to the health claim in Part 4 (Section 4.2.1) of the application and summarised in section 3.2. Cross-references to pertinent human studies (intervention or observational) should be given, as appropriate, in this section.

First, **the relationship** between the consumption of the food/constituent and the claimed effect **should be characterised** by considering:

- the magnitude of the effect and its physiological relevance,
- the study population in which the effect has been observed and whether it is representative of the target population,
- the conditions under which the effect has been achieved or observed (metabolic room, clinical setting, free-living subjects, etc.),
- the sustainability of such effect over time,
- the amount of the food/constituent used to achieve the effect, the usual intakes of the food/constituent in the target population and whether these amounts could be reasonably consumed as part of a balanced diet.

Second, the extent to which the data substantiate **a causal relationship** between the consumption of the food/constituent and the claimed effect should be addressed by considering:

- the consistency of results across studies,
- the magnitude of the effect, its statistical significance, the presence/absence of equally strong evidence, neutral or against,
- if available, an effective dose.

Aspects to be considered are the biological plausibility, alternative explanations for the observed effect, and the specificity of the cause-effect relationship.

3.4. Written summary of data from pertinent non-human studies

This section should address how, and the extent to which the identified or performed pertinent non-human studies (resulting from Part 4, Section 4.2.2) may help to support the relationship between the food/constituent and the claimed effect in humans (e.g. by providing evidence on the mechanisms by which the food/constituent could exert the claimed effect, and on the biological plausibility of the specific claim).

3.5. Overall conclusions

By taking into account the totality of the data (including evidence in favour and not in favour) and by weighing the evidence, the overall conclusions should clearly define the extent to which:

(a) the claimed effect of the food/constituent is relevant for human health,

(b) a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food/constituent and pattern of consumption required to obtain the claimed effect could reasonably be consumed as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

4. Part 4: Body of pertinent scientific data identified

Part 4 contains all pertinent scientific data which form the basis for substantiation of the health claim. Pertinent data means all human and non-human studies, published or unpublished, which are relevant for the substantiation of the health claim, i.e. addressing the relationship between the food/constituent and the claimed effect, including data in favour and data not in favour of such a relationship.

Important notice:

a. Journal abstracts and articles published in newspapers, magazines, newsletters or handouts that have not been peer-reviewed **should not** be cited.

b. Books or chapters of books for consumers or the general public **should not** be cited.

4.1. Identification of pertinent scientific data

4.1.1. Comprehensive review of published human data

Pertinent published human data should be identified through a comprehensive review which addresses the relationship between the food/constituent and the claimed effect in a systematic and transparent manner.

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

4.1.1.1. Authorship

The name, affiliation, declaration of interests and signature of the reviewer(s) responsible for the comprehensive review should be indicated.

4.1.1.2. Background

The food/constituent for which the health claim is made and the claimed effect, together with the outcome measure(s) used to assess the claimed effect, should be defined. In addition, information and a rationale for selecting the outcome measures to assess the claimed effect, stating their relevance and whether they are methodologically valid with respect to their analytical characteristics, should be provided.

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

4.1.1.4. 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).

4.1.1.5. Identification of pertinent published human data

The number of identified publications which have been included (considered pertinent to the health claim) and excluded (considered not pertinent to the health claim) by applying the inclusion and exclusion criteria defined in Section 4.1.1.3 should be indicated.

Publication type	**Number of pertinent publications identified**	**Number of publications excluded**
Human data[1]		
1. Original research		
a. Intervention studies		
b. Observational studies		
2. Pooled analyses of human intervention studies		
3. Meta-analyses of human intervention studies		
4. Pooled analyses of human observational studies		
5. Meta-analyses of human observational studies		
6. Systematic reviews		
7. Other review publications		
8. Guidelines/consensus opinions/text book chapters		
9. Other[2]		

[1] Articles reporting human studies dealing with the effect of the food/constituent on the health outcome forming the basis of the claim.

[2] Articles reporting human studies dealing with the mechanisms by which the food/constituent could be responsible for the health outcome (mechanistic studies), or studies on bioavailability.

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

4.1.2. Unpublished human data

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

4.1.3. Identification of published non-human data

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

4.1.4. Unpublished non-human data

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

4.2. Identified pertinent data

A list of references of the publications considered as pertinent to the health claim identified in Sections 4.1.1 to 4.1.4 (alphabetical order of first authors) should be provided as appropriate in the following sections.

4.2.1. Human data

A list of references of the pertinent published (those studies being included after the comprehensive review) and unpublished human studies (alphabetical order of first authors) in the sections below in accordance with the hierarchy of study design and publication type should be provided.

Copies/reprints of pertinent publications should be provided under **Part 5,** Section 5.2. Full study reports of unpublished studies should be annexed under **Part 5**, Section 5.3.

4.2.1.1. Human intervention studies (original research)

a. Randomised controlled studies

b. Other randomised studies (non-controlled)

c. Controlled, non-randomised studies

d. Other intervention studies

4.2.1.2. Human observational studies (original research)

a. Cohort studies

b. Case-control studies

c. Cross-sectional studies

d. Other observational studies (e.g. case reports)

4.2.1.3. Review publications

a. Systematic reviews, pooled analyses and meta-analyses

b. Other review publications

4.2.1.4. Other

For example: Human studies dealing with the mechanisms by which the food/constituent could be responsible for the claimed effect. These studies also include those on bioavailability (cross-reference to **Part 2** should be given, if appropriate).

4.2.2. Non-human data

A list of references related to pertinent published and unpublished non-human data (alphabetical order of first authors) should be provided.

Copies of articles/reprints of references of published studies should be given under **Part 5,** Section 5.2. Full study reports of unpublished studies should be annexed under **Part 5**, Section 5.3.

5. Annexes to the application

5.1. Glossary and Abbreviations

Used throughout the different Parts. To be presented alphabetically.

5.2. Copies/reprints of pertinent published data

5.3. Full study reports of pertinent unpublished data

5.4. Other

If available, include here, e.g.:

- Scientific opinions of national/international regulatory bodies for health claim authorisation if available, as referred to in **Part 1**, Section 1.3.3.

REFERENCES

Aggett P, Antoine J, Asp N, Bellisle F, Contor L, Cummings J, Howlett J, Müller D, Persin C, Pijls L, Rechkemmer G, Tuijtelaars S and Verhagen H, 2005. Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM). Consensus on criteria. European Journal of Nutrition, 44 (Suppl. 1), 5-30.

Des Jarlais DC, Lyles C and Crepaz N, 2004. Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: The TREND statement. American Journal of Public Health, 94, 361-366.

FDA (Food and Drug Administration), 2009. U.S. Department of Health and Human Services Center for Food Safety and Applied Nutrition: Guidance for Industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims - Final.

FSANZ (Food Standards Australia and New Zealand), Nutrition and health claims: http://www.foodstandards.gov.au/foodmatters/healthnutritionandrelatedclaims/index.cfm.

Health Canada, 2009. Bureau of Nutritional Sciences Food Directorate Health Products and Food Branch: Guidance Document for Preparing a Submission for Food Health Claims.

Higgins J and Green S, 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Available from: www.cochrane-handbook.org.

Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D and Stroup DF, 1999. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. Lancet, 354, 1896-1900.

SCF (Scientific Committee on Food), 2000. Guidelines of the Scientific Committee on Food for the development of tolerable upper intake levels for vitamins and minerals.

Schulz K, Altman D, Moher D and Group. C, 2010. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomized Trials. Annals of Internal Medicine, 152, 726-732.

Stroup D, Berlin J, Morton S, Olkin I, Williamson G, Rennie D, Moher D, Becker B, Sipe T and Thacker S, 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. The Journal of the American Medical Association, 283, 2008-2012.

APPENDICES

Notes to users:

Information requested in Appendices A and B are mandatory. Applicants are advised to follow the instructions given and use the forms provided.

For preparation of the application, refer also to suggested steps in Figure 2.

Content:

Appendix A Application form [Mandatory]

Appendix B Summary of the application [Mandatory]

APPENDIX A

APPLICATION FORM

The application form should be used for an application for authorisation of a health claim pursuant to **Article 13(5) or 14,** or for a modification of an existing authorisation in accordance with **Article 19** of Regulation (EC) No 1924/2006[12] to a Member State of the European Union for the scientific evaluation by the European Food Safety Authority (EFSA).

A separate application form for each health claim is required. It is to be completed by the applicant for inclusion under Part 1, Section 1.2.

Information should be provided where applicable. For ease of completion, references to the related part of the application are given.

DECLARATION and SIGNATURE

Application for authorisation of a health claim pursuant to Article 13(5) or 14, or for a modification of an existing authorisation in accordance with Article 19 of Regulation (EC) No 1924/2006 submitted to:

<Specify the Member State's Competent Authority>

Food/constituent[13] (specify as appropriate):

Proposed wording of the health claim:

Applicant[14]:

Contact person[15]:

It is hereby confirmed to our best knowledge that all existing data which are relevant to the health claim authorisation have been supplied in the application, as appropriate.

On behalf of the applicant:

Signature

Name

Function

Place and date
(yyyy-mm-dd)

[12] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

[13] "Food/constituent" refers to the food category, a food, or constituents (including a nutrient or other substance, or a combination of nutrients/other substances) for which the health claim is made.

[14] 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**.

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

GENERAL INFORMATION (Part 1, Section 1.3)

APPLICANT (PART 1, SECTION 1.3.1)

Applicant[16]:

(Company) Name:

Address:

Country:

Person authorised on behalf of the applicant for communication with EFSA during the procedure (*Notes: To facilitate communication, EFSA requires that there be only one contact person*):

Name:

Company name:

Address:

Country:

Telephone:

Fax:

E-Mail:

SCOPE (PART 1, SECTION 1.3.2)

This application concerns:

☐ **Application for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006**

Please specify:

☐ Reduction of disease risk claim

☐ Claim referring to children's development and health

☐ **Application for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006**

Please specify:

☐ Based on newly developed scientific evidence and/or

☐ Includes a request for the protection of proprietary data

[16] In case more than one company or organisation submit an application, provide their names and addresses.

☐ **Application for a modification of an existing authorisation of a health claim in accordance with Article 19 of Regulation (EC) No 1924/2006**

Please specify:

☐ Modification of an authorised Article 14 health claim

☐ Modification of an authorised Article 13(5) health claim

Indicate whether the health claim applied for complies with:

☐ The general principles referred to in Article 3 of Regulation (EC) No 1924/2006

☐ The general conditions referred to in Article 5 of Regulation (EC) No 1924/2006

☐ The specific conditions referred to in Article 10 of Regulation (EC) No 1924/2006

Indicate whether the application includes:

Proprietary data:	☐ Yes	☐ No
If yes, has a verifiable justification/declaration been provided?	☐ Yes	☐ No
If yes, has the proprietary data in the application been identified?	☐ Yes	☐ No

Confidential data:	☐ Yes	☐ No
If yes, has a verifiable justification/declaration been provided?	☐ Yes	☐ No
If yes, has the confidential data in the application been identified?	☐ Yes	☐ No

NATIONAL AND INTERNATIONAL REGULATORY STATUS (PART 1, SECTION 1.3.3)

State whether approval for this health claim or a similar one has already been sought through any regulatory body for health claim authorisation, either within or outside the European Union.

☐ Yes

☐ No

If yes, specify the regulatory status:

Under consideration:	☐ Yes	☐ No
Approved:	☐ Yes	☐ No
Rejected:	☐ Yes	☐ No
Withdrawn:	☐ Yes	☐ No

HEALTH CLAIM PARTICULARS (Part 1, Section 1.4)

Specify the food/constituent: (Part 1, Section 1.4.1)

Describe the relationship between the food/constituent and the claimed effect, including the outcome measure(s) used to assess the claimed effect in humans: (Part 1, Section 1.4.2)

If known, describe the mechanism(s) by which the food/constituent exerts the claimed effect: (Part 1, Section 1.4.3)

Proposal of the wording of the health claim: (Part 1, Section 1.4.4)

Specify the conditions of use: (Part 1, Section 1.4.5)

APPENDIX B

SUMMARY OF THE APPLICATION

The template provided should be used for the summary of the application for authorisation of a health claim pursuant to **Article 13(5) or 14,** or for a modification of an existing authorisation in accordance with **Article 19** of Regulation (EC) No 1924/2006[17] to a Member State of the European Union for the scientific evaluation by the European Food Safety Authority (EFSA).

GENERAL INFORMATION

Applicant[18]:

(Company) Name:

Address:

Country:

This application concerns:

☐ **Application for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006**

Please specify:

☐ Reduction of disease risk claim

☐ Claim referring to children's development and health

☐ **Application for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006**

Please specify:

☐ Based on newly developed scientific evidence and/or

☐ Includes a request for the protection of proprietary data

☐ **Application for a modification of an existing authorisation of a health claim in accordance with Article 19 of Regulation (EC) No 1924/2006**

Please specify:

☐ Modification of an authorised Article 14 health claim

☐ Modification of an authorised Article 13(5) health claim

[17] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

[18] In case more than one company or organisation submit an application, provide their names and addresses.

Member State of Application

<Specify the Member State's Competent Authority>

HEALTH CLAIM PARTICULARS

Specify the food/constituent:

Describe the relationship between the food/constituent and the claimed effect, including the outcome measure(s) used to assess the claimed effect in humans:

If known, describe the mechanism(s) by which the food/constituent exerts the claimed effect:

Proposal of the wording of the health claim:

Specify the conditions of use:

GLOSSARY

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

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 until such time as the claim is included in the lists of permitted or rejected health claims by Commission Decision.
Application	Means a stand-alone dossier containing the information and scientific data submitted for authorisation of the health claim in question.
Bioavailability	Bioavailability of a nutrient relates to its absorption and may be defined as its accessibility to metabolic and physiological processes (SCF, 2000).
Health claim	Any claim which states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health (as defined in Regulation (EC) No 1924/2006).
Nutrient	Means protein, carbohydrate, fat, fibre, sodium, vitamins and minerals listed in the Annex to Directive 90/496/EEC[19], and substances which belong to or are components of one of those categories (as defined in Regulation (EC) No 1924/2006).
Other substance	Without prejudice to Regulation (EC) No 178/2002[20], it means a substance other than a nutrient that has a nutritional or physiological effect (as defined in Regulation (EC) No 1924/2006).

[19] Council Directive 90/496/EEC of 24 September 1990 on nutrition labelling for foodstuffs. OJ L 276, 6.10.1990, p. 40–44.
[20] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. Official Journal of the European Union OJ L 31, 1.2.2002, p. 1–24.