TECHNICAL REPORT OF EFSA

Frequently Asked Questions (FAQ) related to the EFSA assessment of Article 14 and 13.5 health claims applications[1]

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INTRODUCTION

This frequently asked questions document (FAQ) discusses key issues that are addressed by EFSA in assessment of the scientific evidence submitted for substantiation of health claims in order to assist applicants in preparing applications for claims under Articles 13.5 and 14 of Regulation (EC) No 1924/2006 on nutrition and health claims on foods.

In 2007, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) issued an opinion providing scientific and technical guidance for the preparation and presentation of the application for authorisation of a health claim under Article Article 14/13.5[2] . This EFSA NDA opinion formed the basis for a Commission Regulation (EC) No 353/2008[3] establishing implementing rules for applications for authorisation of health claims as provided for in Article 15 of Regulation (EC) No 1924/2006[4], which applies also to claims submitted under Article 13.5 of the Health Claims Regulation.

The EFSA NDA Panel has also published guidance on administrative and procedural questions which applicants intending to submit applications for health claims authorisation may have[5].

The Standing Committee on the Food Chain and Animal Health at its meeting on the 14 December 2007 adopted guidance on the implementation of Regulation EC (No) 1924/2006 on nutrition and health claims made on foods[6] for (1) interaction with other Community legislation (relating to foodstuffs for particular nutritional uses, novel foods) (2) the use of comparative nutrition claims, and (3) classification of nutrition and health claims, including borderline cases between function claims and reduction of disease risk claims and between claims referring to children's development and health and other health claims.

The FAQ is intended to complement the NDA scientific and technical guidance document for the preparation and presentation of the application for authorisation of a health claim under Article 13.5/14. A draft FAQ, prepared in close collaboration with the NDA Panel, was published in May 2009 on the EFSA website for comments. This document formed the basis for discussion at a technical meeting with experts from industry/applicants for Article 14 and 13.5 health claims, which was held in Brussels on 15th June, 2009. This revised FAQ takes into account the questions/comments received during the public consultation and the discussions at the technical meeting.

1 On request from EFSA, Question No EFSA-Q-2009-00775 finalised on 30 September 2009.

2 http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178623592448.htm

3 http://ec.europa.eu/food/food/labellingnutrition/claims/health_claims_en.htm

4 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32006R1924R(01):EN:NOT

5 http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902594478.htm

6 http://ec.europa.eu/food/food/labellingnutrition/claims/index_en.htm

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Health claims applications are assessed on a case by case basis in the order in which they are received by EFSA and the FAQ will be further updated as appropriate as additional issues are addressed.

The following topics are addressed in this FAQ document:

1. Overview of main issues addressed by the NDA Panel
2. How does the NDA Panel decide whether a claim is substantiated?
3. What are pertinent studies for substantiation of a claim?
4. What is the totality of the available scientific data?
5. To what extent should a food/constituent be characterised?
6. How should the claimed effect be shown to be beneficial to human health?
7. What is a risk factor for the development of a human disease?
8. On what basis does EFSA propose wordings of claims?
9. How does EFSA communicate with applicants?
10. How does EFSA treat proprietary data?
11. How does EFSA treat confidential data?

1. Overview of main issues addressed by the NDA Panel

In assessing each specific food/health relationship that forms the basis of a health claim the NDA Panel considers the extent to which:

- the food/constituent is defined and characterised
- the claimed effect is defined and is a beneficial nutritional or physiological effect ("beneficial to human health")
- a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use)

and, if a cause effect relationship is considered to be established, whether:

- the quantity of food/pattern of consumption required to obtain the claimed effect can be consumed within a balanced diet
- the proposed wording reflects the scientific evidence
- the proposed wording complies with the criteria for the use of claims specified in the Regulation
- the proposed conditions of use are appropriate
- substantiation was dependent on data claimed as proprietary by the applicant.

Because health claims are assessed on a case by case basis, the detailed application of these steps may vary.

2. How does the NDA Panel decide whether a claim is substantiated?

According to Regulation 1924/2006, health claims shall be based on and substantiated by generally accepted scientific evidence (Article 6.1) and a claim should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence (Recital 17).

In assessing each specific food/health relationship that forms the basis of a claim, the NDA Panel makes a scientific judgement on the extent to which a cause and effect relationship is established between consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use). All of the evidence from the pertinent studies is weighed with respect to its overall strength, consistency and biological plausibility, taking into account the quality of individual studies and with particular regard to the population group for which the claim is intended and the conditions of use proposed for the claimed effect. A grade is not assigned to the evidence. While studies in animals or *in vitro* may provide supportive evidence, human data are central for the substantiation of the claim. This is in agreement with the hierarchy of evidence as described in the EFSA guidance to applicants. A rationale/evidence on biological plausibility of the claimed effect should be provided to support the substantiation of the claim.

Each relationship between a food/constituent and a claimed effect is assessed separately. There is no pre-established formula as to how many or what type of studies are needed to substantiate a claim. However, the NDA panel considers what the accepted norms are in the relevant research fields and EFSA consults experts from various disciplines, as appropriate.

Substantiation of reduction of disease risk claims requires evidence on the effect of the food/constituent on risk factors that are predictive of a reduced risk of disease.

The outcome of each assessment is one of three possible conclusions:

1. *A cause and effect relationship has been established between the consumption of the food/constituent and the claimed effect.*

This represents the best judgement of the NDA panel on whether a cause and effect relationship is established between consumption of the food/constituent and the claimed effect by the evidence

provided (i.e. that the claim is substantiated by 'generally accepted scientific evidence').

2. *The evidence provided is insufficient to establish a cause and effect relationship between the consumption of the food/constituent and the claimed effect.*

This represents the best judgement of the NDA panel that although there is scientific evidence supporting a cause and effect relationship, the evidence is not conclusive (i.e. that the claim is not substantiated by 'generally accepted scientific evidence').

3. *A cause and effect relationship has not been established between the consumption of the food/constituent and the claimed effect.*

The NDA panel considers that there is, at most, limited scientific evidence supporting a cause and effect relationship and the claim is not substantiated by 'generally accepted scientific evidence'.

3. What are pertinent studies for substantiation of a claim?

Applicants should provide evidence that shows the extent to which a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect that is applicable to the target group under the proposed conditions of use for the claim. Thus, in presenting studies that are pertinent (i.e. from which scientific conclusions can be drawn for the substantiation of the claim), applicants should consider the following questions:

- Have the studies been carried out with the food/constituent for which the claim is made?
- Have the human studies used an appropriate outcome measure(s) of the claimed effect?
- How do the conditions under which the human studies were performed relate to the conditions of use (e.g. food/constituent quantity) proposed for the claim?
- Have the human studies been carried out in a study group representative of the population group for which the claim is intended? Can the results obtained from the studied population be extrapolated to the target population?
- To what extent can evidence derived from studies in animals/*in vitro* support the claimed effect in humans?

As human data are central for the substantiation of a claim, particular attention should be given to ensuring that the human studies presented are pertinent to the claim. In addition, it is important that the human studies provided represent all available evidence pertinent to the claim, including evidence that supports the relationship as well as equivocal evidence and evidence of no effect and/or opposing effects.

4. What is the totality of the available scientific data?

The totality of data refers to all available studies that are considered pertinent (i.e. the studies from which scientific conclusions can be drawn for substantiation of the claim), including those that support the relationship as well as equivocal studies and studies showing no effect and/or opposing effects.

It is the responsibility of the applicant to provide the totality of the available data. In its assessment the Panel may use data which are not included in the application if they are considered pertinent to the claimed effect.

5. To what extent should a food/constituent be characterised?

Health claims can be made on a food category, a food or a food constituent (e.g. a nutrient, or other substance, or a combination of nutrients/other substances) and these are covered under the term "food/constituent".

The specific food/constituent should be sufficiently defined and characterised to establish that the studies provided for substantiation of the claim were performed with the food/constituent in respect of which the claim is made. Characterisation should be also sufficient to allow appropriate conditions of use to be defined. Although not required for substantiation of a claim, it is in the interest of the

applicant that characterisation should also be sufficient to allow control authorities to verify that the food/constituent which bears a claim is the same one that was the subject of a community authorisation.

The information provided should include those characteristics considered pertinent to the claimed effect, i.e. those that may influence the specific nutritional or physiological effect that is the basis of the claim.

It may be necessary to distinguish between a specific product formulation, a specific constituent or combination of constituents.

If the claim is for an individual constituent, then substantiation of the claim should be based on studies performed with this constituent. However, if the claim is for a specific product formulation or fixed combination of constituents, then studies should be presented on this specific formulation or combination. In the latter case a rationale/evidence should be provided for each constituent proposed to have a role in the claimed effect.

For a food category, information should be provided on variability between individual foods for those characteristics considered pertinent to the claimed effect.

For plant products, information provided should also include the scientific name, the part used and the preparation procedure.

For microorganisms (e.g. bacteria, yeast), as well as species identification, there should be sufficient characterisation (genetic typing) at strain level by internationally accepted molecular methods and strains should be named according to the International Code of Nomenclature. Although not required for substantiation of a claim, it is in the interests of the applicant that strains are deposited in an internationally recognized culture collection (with access number) for control purposes.

For manufacturing processes, information should be provided to show consistency in the final product for those characteristics considered pertinent to the claimed effect.

6. How should the claimed effect be shown to be beneficial to human health?

According to Regulation EC (No) 1924/2006, the use of nutrition and health claims shall only be permitted if the substance in respect of which the claim is made has been shown to have a beneficial nutritional or physiological effect.

In assessing each claim, the NDA Panel makes a scientific judgement on whether the claimed effect is considered to be a beneficial nutritional or physiological effect in the context of the specific claim as described in the application.

The claimed effect should be sufficiently defined to establish that the studies provided for substantiation of the claim were performed with an appropriate outcome measure(s) of that claimed effect. Therefore it may be necessary to distinguish between different possible effects or interpretations. 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 subject of each application.

The claimed effect needs to be specific enough to be testable and measurable by generally accepted methods. For example, “gut health” is too general (unclear what measure can be used) but ‘transit time’ is specific (measurable by generally accepted methods).

In the preparation of an application, a rationale/evidence should be provided that the claimed effect is beneficial in the context of the specific claim.

For function claims, a beneficial effect may relate to maintenance or improvement of a function.

For reduction of disease risk claims, ‘beneficial’ refers to whether the claimed effect relates to the reduction of a risk factor for the development of a human disease.

7. What is a risk factor for the development of a human disease?

Regulation 1924/2006 defines reduction of disease risk claims as 'significantly reduces a risk factor in the development of a human disease'. Thus, for reduction of disease risk claims, the beneficial physiological effect (which the Regulation requires to be shown for the claim to be permitted) is the reduction (or beneficial alteration) of a risk factor for the development of a human disease (not reduction of the risk of disease).

For the purpose of classifying disease, the World Health Organisations (WHO) International Statistical Classification of Diseases and Related Health http://www.who.int/classifications/icd/en/ should be used.

A risk factor is a factor associated with the risk of a disease that may serve as a predictor of development of that disease. To date, the NDA Panel has considered a limited number of disease risk factors, all of them physiological factors that (potentially) may be beneficially altered by diet. Dietary behaviour (e.g. diets with low content of a specific category of foods) would not be acceptable as a risk factor in this context as the beneficial alteration of the risk factor (increased consumption of a specific category of foods) is not a beneficial physiological effect as required by the Regulation.

For reduction of a risk factor to be considered beneficial in the context of a reduction of disease risk claim, it depends on the extent to which it is established that:

- The risk factor is an independent predictor of disease risk (this may be established from intervention and/or observational studies)
- The relationship of the risk factor to the development of the disease is biologically plausible

For some risk factors, there is strong evidence that they meet both criteria. For example, elevated serum LDL cholesterol is a risk factor for coronary heart disease (CHD) for which there is strong evidence for the biological basis through which it can contribute to the development of atherosclerosis (one pathway to CHD). There is also strong evidence that there is an independent association between the risk factor and the incidence of CHD, including evidence that a reduction in the risk factor (by dietary modification and drugs) generally reduces the risk of development of CHD. Reduction in serum LDL cholesterol concentrations therefore may be considered beneficial in the context of a reduction of disease risk claim for CHD.

Similarly, reduction in systolic blood pressure may be considered beneficial in the context of a reduction of disease risk claim for CHD or stroke.

For other risk factors, the evidence may not be as strong. For example, elevated dental plaque level is a risk factor for dental caries for which there is strong evidence for the biological basis through which it can contribute to the development of dental caries. However, while there is evidence that there is an independent association between dental plaque and the incidence of dental caries, it is not generally established that lowering plaque level can lower risk for development of the disease. Nevertheless, if there is evidence that lowering plaque by a specific dietary intervention is accompanied by reduced incidence of dental caries then such a reduction in dental plaque might be considered beneficial in the context of a reduction of disease risk claim for dental caries for that specific dietary intervention.

Except for well established risk factors (e.g. elevated LDL cholesterol for CHD), the extent to which reduction of a risk factor is beneficial in the context of a reduction of disease risk claim needs to be considered on a case by case basis.

8. On what basis does EFSA propose wordings of claims?

For claims for which a cause and effect relationship is considered to be established, EFSA considers whether the proposed wording reflects the scientific evidence and complies with the criteria laid down in the Regulation (e.g. it should not refer only to general, non-specific health benefits of the food/constituent). If not, EFSA proposes an appropriate wording. For reduction of disease risk claims, the wording should refer to the specific risk factor for disease.

It should be noted that the wording adopted by the Commission during authorisation may need to take into account aspects other than agreement with the scientific evidence, e.g. the understanding of consumers. Applicants should address issues related to consumer understanding of the wording of a claim to the Commission following publication of the EFSA opinion. EFSA liaises with the Commission, as appropriate, on scientific aspects of the wording of the claim.

9. How does EFSA communicate with applicants?

All communication between EFSA and the applicant is through the staff of the NDA Unit (not the Panel experts). There are five points during the procedure where direct or indirect communication between EFSA and the applicant may occur.

1. Indirect - during the admissibility check carried out by the Member State through which the application is submitted. EFSA staff liaises with the Member State regarding whether the application fulfils the criteria for the health claim classification under which it was submitted (i.e. Article 14 for development and health of children or reduction of disease risk, or Article 13.5. new science/proprietary data).

2. Direct - before EFSA considers the application complete, EFSA staff communicate with the applicant regarding completeness of the application and compliance with administrative procedures. Completeness checking includes administrative completeness checking, clear identification of food/constituent for which the claim is made (consistency throughout application), clear definition of the claimed effect (a defined claimed effect including identification of endpoint(s) and methods of measurement, identification of a risk factor(s) for disease risk reduction claims) conditions of use. Identification of the food/constituent, the claimed effect and the conditions of use are key decision points for the evaluation.

3. During evaluation - EFSA may request the applicant to provide supplementary information on the application ('stop the clock' procedure). Requests from EFSA staff to applicants for supplementary information are made based on a case by case judgement by the NDA Panel experts. Up to now, such requests generally related to clarification of aspects of data presented in the application. In the light of experience of evaluations gained to date, EFSA has decided to develop further procedures for communication with applicants during evaluation of claims. Specifically, EFSA intends to use the 'stop the clock' procedure to request, when the NDA experts consider appropriate, supplementary information from applicants related to the definition of the claim, e.g. the proposed food/constituent, the claimed effect, risk factors for disease, and conditions of use. Up to now these issues were addressed with applicants only before the application was accepted by EFSA and before evaluation started. The experience of the NDA Panel has shown that issues relating to the definition of these elements of claims that become apparent only during assessment of the application can have a significant bearing on the evaluation. Therefore, EFSA considers that this development in the communication procedures would be helpful both to applicants and the NDA Panel.

If the applicant fails to provide the supplementary information within a time limit as specified by EFSA, EFSA will issue an opinion based on the data provided in the application.

4. Notification- before publication of the adopted opinion EFSA sends applicants a copy of the adopted opinion in advance of publication for their information.

5. Indirect - after publication of the opinion, EFSA replies to requests from the Commission in relation to scientific comments on the opinion submitted during the public comment period (30 days following publication of the opinion) provided for in the Regulation. Such comments may be from applicants (among others). In addition, as appropriate, EFSA may be asked by the Commission for additional advice, e.g. in relation to conditions of use of the claim, or scientific aspects of the wording of the claim.

10. How does EFSA treat proprietary data?

Where evidence for substantiation includes a request for the protection of proprietary data, EFSA only considers whether the claim could not have been substantiated without the proprietary data claimed by

the applicant. In such cases applicants should ensure that all proprietary and non-proprietary data pertinent to the claimed effect are included in the application.

The protection of proprietary data, as appropriate, falls within the responsibility of the European Commission.

11. How does EFSA treat confidential data?

The applicant should keep the designation of confidential information to a minimum.

For transparency reasons, those data and information, which are considered essential for the scientific assessment are released in the opinion, e.g. broad description of the study and main outcome.