DRAFT SCIENTIFIC OPINION

Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Dietetic Products, Nutrition and Allergies (NDA) to draft guidance on scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. This draft guidance has been drawn from scientific opinions of the NDA Panel on such health claims. Thus, this guidance document represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. It is not intended that the document will include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. This draft guidance document was endorsed by the NDA Panel on 25 March 2011, and is released for public consultation from 26 April 2011 to 31 August 2011.

KEY WORDS

Health claims, scientific requirements, appetite ratings, weight management, blood glucose concentrations.

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BACKGROUND AS PROVIDED BY EFSA

Regulation (EC) No 1924/2006[4] harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. According to the Regulation, health claims should only be authorised for use in the Community after a scientific assessment of the highest possible standard has been carried out by EFSA.

EFSA and its NDA Panel have been engaging in consultation with stakeholders and have published guidance on scientific substantiation of health claims since 2007[5]. Most recently, a briefing document on scientific evaluation of health claims was published for consultation in April 2010, followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010[6].

Based on experiences gained with the evaluation of health claims, and to further assist applicants in preparing and submitting their applications for the authorisation of health claims, the NDA Panel is asked to develop guidance documents on the scientific requirements for the substantiation of health claims in selected areas, in addition to the guidance for the scientific substantiation of health claims related to gut and immune function (EFSA-Q-2010-01139).

TERMS OF REFERENCE AS PROVIDED BY EFSA

The NDA Panel is requested by EFSA to develop guidance documents on the scientific requirements for health claims in the following areas:

- Post-prandial blood glucose responses/blood glucose control
- Weight management, energy intake and satiety
- Protection against oxidative damage
- Cardiovascular health
- Bone, joints, and oral health
- Neurological and psychological functions
- Physical performance

Specific issues to be addressed in these guidance documents include:

- which claimed effects are considered to be beneficial physiological effects?
- which studies/outcome measures are appropriate for the substantiation of function claims and disease risk reduction claims?

Each guidance document should be subject to public consultation, and may be followed up as appropriate by scientific meetings with experts in the field.

Before the adoption of each guidance document by the NDA Panel the draft guidance shall be revised, taking into account the comments received during the public consultation. A report on the outcome of the public consultation for each guidance document shall be published. All guidance documents should be finalised by July 2012.

[4] 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.
[5] http://www.efsa.europa.eu/en/nda/ndaclaims.htm
[6] http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf

ASSESSMENT

1. Introduction

To assist applicants in preparing and submitting their applications for the authorisation of health claims, EFSA and in particular its Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) has ongoing consultations with stakeholders, and has published guidance on the scientific substantiation of health claims since 2007[7]. In April 2010, a draft briefing document on the scientific evaluation of health claims was published for consultation and was followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma in June 2010. The draft briefing document has been transformed into a Panel output, taking into account the questions/comments received. This document constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims, and outlines the approach of the NDA Panel to the evaluation of health claims in general. In response to requests from industry, EFSA is engaged in further consultation with stakeholders, and is developing additional guidance on specific types of claims.

The objective of the present public consultation is to discuss with scientific experts in the field the scientific requirements for the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations. This consultation document will be revised to take into account the comments received, in order to provide additional guidance to applicants for the substantiation of health claims in these areas.

The consultation document focuses on two key issues regarding the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

Issues which are related to substantiation and are common to health claims in general (e.g. characterisation of the food/constituent) are addressed in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims [8].

This document has been drawn from scientific opinions of the NDA Panel on health claims related to appetite ratings, weight management, and blood glucose concentrations. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. The document should be read in conjunction with the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

It is not intended that the document should include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations.

[7] http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm

[8] 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.

2. General considerations

2.1. Beneficial physiological effects

According to Regulation (EC) No 1924/2006, the use of health claims shall only be permitted if the food/constituent, for which the claim is made, has been shown to have a beneficial physiological effect. In assessing each claim, the NDA Panel makes a scientific judgement on whether the claimed effect is considered to be a beneficial physiological effect in the context of the specific claim, as described in the information provided and taking into account the population group for whom the claim is intended. 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 (or beneficial alteration) of a risk factor for the development of a human disease (not reduction of the risk of disease). A risk factor is a factor associated with the risk of a disease that may serve as a predictor of development of that disease. Whether or not the alteration of a factor is considered to be beneficial in the context of a reduction of disease risk claim depends on the extent to which it is established that:

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

Except for well established risk factors, the extent to which the reduction of a factor is beneficial in the context of a reduction of disease risk claim needs to be considered on a case-by-case basis.

The NDA Panel considers that the population group for which health claims are intended is the general (healthy) population or specific subgroups thereof, for example, elderly people, physically active subjects, or pregnant women. In its evaluation, the NDA Panel considers that where a health claim relates to a function/effect which may be associated with a disease, subjects with the disease are not the target population for the claim, for example, diabetic subjects. Applications for claims which specify target groups other than the general (healthy) population are the subject of ongoing discussions with the Commission and Member States with regard to their admissibility.

The NDA Panel also considers whether the claimed effect is sufficiently defined to establish that the studies identified for substantiation of the claim were performed with (an) appropriate outcome measure(s) of that claimed effect. Reference to general, non-specific benefits of the nutrient or food for overall good health or health-related well-being may only be made if accompanied by a specific health claim.

2.2. Studies/outcome measures appropriate for substantiation of claims

As human studies are central for substantiation of health claims, this document focuses in particular on such studies. In considering whether the studies provided are pertinent (i.e. studies from which conclusions can be drawn for the scientific substantiation of the claim), the NDA Panel addresses a number of questions, including:

- Whether the studies have been carried out with the food/constituent for which the claim is made. This requirement means that there should be sufficient definition of the food/constituent for which the claim is made, and of the food/constituent which has been investigated in the studies which have been provided for substantiation of the claim. The evaluation also considers how the conditions under which the human studies were performed

relate to the conditions of use (e.g. quantity and pattern of consumption of the food/constituent) proposed for the claim.

- Whether the design and quality of the studies allow conclusions to be drawn for the scientific substantiation of the claim. The evaluation takes into account the hierarchy of evidence as described in the scientific and technical guidance of the EFSA NDA Panel[9], for example, intervention studies generally provide stronger evidence than observational studies. Intervention studies should be appropriately conducted so as to minimise bias. In observational studies adequate control for factors other than the food/constituent known to have an impact on the claimed effect is important. Each health claim is assessed separately and there is no pre-established formula as to how many or what type of studies are needed to substantiate a claim. In this regard, the reproducibility of the effect of the food/constituent as indicated by consistency between studies is an important consideration.

- Whether the studies have been carried out in a study group 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? For studies in groups (e.g. subjects with a disease) other than the target group for a claim (e.g. the general population), the NDA Panel considers on a case-by-case basis the extent to which it is established that extrapolation from the study group to the target group is biologically plausible.

- Whether the studies used (an) appropriate outcome measure(s) of the claimed effect. For this, the NDA Panel considers what is generally accepted in the relevant research fields, and consults experts from various disciplines, as appropriate.

3. Appetite ratings and subsequent energy intake

3.1. Claims on increased satiety and/or reduced sense of hunger/appetite

Claims on changes in different appetite ratings after consumption of a food, including increased satiety and/or reduced sense of hunger/appetite, have been proposed. Different appetite ratings can be measured *in vivo* in humans using validated visual analogue scales (i.e. behavioural assessment). Changes in certain biochemical markers (e.g. cholecystokinin (CCK)) can only be considered in the context of the behavioral assessment.

The beneficial physiological effects of changing appetite ratings in response to food consumption may be a decrease in subsequent energy intake and/or a decrease in body weight. If the health benefit of changing appetite ratings is to decrease subsequent energy intake, subsequent energy intake should be measured using appropriate methods, and the effect should be sustained over time, taking into account possible compensatory effects. If the health benefit of changing appetite ratings is to decrease body weight, body weight changes should be measured. Other beneficial physiological effects of changing appetite ratings in response to food consumption should be specifically indicated, substantiated, and considered on a case-by-case basis. In general terms, changes in appetite ratings after consumption of a "test" food should also be observed after chronic consumption of the food (e.g. after one month), and therefore tests performed on a single occasion would not be considered sufficient for substantiation.

Claims on changes in appetite ratings after food consumption are generally comparative claims (i.e. comparison of the "test" food with the "control" food). In this context, both the test and the control

[9] EFSA (European Food Safety Authority), 2007. Opinion of the Panel on dietetic products, nutrition and allergies (NDA) on a request from the Commission related to scientific and technical guidance for the preparation and presentation of the application for authorisation of a health claim. The EFSA Journal, 530, 1-44.

food should be sufficiently characterised for a scientific evaluation, and comparable with respect to other factors (e.g. energy) than the food/constituent responsible for the claimed effect.

3.2. Claims on reduced energy intake

Claims on reduced *ad libitum* energy intake after consumption of a food/constituent have been proposed.

The beneficial physiological effect of reducing *ad libitum* energy intake during or after consumption of a food/constituent will entirely depend on the context in which the claim is made. The Panel considers that the health benefit of reducing (subsequent) energy intake should be specifically indicated, substantiated, and considered on a case-by-case basis, taking into account possible compensatory effects. In general terms, a reduction in energy intake after consumption of a food/constituent should also be observed after chronic consumption of the food (e.g. after one month), and therefore tests performed on a single occasion would not be considered sufficient for substantiation. If the health benefit of changing energy intake is to decrease body weight, body weight changes should be measured.

Changes in appetite ratings could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect.

Claims on reduced energy intake after food consumption are generally comparative claims (i.e. comparison of the "test" food/constituent with the "control" food/constituent). In this context, both the test and the control food/constituent should be sufficiently characterised for a scientific evaluation, and comparable with respect to other factors (e.g. energy) than the food/constituent responsible for the claimed effect.

A number of claims in relation to reduced energy intake have been proposed for foods based on their reduced, low or no energy content. The Panel notes that these types of claims refer to a property of a food (nutrition claims), and therefore cannot be considered as health claims.

4. Weight management

4.1. Claims on increased energy expenditure

An increase in energy expenditure after acute consumption of a food is not considered a beneficial physiological effect *per se*. However, a sustained increase in energy expenditure may be one of the mechanisms by which a reduction in body weight can be achieved, and therefore measures of energy expenditure can be used as supportive evidence for a claim on body weight loss.

4.2. Claims on body weight maintenance/loss

A sustained reduction in body weight is a beneficial physiological effect for overweight and obese subjects in the general population. To this end, human studies assessing the effects of a food/constituent on body weight changes need to be of appropriate duration (e.g. three months), and the conditions in which this is achieved need to be specified (under energy-restriction, *ad libitum*, etc.). The most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass. However, if the duration of the study is appropriate, measures of body composition are not strictly required for this claim, although these measures could be used as supportive evidence. Body weight change which can be attributed to the loss of body water only is not considered to be a beneficial physiological effect.

A sustained increase in energy expenditure may be one of the mechanisms by which a reduction in body weight can be achieved, and therefore measures of energy expenditure could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect. However, measures of energy expenditure alone cannot be used to substantiate a claim on the reduction of body weight.

A number of claims in relation to body weight management/loss have been proposed for foods based on their reduced, low or no energy content. The Panel notes that this type of claim refers to a property of a food (nutrition claims), and therefore cannot be considered as health claims.

4.3. Claims on body weight maintenance after weight loss

Maintenance of weight loss can be interpreted as contribution to the maintenance of a normal body weight after significant weight loss. In this context, the maintenance of weight loss in overweight and obese subjects without achieving a normal body weight is considered a beneficial physiological effect. Human studies assessing the effects of a food/constituent on body weight maintenance after weight loss need to be of appropriate duration (e.g. six-month follow-up after weight loss), and the conditions under which weight maintenance is achieved need to be specified.

4.4. Claims on increased fat oxidation

An increase in fat oxidation after acute consumption of a food is not considered a beneficial physiological effect *per se*. However, a sustained increase in fat oxidation (e.g. measured by indirect calorimetry) may be one of the mechanisms by which a reduction in body fat can be achieved, and therefore measures of fat oxidation could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect.

4.5. Claims on the reduction of body fat

A sustained reduction in body fat, and particularly abdominal fat, is a beneficial physiological effect for overweight and obese subjects in the general population.

To this end, human studies assessing the effects of a food/constituent on body fat changes need to be of appropriate duration (e.g. three months). Changes in body fat should be measured in human intervention studies using methods with appropriate validity and precision. A sustained increase in fat oxidation (e.g. measured by indirect calorimetry) may be one of the mechanisms by which a reduction in body fat can be achieved, and therefore measures of fat oxidation could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect. However, measures of fat oxidation alone cannot be used to substantiate a claim on the reduction of body fat.

4.6. Claims on the increase of lean body mass

A sustained increase in lean body mass may be a beneficial physiological effect for physically active subjects, including trained individuals. Also a "reduced" loss in lean body mass during energy restriction leading to weight loss can be considered beneficial for overweight and obese subjects even if lean body mass is not increased. To this end, human studies assessing the effects of a food/constituent on lean body mass changes need to be of appropriate duration (e.g. three months). Changes in lean body mass should be measured in human intervention studies using methods with appropriate validity and precision.

4.7. Claims on the reduction of waist circumference

The health benefit of reducing waist circumference in normal weight, overweight and obese subjects is related to the decrease in abdominal/visceral fat. A reduction in waist circumference may not necessarily reflect a change in abdominal/visceral fat, and therefore may not be considered a beneficial physiological effect in isolation. In this context, measurements of changes in abdominal/visceral fat using appropriate methods (e.g. imaging techniques), and appropriate duration of the studies (e.g. three months), are required for the scientific substantiation of the claimed effect. Other health benefits of reducing waist circumference should be specifically indicated, substantiated, and considered on a case-by-case basis (e.g. improvement of the metabolic consequences of increased abdominal fat).

4.8. Claims referring to changes in "body shape"

Body shape can change as a result of changes in body weight and/or body composition. As discussed in previous sections, a reduction in body weight and body fat, and an increase in lean body mass, are considered beneficial physiological effects depending on the context in which the claim is made. Also changes in body shape resulting from changes in body fat distribution (peripheral *vs*. central) in the context of weight maintenance could be considered beneficial even in normal weight subjects, depending on the context of the claim. However, changes in body shape resulting from a reduction in body water are not considered a beneficial physiological effect. In this context, objective and suitable measures of body shape, and appropriate duration of the studies (e.g. three months), are required for the scientific substantiation of the claimed effect.

5. Blood glucose and insulin concentrations

5.1. Claims on the reduction of post-prandial blood glucose responses

Claims on the reduction of post-prandial blood glucose responses refer to the ability of a food/constituent to reduce the blood glucose rise after consumption of a food or meal rich in digestible carbohydrates (i.e. in comparison to a reference food or meal). This ability may be considered a beneficial physiological effect as long as insulin responses are not disproportionally increased (e.g. for subjects with impaired glucose tolerance). Therefore, measures of both glucose and insulin concentrations in the blood, at different time points after consumption of the test and reference food/constituent during an appropriate period of time (i.e. at least two hours), are required for the substantiation of the claim.

Claims have been proposed for food constituents which, when present in carbohydrate-containing foods (e.g. different types of dietary fibre), could reduce post-prandial blood glucose responses to such foods by, for example, decreasing the rate of absorption of available carbohydrates. In this context, both the test and the reference food should be sufficiently characterised for a scientific evaluation and comparable with respect to other factors than the food constituent responsible for the claimed effect (e.g. amount of available carbohydrates, and fat and protein content).

Claims for a beneficial effect of a food/constituent (e.g. non/low-digestible carbohydrates, intense sweeteners and sugar alcohols), when used in replacement of another food/constituent (e.g. digestible carbohydrates) with an independent role in increasing post-prandial glycaemic responses, have been provided. Substantiation may be based on evidence for an independent role of the replaced food/constituent in increasing post-prandial glycaemic responses, together with evidence for the lack of such an effect, or a reduced effect, of the food/constituent which is used for replacement.

With respect to the study population, results from studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet) could be used for the scientific substantiation of these claims.

However, the rationale for extrapolation of results obtained in diabetic subjects under treatment with blood glucose-lowering medications (e.g. oral anti-diabetic medications, insulin) to the target population for the claim (e.g. the general population, or subjects with impaired glucose control) should be provided and considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food/constituent and the medications used on the claimed effect).

5.2. Claims on (long-term) blood glucose control

Improved blood glucose control is a beneficial physiological effect for subjects with impaired blood glucose tolerance. Appropriate outcomes for the scientific substantiation of such claims include glycosylated haemoglobin (HbA1c) measured in intervention studies of appropriate duration (e.g. at least three months). Measurement of the area under the curve of plasma glucose concentrations after a standard oral glucose tolerance test (OGTT) is considered as supportive.

With respect to the study population, results from studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet) could be used for the scientific substantiation of these claims. However, the rationale for extrapolation of results obtained in diabetic subjects under treatment with blood glucose-lowering medications (e.g. oral anti-diabetic drugs, insulin) to the target population for the claim (e.g. the general population or subjects with impaired glucose control) should be provided and considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food/constituent and the medications used on the claimed effect).

5.3. Claims on increased insulin sensitivity

Increasing insulin sensitivity may be a beneficial physiological effect depending on the target population. The hyperinsulinaemic-euglycaemic clamp is an appropriate measure of insulin sensitivity in human intervention studies. Fasting insulin, homeostatic model assessment (HOMA), the insulin sensitivity index (ISI) and the quantitative insulin sensitivity check index (QUICKI) can be used as proxy in epidemiological studies, but not for "short-term" interventions with small numbers of subjects.

CONCLUSIONS

The draft guidance document focused on two key issues regarding the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

The document has been drawn from scientific opinions of the NDA Panel on health claims related to appetite ratings, weight management, and blood glucose concentrations. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas.

GLOSSARY AND ABBREVIATIONS

CCK	Cholecystokinin
HbA1c	Glycosylated haemoglobin
HOMA	Homeostatic model assessment
ISI	Insulin sensitivity index
OGTT	Oral glucose tolerance test
QUICKI	Quantitative insulin sensitivity check index