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TECHNICAL REPORT

Outcome of a public consultation on the Draft Opinion of the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) on a draft guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations[1]

European Food Safety Authority[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

The European Food Safety Authority (EFSA) carried out a public consultation to receive input from the scientific community and all interested parties on a draft guidance document on the scientific requirements for the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations prepared by the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) and endorsed by the Panel for public consultation at its Plenary meeting on 23-25 March 2011. The draft guidance document is based on the experience gained with the evaluation of health claims, and is aimed at further assisting applicants in preparing and submitting their applications for the authorisation of health claims. The written public consultation for this document was open from 26 April 2011 to 31 August 2011. EFSA received comments from 49 interested parties including applicants for health claims, non-governmental organisations, industry organisations and academia. EFSA and its NDA Panel wish to thank all stakeholders for their very useful contributions. The current report summarises the outcome of the public consultation, including a brief summary of the comments received and how the comments were addressed. The NDA Panel prepared an updated version of the guidance document taking into account the questions/comments received. This document was discussed and adopted at the NDA Plenary meeting on 29 February 2012, and is published in the EFSA Journal.

KEY WORDS

Health claims, scientific requirements, appetite, weight management, blood glucose, outcome, public consultation.

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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 the scientific substantiation of health claims, since 2007[5]. Most recently, a briefing document on the 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 was asked to develop a guidance document on the scientific requirements for the substantiation of specific types of health claims.

TERMS OF REFERENCE AS PROVIDED BY EFSA

The NDA Panel is requested by EFSA to develop a guidance document on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. Specific issues to be addressed in this guidance include:

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

The NDA Panel is initially requested to draft a guidance to be released for public consultation in the field of health claims related to appetite ratings, weight management, and blood glucose concentrations.

Before its adoption by the NDA Panel, the draft guidance needs to be revised, taking into account the comments received during the public consultation.

[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

CONSIDERATION

1. Introduction

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 developed a draft guidance document on the scientific requirements for the substantiation of health claims related to appetite ratings, weight management, and blood glucose concentrations. In line with EFSA's policy on openness and transparency, and in order for EFSA to receive comments on its work from the scientific community and stakeholders, EFSA engages in public consultations on key issues. Accordingly, the draft guidance document, which should be read in conjunction with the general guidance document on the evaluation of Article 13.1, 13.5 and 14 health claims[7], was published on the EFSA website for comments (from 26 April 2011 to 31 August 2011). The NDA Panel then prepared an updated version of the guidance document, taking into account the questions/comments received, as appropriate. The updated guidance document was discussed and adopted at the NDA Plenary meeting of 29 February 2012, and is published in the EFSA Journal[8]. EFSA is committed to publishing the comments received during the public consultation, as well as a short report on the outcome of the consultation.

2. Screening and evaluation of comments received

2.1. Comments received

EFSA has received comments from 49 interested parties including applicants for health claims, non-governmental organisations, industry organisations and academia. A summary of the comments received is given below, and all written comments received are listed in the Appendix. Comments related to policy or risk management aspects were considered to be outside the scope of the consultation, and are not covered in this report. Other comments, which were general and not specifically related to the scientific requirements for health claims on appetite ratings, weight management, and blood glucose concentrations, have been taken up already in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

Some comments were considered to be too detailed and technical to be covered in a guidance document, for example comments on experimental design and methods, statistical analysis or requesting exhaustive lists of appropriate outcome measures for claimed effects. It should be noted that the 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, and that it is not possible for the NDA Panel to predict all potential claims, including appropriate outcome measures. Given that health claims are often technically complex and unique, outcome measures for claimed effects may need to be considered in the context of a specific application, and cannot be all cover in a guidance document. The guidance may be updated in the future in the light of additional experience gained with the evaluation of health claims.

2.2. Nature of specific comments

The main issues raised in the comments received are summarised below. EFSA has carefully reviewed all comments and has updated the guidance on the scientific requirements for health claims

[7] 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.

[8] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2012. Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. EFSA Journal, 10(3):2604, 11 pp.

related to appetite ratings, weight management, and blood glucose concentrations, accordingly. The updated guidance document is now published in the EFSA Journal[9].

The structure of the guidance document released for public consultation has changed considerably after taking into consideration the comments received. Whereas the guidance released for consultation aimed to address all health claims related to appetite ratings, weight management, and blood glucose concentrations which had been evaluated, regardless of whether they had been considered by the Panel as beneficial physiological effects *per se*, the revised guidance document has been structured as a guidance to applicants on the beneficial physiological effects identified by the NDA Panel in this field on the basis of the experience gained so far, including the mechanisms which have been proposed by which food/constituent(s) could achieve the claimed effects.

2.2.1. Study population vs. target population

Comments received

- It was proposed that obese and diabetic subjects (on diet only) as well as "pre-diabetic" subjects as part of the general population should be considered as an appropriate target population for health claims on appetite ratings, weight management and blood glucose control.
- Questions were raised on whether elderly subjects could be the target group for claims on weight management, increase in lean body mass, and reduction of body fat, and on whether subjects with metabolic syndrome could be included in the target population for a claim.
- Some comments proposed normal-weight subjects as the target group for claims on weight management and on reduction of body fat.

Panel consideration of comments received

Health claims made on foods cannot relate to the treatment of a disease (e.g. obesity and type 2 diabetes) as per Regulation (EC) No 1924/2006. However, and as stated in the guidance document, 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. Subjects without type 2 diabetes (e.g. impaired glucose tolerance), can be both the target population for health claims and appropriate study subjects for the scientific substantiation of claims made on foods. Similarly, results from studies conducted in overweight or obese subjects treated with lifestyle measures only (e.g. diet and physical activity) could be used for the scientific substantiation of these claims. However, the rationale for extrapolation of results obtained in obese subjects under treatment with medications for weight loss (e.g. inhibitors of intestinal fat absorption and modifiers of central nervous system neurotransmitters) to the target population for the claim should be provided, and will be considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

The guidance document (Section 4.1) has been updated to include this information.

The metabolic syndrome concept was developed to rank subjects with respect to their risk of developing type 2 diabetes/cardiovascular diseases and many definitions/sets of criteria exist. For the purpose of the scientific evaluation of health claims, the study group and the target population should be defined on the basis of the presence (or absence) of disease (e.g. type 2 diabetes, obesity and hypertension), as described above.

Elderly subjects are part of the general population and as such can be both the target population for a claim and the study population, also for claims on increase in lean body mass.

[9] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2012. Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. EFSA Journal, 10(3):2604, 11 pp.

A reduction in body weight and/or a reduction in total body fat may not generally be beneficial physiological effects for the normal-weight population, but would be beneficial for adults with an excess body weight/excess body fat. Also a reduction in abdominal fat, and particularly in visceral fat, is considered a beneficial physiological effect for adults with adverse health effects associated with an excess of abdominal fat.

The guidance document (Sections 4.3 and 4.4) has been updated with this information.

2.2.2. Sustained effects vs. long-lasting effects and reproducibility of the effect

Comments received

- Clarification on the meaning of "sustained effects" was requested and why it should be expected that the effects of a food would persist over time after discontinuation of consumption?
- There were requests for clarification regarding the minimum duration of human studies addressing health outcomes related to appetite ratings, weight management and blood glucose control. It was suggested that the study duration indicated in the guidance (e.g. three months, six months) may not be needed if the claimed effect can be achieved earlier and if the study duration has no impact on the magnitude of the effect. There was a request to express time in weeks rather than in months.
- What did the Panel understand by "reproducibility" of the effect?

Panel consideration of comments received

The Panel wishes to clarify that the scientific requirement for health claims which deals with the sustainability of the effect does not refer to the persistence of the effect after discontinuation of the food/constituent, but rather to the maintenance of the effect over time during continuous consumption of the food/constituent in order to exclude adaptation through compensatory mechanisms or attrition. To address this aspect, measurements of the outcome variable at different time points during the intervention are generally required. An indicative timeframe of what the Panel considers continuous consumption of the food/constituent is given for each type of claim. Shorter-term studies can also be considered for the scientific substantiation of these claims.

As stated in the guidance document, the reproducibility of the effect is indicated by the consistency of results between studies (i.e. an effect of the food/constituent that is observed in one study that can be reproduced under similar circumstances in another study).

The guidance document has been amended to clarify the above, and the indicative study duration has been expressed in weeks as appropriate.

2.2.3. Claims on foods with reduced, low or no energy content

Comments received

- It was questioned why claims proposed for foods based on their reduced, low or no energy content are considered by the Panel as referring to a property of a food (nutrition claims), and therefore cannot be considered as health claims.

Panel consideration of comments received

The Panel realises that the paragraphs referring to health claims made on foods on the basis of their reduced, low or no energy content may have been misunderstood (Sections 3.2 and 4.2 of the draft guidance). The guidance was not meant to indicate that health claims on these foods could not be proposed, but rather to point out that characterisation of foods as meeting the requirements for these nutrition claims (e.g. reduced, low or no energy content) may be insufficient for the scientific substantiation of health claims on the reduction of body fat/body weight. The scientific requirements for health claims made on these foods are as for any other type of food, and therefore specific mention to them has been deleted from the guidance document.

2.2.4. Supportive evidence

Comments received

- Several comments requested special mention in the guidance of the fact that animal studies, *in vitro* studies, and acute (single dose) studies in humans should be accepted as supportive evidence for health claims on, for example, appetite ratings, energy intake, energy expenditure and fat oxidation.

Panel consideration of comments received

As a general point for all claims, animal and *in vitro* studies can be used in support of human studies, which are central for the substantiation of health claims, as already mentioned in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

Acute studies in humans may be considered as supportive evidence for health claims for which evidence of sustained effects during chronic consumption of the food is needed for scientific substantiation.

2.2.5. Methods to assess changes in body composition

Comments received

- Several comments requested more specific guidance on methods which may be considered as appropriate for measuring body composition (fat mass, lean body mass). It was suggested to mention among these: bioelectrical impedance analysis (BIA), air displacement plethysmography (ADP), dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT), as well as waist circumference and the waist-to-hip-ratio.
- There was a question on the meaning of "imaging techniques" in relation to claims on the reduction of waist circumference.

Panel consideration of comments received

The assessment of changes in body composition *in vivo* in humans using methods of appropriate validity and precision may be required for the scientific substantiation of health claims related to the reduction of body fat or to the increase or maintenance (i.e. reduced loss) of lean body mass. As a general point for all claims, the NDA Panel considers what is generally accepted in the relevant research fields when assessing whether the studies provided for substantiation used (an) appropriate outcome measure(s) of the claimed effect (Section 2). Measurements which may be adequate to stratify and characterise population subgroups in large cross-sectional or prospective cohort studies with respect to, for example, body fat distribution (e.g. waist circumference and waist-to-hip-ratio) may not be appropriate to assess changes in body composition (e.g. body fat) in human intervention studies, so that the selection of the method may depend on the study population, the compartment of interest, and the expected change.

Imaging techniques (e.g. DEXA, MRI and CT) are generally appropriate to assess changes in body fat and lean body mass in human intervention studies. Changes in specific body fat compartments can also be assessed reliably by MRI or CT. Anthropometric measurements (e.g. waist-to-hip-ratio, waist circumference and skinfold thickness), even if useful to stratify and characterise population subgroups, may not be appropriate to assess changes in body composition in human intervention studies of short duration, particularly if sample size is small or no changes in body weight are expected. BIA and ADP are generally not appropriate to assess small changes in body fat when used alone, particularly in obese subjects and/or when significant changes in body water compartments occur. These and other body composition techniques have also been used in combination to assess different body compartments.

The guidance document has been updated (Sections 4.1, 4.3, 4.4) to include some of the examples above, but it does not intend to be exhaustive with respect to the methods which may be appropriate to assess changes in body composition in a particular context.

2.2.6. Claims related to changes in appetite ratings

Comments received

- Some comments requested the inclusion in the guidance document of definitions for satiety, appetite, hunger and satiation.
- Some stakeholders suggested that an increase in satiety/reduction in hunger should be considered as beneficial physiological effects *per se*, as eating motivations could have a relationship with positive energy balance and that enhancing satiety or reducing appetite/hunger *per se* could exert beneficial physiological effects in the short-term (pleasure, mood, cognition) medium-term (subjective wellbeing, coping with daily hunger) and long-term (dietary compliance, goal directed behaviour), which could occur independently of reductions in energy intake and body weight.
- There was a request to clearly state that *in vivo* studies demonstrating changes in biochemical markers of satiety (e.g. cholecystokinin (CCK)) can only be considered as supportive of a satiety claim in the context of behavioural assessment.
- There was a request to better specify the requirements for the scientific substantiation of claims on satiety with respect to effect size.
- It was requested to specify in the guidance document the requirements for control foods to be used for the scientific evaluation of claims on satiety and to mention that these claims should be food (matrix) specific, rather than specific for a particular food ingredient.

Panel consideration of comments received

The guidance document has been revised in order to state, as a general point for all claims, that the NDA Panel considers what is generally accepted in the relevant research fields (e.g. guidelines published by scientific societies based on rigorous methodological approaches) when assessing whether the studies provided for substantiation used (an) appropriate outcome measure(s) of the claimed effect (Section 2).

The beneficial physiological effect of changing appetite ratings (e.g. hunger, fullness, satiety, and desire to eat) depends on the context of the claim. All the claims evaluated by the Panel so far related to changes in appetite ratings, which were made in the context of reducing body weight. In this context, evidence for a sustained effect on appetite ratings and on body weight with continuous consumption of the food should be provided. The scientific evidence for an effect on appetite ratings can be obtained from human intervention studies showing an increase in satiety/a reduced sense of hunger or appetite (behavioural assessment) using methods with appropriate validity and precision (e.g. validated visual analogue scales). Evidence for a sustained effect with continuous consumption of the food (in order to exclude adaptation) should also be provided. Changes in certain biochemical markers (e.g. CCK) may support the behavioural assessment.

Claims related to changes in appetite ratings after food consumption may be comparative claims (i.e. comparison of the "test" food with the "control" food). In this context, both the test and the control food should be sufficiently characterised for a scientific evaluation with respect to the factors (e.g. energy, volume, appearance and taste) which may have an impact on the claimed effect.

Claims on other effects of changing appetite ratings in response to food consumption (e.g. effects on mood during energy restriction) should be specifically indicated and substantiated, and will be considered by the Panel in the context of specific applications.

The guidance document (Section 3) has been revised according to the information provided above.

2.2.7. Claims related to the reduction of body fat/body weight

Comments received

- It was suggested that a "sustained increased fat oxidation" should be considered as a beneficial physiological effect *per se*.
- Some comments proposed that a sustained increase in fat oxidation (e.g. measured by indirect calorimetry) as well as a sustained increase in energy expenditure may be mechanisms by which a reduction in body fat/weight can be achieved.
- There was a question as to whether a follow-up period after a weight loss intervention should be required in a study for the substantiation of health claims on weight management/loss.
- Some stakeholders noted that this section mainly addressed overweight adults, and that growth patterns and body composition of infants and children differ largely from those of adults. It is requested that this feature be explicitly explained and that special mention be made of children's claims in this context (e.g. maintenance of body weight may not be beneficial because healthy children are supposed to grow).
- With respect to claims on the reduction of energy intake, it was unclear why control and test foods should be comparable, for example, in terms of energy. When diets where a high energy component (e.g. other carbohydrates) has been replaced by a lower energy component (e.g. fibre) are compared, this requirement may not be appropriate.
- One comment suggested that an increase in energy expenditure observed after every meal (i.e. multiple acute effects) could aid weight loss and therefore could be considered as a beneficial physiological effect *per se*.

Panel consideration of comments received

A sustained (intentional) reduction in total body fat is considered a beneficial physiological effect for adults with an excess body fat in the general population. A reduction in body weight is also considered a beneficial physiological effect for adults with an excess body weight if body fat is reduced. The scientific evidence for the substantiation of health claims on the reduction of body fat can be obtained from human intervention studies showing a reduction in total body fat by using methods with appropriate validity and precision. Surrogate measures of total body fat (e.g. body weight) could be used for the scientific substantiation of these claims if the reduction is sufficiently large so that it could not be attributed to a reduction in lean body mass/body water. Similarly, the scientific evidence for the substantiation of health claims on the reduction of body weight can be obtained from human intervention studies showing a reduction in body weight which could not be attributed to a reduction in lean body mass/body water.

The conditions in which the effect on body fat/body weight is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about 12 weeks, should also be provided.

Changes in appetite ratings, energy intake, energy expenditure or fat oxidation have been proposed in the context of claims related to the reduction of body fat/body weight. Evidence for a sustained effect with continuous consumption of the food (in order to exclude adaptation) on any of these variables may be considered in support of the mechanisms by which the food may exert the claimed effect.

The guidance document has been re-drafted (Section 3.1) to accommodate this information.

For claims related to children with excess body weight, a sustained reduction in weight-for-height scores regardless of absolute body weight may also be considered beneficial. These claims will be considered by the Panel on a case-by-case basis in the context of specific applications.

2.2.8. Claims on body weight maintenance after weight loss

Comments received

- A clear guidance is requested on what is meant by weight maintenance after weight loss.
- Some stakeholders noted that there is no established definition of successful weight loss maintenance after weight loss and that a definition of successful maintenance of lost weight has been proposed as "intentionally losing at least 10 % of initial body weight and keeping it off for at least one year".

Panel consideration of comments received

The guidance is intended to provide a general framework on the type of studies which can provide evidence for the scientific substantiation of health claims made on foods. It is not intended to set outcome requirements for, for example, weight changes, which will be evaluated on a case-by-case basis in the context of specific applications.

The scientific evidence for the substantiation of health claims related to the maintenance of body weight after (intentional) weight loss can be obtained from human intervention studies showing an effect on (limiting) body weight regain after significant weight loss. The conditions in which the effect is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about six months, should be provided.

The guidance document has been amended to clarify this point (Section 4.2).

2.2.9. Claims related to the reduction of abdominal fat

Comments received

- Some comments suggested that there is consensus about the association between reductions in waist circumference and reductions in visceral fat, and that many existing studies have already validated waist circumference against abdominal obesity. Thus, it is requested that simple waist circumference measurements should be sufficient for the scientific substantiation of claims on the reduction of abdominal fat.
- There was a request for clarification on what is precisely understood as objective and suitable measures of body shape, and on what would be an appropriate study duration.

Panel consideration of comments received

A sustained reduction in abdominal fat, and particularly in visceral fat, is considered a beneficial physiological effect for adults with adverse health effects associated with an excess of abdominal fat (e.g. impaired glucose tolerance, dyslipidaemia and high blood pressure).

The beneficial physiological effect of the only claim received by the Panel so far with respect to changes in body shape related to the reduction of abdominal fat and to the improvement of the metabolic variables associated with an excess abdominal fat. Therefore, specific mention to health claims on body shape has been deleted from the guidance.

The scientific evidence for the substantiation of health claims related to the reduction of abdominal fat can be obtained from human intervention studies showing a reduction in abdominal fat using methods with appropriate validity and precision (e.g. imaging techniques). Surrogate measures of abdominal fat (e.g. waist circumference) could be used for the scientific substantiation of these claims if the reduction is sufficiently large so that it could not be attributed to a reduction in lean body mass/body water. The conditions in which the effect is achieved need to be specified (under energy-restriction, eating *ad libitum*, etc.). Evidence for a sustained effect with continuous consumption of the food/constituent over, for example, about 12 weeks, should also be provided.

This information has been included in the revised guidance to further assist stakeholders (Section 4.3).

2.2.10. Claims on the increase/maintenance of lean body mass

Comments received

- It was requested to explicitly mention that slowing or preventing naturally-occurring lean body mass loss in older adults (e.g. over the age of 50) and in inactive individuals is a beneficial physiological effect.

Panel consideration of the comment received

A sustained increase in lean body mass may be a beneficial physiological effect for physically active subjects, including trained individuals. The maintenance (i.e. reduced loss) of lean body mass may also be beneficial, for example, during energy restriction leading to weight loss, or for older adults.

The Panel has taken this comment into consideration and the guidance has been updated accordingly (Section 4.4).

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

Comments received

- There was a request to justify why a decrease in post-prandial blood glucose responses should be achieved without a disproportionate increase in insulin responses for the scientific substantiation of these claims, and to clarify how a "disproportionate increase in insulin concentrations" is defined.
- There was a question on whether a reduction in glucose and/or insulin concentrations (or derivate indices, such as the homeostatic model assessment (HOMA) or the quantitative insulin sensitivity check index (QUICKI)) would be sufficient for the substantiation of these claims. Clarification is requested on whether data on the mechanism, for example decrease in carbohydrate or lipid absorption by the intestine, would be needed in addition, and on whether *in vitro* testing could be sufficient for that purpose.
- More guidance is requested on whether glucose and insulin concentrations should be measured in capillary, venous or arterialised venous blood, and on whether interstitial glucose concentrations should be measured.
- One comment asked to differentiate between the lowering of post-prandial blood glucose by replacing digestible carbohydrates a) by intense sweeteners (non-caloric, do not contribute to overall carbohydrate energy in the diet), b) by fermentable/low-digestible carbohydrates, some providing partly carbohydrate energy, or c) by digestible, but low-glycaemic carbohydrate alternatives providing full energy from carbohydrates.

Panel consideration of comments received

The scientific evidence for the substantiation of health claims on the reduction of post-prandial blood glucose responses can be obtained from human intervention studies showing a decrease in blood glucose concentrations at different time points after consumption of the test food during an appropriate period of time (i.e. at least two hours) while insulin concentrations at different time points are not increased in comparison to the reference food. The requirement for a non-disproportionate increase in insulin concentrations does not refer to the absolute insulin responses in a particular study population (e.g. for subjects with impaired glucose tolerance) with respect to the general population but rather to insulin concentrations in response to the test food as compared to the reference food. The guidance document has been amended to clarify this aspect (Section 5.1).

As a general point for all claims, and as stated in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims, the NDA Panel makes a scientific judgement on the extent to which 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) by considering the strength, consistency, specificity, dose-response, and biological plausibility of the relationship. In this context, data on the mechanisms by which a food/constituent can exert the claimed effect may add to the biological plausibility of the claim, but it is not strictly required for the scientific substantiation of health claims. Also as a general point for all claims, the NDA Panel considers what is generally accepted in the relevant research fields (e.g. guidelines published by scientific societies based on rigorous methodological approaches) when evaluating whether the studies provided for substantiation used (an) appropriate outcome measure(s) of the claimed effect (e.g. use of capillary, venous or arterialised venous blood vs. use of interstitial glucose concentrations; use of raw values vs. use of derivate indices of glucose and insulin concentrations; use of appropriate statistical analyses of data). Section 2 has been revised to highlight this point.

The guidance document only depicts examples of the type of food/constituent for which health claims on the reduction of post-prandial blood glucose responses have been proposed so far and does not intend to be an exhaustive list of possible claims in this area. The guidance may be updated in the future in light of additional experience gained with the evaluation of these claims.

2.2.12. Claims on maintenance of normal blood glucose concentrations and on increased insulin sensitivity

Comments received

- There was a question on why there is no section on claims related to (long-term) maintenance of normal blood glucose concentrations in part 5 of the draft guidance.
- An explanation was requested as to whether only subjects with impaired blood glucose tolerance are to benefit from the long-term maintenance of blood glucose concentrations.
- It was argued that from a clinical point of view, a subject with a diagnosis of diabetes will no longer be without anti-diabetic treatment, so it is questioned how studies could be conducted in "un-medicated" diabetics.
- There was a question on whether claims on the maintenance of normal blood glucose concentrations/improved blood glucose control fall under Article 13 of the claims Regulation, and whether an Article 14 claim could be possible for diabetics, based on reduced HbA1c.
- There was a request to include claims on the improvement of fasting and post-challenge (e.g. standard oral glucose tolerance test (OGTT)) glucose responses.
- It was noted that the use of "biomarkers" other than glycated haemoglobin (HbA1c), such as fasting glucose, continuous interstitial glucose monitoring, OGGT or fructosamine, has been proposed for the scientific substantiation of these claims. There was a proposal to consider fructosamine as a suitable outcome measure in support (complementing, corroborating) of the results obtained for the established HbA1c "biomarker".
- There was a request to mention the HOMA and fasting plasma insulin alone among the appropriate measures of insulin sensitivity not only for epidemiological but also for intervention studies. The insulin sensitivity index (ISI) and/or QUICKI are also suggested as standards for intervention studies.

Panel consideration of comments received

Section 5.2 of the guidance document refers to claims on the (long-term) maintenance of normal blood glucose concentrations, for which measures of blood glucose control are required. For clarity the title of this section has been changed in the revised version of the guidance document.

As suggested in the comments provided, maintenance of normal blood glucose concentrations is considered a beneficial physiological effect for the general population. The guidance document has been amended to reflect this comment (Section 5.2).

With respect to the study population, the first step in the treatment of newly diagnosed type 2 diabetes relies on lifestyle (i.e. diet and physical activity) measures only (Nathan et al., 2009). As already stated in the guidance document, studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet) could be used for the scientific substantiation of these claims. The question about disease risk reduction claims (Article 14) for diabetic subjects based on HbA1c is unclear to the Panel since HbA1c cannot be a risk factor and diabetics cannot be the target population for this claim.

The Panel notes that fasting blood glucose concentrations do not reflect long-term blood glucose control, but considers that measurements of plasma glucose concentrations after a standard OGTT and measurements of fructosamine, can be considered as supportive evidence (i.e. in addition to HbA1c) for the scientific substantiation of these claims. Changes in insulin sensitivity assessed using appropriate (dynamic) outcome measures (e.g. hyperinsulinaemic-euglycaemic clamp, ISI, and QUICKI) could be used in support of a mechanism by which the food/constituent could exert the claimed effect. The guidance has been updated accordingly (Section 5.2).

No claims have been proposed on the reduction of fasting blood glucose or on the reduction of plasma glucose concentrations after an OGTT. Whether any of these outcomes may be considered beneficial physiological effects *per se* will be considered in the context of specific applications. The Panel has also not evaluated health claims related to the (long-term) maintenance of normal blood glucose concentrations and proposing data from continuous (interstitial) glucose monitoring as an outcome measure. The Panel notes that the relationship between measures obtained with different continuous (interstitial) glucose monitoring systems (e.g. mean glucose concentrations) and well-accepted measures of long-term blood glucose control (e.g. HbA1c) has not yet been established.

The guidance may be updated in the future in light of additional experience gained with the evaluation of these claims.

REFERENCES

Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B, American Diabetes Association and European Association for the Study of Diabetes, 2009. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia, 32, 193-203.

GLOSSARY AND ABBREVIATIONS

ADP	Air displacement plethysmography
BIA	Bioelectrical impedance analysis
CCK	Cholecystokinin
CT	Computed tomography
DEXA	Dual energy X-ray absorptiometry
HbA1c	Glycated haemoglobin
HOMA	Homeostatic model assessment
ISI	Insulin sensitivity index
MRI	Magnetic resonance imaging
OGTT	Oral glucose tolerance test
QUICKI	Quantitative insulin sensitivity check index

APPENDIX

FULL LIST OF COMMENTS RECEIVED ON THE DRAFT OPINION OF THE EFSA PANEL ON DIETETIC PRODUCTS, NUTRITION, AND ALLERGIES (NDA) ON A DRAFT GUIDANCE ON THE SCIENTIFIC REQUIREMENTS FOR HEALTH CLAIMS RELATED TO APPETITE RATINGS, WEIGHT MANAGEMENT, AND BLOOD GLUCOSE CONCENTRATIONS

This list contains the comments submitted to EFSA via the public consultation held from 26 April 2011 to 31 August 2011. Comments submitted by individuals in a personal capacity are presented anonymously. Comments submitted formally on behalf of an organisation appear with the name of the organisation.

ORGANISATION	CHAPTER TEXT	COMMENT TEXT
Ashwell Associates Europe Ltd	1. Introduction	General comment I would like to see some mention in these guidance notes about the value of including meta-analyses of individual studies obtained by systematic review. I have always believed that these are very helpful in increasing statistical power and allow well designed studies with smaller effects to add to the conclusions. They also make conclusions from the totality of the evidence which must be one of the panel's main criteria. However, I have noticed several opinions where the meta-analysis has been 'unpicked' so that the studies within it are discarded or retained for individual comment. I find this surprising and would therefore value some guidance on the wisdom of including meta-analysis.
BENEO Institute	1. Introduction	BENEO welcomes the opportunity to provide comments on the subject document. The document mainly provides a summary of and reiterates key aspects that were expressed by the NDA panel in Art. 13.1 and Art. 13.5 related Opinions on claims aiming at appetite ratings, weight management and blood glucose concentrations. We would like to point out that in addition to these remarks it needs to be reiterated for clarification what was stated at the last public EFSA Consultation in December 2010 by Prof. Flynn "that the scientific assessments carried out by the panel are done within the strict legal confines of the Regulation and they have to be seen in that light ..." (see Meeting recordings of December 2nd 2010). This should be equally included in the current Guidance document on health claims related to appetite ratings, weight management, and blood glucose concentrations as well as the two other Guidance documents in preparation, and those announced. Such a clarification is absolutely necessary as it must be pointed out that nutritional assessment in other contexts are

		still valid, e. g. Dietary Reference Values and other nutritional recommendations, food-based dietary guidelines, other opinions, already established food/nutrition-related regulations. Experiences from the public have already questioned well established nutritional assessments including those of other EFSA or even the same NDA panels, because the context is lost.Line 108: Regarding the beneficial physiological effect, could EFSA provide the scientific rationale and criteria on which the NDA panel concludes/concluded that claimed effects are accepted as beneficial physiological effects or is not. Line 109: It will be useful for applicants if the EFSA could provide the scientific rationale and criteria on which the NDA panel concludes/concluded that studies/outcomes measures are appropriate for substantiation of Health Claims aiming at appetite ratings, weight management and blood glucose concentrations.
Danone Research	1. Introduction	We welcome EFSA's initiative to provide additional guidance to applicants for the substantiation of health claims. We acknowledge that the draft guidance is not intended to be an exhaustive list of acceptable beneficial effects, studies or outcome measures, and is mostly based on previously issued evaluations.
DHI Water Environment Health	1. Introduction	We find it very helpful and appreciate that these guidance documents were provided, in order to gain experience from all the assessment work that has been carried out up until now.
ELC	1. Introduction	In order to provide maximum guidance to operators preparing scientific dossiers, the Guidance should provide specific information on criteria for i.e. valid endpoints, markers and methods, and should allow for new approaches as well to support innovation. Unfortunately the draft document rather reflects the findings of those claims already assessed only. In several cases, EFSA refers to combinations of markers as acceptable while a stand alone marker, due to its limited specificity is not. Same applies to modified methods which could be acceptable for the substantiation of a claim. In these cases, combinations should be named and alternative methods discussed or listed.
European Federation of Associations of Health Product Manufacturers (EHPM)	1. Introduction	EHPM would like to thank the European Food Safety Authority (EFSA) for holding this consultation and appreciate very much the opportunity to be able to provide our comments. Whereas the regulations and PASSCLAIM require an assessment of the extent to which cause and effect can be demonstrated between a food category, a food or food constituent, EFSA requires conclusive evidence of cause and effect. This latter standard of proof and the EFSA focus on randomised controlled trials carried out on isolated components and using fully validated, disease-related physiological biomarkers may not always be appropriate to assess state-of-the-art nutrition science. It is the integration of findings from several different types of evidence and the degree of consistency between them that is the scientific standard that needs to be applied to nutrition science, i.e. the totality of the available

data.

The notion of conclusive evidence of cause and effect is not a requirement of the legislation, or of PASSCLAIM. The notion of extent refers to that of a "degree", e.g. either small, moderate or large. The extent of cause and effect is determined by the strength, consistency and biological plausibility of the totality of the available data in support of a beneficial nutritional as well as a physiological effect following consumption of the food category or food/constituent.

The EFSA pharmaceutical approach does not recognise the complexities of research in human studies. EFSA guidance should state more clearly how the evidence is weighed. There should be (a) a section to address the strengths and weaknesses of different sources of evidence that contribute to the totality of the available data; (b) a critical examination of the application of a drug-like, hierarchical assessment model in evidence-based nutrition; (c) a robust, transparent and scientific framework for assessing the strength, consistency and biological plausibility of the evidence.

In general, diet-related diseases are caused by chronic exposure to unbalanced diets and not by acute exposures. The body's physiology may cope with variations in diet through feedback mechanisms, the buffering capacity of homeostasis and, if necessary, by repair mechanisms. Adaptation to habitual consumption of such a diet or diets with unbalanced composition modulates the acute response and produces less dramatic alterations in molecular and physiological responses. Adaptive responses attempt to keep physiology within an individual's normal range. Because of the large variations in "normality", the effects of nutritional intervention (even over two to three months) in the general population may remain hidden because of the dynamic and multifactorial nature of the homeostatic procedures.

Most validated biomarkers currently used in nutrition intervention studies are associated with diagnostic and prognostic use for chronic disease, and since most complex diseases are of late onset, biomarkers are typically associated with surrogate endpoints. Such endpoints would be equivalent to the clinical endpoint. The use of patients/pre-clinical states are common in nutrition science, and of key importance is to weigh up how representative the clinical studies are for the general population. The relevance of studies in patients to the normal healthy population requires a coherent and transparent approach. Furthermore, using the normal general population as subjects in human studies is unlikely to reveal demonstrable physiological effects in short-term RCTs.

Are EFSA's proposed methodologies using certain biomarkers achievable?

Overall, the EFSA guidelines are helpful, but they seem to highlight research needs for the coming decades, not the assessment of current state-of-the-art nutrition science.

European Responsible Nutrition Alliance	1. Introduction	ERNA would like to thank EFSA for making this document available and offering the possibility for consultation. We regret however that the guidance is limited to findings coming from the experiences of EFSA with already submitted requests. This is obviously limited, not only because it is not certain the submitted requests have covered the whole area of effects relating to appetite, weight management and blood glucose, but also because the approach adopted by EFSA has rejected much of the data as non pertinent and the relevance of such data is therefore not covered in this paper. The content is rather general addressing what was not appropriate or sufficient, but with very limited information on what would be appropriate or acceptable. We would have appreciated more comprehensive information with examples of what would be acceptable, and more detailed and state-of-the-art" guidance on criteria for valid endpoints, markers and methods. With such information, the guidance would offer added value. In addition, we believe a technical meeting with experts may be helpful to address this limitation. We hope EFSA will consider the organisation of such technical meetings. Furthermore, the approach does not sufficiently appreciate the totality of currently available knowledge and the limitations of what is achievable in the field of food research. Also, Section 2.1 states that applications for claims that specify target groups other than the general (healthy) population are the subject of on-going discussions with the Commission and member states with regard to their admissibility. This issue needs to be addressed urgently, as nutrition intervention studies in the healthy population are unlikely to show anything at all. A further point is that it would be helpful if the paper could give more clarity or guidance on which claims can be derived from specific endpoints, what population groups and population at risk can be considered as appropriate study groups for claims on general population, what parameters (including value limits) would be considered as normal for physiological effects, how both maintenance and improvements of the physiological function could be demonstrated, and what confounding factors would need to be controlled. That this is possible is demonstrated from several EFSA opinions in which physiological parameters are defined and their limit-values for normality specified (for example for blood pressure in the isoleucine-proline-proline (IPP) and valine-proline-proline (VPP) opinion and for blood lipids in the various opinions dealing with maintenance of normal LDL-cholesterol, normal HDL-cholesterol and triglycerides concentrations. The inclusion of such factual information in the guidance would be useful, as it will provide clarification of the limits of normality for claims in relation to the health effects discussed in this guidance.
ILSI Europe aisbl	1. Introduction	Line 89-100 Overall we welcome this consultation document. It does pull together a number of points on claims relating to appetite, weight management and blood glucose management. At the moment, reference is

		only made to previous EFSA documents. To enable evaluation of the scientific data upon which the guidance is based, we recommend including references from the scientific literature. 101-105 Which criteria would be applied to decide whether or not a scientific meeting would happen? For each guideline document, a scientific meeting would be very useful. 108 It is indeed crucial to know which effects are considered to be beneficial and physiological. It therefore also crucial to know the criteria the Panel applies in order to conclude, case-by-case, whether or not a certain effect is beneficial and physiological. 109 When speaking of the appropriateness of studies we assume the Panel in fact refers to study designs and study population; is that correct? When speaking of the appropriateness of outcome measures, we assume the Panel refers to the validity of such outcomes in terms of whether or not they reflect, or mark, in a meaningful way, effects that are beneficial and physiological; is that correct?
MRC Human Nutrition Research	1. Introduction	We are pleased to have the opportunity to comment on the EFSA draft report on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. This is a well-structured, concise guidance that makes clear reference to other previous documentation by the EFSA related to health claims. There is scope for the addition of some more detail, in particular to distinguish the types of beneficial physiological effects that can be considered as actual benefits, as opposed to mechanistic evidence for an effect.Section 2.1. Beneficial physiological effects (lines 125-142): More clarification is needed on the distinction between an effect per se vs. a mechanism leading to that effect. Although this information is available elsewhere in the document it would be more useful for readers if it was reiterated here.
NB Consulting	1. Introduction	Lines 111 - 113 Characterisation EFSA has already provided a positive opinion on a weight control claims for konjacmannan (1) (3 x 1g is to be consumed before 3 meals per day). Konjacmannan can be well characterised within quite close specifications, as is possible with all such relatively pure ingredients. However, within the opinion it is also indicated that a condition of use is an energy restricted diet – but that is not characterised other than by energy perhaps indicating a broad range of macronutreint composition is acceptable. We also note that EFSA has accepted quite a wide specification for meal replacements for which a weight loss and a weight maintenance claim was found acceptable (2): "Meal replacements for weight loss shall provide not less than 25 % and not more than 50 % of the total energy of the product as protein, not more than 30 % of the total available energy as fat …". Such a wide specification is not usually found acceptable by EFSA. For example, nuts (5 types) were rejected as not characterised for a weight control claim even though they contain a similarly broad range of protein values (5 – 15% energy) and fats (3). The impact of individual foods and individual dishes or meals, as well as individual ingredients, may be successfully studied in the context of inducing changes in appetite/satiety, subsequent food energy intake and weight loss. We would thus urge EFSA to take a case by case approach to characterisation and take a broader perspective in terms of what can be acceptably characterised for health claims. The evidence of the benefit needs to be considered at the same time as the

		characterisation, rather than the two aspects considered separately. As has been demonstrated in the case of meal replacements, a range of composition may be acceptable providing it is consistent with the evidence. 1. EFSA Journal 2010;8(10):1798. [27 pp.]. doi:10.2903/j.efsa.2010.1798. 2. EFSA Journal 2010; 8(2):1466. [19 pp.]. doi:10.2903/j.efsa.2010.1466. 3. EFSA Journal 2011; 9(4):2032. [14 pp.]. doi:10.2903/j.efsa.2011.2032
Nestlé	1. Introduction	Ln 89-92: Nestlé welcomes the EU Nutrition & Health Regulation and its provisions, including EFSA's evaluations of health claim applications.
Rudolf Wild GmbH & Co. KG	1. Introduction	Line 119/120 – Is it planned to publish future lists of beneficial effects, as the process of claim evaluation will be more mature in the future?
SYNPA	1. Introduction	The SYNPA which is representing the French producers of food additives, food enzymes, novel ingredients and functional ingredients, welcomes the opportunity to comment the draft guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations, prepared by the EFSA's NDA panel. The implementation of the Health claims regulation has proved that there is a real need for the operators to have a clear view of the experts' expectations. We believe it could be achieved through the guidance. In order to provide maximum guidance to operators preparing scientific dossiers, the Guidance should provide specific information on criteria for i.e. valid endpoints, markers and methods, and should allow for new approaches as well to support innovation. Unfortunately the draft document rather reflects the findings of those claims already assessed only. In several cases, EFSA refers to combinations of markers as acceptable while a stand alone marker, due to its limited specificity is not. Same applies to modified methods which could be acceptable for the substantiation of a claim. In these cases, combinations should be named and alternative methods discussed or listed. The SYNPA supports the ELC's comments.
Tate & Lyle Plc	1. Introduction	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful

		• Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
Wrigley Science Institute	1. Introduction	In general, the committee should be congratulated for their efforts to develop the proposed "Guidances". I provide some specific comments in some of the sections. One key issue that concerns all claim areas, and not fully developed in the draft scientific opinion, relates to study subject population. Overweight or obese populations can be diverse in terms of their demographics and physical characteristics, e.g. BMI, age, and gender. Thus the panel may wish to provide more specific guidelines for extrapolation of data from the study subject to target/general population of the claim. For example, can a study performed on women be extrapolated to both genders, provided adequate justification is given? If not, or if no satisfactory justification can be given, would it be beneficial to have minimal acceptable proportion of the studied population that should belong to a gender?
DSM Nutritional Products	2. General considerations	General comments We welcome to be given the opportunity to comment on the draft guidances by EFSA which shall be a help to interested parties to successfully substantiate a claim. We would have expected more detailed, "state of the art" guidance which offers specific information on criteria for i.e. valid endpoints, markers and methods. The draft documents seem just to reflect the findings from the assessed claims in those health areas which in turn are based just on the references which have been submitted and do not necessarily reflect state of the art science. In several cases EFSA refers to combinations of markers which could be acceptable for the substantiation of a claim while a stand alone marker (due i.e. its limited specificity) is not, or modified methods which might be acceptable – in those cases combinations should be named and alternative methods discussed or listed. It would be helpful if EFSA i.e. could give guidance what kind of claims can be derived from currently used endpoints, like BMD instead of fractures for bone health claims, and inflammatory parameters and pain scores for joint health ingredients. Furthermore at least with regard to the guidance on bone health etc. we feel the combination of bone health, joint health and oral health in one single document is neither logical nor comprehensible as these are three

		huge indication fields which are biologically extremely diverse and not related. We would therefore favour a split of the guidance into several documents.
DSM Nutritional Products	2. General considerations	General comments We welcome to be given the opportunity to comment on the draft guidances by EFSA which shall be a help to interested parties to successfully substantiate a claim. We would have expected more detailed, "state of the art" guidance which offers specific information on criteria for i.e. valid endpoints, markers and methods. The draft documents seem just to reflect the findings from the assessed claims in those health areas which in turn are based just on the references which have been submitted and do not necessarily reflect state of the art science. In several cases EFSA refers to combinations of markers which could be acceptable for the substantiation of a claim while a stand alone marker (due i.e. its limited specificity) is not, or modified methods which might be acceptable – in those cases combinations should be named and alternative methods discussed or listed. It would be helpful if EFSA i.e. could give guidance what kind of claims can be derived from currently used endpoints, like BMD instead of fractures for bone health claims, and inflammatory parameters and pain scores for joint health ingredients. Furthermore at least with regard to the guidance on bone health etc. we feel the combination of bone health, joint health and oral health in one single document is neither logical nor comprehensible as these are three huge indication fields which are biologically extremely diverse and not related. We would therefore favour a split of the guidance into several documents.
European Federation of Associations of Health Product Manufacturers (EHPM)	2. General considerations	Section 2.1 states that applications for claims that specify target groups other than the general (healthy) population are the subject of on-going discussions with the Commission and member states with regard to their admissibility. This issue needs to be addressed urgently, as nutrition intervention studies in the healthy population are unlikely to show anything at all.
European Health Product Manufacturers	2. General considerations	Section 2.1 states that applications for claims that specify target groups other than the general (healthy) population are the subject of on-going discussions with the Commission and member states with regard to their admissibility. This issue needs to be addressed urgently, as nutrition intervention studies in the healthy

		population are unlikely to show anything at all. Management issue
European Health Product Manufacturers	2. General considerations	EHPM would like to thank the European Food Safety Authority (EFSA) for holding this consultation and appreciate very much the opportunity to be able to provide our comments. Whereas the regulations and PASSCLAIM require an assessment of the extent to which cause and effect can be demonstrated between a food category, a food or food constituent, EFSA requires conclusive evidence of cause and effect. This latter standard of proof and the EFSA focus on randomised controlled trials carried out on isolated components and using fully validated, disease-related physiological biomarkers may not always be appropriate to assess state-of-the-art nutrition science. It is the integration of findings from several different types of evidence and the degree of consistency between them that is the scientific standard that needs to be applied to nutrition science, i.e. the totality of the available data. The notion of conclusive evidence of cause and effect is not a requirement of the legislation, or of PASSCLAIM. The notion of extent refers to that of a "degree", e.g. either small, moderate or large. The extent of cause and effect is determined by the strength, consistency and biological plausibility of the totality of the available data in support of a beneficial nutritional as well as a physiological effect following consumption of the food category or food/constituent. The EFSA pharmaceutical approach does not recognise the complexities of research in human studies. EFSA guidance should state more clearly how the evidence is weighed. There should be (a) a section to address the strengths and weaknesses of different sources of evidence that contribute to the totality of the available data; (b) a critical examination of the application of a drug-like, hierarchical assessment model in evidence-based nutrition; (c) a robust, transparent and scientific framework for assessing the strength, consistency and biological plausibility of the evidence. In general, diet-related diseases are caused by chronic exposure to unbalanced diets and not by acute exposures. The body's physiology may cope with variations in diet through feedback mechanisms, the buffering capacity of homeostasis and, if necessary, by repair mechanisms. Adaptation to habitual consumption of such a diet or diets with unbalanced composition modulates the acute response and produces less dramatic alterations in molecular and physiological responses. Adaptive responses attempt to keep physiology within an individual's normal range. Because of the large variations in "normality", the effects of nutritional intervention (even over two to three months) in the general population may remain hidden because of the dynamic and multifactorial nature of the homeostatic procedures. Most validated biomarkers currently used in nutrition intervention studies are associated with diagnostic and prognostic use for chronic disease, and since most complex diseases are of late onset, biomarkers are typically associated with surrogate endpoints. Such endpoints would be equivalent to the clinical endpoint. The use of patients/pre-clinical states are common in nutrition science, and of key importance is to weigh up how representative the clinical studies are for the general population. The relevance of studies in patients to the normal healthy population requires a coherent and transparent approach. Furthermore, using the normal general population as subjects in human studies is unlikely to reveal demonstrable physiological effects in short-term RCTs. Are EFSA's proposed methodologies using certain

		biomarkers achievable? Overall, the EFSA guidelines are helpful, but they seem to highlight research needs for the coming decades, not the assessment of current state-of-the-art nutrition science.
European Nutraceutical Association (ENA)	2. General considerations	Again the ENA appreciates that EFSA´s NDA panel provides a well-developed draft guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations.
HarlandHall Associates	2. General considerations	Line 121 As a matter of principle, I consider the appropriate study duration should be expressed in weeks. Months is too imprecise, for example is 3 months equivalent to 12 weeks or 84 weeks or 90 days or 93 days? Section 3.1 Line 202 What is the scientific rationale for the chronic exposure to a food for a period of 1 month? Section 4.3 Line 239 What is the rationale for the choice of 3 month for weight loss studies - much of the literature contains studies conducted for shorter periods. Hence is 3 month is it scientifically based? There is concern that small and medium sized enterprises who rely on the published scientific literature to support claims, will have a much restricted use of the scientific literature by the recommendation of this longer time period. While it is considered that studies need to be of a reasonable period to ensure a sustained weight loss, I am unsure of an advantage of 3 months compared to say 8 weeks. The main aspect of longer term studies is a demonstration of better compliance, rather than better assessment of weight loss. The value of long-term RCT to assess weight loss as a result of significant dietary changes is questionable as lifestyles and behaviours have to be taken into consideration, alongside the environmental, cultural and social factors that influence them. Causality becomes much harder to establish because of this interplay of factors. Section 5.3 Line 351 What is the rationale for suggesting the use of HOMA and QUICKI assessment of insulin sensitivity is only appropriate for epidemiological studies. The hyperinsulinaemic-euglycaemic clamp is an invasive and expensive technique. In randomised controlled intervention studies of 6-8 weeks duration the above techniques

		could also be employed.
MRC Human Nutrition Research	2. General considerations	We are pleased to have the opportunity to comment on the EFSA draft report on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. This is a well-structured, concise guidance that makes clear reference to other previous documentation by the EFSA related to health claims. There is scope for the addition of some more detail, in particular to distinguish the types of beneficial physiological effects that can be considered as actual benefits, as opposed to mechanistic evidence for an effect. Section 2.1. Beneficial physiological effects (lines 125-142): More clarification is needed on the distinction between an effect per se vs. a mechanism leading to that effect. Although this information is available elsewhere in the document it would be more useful for readers if it was reiterated here.
Nestlé	2. General considerations	E.g. ln 141-2: We appreciate that EFSA evaluates case-by-case. We encourage, where possible, transparency concerning the criteria applied in each of these case-by-case evaluations.
Tate & Lyle Plc	2. General considerations	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
University of Leeds	2. General considerations	General comment: The guidance does not consider the value of systematic reviews nor meta-analyses which are accepted by NICE in the UK as the highest form of evidence for clinical trials and ensuing decisions regarding prescribing practice. This seems at odds with the pharmaceutical model which appears to have been adopted by EFSA in the development of these guidelines. There is little consideration of the power of systematic and meta-analytic reviews to draw together evidence in a coherent and comparative form, which ought to facilitate the generation of an opinion, whether favourable or unfavourable by the panel. Although the motivation of EFSA guidance on claims is to protect the consumer and to improve the evidence base for claim approval, I have a number of misgivings about the impact of the current guidance on research. On the whole it appears to be narrow in focus and extremely prescriptive and generates the concern that rather than increasing the quality of research in these areas, it will stifle research activity, particularly that funded by the food

		industry, driving smaller concerns away from generating solid evidence for the effectiveness of their products, towards more "creative" less police-able techniques to market their products, which will defeat the object of the entire exercise.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	2. General considerations	For the general function claims, to which extent/how is the matrix effect considered ? Does the effect of an ingredient demonstrated in product A has to be demonstrated in product B to bear a claim ?
Arla Foods a.m.b.a.	2.1. Beneficial physiological effects	We have a general comment to paragraph 2.1 line 147 on the application of claims for groups other than the general healthy population. We think it is important to get a clarification on which groups this will be since it will open up for new possibilities of intervention studies in groups that might be more vulnerable to food interventions and thus those studies might help in getting clear results. We also have one general comment to the indications of duration of various studies set in the guideline. How strict will this be, e.g. will a study on weight loss conducted only for 2 month but with very good results nor be able to include in a dossier for application of health claims?
Ashwell Associates Europe Ltd	2.1. Beneficial physiological effects	139 prospective observational studies
BENEO Institute	2.1. Beneficial physiological effects	Could the EFSA provide a clear definition of the scientific rationale and criteria on which the NDA panel makes its scientific judgment that a claimed effect is accepted as beneficial physiological effects or otherwise is not. The document should provide adequate scientific justification in particular in those cases where the NDA panel did not accept a claimed physiological effect as beneficial, as it was e.g. the case with increased satiety/reduced appetite as stand alone. In this context, we appreciate that the EFSA has acknowledged a reduction of postprandial glucose as a beneficial physiological effect. However, using this as an example, we feel that this stringent effect-targeted evaluation/assessment has thrown several nutrients into the same category only by these evaluated health targets, whereas their diverse role in nutrition is lost. Using this example, for the consumer, no distinction is possible whether the claimed effect "reduction of postprandial glycemia" is based on gastric emptying, use of slower-release carbohydrates, replacement of available carbohydrates by dietary fibres or non-nutritive sweeteners. In our opinion this is a consequence of this pharmacological-type approach chosen by the EFSA without considering the role of the nutrient in the diet. It will lead to misleading the consumer rather than to provide them with appropriate information.

ELC	2.1. Beneficial physiological effects	Lines 143-149 The introduction to this document (lines 96-97) clarifies that it constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. As Article 14.a refers to reduction of disease risk claims, it is not clear why the NDA Panel, in the case of a health claim related to a function/effect associated with a disease, would not consider subjects with that disease as a target population for the claim.
European Nutraceutical Association (ENA)	2.1. Beneficial physiological effects	Lines 132-137 From a scientific point of view it is not comprehensible that just the reduction/beneficial alteration of a risk factor is accepted in the context of disease risk reduction claims. In our view it is unscientific that an outcome like the reduction of the risk of a disease itself is not accepted. If the Regulation actually has an obligatory demand for a change of a risk factor caused by a foodstuff to establish risk reduction claims, this would be extraordinarily questionable. We are convinced that the Regulation must be subject to scientific reality and not the other way round and in this case we request to reconsider the Regulation to enable the NDA panel to provide a scientific opinion based on the totality of the scientific evidence. Currently many opinions of the panel are forced to be "biased" by this unscientific restriction. Lines 143-149 The statement that diabetic subjects should not be the target population for a claim related to appetite ratings, weight management, and blood glucose concentrations is not understandable. First this is a target population that benefits extraordinarily from weight reduction (a normal weight range is one of the main goals for diabetic patients!). From a public health point of view it would be a mistake not to address this target group. Second in Lines 326-332 and 339-345 it is explicitly stated (and appreciated by us) that studies performed in diabetic patients will be accepted. This seems to us as a contradiction! Third we appreciate the discussions regarding target population other than the "healthy" population because in medicine/biology there is no clear line between health and disease. In fact it is even a challenge to study effects of foods or food components with RCTs in a reasonable timeline if a function is not impaired or the physiology/metabolism is not under stress.
European Responsible Nutrition Alliance	2.1. Beneficial physiological effects	Line 138. We do not consider it appropriate to limit beneficial effects only to reduction of disease risk factors. The interpretation by EFSA to consider only a reduction of a risk factor for the development of a human disease as beneficial and not a reduction of the risk of disease is challengeable. As it stands now, it appears that

		EFSA considers that a reduction of the risk of disease is not beneficial for health. It does not fall within EFSA's competence to judge upon this, but is the task of the competent authority (e.g. during the validation phase of an application). For the purpose of the assessment of a beneficial effect for health, both should be considered valid. One must consider that in some cases low intake of the food component is in itself a risk factor for the development of a disease. Line 147. We do not consider that health claims can only be considered to be relevant for the general (healthy) population or specific subgroups thereof. The interpretation of the NDA Panel has no legal justification. Not only does this prevent certain reduction of disease risks from being assessed, it does also create an artificial borderline because of what is considered a disease and what not (e.g. elevated cholesterol or hypercholesterolemia, elevated blood pressure or hypertension, etc.). Furthermore, as can be learned from dietetic therapy, foods can have valuable beneficial effects in people suffering from a disease, disorder or other medical condition and such claims fall under the remit of the claims legislation. In addition, the property to have beneficial effects for patients can also be considered as a beneficial effect to their health. Furthermore, foods for special medical purposes are foods specifically intended for the dietary management of people with disorders, diseases or medical conditions. All health effects, also those beneficial to persons not in good health should therefore be covered under the claims legislation.
ILSI Europe aisbl	2.1. Beneficial physiological effects	125-127 According to Article 13.1 of the Regulation for nutrition and health claims it is allowed to make "Health claims describing or referring to (c) … or reduction in the sense of hunger or an increase in the sense of satiety … may be made without undergoing the procedures laid down in Articles 15 to 19, if they are: Based on generally accepted scientific evidence; and Well understood by the average consumer". 141-142 Which are, according to the Panel, the well-established risk factors in this area? Even in a case-by-case assessment, which may include a variety of considerations, it will be helpful to know the considerations taking into account, as well as the criteria that the Panel applies in order to conclude whether or not an effect on a certain risk factor is beneficial. We would like to recommend that EFSA would list risk factors that they would accept, e.g. elevated eating motivations as a risk factor for overeating and weight gain (or failure of weight

		loss). 143-145 Which age range needs to be studied in order to be able to characterise the general population? Is a 30-50 y old study population sufficient? To what extent can one extrapolate from studies on women only or on men only to both genders; how does the Panel evaluate this, in each of the cases? 145 -149 There remains confusion over the target population for certain claims. We note EFSA's comments in this section regarding ongoing discussion with the Commission and Member States. We would like to ask EFSA to consider as target population, subjects already with the disease if an associated function or effect could be improved by a food (ingredient); or to clarify EFSA's reasons for not doing so. Ln 145-147: Irritable bowel syndrome (IBS) and osteoarthritis (OA) are both in WHO's International Classification of Diseases, whereas the Panel does accept extrapolation of effects shown in people with IBS to claims for people without IBS, but not for OA. So which criteria does the Panel apply in order to decide whether or not effects shown in people with a certain condition can be extrapolated to people without that condition, or with a milder and/or undiagnosed form of that condition? Can effects found in people with e.g. diarrhea, colic, H. pylori infection, impaired joint lower mobility be extrapolated to people without these conditions, or with milder and/or non-diagnosed forms of these conditions? In this context, is obesity/overweight considered a disease? Can results from trials with obese or overweight subjects be applied to the general population? 148 How do 'target groups' differ from 'specific subgroups' of the general (healthy) population (ln 144)? Does their health differ? Which criteria does the Panel apply to decide whether any (specific) (sub)group can be a target group for a certain claim? 152-154 So one can claim more generally 'good health' as long as this is substantiated by a specific, measurable and demonstrated health effect? In other words, the claimed does not have to be limited to the specificity of the demonstrated effect?
MRC Human Nutrition Research	2.1. Beneficial physiological effects	We are pleased to have the opportunity to comment on the EFSA draft report on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. This is a well-

		structured, concise guidance that makes clear reference to other previous documentation by the EFSA related to health claims. There is scope for the addition of some more detail, in particular to distinguish the types of beneficial physiological effects that can be considered as actual benefits, as opposed to mechanistic evidence for an effect.Section 2.1. Beneficial physiological effects (lines 125-142): More clarification is needed on the distinction between an effect per se vs. a mechanism leading to that effect. Although this information is available elsewhere in the document it would be more useful for readers if it was reiterated here.
NATUREX Spain S.L.	2.1. Beneficial physiological effects	Recommendations regarding magnitude of weight loss in a weight loss study • What weight loss (kg) is considered physiologically relevant for a 3-month intervention period? • What weight loss (kg) is considered physiologically relevant between the test product and placebo for a 3-month intervention period?
Rudolf Wild GmbH & Co. KG	2.1. Beneficial physiological effects	Line 146/147 – The legislation in Europe, covering food for particular nutritional needs of type 2 diabetics, was removed recently. This was justified, because the nutritional requirements are the same as for healthy subjects. Taking this into account it would make sense to consider type 2 diabetic subjects and the big group of prediabetes subjects as "general population" that falls under the legislation 1924/2006.
SYNPA	2.1. Beneficial physiological effects	Lines 143 to 149 The introduction to this document (lines 96-97) clarifies that it constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. As Article 14.a refers to reduction of disease risk claims, it is not clear why the NDA Panel, in the case of a health claim related to a function/effect associated with a disease, would not consider subjects with that disease as a target population for the claim.
Tate & Lyle Plc	2.1. Beneficial physiological effects	2.1 line 143 -149 there remains confusion over the target population for certain claims: Whilst we note EFSA's comments in this section vis a vis ongoing discussion with the Commission and Member States. We would ask EFSA to clarify its reasoning for not considering as target population, subjects already with the disease if an associated function or effect is beneficially impacted?
Tate & Lyle Plc	2.1. Beneficial physiological effects	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes

		• Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	2.1. Beneficial physiological effects	Line 132. The European Very Low Calorie Diet Industry Group ("The Industry Group") is not clear on the panel's definition of risk of disease versus risk of development of disease. Line 149. There is confusion as to whether an obese group can be the target of claims or whether this needs to be dealt with by the "further discussion with the Commission and Member States".
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	2.1. Beneficial physiological effects	Are the claims on body shape/ beauty (nutricosmetics) in or out the regulatory scope ? It is stated in the draft that "changes in body shape resulting from changes in body fat distribution […] could be considered beneficial" (section 4.8), so we understand here that physical health is relevant. But what about mental health/well-being/mood, like in the Natural-Push up case where firmer breasts were not considered beneficial ? Taking into account the WHO definition, health is "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity"… How health is defined by EFSA ?
Wrigley Science Institute	2.1. Beneficial physiological effects	The panel notes that studies need to be performed with "..(an) appropriated outcome measure(s) of that claimed effect". The challenge is that there are few established outcome measure(s)/biomarkers demonstrating physiological effects. Furthermore, tools for the assessment of the appropriateness of specific outcome measures are lacking and this deficit could seriously undermine the development supporting science and the justification of claims.
Ashwell Associates Europe Ltd	2.2. Studies/outcome measures appropriate for substantiation of claims	170 Many of the text book claims for vitamins and minerals are based on absolutely no intervention studies. Some of the best scientific evidence comes from good quality observational studies (eg for wholegrain). The emphasise on intervention studies throughout the guidance needs to be diluted to reflect the reality of the type of studies which can be done to reflect that these claims are for foods and not for pharma.
BENEO Institute	2.2. Studies/outcome measures appropriate for substantiation of claims	Line 184: Could the EFSA provide clear criteria when the NDA panel considers an outcome measure as generally accepted in the relevant research fields and thus as appropriate. The document should provide adequate scientific justification in particular in those cases where the NDA panel did not accept an outcome measure as appropriate irrespective that it is accepted and widely used in the corresponding research field. An example is fasting plasma glucose with respect to blood glucose control. Line 167-176: The panel should also allow and express the compensation of weaknesses in reasonably high quality individual studies in light of other studies and the overall evidence. In particular in Art. 13.5 evaluations, studies were rather dismissed individually by their quality without leaving any study for

		consideration/support of the claimed effect. In evidence-based medicine it is common practice that also without supporting level 1 or otherwise "perfect" studies other studies could overcome these within a systematic review of the evidence and a Grade A recommendation is still possible. We have not seen this practice by EFSA. Rather, EFSA appears to expect Grade 1A evidence for every individual study which is hardly expectable from nutritional studies and even in pharmacology rarely seen. It is rather recommended that the EFSA should apply a quality ranking score for studies and define a cut-off of a minimum score for studies that should and can be respected in an evaluation/assessment. This is common practice for instance in nutritional epidemiology.
DHI Water Environment Health	2.2. Studies/outcome measures appropriate for substantiation of claims	Our clients genrally wish for access to consultations with the NDA on what constitutes appropriate biomarkers, before actually carrying out studies. Also, if the documents could give a more structured list of acceptable biomarkers, this would be helpful.
European Responsible Nutrition Alliance	2.2. Studies/outcome measures appropriate for substantiation of claims	Line 160. We note that if the food/food constituent and the substance tested are not exact matches, EFSA excludes the study as not pertinent and not even considers it as supporting data. This approach therefore does not work for complex foods and food groups that cover a range of substances (such as fibre). We believe this is an undue restriction, not supported by the terms of the Nutrition and Health Claims Regulation. The totality of the evidence should be assessed to deliver an opinion on the strength, consistency and plausibility of the health effect.
ILSI Europe aisbl	2.2. Studies/outcome measures appropriate for substantiation of claims	175-176 What does the panel understand by "reproducibility" What does the panel consider as minimum requirement to be reproducible? One repetition? Moreover, it might be that not consistency between studies is important, but rather consistency across a heterogeneous study population, and possibly across a variety of outcome measures that each reflect the effect to be claimed. In other words, one larger study with considerably heterogeneous study population, showing effects on several outcomes that each, in their own way, reflect the effect to be claimed, might demonstrate more consistency than two smaller studies in similar, homogenous study populations and showing effect on the same single outcome. 179-182 We appreciate that this is a case-by-case evaluation, but fail to see how the criteria underlying such evaluation could be case-by-case. It would be helpful to know the considerations taking into account, as well as the criteria that the Panel applies in order to conclude whether or not a certain extrapolation is biologically plausible. Ln 183-185: We would like to note that appetite ratings using questionnaires are accepted in the relevant research field.
McCORMICK France SAS	2.2. Studies/outcome measures appropriate for substantiation of	• Claims based on a category of ingredients should be permitted if they reflect common dietary practice. Specifically, a category of spices/herbs such as "pungent" spices could be established for the purpose of making satiety/weight management claims. The specific spices/herbs that fall under this classification (e.g., red

	claims	pepper, ginger, black pepper, turmeric) would be identified and tested using the appropriate methodology. Such studies would compare "test" and "control" foods seasoned with one or more of these spices over a period of two or more days and compare outcomes of interest (i.e., satiety ratings, subsequent energy intake). The availability of such claims is appealing from a public health perspective because dietary guidelines recommend a variety of foods and such a practice is likely to lead to higher compliance than with repeated use of a single food.
McCORMICK France SAS	2.2. Studies/outcome measures appropriate for substantiation of claims	Characterization of the object of the claim (e.g., spice/herb) should not be so specific as to limit the usefulness of the claim. For spices/herbs the characterization could be on their purported bioactive component(s) (e.g., capsaicin for red pepper, piperine for black pepper, curcumin for turmeric).
NATUREX Spain S.L.	2.2. Studies/outcome measures appropriate for substantiation of claims	Recommendations regarding body weight reduction measurements: • Is there a specific medical-grade scale recommended to measure body weight? • Is the measurement of body weight by DEXA acceptable to EFSA? • Is a sensitivity of 0.1 kg acceptable to EFSA? Recommendations regarding reporting of body fat and body fat reduction measured by DEXA: DEXA provides information on the percentage of body fat as a proportion of the whole body. DEXA also provides information on the lean mass and bone mineral content allowing a total body weight to be calculated. However, overall DEXA measurements for total body weight are not as accurate as a medical-grade scale. • Would EFSA agree that it is more appropriate to report the body fat mass (kg) by multiplying the % body fat result from the DEXA scan by the body weight as measured from a medical-grade scale? For the calculation of body composition using bioelectrical impedance, the manufacturer equation imbedded in the software is typically utilized. However, alternative equations exist (for instance and non-exhaustively the Gray equation (Gray et al., 1989) or the Segal equation (Segal et al., 1988)), which seem more adapted for overweight and obese population (Braulio et al., 2010). • Does EFSA have an opinion on whether it is more to appropriate to accept the manufacturer's equation or if an obesity-specific equation should be applied? • If an obesity-specific equation is more valid, does EFSA have a recommendation about which particular equation should be applied? For the calculation of body fat, skinfold measurements may be taken and a formula applied to directly or

		indirectly obtain percentage body fat (Jackson and Pollock, 1978;van der Ploeg et al., 2003). • Does EFSA have a recommendation on which equation is most relevant for calculating body fat percentage from skinfold measurements? Body fat reduction is often reported as the difference in body fat (expressed either as kg or as %) between the start and completion of the study. However, due to the large differences in body fat composition in men and women, the resulting standard deviations are extremely large, and often no significant differences are detected. • Would EFSA agree that it is more appropriate to report the % change in body fat, thereby normalizing the differences between the physiology of men and women? Various questionnaires have been used to monitor and calculate physical activity changes in short- to medium-term intervention studies (e.g. 3 months). • Which validated physical activity questionnaires are recommended to monitor and calculate physical activity score in short- to medium-term intervention studies (e.g. 3 months)? • Is the IPAQ recommended to monitor and calculate physical activity score in short- to medium-term intervention studies (e.g. 3 months)?
Rudolf Wild GmbH & Co. KG	2.2. Studies/outcome measures appropriate for substantiation of claims	Line 175/176 – What is considered as an approbiate reproducibility / consistency between studies? Is always a minimum of two studies required? A well designed "big" single study should be sufficient.
Tate & Lyle Plc	2.2. Studies/outcome measures appropriate for substantiation of claims	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD	2.2. Studies/outcome	Line 177. Studies using VLCDs can only be implemented in the obese: regulations regarding their use in the

Industry Group	measures appropriate for substantiation of claims	"normal" population prevent such studies in the "target population". As a result, it would appear that such intervention studies for VLCDs may not be considered.
Wrigley Science Institute	2.2. Studies/outcome measures appropriate for substantiation of claims	Line 164 - 166–. In relation to quantity and pattern of consumption, it is noteworthy that the changes in appetite ratings or weight management observed under experimental situations (laboratory conditions) often do not directly translate to ecological situations (free living consumers). Discrepancies may be derived from confounders associated in ecological situations while ideal controls can be applied in experimental conditions. With this in mind, the panel may wish to define conditions under which demonstrations of efficacy under experimental conditions may be allowed for example, if a defined proposed mechanism of action is being tested. Alternatively the panel may wish to provide guidance on ecological studies under which a specific characterization of tested food/constituents is unreasonable, e.g. a diet lowered in fat, or increased in proteins, or providing a lower glycaemic load to produce a weight loss.
Health Canada	3. Appetite ratings and subsequent energy intake	Based on the information provided in the March 2011 Draft Guidance, it is our understanding that we share a common approach to the following: ¿ Claims on change in appetite ratings after food consumption are comparative claims requiring the comparison between the test food and a control food. The document also states that both the test and control foods should be sufficiently characterized and comparable with respect to factors (e.g. energy) other than the food/constituent responsible for the claimed effect. ¿ Changes in certain biochemical markers can only be considered as supportive in the context of the behavioural assessment. ¿ Reporting of a reduction of subsequent food intake is not appropriate in supporting a health claim about a reduction of energy intake unless the effect is shown in longer term studies.
ILSI Europe aisbl	3. Appetite ratings and subsequent energy intake	186 Reduced appetite can also lead to sustainable weight management without immediate and significant reduction in energy intake. For example in pharma and alcohol research the craving for alcohol can be calmed down by learning and thus changing behaviour little by little (Heinälä et al 2001, J Clin Psychopharmacol. 21: 287-92).
Kellogg Europe	3. Appetite ratings and subsequent energy intake	Section 3. Appetite ratings and subsequent energy intake It is recommended to change this title in 'appetite control: ratings of hunger and satiety and energy intake regulation', This as appetite ratings per se do not have to be directly linked with energy intake as people do not always eat based on their feelings of appetite but regularly due to other constraints like habit or availability or

		social pressure etc.
NB Consulting	3. Appetite ratings and subsequent energy intake	Lines 204 – 207 and lines 222- 226 EFSA refers to "test" and "control" foods. However, many intervention studies on appetite/satiety (non- acute studies), energy intake and weight loss are constructed with a "before and after" methodology. EFSA should accept properly conducted, well designed studies of this nature as these studies can often represent more realistic conditions than a test vs. control design. In particular, for diets that are on an ad libitum basis, there is difficulty in devising an appropriate control diet, the control in practice being the prior habitual diet. If energy intake is to be measured at all to validate claims, then it must be the TOTAL dietary intake that is measured and EFSA seems to accept in the document that methods are available. Thus, within the limits of the methodology, the measurement (characterisation) of the dietary intake from the habitual diet can be just as good as the measurement of the dietary intake that includes the intervention. Therefore, the habitual diet should be able to represent the "control diet".
Tate & Lyle Plc	3. Appetite ratings and subsequent energy intake	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	3. Appetite ratings and subsequent energy intake	Appetite ratings are subjective and there is enormous variation between individuals in their response to different interventions. Appetitive ratings are a relatively "soft" endpoint whilst weight, body weight and composition are harder endpoints. Thus care must therefore be taken in using appetite ratings to substantiate health claims.
Unilever Research & Development	3. Appetite ratings and subsequent energy intake	We recommend adding these definitions: Satiety: "Processes that act to inhibit eating post-prandially and/or reduce intake at later meals, including associated motivational states"

Appetite: "The general motivational state or drive to seek and eat food"

•EFSA is ambiguous whether satiety enhancement per se is a relevant physiological benefit, though it fulfils the Section 2.1 criteria. We therefore recommend in line 189 and elsewhere clarity that satiety enhancement (reductions in eating motivations) per se is a physiological benefit. This would align with and reflect views of the expert research community, including the research strategy and expert bodies of the EC itself. Points below underpin this.

•Experts in this field can quantitatively measure and compare eating motivations between different foods and populations, based on individually 'subjective' ratings, with methods that are objective, sensitive and unbiased at group level. In other guidance, use of validated questionnaires is accepted by EFSA as evidence for physiological benefits (e.g. gastrointestinal discomfort- www.efsa.europa.eu/en/consultationsclosed/call/nda100928.pdf). To acknowledge this and the current state of science, we recommend citing accepted methodology in the research field (Blundell, J. et al. Obesity Reviews 2010;11(3):251-270).

•Eating motivations are a mechanistic target for existing and proposed pharmaceutical approaches to weight management, explaining about 30% of the probability of initiating eating (Mattes RD.. Physiology & Behavior 2010;100:22-32) and 10-15% of variation in subsequent energy intake (Drapeau V et al. Br J Nutr 2005;93:273-80). This is well above the sustained changes in energy balance that would prevent or cause obesity (Hill JO et al.Science 2003;299:853-855). Eating motivations are clearly not the only determinant of energy intake and body weight, but reflect physiological drivers of behaviour that are amenable to food-based interventions. We recommend that a sustained high level of eating motivation is recognised as a risk factor for a positive energy balance, which is a direct and required determinant of obesity.

•We recommend recognition that eating motivations have a biologically plausible relationship with positive energy balance and thus also health. Research on eating motivations and satiety enhancement is carried out by a global academic community with substantial public funding, underpinned by a widely accepted view that this can confer beneficial physiological effects. The EC itself provides significant support for research to understand and enhance the satiating effects of foods (e.g. ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/kbbe/b-wp-201002_en.pdf). EC research programme documents also repeatedly link satiety to health benefits, implicitly and explicitly (e.g. www2.spi.pt/fahre/docs/fahre_draft_synthesis_of_research_needs_270111_merged.pdf). Furthermore, most national scientific research programmes also support research on understanding and technical routes to influence eating motivations, making clear links between this and public health.

•Given that 1) effects on (acute) post-ingestive eating motivations are quantitatively measurable and

		comparable between products in an objective and unbiased way, 2) eating motivations have a clearly plausible relationship in the development of a disease (and may indeed be seen as risk factor), and 3) reduced eating motivations (eg hunger, craving, etc) can benefit consumers independently (as an adjunct to other steps to manage energy intake or body weight): We recommend explicit clarity that limited claims referring to and validated only by evidence of eating motivations can be scientifically supported where other substantiation criteriria are met.
Arla Foods a.m.b.a.	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	We understand it as for a claim linking increased satiety and energy intake influence on satiety on energy intake should be sustainable over time and a duration period (study period in human intervention studies) of 1 month is mentioned. For a claim linking increased satiety to decreased body weight it is stated that body weight changes should be measured. However no duration period for a human study is mentioned. We like this to be added.
Ashwell Associates Europe Ltd	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	204 Changes in appetite ratings can often be made on an absolute basis- this should be acknowledged.
Ashwell Associates Europe Ltd	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	200 Measurements of appetite are only done in short term situations and so the reference to chronic consumption is misleading. Better to say that several tests should be performed over a period of a few weeks to show the effect has been maintained. However, it should also be recognised that reduced intake might be due to reduced appetite in the early stages but due to other factors after that.
Ashwell Associates Europe Ltd	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	198 Additional beneficial effects of reduced appetite should be mentioned such as avoidance of hunger at unwanted periods of the day (e.g. mid morning) and reduced feelings of hunger during food restriction. Consumption of a reduced energy food or following a weight management programme itself provides for a reduced energy intake. In this case, reduced eating motivations would reflect a reduced hunger feeling independent of any added effect on energy intakes or rates of weight loss. So effects on energy intake or weight loss are not necessary to substantiate a claimed effect on eating motivations, which may still be beneficial for consumers
BENEO Institute	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 204 – 207: The control food for these kind of tests can be chosen based on several criteria, including comparable volume, appearance, taste and energy content. From a practical point of view it is often not feasible to account for all these criteria in parallel when designing a control and test food. Energy is not always the first factor to balance. For instance, it may be scientifically more relevant to aim for similar volume and texture than for the same energy content (and adjust for differences in energy in later data analysis). The example “energy” should thus be complemented with other criteria such as “volume, appearance or taste” to clarify that an

		appropriate control food is not only one with a matched energy content, but should be considered on a case-by-case basis.
BENEO Institute	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 190: Use of "validated" visual analogue scales are suggested for the assessment of appetite ratings. According to Stubbs et al (2000), the reliability and validity of a rating scale can be difficult to demonstrate unequivocally since there are often few if any objective measures of the trait with which to compare the rating system. Likewise, Livingstone et al (2000) sees an objective assessment of the validity of VAS problematic. However, there are basic scales that according to Blundell et al (2010) enjoy a history of widespread and consistent use and acceptance over several decades in many different countries and laboratories, with different test stimuli and subject groups. Thus, these basic scales described in Blundell et al (2010) are in essential agreement to the principles illustrated in chapter 2 line 184. There, appropriate outcome measures are described as those which are generally accepted in the fields. Consequently, instead using "validated" as descriptor it seems more appropriate to term it "generally accepted" visual analogue scales (VAS) in the guidance document. "Generally accepted" in terms of "according to the methodological standards in scientific research on eating motivations". Line 193: The panel considered increased satiety and/or reduced sense of hunger/appetite beneficial only if linked to a decrease in subsequent energy intake or body weight. This view disagrees with the scientific consensus in the corresponding research fields (e.g. Blundell et al. 2010). Increased satiety and/or reduced sense of hunger/appetite per se are widely accepted as a valid and legitimate stand-alone claim (e.g. Blundell et al. 2010). One example to illustrate this is the reduced sense of hunger during food/diet energy restriction, clearly a beneficial physiological effect as such. The guidance document should thus acknowledge an increase in satiety / reduced appetite as 'beneficial' effect per se. Line 196: "Appropriate methods" are demanded for the measurement of energy intake. It will be useful for applicants to see more information and details what is considered "appropriate" and which particular method is not. Line 196-203: The guidance document specifies that effects should be "sustained over time, taking into account possible compensatory effects". The underlying rationale is, according to line 196-197, to ensure absence of compensatory effects when the "test" food is consumed on more than a single occasion, i.e. for a certain period of time. Hence, chronic consumption is key but not necessarily the repeated measurement of appetite/energy intake. It should still be

		sufficient to prove the absence of compensatory effect with the testing carried out only once as long as this will be at the end of a chronic consumption period. Thus, line 200-203 of the guidance document should rather read "In general terms, changes in appetite ratings after consumption of a test food should be observed after chronic consumption of the food/constituent (e.g. after one month) and therefore observing changes in appetite ratings only after a single consumption of the test food would not be considered sufficient for substantiation." Line 201: The time regarded as "chronic consumption" is exemplified as "after one month". Could the EFSA be more clear in that it is stated that this is not meant as the "minimum" or "maximum" intervention length required. The guidance should acknowledge that periods of chronic consumption other than 1 months e.g. 2 weeks or 3 months may be appropriate durations, too.
Biofortis	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	What does long term/sustained effect suggest ? Does it mean that the product has to be taken continuously (eg phytosterols which have to be consumed for the whole life), or temporarily with then a maintained effect (such as meal replacements) ?
Biofortis	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Is a claim about satiety itself achievable/pertinent ? To develop a weight loss product, what is the more pertinent, a claim about satiety leading to a body weight reduction, or a claim about body weight reduction showing an increased satiety as a mechanism ? (cf EFSA-Q-2008-396)
Cargill	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 196: "if the health benefit of changing appetite ratings is to decrease subsequent energy intake, subsequent energy intake should be measured using appropriate methods". 1. Appetite regulation and subsequent food intake are determined by multiple factors and often social influences override physiological signals. In measurement of the effects of foods/ ingredients for appetite and food intake control, inevitably compromises need to be made between precision (tightly controlled laboratory studies) and naturalness (free living conditions). Although, the panel does acknowledges the beneficial effects of changing appetite with concomitant decreases in energy intake (without link to body weight reduction) to what extent will data, generated in laboratory studies and where subjects are devoid of any external influences, be allowed to be extrapolated to the free living situation and still be considered physiologically relevant? 2. Also according to the Panel enhancing fullness or satiety and/or control hunger should be accompanied with reductions in energy intake. Nevertheless, controlling hunger can confer a benefit as such for example for those that are on a weight management diet providing ways for appetite control and to cope with daily hunger. Such beneficial effects could be seen independent of a reduction in energy intake. For example, perceived hunger has been shown to predict failure to lose weight in clinical trials (Womble et al. 2001); and perceived

		deprivation (not eating what or as much as one would like) is linked to susceptibility to weight gain (Markowitz et al. 2008).
Danone Research	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	193-203 We would like to have a better understanding of the rationale why satiety is not considered as a beneficial physiological effect. Is it mandatory to combine Visual Analogue Scales (VAS) with food intake to be able to claim on appetite? Is it mandatory to combine VAS with body weight assessment to be able to claim on appetite?200-203 There is limited literature on satiety studies beyond 2 weeks. Indeed, most of the evidence is built after 1 or 2 weeks of intervention. Therefore, what is the rationale for the choice of an intervention period of 1 month? 205-207 In the case that all characteristics (e.g. macronutrients or volume) of a test product and control product could not be the same, would it be sufficient to have both products equivalent in terms of energy? General comments For satiety and/or reduced sense of hunger/appetite claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DSM Nutritional Products	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	LINES 193-194 "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.": A (sustained) increase of satiety or decrease in appetite should be acknowledged as a beneficial effect per se which should be permitted to be claimed if substantiated, without having to prove energy intake reduction or weight reduction. A parallel can be drawn to the claims on cardiovascular health: there, the maintenance of normal LDL-cholesterol concentrations per se is considered a beneficial effect. No other secondary endpoints are being asked for such as for instance the reduction of intima thickness or even further cardiovascular events. Dietary measures to achieve normal LDL-cholesterol concentrations are acknowledged as beneficial. Likewise, appetite reduction is in its self a physiological benefit without asking for further substantiation. Appetite control and / or reduction has a clear plausible relation with energy intake, energy balance and weight control. Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while EFSA requires in addition a physiological, functional outcome, i.e. reduction of energy intake or

		weight. This is, in our view, neither scientifically correct nor in line with the Regulation. This can be directly derived from the text of the Regulation where in Art 13.1 it reads "Health claims describing or referring to.. c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet, which are indicated in the list provided for in paragraph 3 may be made… The reduction of the sense of hunger or an increase in the sense of satiety are listed, independently from their consequences on other measures like energy intake, as health claims. Furthermore Art.13.1 b) also refers explicitly to psychological and behavioural function claims.This is in agreement with Blundell et al (2010) who states that for product claims, the demonstration of an effect on food intake should not be required in addition. For example where energy intake is already being effectively controlled through other means (low energy foods, reduced energy diet plans etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake. References: Blundell J, de Graaf C, Hulshof T, et al. Appetite control: methodological aspects of the evaluation of foods. Obesity Reviews. Obes Rev. 2010 Mar;11(3):251-70.
DSM Nutritional Products	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	LINES 201-203 "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.": However, reduced satiety for shorter periods of time than a month should also be considered as useful for consumers to simply minimize the dysphoria of hunger feelings at specific occasions. In certain cases even a couple of days may be of physiological benefit, for instance to prevent the physiological discomfort in having a low energy intake. In this case there is no direct link to energy intake. LINES 204-207 "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 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.": Clarification is sought on the meaning of "sufficiently characterized". In nutritional research, a particular ingredient or macronutrient is often exchanged for another one. Would "balanced on energy content" suffice in this context?
DSM Nutritional	3.1. Claims on	LINS 193-194 "The beneficial physiological effects of changing appetite ratings in response to food

Products	increased satiety and/or reduced sense of hunger/appetite	consumption may be a decrease in subsequent energy intake and/or a decrease in body weight.": A (sustained) increase of satiety or decrease in appetite should be acknowledged as a beneficial effect per se which should be permitted to be claimed if substantiated, without having to prove energy intake reduction or weight reduction. A parallel can be drawn to the claims on cardiovascular health: there, the maintenance of normal LDL-cholesterol concentrations per se is considered a beneficial effect. No other secondary endpoints are being asked for such as for instance the reduction of intima thickness or even further cardiovascular events. Dietary measures to achieve normal LDL-cholesterol concentrations are acknowledged as beneficial. Likewise, appetite reduction is in its self a physiological benefit without asking for further substantiation. Appetite control and / or reduction has a clear plausible relation with energy intake, energy balance and weight control. Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while EFSA requires in addition a physiological, functional outcome, i.e. reduction of energy intake or weight. This is, in our view, neither scientifically correct nor in line with the Regulation. This can be directly derived from the text of the Regulation where in Art 13.1 it reads "Health claims describing or referring to.. c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet, which are indicated in the list provided for in paragraph 3 may be made… The reduction of the sense of hunger or an increase in the sense of satiety are listed, independently from their consequences on other measures like energy intake, as health claims. Furthermore Art.13.1 b) also refers explicitly to psychological and behavioural function claims.This is in agreement with Blundell et al (2010) who states that for product claims, the demonstration of an effect on food intake should not be required in addition. For example where energy intake is already being effectively controlled through other means (low energy foods, reduced energy diet plans etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake.
ELC	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Lines 194-196 Multiple factors, physiological and social, play a role in appetite regulation and subsequent food intake. To what extent should extrapolations of energy intake in controlled laboratory studies, where subjects are devoid of any external influences, be considered relevant to the free living situation? We would appreciate further details on this point in the final guidance.
ELC	3.1. Claims on	Lines 193-194 A (sustained) increase of satiety or decrease of appetite should be acknowledged as a beneficial

	increased satiety and/or reduced sense of hunger/appetite	effect per se, without having to prove energy intake reduction or weight reduction. Controlling hunger can confer a benefit as such, for example, for those that are on a weight management diet. Such beneficial effects could be viewed independently of a reduction in energy intake. For example, perceived hunger has been shown to predict failure to lose weight in clinical trials [Womble, L. G., Williamson, D. A., Martin, C. K., Zucker, N. L., Thaw, J. M., Netemeyer, R., et al. (2001). Psychosocial variables associated with binge eating in obese males and females. International Journal of Eating Disorders, 30(2), 217–221]; and perceived deprivation (not eating what or as much as one would like) is linked to susceptibility to weight gain [Jessica Tuttman Markowitz, Meghan L. Butryn, Michael R. Lowe. Perceived deprivation, restrained eating and susceptibility to weight gain. Appetite 51 (2008) 720–722]. Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while EFSA requires in addition a physiological, functional outcome, i.e. reduction of energy intake or weight. This is, in our view, neither scientifically correct nor in line with the Regulation. This can be directly derived from the text of the Regulation where in Art 13.1 it reads "Health claims describing or referring to c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet, which are indicated in the list provided for in paragraph 3 may be made." A "reduction of the sense of hunger" or an "increase in the sense of satiety" are listed, independently from their consequences on other measures like energy intake, as health claims. Furthermore Art.13.1 b) also refers explicitly to psychological and behavioural function claims. This is in agreement with Blundell et al (2010) [Blundell J, de Graaf C, Hulshof T, et al. Appetite control: methodological aspects of the evaluation of foods. Obes Rev. 2010 Mar; 11(3):251-70] stating that for product claims, the demonstration of an effect on food intake should not be required in addition. For example where energy intake is already being effectively controlled through other means (low energy foods, reduced energy diet plans etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake.
European Responsible Nutrition Alliance	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 193. A (sustained) increase of satiety or decrease in appetite should be acknowledged as a beneficial effect per se which should be permitted to be claimed if substantiated, without having to prove energy intake reduction or weight reduction. Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while the EFSA approach requires in addition a physiological, functional outcome, i.e. reduction of energy intake or weight. This is an undue restriction, neither scientifically correct nor in line with the Claims Regulation. Both reduction in the sense of hunger and increase in the sense of satiety are claims explicitly accepted as health claims, eligible under Article 13 of the Regulation, independently from further

		consequences such as energy intake. If energy intake is already being effectively controlled through other means (low energy foods, reduced energy diet plans etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake. In these cases increased satiety or reduced sense of hunger could be considered as psychological or behavioural function claims, both also accepted under the terms of Article 13. Line 196. It would be helpful if EFSA could specify what methods it would judge acceptable for such measurements. Line 201. Reduced satiety for shorter periods of time than a month, several days, should also be considered as useful for consumers to simply minimize the dysphoria of hunger feelings at specific occasions. Line 206. It would be good if EFSA could further specify how it expects characterization to be sufficient in this case. Line 207. It is not clear why control and test food should be comparable, e.g. in terns of energy. This may not even be necessarily appropriate, for example, when comparing diets with zero or lower calorie component (e.g. fibre) replacing a higher calorie component (e.g. other carbohydrate). It cannot be requested to add energy to the test diet given that the whole intention is to reduce its energy content. With such interventions, changes in appetite rating should be accepted, irrespective of whether they led to weight/body fat reduction.
FederSalus	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	The measure of biochemical markers (cholecystokinin - CCK) is not practically applicable in a general population. Moreover CCK explains only 20% of satiety sensation. In order to substantiate the change in appetite ratings, we think it is important to measure overtime (beyond 1 month) the following: 1. VAS (Visual analogue scale about subjects appetite) 2. Semi quantitative alimentary diaries 3. Body weight. The investigation should be a randomized longitudinal study in which the "control" food is habitual food / meals and the "test" food should contain the food or the food component for which the health claims is required. Methodologically, an important aspect is that both "control" people and "experimental" people may maintain their respective habitual alimentation with exception of only small modification, if the case.
HarlandHall Associates	3.1. Claims on increased satiety	Line 202 What is the scientific rationale for the chronic exposure to a food for a period of 1 month?

	and/or reduced sense of hunger/appetite	
Health Canada	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Clarification needed • The EFSA Panel on Dietetic Products, Nutrition and Allergies (Panel) reports that 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. However, it is not clear whether the Panel considers increased satiety and/or reduced sense of hunger/appetite to have beneficial physiological effects by themselves in justifying claims related to appetite ratings (e.g. 'satiety' claims), when these effects are substantiated by subjective rating using commonly accepted scales such as the visual analogue scales (VAS). Clarification would be helpful because the document acknowledges that claims on changes in appetite ratings after food consumption are generally comparative claims (line 204) and could be considered substantiated after chronic consumption of the food (line 201), while also noting that changes in appetite ratings could be used as evidence for a mechanism by which a food/constituent could exert the claimed effect on reduced energy intake (line 220). • There is no indication whether a claim on satiety, reduced energy intake, or weight management could be made in relation to an ingredient independently of the food to which it is added, or only to the foods which correspond to tested food products as sold and consumed. For example, if an ingredient X is added to a number of foods and the foods were shown to significantly reduce energy intake, would another food to which ingredient X is added be eligible to carry the claim without testing? Methodological issues The Food Directorate of Health Canada is currently preparing a guidance document on the scientific requirements for the substantiation of claims on satiety. We would be pleased to share this document with the Panel when it is ready for public comments. We are interested in knowing whether the Panel has addressed the following methodological issues when assessing studies that are used to support satiety and related claims. 1. The Panel considers changes in appetite ratings only after chronic consumption of the test food (i.e. tests performed on a single occasion of the food would not be considered sufficient for substantiation). This is in contrast to how satiety studies are generally conducted at present. While such studies are not standardized, they are primarily based on appetite ratings from single meal experiments. 2. If the Panel considers only longer term studies (e.g. after one month) to be acceptable, it is not clear how the Panel would judge the appropriateness of long term appetite ratings studies to support claims on satiety and/or reduction of energy intake.It would be helpful if guidance on longer studies is provided, e.g. Is the test food

		required to be consumed on a daily basis? Is the assessment of appetite ratings only required at the beginning and at the end of the study or throughout the study period? Should environmental factors affecting appetite sensations and eating behaviours of study participants in free living conditions be controlled? What is the difference in appetite ratings between the control and the test foods that would be considered meaningful? 3. What methods would be considered appropriate by the Panel for the measurement of energy intake after chronic consumption of the food to support claims on reduced energy intake?
HFMA	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 194. The regulation specifically refers in Article 13.1 (c) to claims for reduction in the sense or hunger or an increase in the sense of satiety. Hence claims for these effects should be acceptable without the need for evidence of consequential effects.
ILSI Europe aisbl	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	200 People on a diet often feel hungry and therefore can suppression of hunger in the context of a low caloric diet be considered a beneficial physiological effect? The idea would be to suppress the hunger so that people would be able to stick to the diet and maintain or even lose weight. Would a claim like: helps you to feel less hungry while being on a diet, be acceptable to EFSA? 200-203 Clarification is needed for what is required to address the 'chronic consumption' criterion, and acknowledgement that varying durations (e.g. other than one month) may be justified. Based on our interpretation of this, we would like to recommend a more explicit text such as, 'Where claims are based on an acute response period (e.g. hours or days), these effects must also be shown to be apparent (i.e. still able to be demonstrated) after chronic consumption period of at least 15-30 days, to be assessed on a case-by-case basis.' We would like to recommend additional guidance on how often the food should be consumed during the chronic consumption period, considering that people do not eat every day the exactly the same food. 204 We agree that eating motivation claims are generally comparative, but non-comparative ('absolute') claims are also possible. We therefore recommend explicit acknowledgement of the potential to also make claims based on e.g. duration of effect or effects relative to energy content, or other measures, where these are based on appropriate methods, to be considered on a case-by-case basis. Based on the 'general guidance for article 13.1, 13.5 and 14 health claims evaluation', only 2 types of comparative claims have been defined as 'eligible claims' such as replacement claims and when the

		absence/reduced content of a food is responsible of the effect. In this context, in which category belong claims on changes in appetite ratings that are generally comparative claims? 206 What is the sufficient characterisation required? What means comparable and what would be the most appropriate design? In the opinion regarding protein and satiety, it was considered that it was not possible to conclude to the effect of the proteins by themselves as they were replacing other macronutrients that could be also involved in the obtained effect. 207 As choices have to be made to compare control and test foods appropriately, is energy the first factor to balance when not possible to balance both the energy, volume, macronutrients ?
ILSI Europe aisbl	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	193-200 A (sustained) increase of satiety or decrease in appetite should be acknowledged as a beneficial effect per se which should be permitted to be claimed if substantiated, without having to prove energy intake reduction or weight reduction. Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while EFSA requires in addition a physiological, functional outcome, i.e. reduction of energy intake or weight. This is, in our view, neither scientifically correct nor in line with the Regulation. This can be directly derived from the text of the Regulation where in Art 13.1 it reads "Health claims describing or referring to.. c) without prejudice to Directive 96/8/EC, slimming or weight control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet, which are indicated in the list provided for in paragraph 3 may be made… The reduction of the sense of hunger or an increase in the sense of satiety are listed, independently from their consequences on other measures like energy intake, as health claims. Furthermore Art.13.1 b) also refers explicitly to psychological and behavioural function claims. This is in agreement with Blundell et al (2010) who states that for product claims, the demonstration of an effect on food intake should not be required in addition. For example where energy intake is already being effectively controlled through other means (low energy foods, reduced energy diet plans etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake.

		As stated in LN183-185: the panel defines an appropriate outcome measure for the claimed effect as what is generally accepted in the relevant research fields. Appetite ratings using questionnaires are accepted in the relevant research fields and should therefore be relevant measures for subjective feelings if the claim is considering only subjective feelings and not subsequent energy intake. 194 If the validated beneficial physiological effect of changing appetite ratings in response to food is a decrease in subsequent energy intake and/or a decrease in body weight, will it be possible to claim on appetite ratings that thus would be the mechanisms of action of the health effect? The beneficial effects of changing appetite ratings in food consumption, take in account only the "quantity" point of view, without taking in account "the quality"! Meaning that one subject can modify its diet which could become more balanced, with the same caloric value, but with an intake more beneficial and healthy for the organism... then can we ignore a such healthy modification? Furthermore, what happens if the population eat a same caloric diet but with high intake of fibers? It seems that fibers can compromise energy intake. Then it would be more efficient to talk about quantity of caloric values absorbed by the intestine, doesn"t it? 196 Please clarify what “appropriate methods” are; would those described by Blundell et al. (Obesity Reviews 2010; 11(3): 251-270) be accepted? Could you clarify “the effect should be sustained over time” (does this mean, 2 weeks, one month, etc.). 199 Could testimonials tests and consumers enquiries be considered in evaluating the effect of appetite changes?
ILSI Europe aisbl	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	188-192 We recommend explicit recognition that eating motivations have a biologically plausible relationship with positive energy balance. In support of this, we note that research on eating motivations and satiety enhancement is carried out by a global academic community with very substantial public funding, underpinned by a widely accepted view amongst experts that this can confer beneficial physiological effects. Indeed the European Commission itself (via the Directorate General for Research & Innovation) has provided significant support for research intended to understand and enhance the satiating effects of foods (e.g. ‘...to identify dietary components/food structure that can help to control food intake and to develop food prototype that control satiety’ - ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/kbbe/b-wp-201002_en.pdf). EC research programme documents repeatedly link satiety to health benefits implicitly and explicitly (e.g.

		'…activities relevant to health include satiety control through food structures…' - www2.spi.pt/fahre/docs/fahre_draft_synthesis_of_research_needs_270111_merged.pdf). Furthermore, most national scientific research programmes also support research activities focused on understanding and technical routes to influence eating motivations, making clear links between this and public health. Given that 1) effects on (acute) post-ingestive eating motivations are quantitatively measurable and comparable between products in an objective and unbiased way, and 2) eating motivations have a clearly plausible relationship in the development of a disease (and may indeed be seen as risk factor): We recommend explicit clarity that limited claims referring to and validated only by evidence of eating motivations can be scientifically supported where other substantiation criteria are met. 191 Which biomarkers can be considered in the context of behavioral assessment? Will those identified by Delzenne et al. (Obesity Reviews 2010; 11(3): 234-250) be considered? 193-200 The text limits specific mention of possible beneficial effects of changing appetite ratings to changes in energy intake or body weight, which must be separately substantiated. We recommend that additional beneficial effects of reduced eating motivations – which may be independent of direct effects on energy intake or body weight - are also specifically recognised and cited here, including: reduced feelings of hunger during food restriction, reduced food 'cravings', enhanced acceptance or tolerance to dietary behaviour change, supporting beneficial changes in food choices, etc. Where consumption of a reduced energy food or weight management programme itself provides for a reduced energy intake, reduced eating motivations would reflect a reduced hunger dysphoria independent of any added effect on energy intakes or rates of weight loss. In this context, effects on energy intake or weight loss are not necessary to substantiate a claimed effect on eating motivations, which may still be beneficial for consumers. This would also be consistent with other EFSA guidance, e.g. that reducing gastrointestinal discomfort (based on self-report questionnaires) is considered a beneficial physiological effect (www.efsa.europa.eu/en/consultationsclosed/call/nda100928.pdf).
ILSI Europe aisbl	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	188-192 Motivational ratings of appetite should be explicitly recognised as a valid and accepted expression of changes in the motivational state of consumers, when appropriate methodology is used. Accordingly, we recommend consistent use of the term 'eating motivations' (ie, what has been measured) rather than 'appetite ratings' (ie, the method of measurement). This would be consistent with the rest of the text (e.g. 'fat oxidation' rather than 'reduction in the respiratory quotient'). EFSA opinions to date and this guidance express ambiguity regarding whether satiety enhancement per se is a relevant physiological benefit, although it fulfils the criteria described in Section 2.1. We therefore recommend that EFSA express a clear and consistent view that satiety enhancement (reductions in eating motivations) per se is a relevant physiological benefit (in line 189 and elsewhere). This would eliminate the continuing ambiguity, and align with and appropriately reflect the views of the expert research community - including the

		research strategy and expert bodies of the EC itself (as cited below). Subsequent points here underpin the validity of this position: • Experts in the relevant research field can quantitatively measure and compare eating motivations between different foods and populations, based on individually 'subjective' ratings, with methods that are objective, sensitive and unbiased at a group level. These ratings are the current standard for validation of corresponding physiological measures reflecting underlying mechanisms (e.g. neural and hormonal responses). In other guidance, use of validated questionnaires is explicitly accepted by EFSA as evidence for physiological benefits (reducing gastrointestinal discomfort) - www.efsa.europa.eu/en/consultationsclosed/call/nda100928.pdf). To more clearly convey this point and the current state of science and methodological standards, we recommend citing the availability of established methodology for eating motivations ('appetite ratings'), which is widely accepted in the relevant research field (Blundell et al. Obesity Reviews 2010; 11(3):251-270). • Reducing eating motivations is the mechanistic basis for many existing and proposed pharmaceutical approaches to weight loss and control. Furthermore the research literature finds that appetite motivations explain about 30% of the probability of initiating a meal or snack (Mattes. Physiology & Behavior 2010; 100: 22-32) and 10-15% of variation in subsequent energy intake (Drapeau et al. Br J Nutr 2005; 93: 273-80). The latter is well above the sustained changes in energy balance that would prevent or cause obesity (Hill et al. Science 2003; 299: 853-855). Eating motivations are clearly not the only determinant of energy intake and body weight, but reflect physiological drivers of behaviour that are amenable to food-based interventions. To clarify the position, we recommend that a sustained high level of eating motivation be seen as a risk factor for developing a positive energy balance, which is a direct and required determinant of obesity.
Kellogg Europe	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	3.1 Claims on increased satiety and/or reduced sense of hunger/appetite Line 190: The term validated visual analogue scales suggest that the panel believes that this might not be the case. The panel does not write 'validated food intake methods' either. In the publication of Blundell et al. (Appetite control: methodological aspects of the evaluation of foods: Obesity reviews: volume 11: issue 3: March 2010, page 251-270) reliability and validity of VAS are discussed and it was concluded that VAS are measuring what they are purported to capture. Therefore we suggest that the panel refers to the publication of Blundell et al. 2010 for how appetite ratings should be measured and analysed as best practice. Lines 193-200 In this opinion EFSA limits possible beneficial effects of changing appetite ratings specifically to changes in

		energy intake or body weight and which must be separately substantiated. It is recommended that additional beneficial effects of reduced eating motivations are also specifically cited, including but not limited to: • reduced feelings of hunger during food restriction, • enhanced acceptance or tolerance to dietary behaviour change, • Avoidance of hunger at unwanted periods of the day (e.g. mid morning) • supporting beneficial changes in food choices, • hunger in relation to distraction and cognition • hunger in relation to mood • etc. Where consumption of a reduced energy food or weight management programme itself provides for a reduced energy intake, reduced eating motivations would reflect a reduced hunger feeling independent of any added effect on energy intakes or rates of weight loss. Within this context, effects on energy intake or weight loss are not necessary to substantiate a claimed effect on eating motivations, which may still be beneficial for consumers. Lines 200-203 Clarification is needed for what is required to address the "chronic consumption" criterion. Based on our interpretation of this, we recommend text such as, "Where claims are based on an acute response period (eg hours or days), these acute effects must also be shown to be maintained (ie still able to be demonstrated) after chronic consumption period of at least 30 days." Line 204 We agree that eating motivation claims are generally comparative, but non- comparative ("absolute") claims are also possible. We therefore recommend explicit acknowledgement of the potential to also make claims based on e.g. duration of effect or effects relative to energy content, or other measures, where these are based on appropriate methods, to be considered on a case-by-case basis.
Kraft Foods R&D	3.1. Claims on increased satiety and/or reduced sense	- (l193) Will it be possible to claim on appetite ratings changes without a decrease of energy intake? If yes, to which conditions?

of hunger/appetite	- (l193) In previous published 13.1 and 13.5 opinions on satiety claims, the reduction of appetite ratings have been qualified as 'might be beneficial for health'. What is the meaning of the expression 'might be'? What are the consequences to obtain a validation of the request? Why this is not mentioned in this draft guidance document? - (l194) If the validated beneficial physiological effect of changing appetite ratings in response to food is a decrease in subsequent energy intake and/or a decrease in body weight, will it be possible to claim on appetite ratings that thus would be the mechanisms of action of the health effect? - (l196) Regarding energy intake measurement, which methods are considered appropriate? - (l197) Regarding the sustainability over time of the effect of energy reduction, what is the appropriate period of time? Would the next meal be sufficient or at least 24h should be considered to evaluate compensatory effects? - (l199) Could the prevention of overconsumption demonstrated by the consumption of a energy-reduced test product which does not affect energy intake (no compensatory effect) in comparison to a control product be considered as a beneficial effect? - (l199) In addition to physiological effects, will psychological effects such as impact on mood or well-being be considered as possible beneficial effects? Could it be addressed in the future guidance document on psychological and neurological function? Are effects on subjective well-being in the scope of this regulation? - (l199) Could testimonials tests and consumers enquiries be considered in evaluating the effect of appetite changes? - (l201) Why the duration of one month is suggested as relevant to evaluate chronic consumption? Would demonstration based on duration inferior to one month accepted? (there are very few examples of published studies measuring appetite during more than 2 weeks) - (l204) Based on the 'general guidance for article 13.1, 13.5 and 14 health claims evaluation', only 2 types of comparative claims have been defined as 'eligible claims' such as replacement claims and when the absence/reduced content of a food is responsible of the effect. In this context, in which category belong claims on changes in appetite ratings that are generally comparative claims? - (l206) What is the sufficient characterisation required? What means comparable and what would be the most appropriate design? In the opinion regarding protein and satiety, critics were expressed by the panel because it was not possible to conclude to the effect of the proteins by themselves as they were replacing other macronutrients that could be also involved in the obtained effect.

		- (l207) As choices have to be made to compare control and test foods appropriately, is energy the first factor to balance when not possible to balance both the energy, volume, macronutrients ?
McCORMICK France SAS	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	3.1 Characterization of the food vehicles used for satiety claims (both the "test" food and the "control" food) should not be so specific that the claim can be used for only that food. For example, a claim authorized for red pepper and satiety based on studies that used pasta sauce with and without this spice as the "test" and "control" foods, respectively should not be restricted exclusively to red pepper in pasta sauce. It is appropriate that the same food vehicle be used in the study with and without the claimed ingredient, but the food vehicle itself should not become part of the claim. • The requirement for a minimum of one week duration for satiety studies that demonstrate reduced subsequent energy intake may be inappropriate for some foods/ingredients because it will not reflect intended usage patterns and could lead to confounded outcomes. Specifically, subjects required to use the same food at each intervention for one week may find the food increasingly unappealing due to monotony (or aversion in extreme cases) and this factor could mask any effect of the test ingredient. It is recommended that a minimum of two days be considered sufficient for the substantiation of such claims on a case-by-case basis. • The previous comment also applies to studies that report changes in appetite ratings. It is recommended that a minimum duration of two days be applied to studies that measure this endpoint on a case-by-case basis.
Mead Johnson Nutrition	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 191 indicates that for substantiation of claims on appetite and reduced sense of hunger/appetite, changes in certain biochemical markers can only be considered in the context of the behavioral assessment. What behavioral assessment methods would be considered relevant for substantiating these claims? And what would be relevant behavioral assessment methods for infants and children?
MRC Human Nutrition Research	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Section 3.1. Claims on increased satiety and/or reduced sense of hunger/appetite (lines 188-207): The use of the various measures to substantiate claims based on biochemical parameters, behavioural outcomes and health outcomes is unclear and more precision is needed on the type of evidence required for each type of claim. We suggest re-structuring the information provided in section 3.1 in the following way to enhance clarity: Lines 189 to 192. Add the following clarification after first sentence (after "have been proposed"): "These claims may involve a change in appetite ratings alone, or changes in other parameters (e.g. energy intakes; body weight) that result from appetite changes". Remove remaining of line 189 up to line 192, which will be explained later. Lines 193 -203. Replace current text with: "To be considered substantiated, claims on changes in appetite ratings after consumption of a test food, including increased satiety and/or reduced sense of hunger/appetite, should be based on human studies that meet the following two criteria: - Use validated behavioural assessment methods (e.g. visual analogue scales) - Demonstrate a sustained effect on appetite ratings over time after chronic consumption (e.g. after one month) taking into account possible compensatory effects. Appetite tests performed on a single occasion would not be considered sufficient for substantiation.

		Claims on appetite changes based on in vitro studies or in vivo studies demonstrating changes in biochemical satiety markers (e.g. cholecystokinin), can only be considered in the context of behavioural assessment. That is, such laboratory outcomes can be used as supportive evidence alongside behavioural assessment outcomes but not as sufficient conclusive evidence that a change in appetite occurs. Claims on changes in energy intakes resulting from a change in appetite ratings, such as a decrease in subsequent energy intake, should be substantiated with human studies that meet the following three criteria: - Measure subsequent energy intake using appropriate methods - Use validated behavioural assessment methods (e.g. visual analogue scales) to measure appetite - Demonstrate a sustained effect over time on energy intakes, taking into account possible compensatory effects. Claims on changes in body weight resulting from appetite changes should be substantiated by human studies that also measure appetite changes and body weight changes with appropriate methods and that demonstrate a sustained effect over time on body weight, with a minimum duration of 3 months. Claims for any other beneficial physiological effects that may result from changing appetite ratings in response to food consumption should be specifically indicated, substantiated, and considered on a case-by-case basis." Lines 204-207. Replace current text with: "If the claim is a comparative claim (i.e. comparison of the "test" food with the "control" food), both the test and the control 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. the two foods should be of comparable energy load)." Section 3.2. Lines 220-221: We suggest that this sentence is re-worded for clarity, consistently with the structure suggested for section 3.1. For instance, we propose: "Claims on reduced energy intakes based exclusively on changes in appetite ratings would not be considered sufficient for substantiation. Changes in appetite ratings in this context however, can be used as evidence for a mechanism by which the food/constituent could exert the claimed effect".
Nutraveris	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	While 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, what is the right way to substantiate the efficacy of an ingredient on satiety, see below ? 1) primary outcome = satiety secondary outcome = energy uptake and/or weight management OR 2) primary outcome = weight management secondary outcome = appetite and/or energy uptake OR

		3) primary outcome = energy uptake secondary outcome = appetite and/or weight management Moreover, are questionnaires (Three factors eating questionnaire (TFEQ), Dutch eating behavior questionnaire (DEBQ)) and visual analogue scale (on appetite ratings, prospective consumption, desire to eat, etc...) sufficient to substantiate satiety? Finally, the target population is healthy people, are obese but non treated considered as healthy people as well as overweight poeple?
Rudolf Wild GmbH & Co. KG	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 196 – How long need the effect be sustained over time? Line 201/202 – Is a chronic consumption really approbiate? A single occasion should also provide sufficient information. It would be better to reproduce the effect of a single occasion than to go into chronic consumption, as a single occasion mimics "real life". What is meant with "chronic consumption of the food"? Does it mean the consumption of the test food one time per day over one month ?
SYNPA	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Lines 193-194: "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." The SYNPA supports the ELC's comments. We would like to underline that a (sustained) increase of satiety or decrease of appetite should be acknowledged as a beneficial effect per se, without having to prove energy intake reduction or weight reduction. Controlling hunger can confer a benefit as such, for example, for those that are on a weight management diet. Such beneficial effects could be viewed independently of a reduction in energy intake (Womble, L. G. et al, 2001; Jessica Tuttman Markowitz et al, 2008) Claims on satiety/control of appetite are to be seen rather in the context of psychological and behavioural effects while EFSA requires in addition a physiological, functional outcome, i.e. reduction of energy intake or weight. This is, in our view, neither scientifically correct nor in line with the Regulation. A "reduction of the sense of hunger" or an "increase in the sense of satiety" are listed, independently from their consequences on other measures like energy intake or the nutritional quality of food intake, as health claims. References: Blundell J, de Graaf C, Hulshof T, et al. Appetite control: methodological aspects of the evaluation of foods. Obesity Reviews. Obes Rev. 2010 Mar;11(3):251-70. Line 196: "if the health benefit of changing appetite ratings is to decrease subsequent energy intake,

		subsequent energy intake should be measured using appropriate methods". The SYNPA supports the ELC's comments. Appetite regulation and subsequent food intake are determined by multiple factors and often social influences override physiological signals. Although, the panel does acknowledge the beneficial effects of changing appetite with concomitant decreases in energy intake (without link to body weight reduction) to what extent will data, generated in laboratory studies and where subjects are devoid of any external influences, be allowed to be extrapolated to the free living situation and still be considered physiologically relevant? Also according to the Panel enhancing fullness or satiety and/or control hunger should be accompanied with reductions in energy intake. Nevertheless, controlling hunger can confer a benefit as such for example for those that are on a weight management diet providing ways for appetite control and to cope with daily hunger. Such beneficial effects could be seen independent of a reduction in energy intake. For example, perceived hunger has been shown to predict failure to lose weight in clinical trials (Womble et al 2001); and perceived deprivation (not eating what or as much as one would like) is linked to susceptibility to weight gain (Markowitz et al, 2008). line 201: "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." However, reduced satiety for shorter periods of time than a month, several days, should also be considered as useful for consumers to simply minimize the dysphoria of hunger feelings at specific occasions.
Tate & Lyle Plc	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	190: Which Vas scores have been validated? If the product is taken at breakfast, do we need to measure VAS scores until lunch or until dinner? Do we need to measure food intake at lunch and at dinner or only at lunch? 191: Which biomarkers can be considered in the context of behavioral assessment? Delzenne et al on behalf of ILSI recently published a nice overview about biomarkers. Can this review be of guidance? 196: What methods can be used to appropriately measure energy intake. Please specify. Blundell et al on behalf of ILSI recently published a nice overview about the methodology. Can this review be of guidance? 198-200: People on a diet often feel hungry and therefore can suppression of hunger in the context of a low

		caloric diet be considered a beneficial physiological effect? I.e. suppressing hunger, enabling people to stick to the diet and maintain or even loose weight. Suggested claim wording: helps you to feel less hungry while being on a diet. 201: Chronic consumption mean at least for one month or what is the minimum? Can EFSA expand on the science behind this statement about the duration? Does the body try to compensate within one month?
Tate & Lyle Plc	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Since VLCDs are ketogenic in their nature, the Industry Group questions whether is it appropriate to use data that compares appetite and satiety ratings from other non-VLCD diets (which are also ketogenic) to non-ketogenic diets of the same energy content, to allow the claims of ketosis on reduction in appetite.
TNO	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	lines 198-199 We fully agree with the requirement to show sustained effects in studies of sufficient duration. With respect to appetite ratings, we would like to emphasize that feelings of increased satiety or reduced sense of hunger/appetite may indeed have other beneficial effects in addition to decreasing subsequent energy intake or decreasing body weight. We refer to effects such as enhanced attention, mood, well being – the Guidance does not address the question whether such effects would be considered a health benefit, nor what additional measures would be required to support these beneficial effects of changing appetite ratings.
Unilever Research & Development	3.1. Claims on increased satiety	Lines 188-192 (‘Claims on changes in different appetite ratings…’) – • Motivational ratings of appetite should be explicitly recognized as a valid and accepted expression of

	and/or reduced sense of hunger/appetite	changes in the motivational state of consumers, when appropriate methodology is used. Accordingly, we recommend consistent use of the term 'eating motivations' (ie, what has been measured) rather than 'appetite ratings' (ie, the method of measurement). This would be consistent with the rest of the text (eg 'body weight' rather than 'mass recorded on a weighing scale', 'fat oxidation' rather than 'reduction in the respiratory quotient', and so on). Lines 193-200 ('The beneficial physiological effects of changing appetite ratings…') • The text implies possible beneficial effects of changing appetite ratings occur only through changes in energy intake or body weight, which must be separately substantiated. We recommend that additional beneficial effects of reduced eating motivations – often independent of direct effects on energy intake or body weight - are also specifically recognised and cited, including: reduced feelings of hunger during food restriction, reduced food 'cravings', enhanced acceptance or tolerance to dietary change, etc. Where consumption of a reduced energy food or weight management programme itself provides for a reduced energy intake, reduced eating motivations would reflect a reduced hunger dysphoria independent of any added effect on energy intakes or weight loss. In this context, effects on energy intake or weight loss are not necessary to substantiate a claimed effect on eating motivations, which is still beneficial for consumers. This is also consistent with other EFSA guidance, e.g. that reducing gastrointestinal discomfort is considered a beneficial physiological effect. Lines 200-203 Clarification is needed for what is required to address the 'chronic consumption' criterion, and that varying durations (eg other than one month) may be justified. We recommend explicit text such as, 'Where claims are based on an acute response period (eg hours or days), these effects must also be shown to be apparent (ie still able to be demonstrated) after chronic consumption period of at least 15-30 days, to be assessed on a case-by-case basis.' Line 204 ('Claims on changes in appetite ratings...') Whilst eating motivation claims are generally comparative, non-comparative ('absolute') claims are also possible. We therefore recommend recognition of the potential to also make non-comparative claims based on e.g. duration of effect or effects relative to energy content, or other measures, where these are based on appropriate methods, to be considered on a case-by-case basis.
University of	3.1. Claims on	Section 3 The document refers to 'food' throughout and it is assumed that this also includes caloric or even

Aberdeen Rowett Institute	increased satiety and/or reduced sense of hunger/appetite	acaloric beverages, since liquid-solid features of food, energy and nutrient intake are relevant to investigation of appetite and body weight. Section 3 The document uses the term 'food', 'test food' and 'control food' within the context of a suggested one-month period. Humans eat meals, snacks and beverages, rather than test foods, and many manipulations will include the test food as part of a meal. An additional comment to include 'meal' in context of eating in subjects in a free-living environment would be beneficial. Section 3 The comparison of a 'test food' is not relevant for all occasions, for example when applying to ad libitum feeding, particularly when a period of a month is applied. Also, how many times would a comparison need to be made ? Section 3 An additional comment on specific macronutrient effects would be beneficial since many studies of appetite alter macronutrient composition both as the dietary change and as an outcome measure of assessing feeding behaviour e.g. low fat weight loss diets or high-protein weight loss diets
University of Leeds	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 189 - 190: The issue of validation is raised with respect to use of visual analogue scales but no indication of what these measures should be validated against is considered. Blundell et al., 2010 (Obesity Reviews 11, 251-270, ILSI Supplement): Blundell et al., 2010 discuss the validity and reliability of these VAS and best practice in their use and analysis. Consideration of these issues could improve the guidance suggested. Lines 193 – 200: EFSA guidance appears to be limited to the beneficial effects of changing appetite ratings only insofar as concomitant changes in energy intake or body weight are observed. It does not allow for the view that a reduction in hunger per se, for example, could be a beneficial effect in its own right. Benefits of satiety in the short- (pleasure, mood, cognition) medium- (subjective wellbeing, coping with daily hunger) and long-term (dietary compliance, goal directed behaviour) are all possible and could occur independently of reductions in energy intake and body weight. There have been a number of presentations on the evidence for these effects and a paper has been produced by ILSI which details these (Hetherington et al., under review). This paper is consistent with the comment that 'Subjective appetite and food intake measures are related, but are different consumer benefits/claims areas, which can vary independently of each other'(Blundell et al., 2010, p261-262) but which has not been afforded due consideration by the guidance. Lines 200-203: The EFSA draft guidance states that 'In general, 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 test performed on a single occasion would not be considered sufficient for substantiation'. This is quite a vague statement and clarification is required to explain more clearly the 'chronic consumption' criterion. This rigid recommendation will as outlined in my general comments, stifle research, rather promote

		research excellence and will disenfranchise those bodies amongst whom EFSA would seek to encourage greater cooperation. Over the last two decades of appetite research acute studies of the effects of foods/food components on satiation and satiety based on a single administration of the food/food component on a single occasion form the body of the research evidence. The draft guidance effectively renders the results of such studies unimportant/redundant. It is my view that this immense body of research is hugely valuable and could be supportive of a satiety claim. Under conditions of normal use the consumer might not be likely to consume the test food on a daily basis. Thus to state that the acute effects of a food/food component on appetite ratings should be demonstrable over more than one test occasion (e.g. once a week over a 4 week period) may offer some value to the consumer and promote increased consumption of the satiety enhancing product with benefits for other behaviours. Line 204: It should be acknowledged that claims on changes in appetite ratings after food consumption can be non-comparative
University of Leeds, Leeds, UK	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 189 - 190: It is stated that 'Different appetite ratings can be measured 'in vivo in humans using validated visual analogue scales'. In this respect it would be useful to refer to the VAS scales recommended by Blundell et al., 2010 (Obesity Reviews 11, 251-270, ILSI Supplement): Hunger, fullness, satiety, desire to eat and prospective consumption. Blundell et al., 2010 discuss the validity and reliability of these VAS and best practice in their use and analysis. Lines 193 – 200: This section of the EFSA draft guidance appears to limit the beneficial effects of changing appetite ratings to those which occur with concomitant changes in energy intake or body weight. It does not allow for the view that a reduction in hunger per se, for example, could be a beneficial effect in its own right. Benefits of satiety in the short- (pleasure, mood, cognition) medium- (subjective wellbeing, coping with daily hunger) and long-term (dietary compliance, goal directed behaviour) are all possible and could occur independently of reductions in energy intake and body weight. With respect to changes in energy intake, this draft guidance is at odds with the paper by Blundell et al., 2010 (Obesity Reviews 11, 251-270, ILSI Supplement) which states (p. 261) 'It is important to emphasise that the validity of self-report measures is not defined by or dependent on their correlation with behavioural measures of eating (Hill et al., 1995, International Journal of Obesity 19:361-375). This paper refers to the fact that people often eat when they have a low reported hunger (and vice versa) but that this 'does not invalidate self reports as a reflection of intensity of a specific feeling or state or aspect of eating motivation' (Blundell et al., 2010, p261-262).

		Furthermore, with regard to product claims it is stated that 'where energy intake is already being effectively controlled through other means (low energy foods, reduced-energy diet plans, meal replacements etc.) then the benefit of enhancing satiety or reducing appetite may be simply to minimise the dysphoria of hunger feelings , independent of further changes in intake'. Blundell and colleagues (2010) go on to state that 'Subjective appetite and food intake measures are related, but are different consumer benefits/claims areas, which can vary independently of each other'. This indicates that subjective appetite and measures of energy intake need a different set of agreed/validated measures. Lines 200-203: The EFSA draft guidance states that 'In general, 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 test performed on a single occasion would not be considered sufficient for substantiation'. Here more clarification on what is required to achieve the 'chronic consumption' criterion. The present guidance is a little vague. It is also my view that such a rigid recommendation will stifle research, not promote it, and it won"t create the level playing field that was intended. The majority of studies of the effects of foods/food components on satiation and satiety are acute studies consisting of a single administration of the food/food component on a single occasion. Under the draft guidance the results of such studies (carried out over the last 20 years plus) appear redundant but could clearly still be supportive of a satiety claim. Given that the consumer might not be likely to consume the test food on a daily basis (under conditions of normal use) it would be preferable to state that the acute effects of a food/food component on appetite ratings should be demonstrable over more than one test occasion (e.g. once a week over a 4 week period).
University of Limerick	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Line 193: biased in support of claims to decrease in energy intake and/or bodymass. Should be "change in" to accommodate changes in appetite, weight (mass) management that are required to be positive for health benefit. This recommended edit should be followed throughout this section.
VAB-nutrition	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Ln 189-192. Only behavioral assessment seems to be recognized as a relevant measure, and there is a wide variety of methodologies in this area. Can the panel provide additional guidance or examples about precise experimental designs which can be acceptable or not acceptable (namely relatively to settings, timings to and from previous/next eating event, duration, etc…) Ln 204-207. The test food is required to be comparable to the control food, especially in terms of energy. This requirement or at least its wording does not seem appropriate. Indeed, if the beneficial change associated to increased satiety is a decrease in energy intake or in body weight (see ln 193-198), and if this is appropriately

		assessed in the study, the nutritional composition of the tested food relatively to the control food should not matter. Indeed, it can be hypothesized that the "satiating potency" of a food is not a function of its energy content. For a similar weight ingested, a protein-rich food can be more satiating than a lipid-rich food, while having a lower energy content. It can also be imagined that an energy-dense food could be more satiating that its lower-energy counter-art and that it leads to an overall lesser energy intake, which is the point which matters as it is the one which is linked to decreased weight. Similarly, some foods or food ingredients may generate satiety by other means that their nutritional content (specific flavors, for example).
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	For EFSA, what does satiety mean : the absence of hunger between two meals or the mechanism leading to the cessation of food intake ? Line 187 : claims on reduced sense of hunger/appetite : does it mean that reduced sense of hunger has the same signification than reduced appetite for EFSA ? The choice of that wording is ambiguous. Lines 193-194 : which protocol to study increased satiety ? protocol where primary outcome is weight management and secondary outcome is energy uptake and appetite or protocol where primary outcome is energy uptake and secondary outcome is weight management and appetite ?
Wageningen Universiety	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	In line 193 it is noted that "the beneficial physiological effects of changing appetite rating in response to food consumption may be a decrease in subsequent energy intake and/or a decrease in body weight." This sentence reflects the position that beneficial physiological effects with respect to satiety can only exist in relation to measured food intake and/or body weight. We do not agree with this position. We hold the view that an increase in satiety can be considered as a beneficial physiological effect on its own. It does not need not be accompanied by reduction in measured food intake and/or body weight. In this context we agree with a recent paper published by ILSI in the journal Obes Rev 2010;11:251-70, "Appetite control: methodological aspects of the evaluation of foods". This paper was written by 11 scientists in field of satiety, coming from 5 universities and 3 food industries. "It is important to emphasize that the validity of self-report measured is not defined by or dependent on their correlation with behavioural measures of eating. ….. With respect to product claims, demonstration of an effect on food intake is also not required. For example… where energy intake is already being effectively controlled through other means … , then the benefit of enhancing satiety or reducing appetite may be simply to minimize the dysphoria of hunger feelings, independent of further changes in intake" In the conclusion if this paper it is stated that the "use of self-report scales (with or without related biomarkers or behavioural measures) should be strongly supported as a standard, accepted methodological approach to substantiate claims relating to effects of foods on the relevant feelings states and eating motivation "

		Satiety, food/energy intake and body weight management are different concepts that are measured with different tools. Although these concept are meaningfully related to each other, they are different claims and therefore they need a different set of agreed validated measurements. In the EFSA scientific opinion on health claims related to gut and immune function (EFSA Journal 2011; 9(4): 1984) it is noted under paragraph 3.2. "Reducing gastrointestinal discomfort is considered an indicator of improved gastro-intestinal function, and is considered to be a beneficial physiological effect. Appropriate outcome measures of the claimed effect in human studies include validated questionnaire(s)...." We think that this case is comparable to "satiety". We do not understand, why in the case of GI discomfort, validated subjective rating scales are considered beneficial physiological effects, and why this should not be the case for satiety. Line 200-203. "In general, 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 test performed on a single occasion would not be considered sufficient for substantiation ". Although we agree with the idea that satiety claims should only be allowed after demonstration of a repeated effect, this formulation is still rather vague. We propose: "In general, a satiety claim for a particular satiety enhancing food product needs a higher (> 10 %) sustained satiety score compared to an appropriate control product with the same energy content (cf. Blundell et al, Obes Rev). This effect need to be demonstrated for at least 4 times during daily administration of the test food for the period of one month." The proposal for the factor 4 comes from the perspective that weekly measurements of satiety are feasible within a satiety study context. The proposal for daily administration allows for adaptation effects to occur, and such a time frame may be meaningful to consumers.
Wrigley Science Institute	3.1. Claims on increased satiety and/or reduced sense of hunger/appetite	Lines 186 – 203 – Behavioral assessment is a relevant measurement approach for appetite ratings and subsequent energy intake. However a clear definition of chronic consumption seems to be missing. It is appropriate to define single occasion as insufficient to substantiate a claim about reduction in appetite ratings. Chronic consumption as opposed to single consumption may be interpreted in multiple ways, however. The panel may wish to further discuss minimum requirements for experimental designs in regards to duration; frequency; and timing, for example changes in appetite ratings following intake of the food/constituent observed at least once per week for one month. Lines 204-207 require for the test food to be comparable to the control food, especially in terms of its energy contents. This requirement or at least its wording does not seem appropriate. Oral processing of food is a part of the satiation process. Satiety may be achieved means other than than their nutritional contents, for example eating rate and specific flavors. The main focus of the claim is the beneficial change in increase of satiety or decrease in energy intake or in body weight (see ln 193-198). With this in mind, a study may demonstrate

		equivalency in satiety between two comparable food/constituent while one has lesser energy content. For example, a protein-rich food can be more satiating than a lipid-rich food of the same weight. Another example would be that consumption of an energy-dense food could be more satiating than its lower-energy counter-part and thus leads to an overall lesser energy intake. Achievement of overall lesser energy intake should be a driving factor for weight loss and thus the panel may wish to consider or allow that the "satiating potency" of a food does not need to be a function of its energy content.
Ashwell Associates Europe Ltd	3.2. Claims on reduced energy intake	227 "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." This paragraph is very surprising and could have the effect of dissuading companies from submitting claims for low calorie foods such as very low energy diets (VLED) or intense sweeteners. Is this what EFSA intend? Responsible companies want to submit claims that their products can help within a calorie controlled diet and want to submit evidence from studies which show their products being used in controlled or real life situations. In fact in the case of sweeteners, the NDA panel concluded that "a cause and effect relationship has not been established between the consumption of foods and beverages in which sugars have been replaced by intense sweeteners and contribution to the maintenance or achievement of a normal body weight". So was the claim submission unnecessary and would it be better for the sweetener industry to focus on the fact that their product contains zero calories and allow the consumer to draw their own conclusions? Those who argue that sweetener consumption leads to increased appetite or compensation by other means would not be very happy about this! In fact, the sweetener industry is quite ready to admit that some compensation does occur, but will still argue that there is sufficient evidence to show energy reduction and weight loss with sweetener use in several studies (de la Hunty A, Gibson S, Ashwell M. A review of the effectiveness of aspartame in helping with weight control. BNF Nutrition Bulletin 2006;31:115-128).
BENEO Institute	3.2. Claims on reduced energy intake	Line 215-218: The guidance document specifies that "a reduction in energy intake after consumption of a food/constituent should be also be observed after chronic consumption of the food". The underlying rationale is, according to line 214-215, to ensure absence of compensatory effects when the "test" food is consumed on more than a single occasion, i.e. for a certain period of time. Hence, chronic consumption is key but not necessarily the repeated measurement of energy intake. It should still be sufficient to prove the absence of compensatory effect with the testing carried out only once as long as this will be at the end of a chronic consumption period. Thus, line 215-216 of the guidance document should rather read "In general terms, a reduction in energy intake after consumption of a food/constituent should be observed after chronic consumption of the food/constituent (e.g. after one month) and therefore observing changes in energy intake only after a single consumption of the test food would not be considered sufficient for substantiation." Line

		216: The time regarded as "chronic consumption" is exemplified as "after one month". We understand that this is not meant as the "minimum" or "maximum" intervention length required. The guidance should acknowledge that periods of chronic consumption other than 1 months e.g. 2 weeks or 3 months may be appropriate durations, too. Line 222-226: The control food for these kind of tests could be chosen based on several criteria, including comparable volume, appearance, taste and energy content. From a practical point of view it is often not feasible to account for all these criteria in parallel when designing a control and test food. Energy is not always the first factor to balance. For instance, it may be scientifically more relevant to aim for similar volume and texture than for the same energy content (and adjust for differences in the later data analysis). The example "energy" should thus be complemented with other criteria of such as "volume, appearance or taste" to clarify that an appropriate control food is not only one with a matched energy content, but should be considered on a case-by-case basis.
Danone Research	3.2. Claims on reduced energy intake	211-219 In order to consider reduced energy intake as a beneficial physiological effect, is it sufficient to demonstrate a reduced energy intake in the absence of a compensatory effect? Could the Panel clarify the target population? What kind of subjects could be included in the study (overweight, obese…)? 215-218 What is the rationale for the choice of an intervention period of 1 month? We would like the Panel to clarify the minimal frequency of measurements required (e.g.periodic or daily measurements). 222-226 In the case that all characteristics (e.g. macronutrients or volume) of a test product and control product could not be the same, would it be sufficient to have both products equivalent in terms of energy? General comments For reduced energy intake claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DSM Nutritional Products	3.2. Claims on reduced energy intake	LINES 215-218 "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.": As indicated in paragraph 3.2 the beneficial physiological effect of reduction of ad libitum energy intake during or after consumption of a food/constituent will entirely depend on the context in which the claim is made. Reduced energy intake for shorter periods of time than a month, several days or also one day, should also be considered as useful for consumers to regulate their energy intake if body weight loss is not the goal, but only to reduce their energy intake at specific occasions, whereas a longer period should be needed in case body weight loss is the intention behind food/constituent use. However, reduced energy intake is a beneficial effect on its own.
European Responsible	3.2. Claims on reduced energy	Line 215. As indicated in paragraph 3.2 the beneficial physiological effect of reduction of ad libitum energy intake

Nutrition Alliance	intake	during or after consumption of a food/constituent will entirely depend on the context in which the claim is made. Reduced energy intake for shorter periods of time than a month, several days or also one day, should also be considered as useful for consumers to regulate their energy intake if body weight loss is not the goal, but only to reduce their energy intake at specific occasions, whereas a longer period should be needed in case body weight loss is the intention behind food/constituent use. Line 224. It is not clear why control and test food should be comparable, e.g. in terns of energy. This may not even be necessarily appropriate, for example, when comparing diets with zero or lower calorie component (e.g. fibre) replacing a higher calorie component (e.g. other carbohydrate). It cannot be required to add energy to the test diet given that the whole intention is to reduce energy intake. With such interventions, changes in energy intake should be accepted, irrespective of whether they led to weight/body fat reduction. Line 227. This is in contrast to the field of fat/cardiovascular disease where claims for a beneficial effect of the absence (or reduced content) of a food constituent in a food or category of food on for example LDL-cholesterol concentrations have been proposed and accepted without them being considered as nutrition claims.
FederSalus	3.2. Claims on reduced energy intake	No comment. Moreover, for intervention, see the methods used in paragraph 3.1
ILSI Europe aisbl	3.2. Claims on reduced energy intake	208 According to the Panel, enhancing fullness or satiety and/or control hunger should be accompanied with reductions in energy intake. Nevertheless, controlling hunger can confer a benefit as such for example for those that are on a weight management diet providing ways for appetite control and to cope with daily hunger. Such beneficial effects could be seen independent of a reduction in energy intake. For example, perceived hunger has been shown to predict failure to lose weight in clinical trials (Womble et al. 2001, Int J Obes Relat Metab Disord. 25: 340-345); and perceived deprivation (not eating what or as much as one would like) is linked to susceptibility to weight gain (Markowitz et al. 2008, Appetite 51: 720-722). 216 The lack of compensation needs to be demonstrated but it needn"t take a month. For example, a 10 day study has been reported (King et al. 2005, Br J Nutr. 93: 911-915).

211-219

We recommend EFSA express clarity on the view that reducing energy intake is a beneficial physiological effect on its own, in that this is a biologically plausible factor in dietary relationships with positive energy balance. Even modest reductions in energy intake on a sustained basis would confer a population health benefit (Hill et al. 2003, Science 299: 853-855), although changes in weight for individuals might be very small. Also, lines 193-194 state that reduced energy intake itself is a beneficial physiological effect; we believe that latter reflects best the scientific state of the art.

What is the rationale to demand a chronic consumption (e.g. one month), knowing that a potential benefit might be to reduce energy intake only for few days following a period of overeating? Reduction and maintenance of body weight might both be the desired benefit.

215

What is meant by compensatory effects? On the test day itself, the day after or one month after?

The beneficial physiological effect of reduction of ad libitum energy intake during or after consumption of a food/constituent will entirely depend on the context in which the claim is made. Reduced energy intake for shorter periods of time than a month, several days or also one day, should also be considered as useful for consumers to regulate their energy intake if body weight loss is not the goal, but only to reduce their energy intake at specific occasions, whereas a longer period should be needed in case body weight loss is the intention behind food/constituent use.

Ln 215-218

What is the rationale for defining “one month” as chronic consumption, and therefore as relevant? How often during this month the food should be consumed?

220

If changes of appetite ratings are recognised as the mechanisms of action in an opinion, will it be possible to claim on appetite?

227-229 and 250-252

We understand this to mean that EFSA considers that these types of claims are ‘out of scope’ for health claims. For example, the reduction of energy intake due to a reduced, low or no energy content (which may as an example come from the use of high potency sweeteners) and so form an important part of a calorie controlled diet, are nutrition claims? And thereby information on inclusion/use of such products as part of a calorie

		controlled diet are not health claims?
Kraft Foods R&D	3.2. Claims on reduced energy intake	- (l220) If changes of appetite ratings are recognised as the mechanisms of action in a opinion, will it be possible to claim on appetite?
Kraft Foods R&D	3.2. Claims on reduced energy intake	- (l211) Why maintenance of energy intake/prevention of overconsumption is not discussed as a potential health benefit that could be more realistic for a sole food to achieve?
MRC Human Nutrition Research	3.2. Claims on reduced energy intake	Section 3.1. Claims on increased satiety and/or reduced sense of hunger/appetite (lines 188-207): The use of the various measures to substantiate claims based on biochemical parameters, behavioural outcomes and health outcomes is unclear and more precision is needed on the type of evidence required for each type of claim. We suggest re-structuring the information provided in section 3.1 in the following way to enhance clarity: Lines 189 to 192. Add the following clarification after first sentence (after "have been proposed"): "These claims may involve a change in appetite ratings alone, or changes in other parameters (e.g. energy intakes; body weight) that result from appetite changes". Remove remaining of line 189 up to line 192, which will be explained later. Lines 193 -203. Replace current text with: "To be considered substantiated, claims on changes in appetite ratings after consumption of a test food, including increased satiety and/or reduced sense of hunger/appetite, should be based on human studies that meet the following two criteria: - Use validated behavioural assessment methods (e.g. visual analogue scales) - Demonstrate a sustained effect on appetite ratings over time after chronic consumption (e.g. after one month) taking into account possible compensatory effects. Appetite tests performed on a single occasion would not be considered sufficient for substantiation. Claims on appetite changes based on in vitro studies or in vivo studies demonstrating changes in biochemical satiety markers (e.g. cholecystokinin), can only be considered in the context of behavioural assessment. That is, such laboratory outcomes can be used as supportive evidence alongside behavioural assessment outcomes but not as sufficient conclusive evidence that a change in appetite occurs. Claims on changes in energy intakes resulting from a change in appetite ratings, such as a decrease in subsequent energy intake, should be substantiated with human studies that meet the following three criteria: - Measure subsequent energy intake using appropriate methods

		- Use validated behavioural assessment methods (e.g. visual analogue scales) to measure appetite - Demonstrate a sustained effect over time on energy intakes, taking into account possible compensatory effects. Claims on changes in body weight resulting from appetite changes should be substantiated by human studies that also measure appetite changes and body weight changes with appropriate methods and that demonstrate a sustained effect over time on body weight, with a minimum duration of 3 months. Claims for any other beneficial physiological effects that may result from changing appetite ratings in response to food consumption should be specifically indicated, substantiated, and considered on a case-by-case basis." Lines 204-207. Replace current text with: "If the claim is a comparative claim (i.e. comparison of the "test" food with the "control" food), both the test and the control 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. the two foods should be of comparable energy load)." Section 3.2. Lines 220-221: We suggest that this sentence is re-worded for clarity, consistently with the structure suggested for section 3.1. For instance, we propose: "Claims on reduced energy intakes based exclusively on changes in appetite ratings would not be considered sufficient for substantiation. Changes in appetite ratings in this context however, can be used as evidence for a mechanism by which the food/constituent could exert the claimed effect".
Rudolf Wild GmbH & Co. KG	3.2. Claims on reduced energy intake	Line 215-218 - Is a chronic consumption really approbiate? A single occasion should also provide sufficient information. It would be better to reproduce the effect of a single occasion than to go into chronic consumption, as a single occasion mimics "real life".
SYNPA	3.2. Claims on reduced energy intake	line 215: "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." As indicated in paragraph 3.2 the beneficial physiological effect of reduction of ad libitum energy intake during or after consumption of a food/constituent will entirely depend on the context in which the claim is made. Reduced energy intake for shorter periods of time than a month, several days or also one day, should also be considered as useful for consumers to regulate their energy intake if body weight loss is not the goal, but only to reduce their energy intake at specific occasions, whereas a longer period should be needed in case body weight loss is the intention behind food/constituent use.

Tate & Lyle Plc	3.2. Claims on reduced energy intake	215: What is meant by compensatory effects: on the test day itself, the day after or one month after? 227-229: We understand this to mean that EFSA considers that these types of claims are 'out of scope' for health claims. For example, the reduction of energy intake due to a reduced, low or no energy content (which may as an example come from the use of high potency sweeteners) and so form an important part of a calorie controlled diet, are nutrition claims? And thereby information on inclusion/use of such products as part of a calorie controlled diet is not health claims?
Tate & Lyle Plc	3.2. Claims on reduced energy intake	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	3.2. Claims on reduced energy intake	Line 209. While evidence for reduced energy intake may be interesting, the critical variable would be maintenance of bodyweight reduction: therefore evidence supporting a claim for maintenance of reduced energy intake would tend to be somewhat "soft". Evidence for maintenance of bodyweight would be much stronger evidence.
TNO	3.2. Claims on reduced energy intake	We agree that reduced energy intake may be considered a beneficial physiological effect (depending on the target population). Energy intake can be measured in numerous ways, not all of which are appropriate in the setting of a relatively short-term (e.g. one month) intervention study and depending on the size of the population. It would be helpful if the Panel would refer to publications in which the appropriateness of energy intake measures is reviewed.
Unilever Research & Development	3.2. Claims on reduced energy intake	Lines 211-219 We recommend EFSA express clarity on the view that reducing energy intake is a beneficial physiological effect on its own, in that this is a biologically plausible factor in dietary relationships with positive energy balance. Even modest reductions in EI on a sustained basis would confer a population health benefit (Hill JO et al., Obesity and the environment: Where do we go from here? Science 2003;299:853-855), although changes in

		weight for individuals might be very small.
University of Leeds, Leeds, UK	3.2. Claims on reduced energy intake	Lines 215-216: The EFSA draft guidance states that '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'. Here more clarification on what is required to achieve the 'chronic consumption' criterion. The present guidance is a little vague. The majority of studies of the effects of foods/food components on satiation and satiety are acute studies consisting of a single administration of the food/food component on a single occasion. Under the draft guidance the results of such studies (carried out over the last 20 years plus) appear redundant but could clearly still be supportive of a claim on reduced energy intake. Given that the consumer might not be likely to consume the test food on a daily basis (under conditions of normal use) it would be preferable to state that the acute effects of a food/food component on food intake should be demonstrable over more than one test occasion (e.g. once a week over a 4 week period). Here, as with effects on satiety/hunger/appetite – section 3.1, it is important to demonstrate that acute effects can be maintained (i.e. still demonstrated) over a longer period (e.g. at least 1 month).
University of Limerick	3.2. Claims on reduced energy intake	Line 208 3.2 Claims on reduced energy intake. Unless specified to the contrary there should also be a section 3.3. Claims on inv=creased energy intake
VAB-nutrition	3.2. Claims on reduced energy intake	Ln 224-226. The test food is required to be comparable to the control food, especially in terms of energy. This requirement or at least its wording does not seem appropriate. Indeed, if the beneficial change associated to increased satiety is a decrease in energy intake or in body weight (see ln 193-198), and if this is appropriately assessed in the study, the nutritional composition of the tested food relatively to the control food should not matter. Indeed, it can be hypothesized that the "satiating potency" of a food is not a function of its energy content. For a similar weight ingested, a protein-rich food can be more satiating than a lipid-rich food, while having a lower energy content. It can also be imagined that an energy-dense food could be more satiating that its lower-energy counter-art and that it leads to an overall lesser energy intake, which is the point which matters as it is the one which is linked to decreased weight. Similarly, some foods or food ingredients may generate satiety by other means that their nutritional content (specific flavors, for example). Ln 227-229: the wording of this sentence appears unclear. A claim about a reduced energy intake should be possible for a food low or reduced in energy, provided that the required scientific support is given (i.e. demonstration in human studies that the intake of the food actually leads to a decreased energy intake and not mere calculation of the theoretical "missed" energy).

		This point also raises the general question of the health claims that can be associated to nutrition claims. The EC 1924/2006 regulation stipulates that "the presence, absence or reduced content in a food or category of food of a nutrient or other substance in respect of which the claim is made has been shown to have a beneficial nutritional or physiological effect, as established by generally accepted scientific evidence" (art 5.1.a) This means that the nutrition claims are allowed when they correspond to a benefit for the consumer, even if the mention of this benefit is not allowed through the nutrition claim itself. However, because these nutrition claims have been allowed based on generally accepted scientific evidence, the corresponding (or a corresponding) health claim should be allowed. This is likely to be the case soon for vitamins and minerals and other nutrients, as they have been favorably evaluated for claim(s) pursuant to art 13-1, but some nutrition claims have not yet a favorably evaluated corresponding health claim. This is in particular the case for food with no, low or reduced energy content.
Wageningen Universiety	3.2. Claims on reduced energy intake	In the draft opinion it is indicated : In general terms, a reduction in energy intake after consumption of a food/constituent should also be oberved afterchronic consumption ofthe food (e.g. after one month), and therefore tests performed on a single occasion would not be considered sufficient for substantiation. With respect to the time frame, we propose a similar formulation for reduced energy intake as for satiety. The current formulation is rather vague. "In general, a reduced energy intake claim for a particular energy intake reducing functional food product needs a lower (> 10 %) observed food intake at a testmeal (after a preload) compared to an appropriate control product with the same energy content. This effect needs to be demonstrated for at least 4 times during daily administration of the test food for the period of one month." Such a time frame allows for adaptation to occur. The number 4 refers to weekly measurement which be feasible in a energy intake study. The timing of one month may be valuable time frame for consumers.
Wrigley Science Institute	3.2. Claims on reduced energy intake	Lines 208-219 – As mentioned for lines 186-203, a clearer definition of chronic consumption seems to be missing.Lines 224-226 - As mentioned for lines 204-207, achievement of lesser energy intake due to consumption of equal amount of lower energy food/constituents should be allowed as well as due to consumption of less amount of food/constituents with the same energy contents. Lines 227-229: This section is rational, however a claim in relation to a reduced energy intake should be allowed based on a food with reduced energy content as long as the required scientific support is provided (i.e. human efficacy that the chronic consumption of the food/constituents lead to actual decreased energy intake

		instead of theoretical energy gap based on the calculated differences). Another argument is the question regarding the health claims associated with nutrition claims. The EC 1924/2006 regulation states that "the presence, absence or reduced content in a food or category of food of a nutrient or other substance in respect of which the claim is made has been shown to have a beneficial nutritional or physiological effect, as established by generally accepted scientific evidence" (art 5.1.a). Thus, it allows nutrition claims, provided that there are established scientific evidences to link with consumer benefits, while the health benefit itself is not allowed to accompany nutritional claims. Recent art 13-1 opinions on claims related to some vitamins and minerals provided supporting evaluations to the submitted claims. These claims on vitamins and minerals were permitted based on generally accepted scientific evidence on causality between these nutrients and the corresponding health benefits.
AESGP - Association of the European Self-Medication Industry	4. Weight management	What does EFSA consider as biological significance in the area of weight and fat loss? Will set guidelines be used? While it is clear what study design might be needed, it is not sufficiently clear what levels of change are needed with regard to the effect of a food/ingredient (where specific guidelines exist for medicines).
Biofortis	4. Weight management	What does long term/sustained effect suggest ? Does it mean that the product has to be taken continuously (eg phytosterols which have to be consumed for the whole life), or temporarily with then a maintained effect (such as meal replacements) ?
GlaxoSmithKline	4. Weight management	The suggestions made in the area of duration of studies, population to use, mechanisms etc. are useful. Further clarity would be useful by giving reference to suitable measures of body fat and lean body mass. What does the Panel view as biological significance in the area of weight and fat loss- will they be using set guidelines? It's clear what study design might be needed but not what levels of change are needed with regard to the effect of a food/ ingredient (guidelines exist for medication). It would be useful if this detail could be provided.
ILSI Europe aisbl	4. Weight management	230 Would claim on foods combination/diet/programs rather than on one single food be eligible?
Kraft Foods R&D	4. Weight management	(l230) would claim on foods combination/diet/programs rather than on one single food be eligible?
Mead Johnson Nutrition	4. Weight management	What is the importance of a food's glycemic index for healthy weight management (lines 230 to 303) and for blood glucose regulation (lines 304 to 345)?
Mead Johnson Nutrition	4. Weight management	The guidance on weight management (lines 230 to 303) does not describe the effects of early nutrition on weight management. Early biomarkers (like leptin, adiponectin and growth factors) are considered to be related

		to long-term outcomes like weight management and obesity. Will early biomarkers, according to the NDA panel, be valid in a disease-risk factor reduction claim? And are biomarkers derived from saliva as relevant as biomarkers derived from blood? (this method is less invasive for infants and children then blood draw).
Mead Johnson Nutrition	4. Weight management	The guidance on weight management (lines 230 to 303) does not describe the effects of early nutrition on weight management. Early markers can include early growth patterns (like rapid growth and early adiposity rebound), sleep disturbances, and others. According to the NDA panel, which early markers have an established relationship to long-term outcomes like weight management and obesity?
Mead Johnson Nutrition	4. Weight management	Lines 236 to 303 describes beneficial effects related to growth and body composition and might not be suitable for claims intended for infants and children. In addition, this section mainly addresses overweight. Growth patterns and body composition of infants and children differ largely from those of adults. For example, maintenance of body weight is not always beneficial, because children are supposed to grow. What would be beneficial outcomes that are considered as beneficial effects with regard to weight management during childhood? What would be considered by the NDA panel as healthy growth, and what would be a normal range for healthy growth?
Mead Johnson Nutrition	4. Weight management	Section 4 (lines 230 to 303) describes requirements for claims on weight management and is almost entirely related to claims for the general healthy population. As early nutrition has a very important role in determining and predicting healthy weight management later in life, we would like to ask the NDA panel to address the general criteria that will be applied in evaluation of weight management related health claims specifically intended for pediatric populations.
NATUREX Spain S.L.	4. Weight management	Follow-up recommendations in a weight loss study • Are follow-up periods after the intervention period required in a body weight loss study? • If yes, what is the minimum follow-up period? • What are the compulsory measurements to perform as part of the follow-up?
NATUREX Spain S.L.	4. Weight management	Physical activity recommendations in a weight loss study In combination with dietary energy restrictions, increased physical activity can results in additional and prolonged weight loss. An internationally accepted method for measuring physical activity is the IPAQ questionnaire. • Is the IPAQ questionnaire the most reliable method to assess physical activity or are there other acceptable methods to determine physical activity?

		• Have any validated pedometers/accelerometers been recommended? An increase in physical activity of 1000 steps per day over the current level of physical activity is often recommended in weight loss studies. The figure of 1000 steps per day may have originated from the Japanese government's attempts to increase physical activity and thereby decrease obesity. In addition, it has recently been reported in an epidemiological study that the likelihood of having metabolic syndrome was 10% less for each additional 1,000 steps per day (Sisson et al., 2010). • Therefore, is a physical activity increase of 1000 steps/day acceptable? • Should a controlled increase in physical activity be set as a fixed number of steps or as a % from baseline physical activity?• If neither of these proposals are acceptable to EFSA, what level of increased physical activity is recommended in a weight loss study? Questionnaire recommendations for measurement of physical activity in weight loss studies Various questionnaires have been used to calculate physical activity, and the results of which used to calculate a physical activity score for the Harris- Benedict equation. • Which validated physical activity questionnaires are recommended to calculate the physical activity score for the Harris-Benedict equation? • Is the IPAQ recommended to calculate the physical activity score for the Harris-Benedict equation? Sisson,S.B., S.M.Camhi, T.S.Church, C.Tudor-Locke, W.D.Johnson, and P.T.Katzmarzyk. 2010. Accelerometer-determined steps/day and metabolic syndrome. Am. J Prev. Med. 38:575-582. Not relevant
NATUREX Spain S.L.	4. Weight management	Dietary restriction recommendations in a weight loss study It has often been reported that 0.5 kg of fat has about 3,500 kcal (Katan and Ludwig, 2010). Thus, a daily reduction of 500 kcal below the required energy intake is often proposed in weight loss studies to encourage a weight loss of 0.5 kg of fat per week. • Should a restriction in calorie intake be set as a fixed kcal amount or as a percentage of subject's baseline calorie intake (as defined by the Harris Benedict equation)? • If a fixed kcal restriction is preferable, would a 500-kcal restriction (from the Harris Benedict line) be acceptable? • If a percentage restriction is preferable, would a 15 % restriction (from the Harris Benedict equation) be acceptable? • If neither of these proposals is acceptable to EFSA, what energy intake deficit is recommended in a weight loss study? Katan,M.B., andD.S.Ludwig. 2010. Extra Calories Cause Weight Gain-But How Much? JAMA: The Journal of the American Medical Association 303:65.
NATUREX Spain	4. Weight	Energy restriction recommendations in a weight loss study

S.L.	management	Energy restrictions, in the form of dietary restrictions and increased physical activity are associated with greater weight loss than compared to dietary restrictions alone, as long as the energy restriction is not severe (Donnelly et al., 2009). In addition, follow-up studies have shown that diet plus exercise programs resulted in 20% greater sustained weight loss after one year, compared to a dieting program alone (Curioni and Lourenco, 2005). • In this respect, does EFSA agree that a combination of dietary restrictions and increased physical activity be applied in weight loss studies? Curioni,C.C., andP.M.Lourenco. 2005. Long-term weight loss after diet and exercise: a systematic review. Int J Obes. (Lond) 29:1168-1174. Donnelly,J.E., S.N.Blair, J.M.Jakicic, M.M.Manore, J.W.Rankin, and B.K.Smith. 2009. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med. Sci. Sports Exerc. 41:459-471.
NATUREX Spain S.L.	4. Weight management	Age range recommendations of a weight loss study population Individuals older than 18 years are considered to be in the adult population but adult body mass, bone growth and height might not be achieved until the age of 20 or 21 (American Medical Association, 2004). • Given that the anthropometric parameters of this sub-population can change rapidly, does EFSA have an opinion on whether this sub-population should be included in intervention studies focused on body weight and body composition? • If those aged 18-21 are excluded from the trial design, will the proposed health claim have to reflect that the product is excluding those in the 18-21 age range? During menopause, the body composition of females may change significantly (Lovejoy et al., 2008). • Does EFSA have an opinion on whether this sub-population should be included in intervention studies focused on body weight and body composition? • If this sub-population should not be considered for study, what should be the basis for exclusion – age or estrogen level? • If menopausal women are excluded from the trial design, will the proposed health claim have to reflect that the product is excluding menopausal women? • Can the results obtained from a study of a population aged 20-45 years be extrapolated to those less than 18

		years old? • If not, will a separate study for this sub-population need to be conducted separately? • Can the results obtained from a study of a population aged 20-45 years be extrapolated to the elderly (>70 years)? • If not, will a separate study for this sub-population need to be conducted separately? • Can the results obtained from a study of a population aged 55-85 years be extrapolated to the general population? • What should a sub-population aged 20-45 years be referred to as: "adults", "middle aged", "early-life adults"? American Medical Association. 2004. Family Medical Guide. 4th ed. Lovejoy,J.C., C.M.Champagne, L.De Jonge, H.Xie, and S.R.Smith. 2008. Increased visceral fat and decreased energy expenditure during the menopausal transition. International Journal of Obesity 32:949-958.
NATUREX Spain S.L.	4. Weight management	Gender composition recommendations of a weight loss study population The opinion of EFSA is sought in relation to the gender composition of the study population. Many open design weight loss intervention studies report a significantly larger number of female volunteers compared to male volunteers. The difference in interest between the sexes to participate in a weight loss study may reflect a gender-specific desire of the general population to lose weight. • Is an open design weight loss study, in which female volunteers represent a significant number of the study population (for example 90%) acceptable to EFSA? • If an open design is acceptable, is a post-hoc test required to conduct an analysis by gender (considering that the final number of men and women is not predetermined)? Alternatively, a balanced design is proposed, in which an equal number of men and women are assigned to the test and placebo groups. • Is a balanced design acceptable to EFSA even if it does not represent the desire of the general population? • If a balanced design is acceptable, is a stratified analysis by gender required? • It may be reasonably assumed that a significant difference observed between the test and placebo group in the entire study population may not be observed in either, or both of, the gender-specific stratified analyses. In

		this instance, does EFSA advise the sample size calculations be based on observing a significant difference between the test and placebo groups within genders? A further alternative is a semi-open design, in which there is an arbitrary limit (for example 60 or 70%) set for one gender. The purpose of this design is to reflect the desire of one section of the population to participate in a weight loss study and, on the other hand, to attempt to remain close to the demographics of the general population. • Is a semi-open design weight loss study, in which female volunteers represent a larger number of the study population than men (for example 60:40 or 70:30) acceptable to EFSA? • If an open design is acceptable, is a post-hoc test required to conduct an analysis by gender (considering that the final number of men and women is not predetermined)?
NATUREX Spain S.L.	4. Weight management	Recommendations regarding initial BMI of the study population in a weight loss study In the current draft scientific opinion from EFSA (lines 326-327, EFSA 2011) states that "studies conducted in diabetic subjects treated with lifestyle measures only (e.g. diet) could be used for the scientific substantiation of these claims" (Section 5.1). • Can this statement be extrapolated to weight loss studies, in that obese subjects (BMI 30 – 34.9 kg/m2), who are not undergoing treatment for obesity, can form part of the study population for health claims targeted at the general population? Recommendations regarding restrictions of the study population in a weight loss study The following groups are regularly included in the exclusion criteria in weight loss studies: a) Women who began taking oral contraceptives or hormone replacement therapy recently, within the last 6 months. b) Volunteers who have quit smoking in the last 6 months or who plan on quitting/altering smoking habits during their participation in this intervention trial. • Does EFSA have an opinion on whether a time period of 6 months is sufficient or whether this time period is excessively restrictive? EFSA. 2011. Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. EFSA Journal in press.

Tate & Lyle Plc	4. Weight management	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4. Weight management	The panel should make clear the differences in claims regarding weight loss and weight management after weight loss, as well as claims relating to weight maintenance only where there is no indication of prior weight loss.
University of Aberdeen Rowett Institute	4. Weight management	Section 4 The document suggests a one-month chronic consumption of the 'food', and this seems reasonable to show durability of effect on appetite. However, following on from this, is a suggestion of a three-month period for claims in body weight maintenance/loss. From a pragmatic point of view, it is unlikely that subjects would adhere to a dietary intervention study for this duration. It may be that after one month a follow-up of weight could be conducted at three-months for assessment of body weight.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	4. Weight management	Target populations : Obese/overweight/diabetic subjects are not healthy people, are claims targeting this group admissible in the scope of the regulatory ? Are claims targeting people with metabolic syndrom (with or without medication) admissible in the scope of the regulatory ? As the number of obese/overweight subjects is constantly increasing, would datas obtained in these groups extrapolable to general population ? Sections 4.2 and 4.6 (claims on body weight maintenance/loss and claims on the increase of lean body mass) : Can a product bear a claim to maintain/get back to a normal weight in a situation of physiological but nevertheless deleterious weight loss like in sarcopenia ? What about claims targeting elderly people with risk of malnutrition, are they admissible in the scope of the regulatory ?

Ashwell Associates Europe Ltd	4.1. Claims on increased energy expenditure	231 An increased thermic effect after every meal could be a beneficial effect and could aid weight loss in the short an long term. This is different to a sustained increase in energy expenditure and should also be mentioned here.
BENEO Institute	4.1. Claims on increased energy expenditure	Line 232: Energy expenditure is one component of energy balance like energy intake is. There is a biologically plausible relation to energy balance and weight management. Energy expenditure is commonly regarded as a critical factor contributing to successful energy regulation in normal individuals, as well as to the dysregulation of energy balance that characterizes obesity (Riccardi et al, 2004). It should thus be acknowledged as beneficial physiological effect per se. Line 233: Clarification should be provided what is understood and accepted as an "sustained increase".
European Responsible Nutrition Alliance	4.1. Claims on increased energy expenditure	Line 232. We would not agree with the position that sustained increased energy expenditure per se is not considered a beneficial effect but needs to be associated to weight loss. The same reasoning is not applied to reduced energy intake, which is considered as a beneficial effect per se, without the need to be associated to weight loss. Linking both concepts together is an unduly restrictive attitude. Sustained increased energy expenditure should be considered as a beneficial effect per se.
FederSalus	4.1. Claims on increased energy expenditure	To measure energy expenditure as supportive evidence for a claim on body weight loss, we propose the use of arm calorimetry, for instance Arm – Band.
ILSI Europe aisbl	4.1. Claims on increased energy expenditure	232-235 Given that energy expenditure is an inherent component of energy balance, a relationship of energy expenditure with obesity risk is clearly biologically plausible, a sustained effect (rise) in energy expenditure reduces the risk of positive energy balance. On this basis we therefore recommend that a sustained rise in energy expenditure per se should be seen as a beneficial physiological affect. 233 Can the panel clarify what they mean with "sustained increase" in energy expenditure?
Kraft Foods R&D	4.1. Claims on increased energy expenditure	- (l234) what is the appropriate period of time to demonstrate the sustained effect?
MRC Human Nutrition Research	4.1. Claims on increased energy	Section 4.1. Lines 232-235. We suggest that this sentence is slightly reworded for clarity and consistency with

	expenditure	the previous sections. We propose: "An increase in energy expenditure after acute consumption of a food is not considered a beneficial physiological effect per se and so would not be considered sufficient for substantiation. However, a sustained increase in energy expenditure may be one of the mechanisms by which a reduction in body weight can be achieved. Therefore measures on energy expenditure can be used as supportive evidence for a mechanism by which the food/constituent could exert weight loss". Section 4.5. Lines 271-275. We suggest that this sentence is re-worded for clarity and consistency with the previous text. We propose: "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, although it is not a physiological effect per se. Therefore measures of fat oxidation alone cannot be considered sufficient to substantiate a claim on the reduction of body fat but could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect".
Tate & Lyle Plc	4.1. Claims on increased energy expenditure	232-235: Please explain why an increase in energy expenditure is not considered a beneficial physiological effect per se? What would be needed to consider it as beneficial?
Tate & Lyle Plc	4.1. Claims on increased energy expenditure	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.1. Claims on increased energy expenditure	Line 231. The most important variable in relation to increased energy expenditure after weight loss is physical activity. Any evidence supporting a claim for a food component in raising energy expenditure would have to be from studies in which physical activity was very carefully monitored and recorded. Such studies would be extremely difficult and it is unlikely that any such claims could be adequately substantiated.

Unilever Research & Development	4.1. Claims on increased energy expenditure	Lines 232-235 Given that energy expenditure is an inherent component of energy balance, a relationship of energy expenditure with obesity risk is clearly biologically plausible, a sustained effect (rise) in energy expenditure reduces the risk of positive energy balance. On this basis we therefore recommend that a sustained rise in energy expenditure per se should be seen as a beneficial physiological effect.
University of Leeds, Leeds, UK	4.1. Claims on increased energy expenditure	Line 232-233: It should be acknowledged that an increase in energy expenditure observed after every meal (i.e. multiple acute effects) could aid weight loss and therefore be a physiological beneficial effect.
University of Limerick	4.1. Claims on increased energy expenditure	Line 232 "energy expenditure" is ill-defined. Requires clarification on the components of energy expensiture most relevant for consideration i.e basal or resting EE, NEAP etc.
Arla Foods a.m.b.a.	4.2. Claims on body weight maintenance/loss	The headline is misleading since the text only covers weight loss.
Ashwell Associates Europe Ltd	4.2. Claims on body weight maintenance/loss	250 This paragraph is very surprising and could have the effect of dissuading companies from submitting claims for low calorie foods such as very low energy diets (VLED) or intense sweeteners. Is this what EFSA intend? Responsible companies want to submit claims that their products can help within a calorie controlled diet and want to submit evidence from studies which show their products being used in controlled or real life situations. In fact in the case of sweeteners, the NDA panel concluded that “a cause and effect relationship has not been established between the consumption of foods and beverages in which sugars have been replaced by intense sweeteners and contribution to the maintenance or achievement of a normal body weight”. So was the claim submission unnecessary and would it be better for the sweetener industry to focus on the fact that their product contains zero calories and allow the consumer to draw their own conclusions? Those who argue that sweetener consumption leads to increased appetite or compensation by other means would not be very happy about this! In fact, the sweetener industry is quite ready to admit that some compensation does occur, but will still argue that there is sufficient evidence to show energy reduction and weight loss with sweetener use in several studies (de la Hunty A, Gibson S, Ashwell M. A review of the effectiveness of aspartame in helping with weight control. BNF Nutrition Bulletin 2006;31:115-128).
Ashwell Associates Europe Ltd	4.2. Claims on body weight maintenance/loss	241 The guideline states in line 241 that “The most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass”. In this context the demonstration of significant fat loss should override the duration of the intervention. Better to suggest that data on body weight should be accompanied by data on body composition rather than saying these should be used as

		supporting evidence (line 244)
BENEO Institute	4.2. Claims on body weight maintenance/loss	Line 237: It will be useful for applicants if the EFSA could provide precise information what is understood and accepted as "sustained reduction in body weight". Line 239: The time regarded as "appropriate duration" is exemplified as "three months". Clarification should be provided that this is not to be understood as the "minimum" or "maximum" intervention length required. The guidance should acknowledge that periods other than 3 months e.g. 2 or 6 months may be appropriate durations, too. Line 242-243: Guidance should define what is the appropriate study duration when measures of body composition are not strictly required and, vice versa, the study length where measures of body composition are required in parallel. The guidance document should be supplemented for transparency reasons with the scientific judgments and justifications for these distinctions. Line 243: Further clarification should be provided on the different measures of body composition analysis considered appropriate. Well established and generally in science accepted measures include bioelectrical impedance analysis (BIA), air displacement plethysmography (ADP), Dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT) as well as waist circumference or the waist-to-hip-ratio. All of these measures provide information on body composition which could be used as supportive evidence for claims on body weight maintenance/loss.
Danone Research	4.2. Claims on body weight maintenance/loss	237-245 Could maintenance of body weight be considered as a beneficial physiological effect in certain target populations, for instance: - Maintenance of a stable body weight in postmenopausal women? - Limitation of the magnitude of weight gain to delay the onset of obesity in overweight subjects? If yes, what should the primary criteria in clinical studies be and what are the possible secondary criteria? General comments In the case that all characteristics (e.g. macronutrients or volume) of a test product and control product could not be the same, would it be sufficient to have both products equivalent in terms of energy? Overweight and/or obesity is the result of a chronic energy imbalance. In order to claim on body weight maintenance/loss, would it be sufficient to demonstrate an improvement in energy balance?

		If yes, could energy balance be used as a primary criteria in clinical studies? In that case, what methods would be appropriate to measure the changes in energy balance? For body weight maintenance/loss claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DHI Water Environment Health	4.2. Claims on body weight maintenance/loss	ln 239: Does the duration of the study have any bearing on what can be claimed? E.g. if the duration of the study was three months, should the claim elaborate on the fact that the effect has not been proven beyond three months duration?
DSM Nutritional Products	4.2. Claims on body weight maintenance/loss	LINES 238-239: "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)": It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is by all means possible within 2-4 weeks, so a minimum duration of 2-4 weeks for a weight loss study should be sufficient to support such claim while we agree that for a weight maintenance study 3 months might be needed. EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. line 246-249 "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.": Sustained increase in energy expenditure again is in itself a beneficial effect, even though it may not be an evidence for weight reduction. However, clarification is sought on the meaning of "sustained increase in

		energy expenditure". References: Pischon T, Boeing H and Hoffman K et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med 2008; 359:2105-20.
DSM Nutritional Products	4.2. Claims on body weight maintenance/loss	LINES 238-239: "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)": It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is by all means possible within 2-4 weeks, so a minimum duration of 2-4 weeks for a weight loss study should be sufficient to support such claim while we agree that for a weight maintenance study 3 months might be needed. EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. LINES 246-249 "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.": Sustained increase in energy expenditure again is in itself a beneficial effect, even though it may not be an evidence for weight reduction. However, clarification is sought on the meaning of "sustained increase in energy expenditure".
ELC	4.2. Claims on body weight	Lines 237-239 It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the

	maintenance/loss	reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is by all means possible within 1 or 2 months, so a minimum duration of 1 month for a weight loss study should be sufficient to support such claim while we agree that for a weight maintenance study 3 months might be needed.
European Responsible Nutrition Alliance	4.2. Claims on body weight maintenance/loss	Line 238. It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is possible within 1 or 2 months, so a minimum duration of 1 month for a weight loss study should be sufficient to support such claim. We accept that weight management is a different claim, requiring a longer period (3 months). EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. It would helpful if EFSA could clarify how this should be measured to be acceptable in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well. According to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. Line 250. This is in contrast to the field of fat/cardiovascular disease where claims for a beneficial effect of the absence (or reduced content) of a food constituent in a food or category of food on for example LDL-cholesterol concentrations have been proposed and accepted without them being considered as nutrition claims.
ILSI Europe aisbl	4.2. Claims on body weight maintenance/loss	236 Can weight maintenance in the general population and in elderly can be considered as a health benefit? Clarification of the title of 4.2 needed; in this paragraph, nothing is said on “body weight maintenance” 237-245 Which criteria should be used to characterise ‘obese subjects’ (BMI, metabolic parameters,…)?

		We recommend better guidance on the range of evidence (including duration of effect) that could be acceptable for substantiating claims for weight loss and or claims of weight maintenance (other than reduced rate of gain after weight loss, as described in Section 4.3). For example, we recommend that demonstration of weight loss should be considered from suitably powered studies of 4-12 weeks duration. We also recommend stating that demonstration of a reduced rate of weight gain over 3 months or longer in an intervention population relative to the general population could be a basis for weight maintenance claims. It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is by all means possible within 1 or 2 months, so a minimum duration of 1 month for a weight loss study should be sufficient to support such claim while we agree that for a weight maintenance study 3 months might be needed. How should body fat mass reduction be measured to be acceptable to EFSA? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence as well (Pischon et al 2008 N Engl J Med. 359: 2105-20).
KELLOGG"S	4.2. Claims on body weight maintenance/loss	Study Duration – lines 239, 270, 290, 281 Short term weight loss programs can motivate consumers to achieve a reduction in body weight over period of time they see as attainable, by making the relatively simple dietary changes required by the Program. Their prime motivation is normally to improve personal appearance or achieve a particular garment size, rather than health. Having achieved this early short-term success, individuals are more likely to continue to make dietary and lifestyle changes in order to consolidate their achievement, or to continue on to further weight loss. This is supported by studies which indicate that people, who believe that they can control their weight, continue to engage in effective weight control behaviours (Byrne, 2002). Other work suggests that short-term weight loss is a significant predictor of successful longer-term weight loss (Fabricatre et al, 2009; Wadden & Stunkard, 1986; Dubbert & Wilson, 1984). Low self belief in being able to initiate and maintain dietary & lifestyle changes is a major barrier to initiating and continuing a weight loss program is. Excess body weight is per se a major risk factor and marker for the development of cardiovascular disease (CVD) (WHO, Report 916, 2003; AHA, 2010 http://www.americanheart.org/presenter.jhtml?identifier=4726). Therefore for overweight people, any significant amount of weight loss represents a health benefit. In this respect, overweight individuals who successfully achieve a body weight reduction of 1-2 kg over a 2 week period benefit from a reduced risk for cardiovascular events.The National Heart, Lung and Blood Institute

		(NHLBI) guidelines recommend a weight loss rate of 5 – 10% over the period of 6 to 12 months (NHBI North American Association for the Study of Obesity www.nhlbi.nih.gov; International Diabetes Foundation, 2006). This translates to approximately the rate of weight loss 0.5-1 kg per week, which corresponds to the recommendations of this 2 Week Program. In addition to body weight reduction as an independent disease risk factor per se, reduced blood pressure is one of the secondary benefits of reducing excess weight. Reduced blood pressure, itself a major risk factor for CVD, occurs with in the first weeks of body weight reduction. A review by Pi-Sunyer (1993) stated that significant short-term effects of blood pressure can occur even if 'ideal weight' has not been reached. For example, in a study using 49 hypertensive, overweight patients, blood pressure fell by 2.2/1.5mm Hg (P=0.01) in those who lost <3kg (Ramsay et al., 1978). In addition, MacMahon and colleagues (1985) reported a 1-3mmHg decrease in systolic and diasystolic blood pressure per kg of weight loss among a group of obese women. A recent study, in which 32 healthy individuals (BMI 33.8 ± 0.7) participated in a 7-day diet and exercise trial, suggested that short-term dietary treatment can also improve hypertension, particularly systolic blood pressure ($p < 0.05$) (Solomon et al, 2009).
KELLOGG"S	4.2. Claims on body weight maintenance/loss	Line 238. Human studies assessing the effects of a food/constituent on body weight changes need to be of appropriate duration (e.g. three months). The weight loss should be fat loss and other health outcomes such as TAG should be considered. The guideline goes on to state that "The most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass" surely if this is the case then if you can demonstrate fat loss then it doesn't matter what the duration of the intervention is. Body weight claims should be accompanied by body fat data at all times to remove this ambiguity. 1. Question the appropriate duration? 2. Question that if one can demonstrate a health benefit other than fat loss then why do you need to specify a time limit
Kraft Foods R&D	4.2. Claims on body weight maintenance/loss	- (l237) Which criteria should be used to characterise 'obese subjects' (BMI, metabolic parameters,…)? - (l239) On which rationale is based the proposed duration (3 months for evaluating body weight changes? Would demonstrations of less than 3 months be accepted? - (l242) What is the recommended methodology to measure a loss of body fat mass? - (l242) What should be the appropriate expected ranges of efficacy for weight and body fat mass reduction?
McCORMICK France SAS	4.2. Claims on body weight maintenance/loss	• Claims pertaining to changes in body weight (i.e., weight loss) should be permitted to be substantiated with studies of no less than one month duration rather than no less than three months. One month is sufficient to identify a true effect; and longer studies are very difficult to perform in free living subjects – who are the intended target for such claims. Three month studies are more likely to reflect dietary compliance rather than a

		physiological mechanism(s). Intent-to-treat analysis of such studies may be appropriate for meal-replacement claims where a physiological mechanism is not involved. • The title of section 4.2 should not include the term "maintenance" because this topic is covered in section 4.3.
SYNPA	4.2. Claims on body weight maintenance/loss	Lines 237-239: "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 […]". It is not clear what is the rationale behind asking for (at least) 1 month study duration to support a claim on the reduction of energy intake (see line 216) while for weight loss an appropriate study duration of 3 month is indicated. A significant reduction in body weight is by all means possible within 1 or 2 months, so a minimum duration of 1 month for a weight loss study should be sufficient to support such claim while we agree that for a weight maintenance study 3 months might be needed. EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. A study which shows that the control group maintains its weight, but the placebo adds weight should be acceptable as well for a weight maintenance claim. References: Pischon T, Boeing H and Hoffman K et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med 2008; 359:2105-20.
Tate & Lyle Plc	4.2. Claims on body weight maintenance/loss	243: which measures of body composition are validated? Waist-hip ratio or DEXA or otherwise? 250-252: We understand this to mean that EFSA considers that these types of claims are 'out of scope' for health claims. For example, the reduction of energy intake due to a reduced, low or no energy content (which may as an example come from the use of high potency sweeteners) and so form an important part of a calorie controlled diet, are nutrition claims? And thereby information on inclusion/use of such products as part of a calorie controlled diet is not health claims?
Tate & Lyle Plc	4.2. Claims on body weight maintenance/loss	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and

		sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.2. Claims on body weight maintenance/loss	The Industry Group has a number of concerns regarding this part of the guidance. Line 239. The use of three months to allow a health claim is too short. There is a requirement by most obesity experts to have data extending over at least one-to-two years to substantiate an effect on body weight that can be sustained in the longer term. Line 241. Where there is a reduction in body weight which is seen as a health advantage, it is essential that there is data to underpin that the target tissue for weight loss is primarily fat and not lean body mass. Therefore body composition data should be mandatory to assure that it is fat and not lean body mass that is being lost, especially if the panel insist on only three months of data. Line 248. Energy reduction in a diet is the most effective way of producing weight loss. To not allow this as a health claim, where this is part of the weight loss programme, disallows all health claims where weight loss is due to the energy deficit in the diet, as well as allowing inappropriate, nutritionally incomplete diets to be in free use.
Unilever Research & Development	4.2. Claims on body weight maintenance/loss	Lines 238-241 We recommend better guidance on the range of evidence (including duration of effect) that could be acceptable for substantiating claims for weight loss and or claims of weight maintenance (other than reduced rate of gain after weight loss, as described in Section 4.3). For example, we recommend that demonstration of weight loss should be considered from suitably powered studies of 4-12 weeks duration. We also recommend stating that demonstration of a reduced rate of weight gain over 3 months or longer in an intervention population relative to the general population could be a basis for weight maintenance claims.
University of Leeds	4.2. Claims on body weight maintenance/loss	Lines 238-239: It is stated that '…….human studies assessing the effects of a food/constituent on body weight changes need to be of appropriate duration (e.g. three months). The guidance does not justify how or why this particular duration was considered appropriate. In my opinion it seems arbitrary and although this appears to be an example, I fear it will be taken literally and force research to conform to a 12 week intervention irrespective of more important scientific considerations. Weight loss demonstrated over a shorter period (e.g. 2-4 weeks) could still be a valid indicator of effect particularly where this could be demonstrated not to be due to loss of body water (lines 244-245). In support of this there is plentiful evidence that short-term weight loss is a significant predictor of longer-term success at weight loss (e.g. Wadden TA, Letizia KA. Predictors of attrition and weight loss in patients treated by moderate and severe caloric restriction. In: Wadden TA, Van Itallie TB

		(eds). Treatment of the SeriouslyObese Patient. The Guilford Press: New York, 1992, pp. 383–410. Lines 241-242: It is stated that 'The most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass'. My view is that data on body weight should be accompanied by data on body composition rather than saying that measures of body composition could be used as supporting evidence (line 244). Note however that there are issues with measurement and the guidance once more appears rigid in terms of the accepted measurement of body fat.
University of Leeds, Leeds, UK	4.2. Claims on body weight maintenance/loss	Lines 238-239: It is stated that '…….human studies assessing the effects of a food/constituent on body weight changes need to be of appropriate duration (e.g. three months). It is not clear how this particular duration (which seems a little arbitrary and unrealistic) was decided upon. Weight loss demonstrated over a shorter period (e.g. 2-4 weeks) could still be beneficial as this would be unlikely to be attributable to loss of body water alone (lines 244-245). Studies also indicate that short-term weight loss is a significant predictor of longer-term success at weight loss (e.g. Wadden TA, Letizia KA. Predictors of attrition and weight loss in patients treated by moderate and severe caloric restriction. In: Wadden TA, Van Itallie TB (eds). Treatment of the SeriouslyObese Patient. The Guilford Press: New York, 1992, pp. 383–410. Lines 241-242: It is stated that 'The most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass'. In this context it seems important to demonstrate of significant fat loss regardless of the duration of the intervention. It would be preferable to suggest that data on body weight should be accompanied by data on body composition rather than saying that measures of body composition could be used as supporting evidence (line 244).
University of Limerick	4.2. Claims on body weight maintenance/loss	Line 237 and on... In the 21st century, change in body weight (strictly body mass) should not be considered the primary goal. Body mass is too blunt an instrument/biomarker on which to base a health claim. The reference biomarker should be a change in body composition as the primary outcome with specific reference to change in fat tissue mass and lean tissue mass and change in regional distribution of these components appropriate to the health claim under consideration.
VAB-nutrition	4.2. Claims on body weight maintenance/loss	Ln 237-242. Body weight maintenance/loss is said to be beneficial for overweight and obese subjects in the general population. Does this mean that the target population of such claims is restricted to overweight and obese subjects? It could be argued that maintenance of body weight is a beneficial effect for normal weight people as it prevents evolution towards overweight and possibly obesity. Can the Panel comment on this? Ln 244-245. Although it is clear that loss of body water cannot be an acceptable mean to decrease body weight, isn't there any benefit of reduction of body water, when this body water is in excess (oedemas)? Potential

		claims should in this case avoid any reference to body weight. Can the corresponding sentence in the guidance be clarified so that it does not exclude or seem to exclude any claim on body water loss? Ln 250-252. The test food is required to be comparable to the control food, especially in terms of energy. This requirement or at least its wording does not seem appropriate. Indeed, if the beneficial change associated to increased satiety is a decrease in energy intake or in body weight (see ln 193-198), and if this is appropriately assessed in the study, the nutritional composition of the tested food relatively to the control food should not matter. Indeed, it can be hypothesized that the "satiating potency" of a food is not a function of its energy content. For a similar weight ingested, a protein-rich food can be more satiating than a lipid-rich food, while having a lower energy content. It can also be imagined that an energy-dense food could be more satiating that its lower-energy counter-art and that it leads to an overall lesser energy intake, which is the point which matters as it is the one which is linked to decreased weight. Similarly, some foods or food ingredients may generate satiety by other means that their nutritional content (specific flavors, for example). Others. 1-Weight management in the long term often proceeds from dietary changes involving more than a specific food or ingredient. It might be –for example- that a diet lowered in fat, or increased in proteins, or providing a lower glycaemic load will produce a weight loss. It can also be that a set of different foods (e.g. "foods with reduced fat content" or "foods with enhanced protein content") can be proposed as susceptible to bear a weight reduction claim(or an associated claim). In both these cases, food characterization might be difficult to provide in a manner which would fulfill EFSA's requirements. Can the panel comment on this question and provide appropriate guidance? 2- Overweight or obese populations can be diverse. They can gather people with different BMIs and of various ages. When extrapolating the result from the studied to the target population, should the BMI (or age) range be the standard deviation of the sample? Or the min-max range? Or any other measure? Diversity can also come from gender difference. In that respect, can a study performed on women can be extrapolated to both genders, provided adequate justification is given? If not, or if not satisfactory justification can be given, what is the minimal proportion of the studied population that should belong to a gender? In the same area, can the Panel clarify whether or not the results from a study carried out in a population composed of (i) both obese and overweight adult subjects or (ii) only obese adult subjects can be extrapolated to the general adult population?
Arla Foods a.m.b.a.	4.3. Claims on body weight maintenance	The paragraph includes weight maintenance after weight loss in overweight and obese persons. We think that achieving a weight maintenance in normal weight persons also is a beneficial effect i.e. weight maintenance in

	after weight loss	normal weight persons is always beneficial. How could this be addressed? We think that a six month period of weight maintenance after weight loss is a long period. If very clear results are obtained during a shorter study, how will that be considered?
Ashwell Associates Europe Ltd	4.3. Claims on body weight maintenance after weight loss	255 Very pleased to see that maintenance of a weight loss without achieving normal body weight is considered a beneficial effect.
Ashwell Associates Europe Ltd	4.3. Claims on body weight maintenance after weight loss	237 Agree that the loss of body water is not a beneficial change. However, loss of body water due to mobilisation of liver and muscle glycogen is usually over by two weeks when on a reduced calorie regime. The suggestion that 3 months is appropriate duration is an unrealistic requirement for study length. More leeway should be given here for studies longer than two weeks. Even short term weight loss programmes (2-4 weeks)can motivate consumers to achieve a reduction in body weight over period of time they see as attainable, by making some relatively simple dietary changes. Having achieved this early short-term success, individuals are more likely to continue to make dietary and lifestyle changes in order to consolidate their achievement, or to continue on to further weight loss. This is supported by studies which indicate that people, who believe that they can control their weight, continue to engage in effective weight control behaviours (Byrne SM. Psychological aspects of weight maintenance and relapse in obesity. J Psychosom Res 2002;53:1029-36.). Other work suggests that short-term weight loss is a significant predictor of successful longer-term weight loss.
BENEO Institute	4.3. Claims on body weight maintenance after weight loss	Line 253: Also maintenance of a stable (not essentially normal) body weight without preceding weight loss is a beneficial physiological effect, if a control group without intervention or on a placebo shows increases in body weight over an intervention period. Line 258: The time considered as “appropriate duration” is exemplified as “six months follow-up after weight loss”. Clarification should be provided that this is not meant as the “minimum” or “maximum” follow-up/intervention length required. The guidance should acknowledge that periods of other than 6 months e.g. 3 or 12 months may be appropriate durations, too.
DHI Water Environment Health	4.3. Claims on body weight maintenance after weight loss	ln 258: Does the duration of the study have any bearing on what can be claimed? E.g. if the duration of the study was six months, should the claim elaborate on the fact that the effect has not been proven beyond six months duration?
DSM Nutritional Products	4.3. Claims on body weight maintenance after weight loss	lines 254-255 "Maintenance of weight loss can be interpreted as contribution to the maintenance of a normal body weight after significant weight loss.”:

		Clarification is sought as to what would be considered a "significant weight loss". lines 257-259 "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. ": Could EFSA please specify why in this case the study duration is seen differently than under i.e. 4.2 maintenance of body weight? (i.e. 6 month vs. 3 month). Three months would seem to us to be an acceptable period in both cases. It is important is to specify against the control situation both for weight loss as well as weight maintenance. lines 261-265 "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.": In obesity, a low fat oxidation capacity is observed and considered as a risk factor to become obese. Therefore increase in fat oxidation can be considered as a beneficial effect per se.
ELC	4.3. Claims on body weight maintenance after weight loss	Lines 257-259 Could EFSA please specify why in this case the study duration is seen differently than under i.e. 4.2 maintenance of body weight? (I.e. 6 month versus 3 month). Three months would seem an acceptable and sufficient period in both cases.
European Responsible Nutrition Alliance	4.3. Claims on body weight maintenance after weight loss	Line 258. It would be good if EFSA could clarify what scientific rationale exist to justify that in this case the study duration must be seen differently than under i.e. 4.2, maintenance of body weight? (i.e. 6 month vs. 3 month). Three months would seem an acceptable period in both cases.
FederSalus	4.3. Claims on body weight maintenance after weight loss	253 To avoid any misunderstanding about "conditions under which weight maintenance is achieved need to be specified" the health claim should prove that during 6 months follow up people's alimentation (by alimentary diary), appetite (by VAS) and energy expenditure (by arm band) should be constant.
HarlandHall Associates	4.3. Claims on body weight maintenance after weight loss	Line 239 What is the rationale for the choice of 3 month for weight loss studies - much of the literature contains studies

		conducted for shorter periods. Hence what the rationale is for 3 month and is it scientifically based? There is concern that small and medium sized enterprises who rely on the published scientific literature to support claims, will have a much restricted use of the scientific literature by the recommendation of this longer time period. While it is considered that studies need to be of a reasonable period to ensure a sustained weight loss, I am unsure of an advantage of 3 months compared to say 8 weeks. The main aspect of longer term studies is a demonstration of better compliance, rather than better assessment of weight loss. The value of long-term RCT to assess weight loss as a result of significant dietary changes is questionable as lifestyles and behaviours have to be taken into consideration, alongside the environmental, cultural and social factors that influence them. Causality becomes much harder to establish because of this interplay of factors.
ILSI Europe aisbl	4.3. Claims on body weight maintenance after weight loss	253 Can clinical studies include an intervention on lifestyle (e.g. physical activity)? For instance, test product + physical activity vs. control product + physical activity. 255 What is considered as a significant weight loss? 258 Could EFSA kindly specific why in this case the study duration is seen differently than under i.e. 4.2 maintenance of body weight? (i.e. 6 month vs. 3 month). Three months would appear to be an acceptable period in both cases. 258-259 Is a simple follow-up during normal life habits considered a specific enough condition?
Kraft Foods R&D	4.3. Claims on body weight maintenance after weight loss	- (l255) what is considered as a significant weight loss? - (l258) How is substantiated the appropriate duration for body weight maintenance after weight loss (e.g. six months)?
NB Consulting	4.3. Claims on body weight maintenance after weight loss	Lines 237 - 241 The consultation paper mentions that a sustained weight loss is a health benefit. However, even a 5% weight loss that can be achieved within 4 weeks in the moderately obese and has health benefits. For example in women weighing 90 kg a weight loss of 1kg per week is acceptable (based e.g. on UK NICE Guidance). Such weight loss can be achieved on an ad lib diet and significant fat loss can also be demonstrated over such a period. Further a 5% weight loss can also confer significant other health benefits such as reduced blood pressure and reduced cholesterol. It is thus not reasonable to expect all intervention studies to go beyond

		one month. The cost of longer studies is a great disadvantage for SMEs. The difficulty in finding subjects who are able to participate in a study for as long as 3 months adds impracticality and could lead to high drop out rates. Lines 241-245 EFSA states a benefit of weight loss is fat loss. However, surely other consequential health benefits of weight/fat loss such as lower blood pressure, lower blood lipids and better blood glucose control are more important. In reference to comments on earlier sections, these parameters can be measured in a "before and after" study design, especially in studies where ad lib intake is used, and a specific control is not required for comparison; indeed a control diet that did not result in weight/fat loss might even be considered unethical. Lines 254-259 Weight maintenance is mentioned in the context of maintenance of weight lost with a requirement for 6 months study as a follow up. Again this is impractical in terms of intervention studies and a shorter time scale should be acceptable, for example 2 months. Longer term maintenance is more a matter of individual compliance than a reflection of the ability of a food to assist in weight maintenance which can be demonstrated over a shorter time frame.
SYNPA	4.3. Claims on body weight maintenance after weight loss	line 258 "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)" Could EFSA please specify why in this case the study duration is seen differently than under i.e. 4.2 maintenance of body weight? (i.e 6 month vs 3 month). Three months would seem to us to be an acceptable period in both cases.
Tate & Lyle Plc	4.3. Claims on body weight maintenance after weight loss	258 Why are at least a six months studies on weight maintenance after weight loss needed while body weight maintenance/loss studies just need to last for 3 months. What would be the rationale for it being longer?
Tate & Lyle Plc	4.3. Claims on body weight maintenance after weight loss	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.3. Claims on body weight maintenance	Line 257. There is no clear guidance on what is meant as weight maintenance after weight loss. The panel need to put some figures behind this: for example, a variation of plus or minus 3% of minimal weight achieved

	after weight loss	during the weight loss phase of management over a period of time of at least one year. Currently there is no clarity as to what is meant by weight loss maintenance. Line 258. Again the recommendation for body weight loss maintenance is for at least one year of study and not six months after the initial weight loss.
University of Limerick	4.3. Claims on body weight maintenance after weight loss	Line 254 and on.... Again, "normal" body mass is not readily defined, theerfore reference to the maintenance of "normal" body mass is ill-advised as a guideline for a scientific requirement in substantiation of a health claim. The comment related to section 4.3 is as relevant here, so is re-stated In the 21st century, change in body weight (strictly body mass) should not be considered the primary goal. Body mass is too blunt an instrument/biomarker on which to base a health claim. The reference biomarker should be a change in body composition as the primary outcome with specific reference to change in fat tissue mass and lean tissue mass and change in regional distribution of these components appropriate to the health claim under consideration.
Wrigley Science Institute	4.3. Claims on body weight maintenance after weight loss	Lines 253-259 –It is noted that maintenance of weight loss without achieving normal weight is considered a benefit to consumers. To demonstrate that the effect lasts for 6 month after weight loss seems reasonable. However, it is probably unreasonable to make the definition as maintaining all of weight loss since studies suggest that most, if not all, behavioral weight loss interventions resulted in weight regain of various levels. There is no established definition of successful weight loss maintenance after weight loss. A suggested definition of successful maintenance of lost weight was proposed by Wing and Hill (Annu Rev Nutr. 2001;21:323-341) as "intentionally losing at least 10% of initial body weight and keeping it off for at least 1 year". In line with guidance from the panel, the definition might reasonably be considered as losing at least 10% of initial body weight after the trial and maintaining this at 6 month after the trial.
BENEO Institute	4.4. Claims on increased fat oxidation	Line 261-262: Subjects prone to obesity show reduced ability to oxidize fat. Furthermore, in obese subjects undergoing a weight loss treatment, a low rate of fat oxidation at the end of the weight-reduction period predicts weight gain in the following year (Riccardi et al 2004). A reduced or decrease of fat oxidation could be regarded as risk factor for the development of overweight. An increase in fat oxidation or a lower suppression of fat oxidation after acute or chronic consumption of a food/constituent should thus be considered as beneficial effect per se. Line 262: Clarification should be provided what is accepted as "sustained increase". Line 263: A sustained increase of fat oxidation should also serve as evidence for a mechanism by which a

		reduction in body weight can be achieved, i.e. not only limited to body fat related claims.
European Responsible Nutrition Alliance	4.4. Claims on increased fat oxidation	Line 261. We would not agree with the position that sustained increased fat oxidation per se is not considered a beneficial effect but needs to be associated to a reduction in body fat . Linking both concepts together is an undue restrictive attitude. Sustained increased fat oxidation should be considered as a beneficial effect per se.
FederSalus	4.4. Claims on increased fat oxidation	260 For human studies as an indirect measure of fat oxidation may be used the measure of respiratory exchange ratio obtained from indirect calorimetry .
ILSI Europe aisbl	4.4. Claims on increased fat oxidation	261 Would "An increase in fat oxidation after chronic (rather than "acute") consumption of a food" be considered a beneficial physiological effect per se"? 261-265 Would the Panel consider decreased fat oxidation as a risk factor for overweight and obesity, in the context of a disease risk (factor) reduction claim? How is a 'sustained increased in fat oxidation' defined? Can the period of chronic consumption be defined? Would the Panel consider "an increase in fat oxidation" as beneficial for health in the specific context of active body weight reduction or reduced-body weight maintenance, when it is known that a "low rate of fat oxidation" is a "risk factor" for body weight gain and regain?
Kraft Foods R&D	4.4. Claims on increased fat oxidation	- (l262) what is the appropriate period of time to demonstrate the sustained effect? - (l264) how the mechanisms of actions could be integrated in the wording?
Tate & Lyle Plc	4.4. Claims on increased fat oxidation	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD	4.4. Claims on	Line 262. This would only be the case where there was also a negative energy balance in relation to food

Industry Group	increased fat oxidation	consumption. Increased fat oxidation will occur in the presence of low carbohydrate in the diet but increased amounts of protein and fat to isocaloric levels will result in increased fat oxidation but no weight loss.
AESGP - Association of the European Self-Medication Industry	4.5. Claims on the reduction of body fat	Would it be possible to make reference to a suitable measurement of body fat?
Arla Foods a.m.b.a.	4.5. Claims on the reduction of body fat	The paragraph states that reduction of body fat in over weight or obese person is beneficial. We think that this could be beneficial for normal weight persons as well. It is also stated that changes in body fat should be measured with appropriate methods. It is good if those methods could be specified.
Ashwell Associates Europe Ltd	4.5. Claims on the reduction of body fat	269 Again suggest that 3 months is not given as an appropriate duration for reasons given previously. This is the section to spell out the suggested methods for measuring reduction of body fat. Currently the method of doing this by measuring fat oxidation is given too much prominence. A later section (line 289) mentions imaging techniques. These should be mentioned here alongside impedance measurements since many of these have been validated against imaging techniques (Maddalozzo, G. F., Cardinal, B. J., Snow, C. M. (2002) Concurrent Validity of the BOD POD and Dual Energy X-Ray Absorptiometry Techniques for Assessing Body Composition in Young Women. Journal of the American Dietetic Association, 102(11): pp1677-1679). Plethysmography, of course, preceded both of these techniques (Mccrory, M. A., Gomez, T. D.. Bernauer, E. M., Molé, P. A. (1995) Evaluation of a new air displacement plethysmograph for measuring human body composition. Medicine and Science in Sports and Exercise, 27(12): pp1692-1697.)
BENEO Institute	4.5. Claims on the reduction of body fat	Line 267: Clarification should be provided what is understood and accepted as “sustained reduction”. Line 268: Reduction of body fat is not only a beneficial effect to overweight and obese individuals (defined by their BMI) and should not only be limited to them. It should also be considered as beneficial effect to normal weight people, for instance those at the upper BMI limit being at risk for becoming overweight.Line 270: The time regarded as “appropriate duration” is exemplified as “three months”. Clarification should be provided that this should not be understood as “minimum” or “maximum” intervention length required. The guidance should acknowledge that periods of other than 3 months e.g. 2 or 6 months may be appropriate durations, too. Line 271: Further clarification should be included in the guidance document on the different measures of body fat composition analysis considered appropriate by EFSA and those which are not considered by EFSA as methods with appropriate validity and precision. Well established and generally in science accepted measures for body fat composition include bioelectrical impedance analysis (BIA), air displacement plethysmography (ADP), Dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT).

Danone Research	4.5. Claims on the reduction of body fat	270-271 What methods are appropriate to measure changes in body fat? General comment For reduction of body fat claims, we would like to know what should be the primary criteria in clinical studies and possible secondary criteria.
DSM Nutritional Products	4.5. Claims on the reduction of body fat	LINES 267-268 "A sustained reduction in body fat, and particularly abdominal fat, is a beneficial physiological effect for overweight and obese subjects in the general population.": The reduction of abdominal fat can also be beneficial for normal weight persons, not only for overweight and obese. It might be for example of benefit in the elderly which are often normal or even underweight but where the muscle mass decreases while fat mass increases. This should be considered in this passage (see also points 4.6, 4.7 and 4.8, specifically line 299) EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death.
ELC	4.5. Claims on the reduction of body fat	Lines 267- 268 The reduction of abdominal fat can also be beneficial for normal weight persons, not only for the overweight and obese. It might be, for example, of benefit in the elderly who are often normal or even underweight but where the muscle mass decreases while fat mass increases. This should be considered in this passage as under paragraphs 4.6, 4.7 and 4.8. EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as

		supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) [Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med. 2008: Nov 13; 359(20):2105-20] general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death.
European Responsible Nutrition Alliance	4.5. Claims on the reduction of body fat	Line 268. We believe that reduction of abdominal fat can also be beneficial for normal weight persons, not only for overweight and obese. It might be for example of benefit in the elderly which are often normal or even underweight but where the muscle mass decreases while fat mass increases. It would be helpful if EFSA would consider this (as well as in chapters 4.6, 4.7 and 4.8, and specifically in line 299).
ILSI Europe aisbl	4.5. Claims on the reduction of body fat	266 Is it possible to have a wording of a claim mentioning ‘body shape’ when the health beneficial effect is a reduction in body fat mass for example? If only the fat mass is reduced in the periphery but not visceral fat, is this considered beneficial to health? 267 Would it be possible to obtain a claim on "reduction of body fat" by showing a decrease of fat mass, without decrease of body weight linked to an increase of lean mass related to an increase of physical exercise? 268 Does the statement "overweight and obese subjects in the general population" mean that the “general healthy” population can include overweight and obese subjects? Ln 267-268 Lean people may also want to reduce their amount of body fat, and change their body shape; such effects are therefore beneficial. Apart from that people may feel better ‘esthetically’ (an effect also involved in increasing lean body mass; § 4.6), they will move ‘further away’ from being overweight. It is comparable to decreasing LDL- or total cholesterol within the ‘normal’ range, which is also considered to be relevant for health. 268 Could individuals with normal weight also be targeted by the claim, as some might be at risk of becoming overweight? The reduction of abdominal fat can also be beneficial for normal weight persons, not only for overweight and obese. It might be for example of benefit in the elderly which are often normal or even underweight but where the muscle mass decreases while fat mass increases. This should be considered in this passage (see also points 4.6, 4.7 and 4.8, specifically line 299). EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA.How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence as well (Pischon et al 2008 N Engl J Med. 359: 2105-20). 271 Apart from indirect calorimetry, which methods would be appropriate to measure fat oxidation? What should be understood by “appropriate validity and precision”? How is ‘sustained’ defined here?

Kraft Foods R&D	4.5. Claims on the reduction of body fat	- (l268) why individual with normal weight are not targeted by the claim, as some might be at risk of being overweight? - (l270) what is the appropriate period of time to demonstrate the sustained effect? How it is substantiated? - (l271) which methods would be appropriate to measure fat oxidation? What should be understood by "appropriate validity and precision"
MRC Human Nutrition Research	4.5. Claims on the reduction of body fat	Section 4.1. Lines 232-235. We suggest that this sentence is slightly reworded for clarity and consistency with the previous sections. We propose: "An increase in energy expenditure after acute consumption of a food is not considered a beneficial physiological effect per se and so would not be considered sufficient for substantiation. However, a sustained increase in energy expenditure may be one of the mechanisms by which a reduction in body weight can be achieved. Therefore measures on energy expenditure can be used as supportive evidence for a mechanism by which the food/constituent could exert weight loss". Section 4.5. Lines 271-275. We suggest that this sentence is re-worded for clarity and consistency with the previous text. We propose: "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, although it is not a physiological effect per se. Therefore measures of fat oxidation alone cannot be considered sufficient to substantiate a claim on the reduction of body fat but could be used as evidence for a mechanism by which the food/constituent could exert the claimed effect".
SYNPA	4.5. Claims on the reduction of body fat	lines 267-268 "A sustained reduction in body fat, and particularly abdominal fat, is a beneficial physiological effect for overweight and obese subjects in the general population." The "overweight and obese subjects in the general population" is noticed. Does it mean that the general population can include overweight and obese subjects that are by definition, not considered as healthy? And is it possible to obtain a claim on "reduction of body fat" face to evidences showing a decrease of fat mass, without decrease of body weight linked to an increase of lean mass related to an increase of physical exercise? The reduction of abdominal fat can also be beneficial for normal weight persons, not only for overweight and obese. It might be for example of benefit in the elderly which are often normal or even underweight but where the

		muscle mass decreases while fat mass increases. This should be considered in this passage (see also points 4.6, 4.7 and 4.8, specifically line 299) EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. How should this be measured to be acceptable to EFSA and in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well, as according to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. line 286: "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…." See also comments for Section 4.2 and 4.5. Reduction in waist circumference can provide additional supporting evidence for weight loss and reduction of body fat, also when they are not measured by imaging techniques. Further it is not clear why a study duration of 3 months is indicated for reduction of waist circumference as a significant reduction in waist circumference is possible within 1 or 2 months, so a minimum duration of 1 month for reduction in waist circumference should be sufficient to support such claim.
Tate & Lyle Plc	4.5. Claims on the reduction of body fat	If only the fat mass is reduced in the periphery but not visceral fat, is this considered beneficial to health? 271: what methods are validated to measure body fat? DEXA, waist-hip ration, or otherwise?
Tate & Lyle Plc	4.5. Claims on the reduction of body fat	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD,

		diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.5. Claims on the reduction of body fat	Line 272. If claims on increase fat oxidation are made them body composition data needs to be presented simultaneously.
University of Leeds	4.5. Claims on the reduction of body fat	Lines 269-270: It is stated that '…….human studies assessing the effects of a food/constituent on body fat changes need to be of appropriate duration (e.g. three months)'. Again, the rationale for this particular duration is not evident. In this section it would be useful to specify the recommended methods for measuring body fat but there is a need to consider a wider range of methods as these may be more or less appropriate and cost effective to particular study designs. Methods utilising bioimpedance and air displacement plethysmography should be considered alongside measures of fat oxidation (indirect calorimetry).
University of Leeds, Leeds, UK	4.5. Claims on the reduction of body fat	Lines 269-270: It is stated that '…….human studies assessing the effects of a food/constituent on body fat changes need to be of appropriate duration (e.g. three months). It is not clear how this particular duration (which seems a little arbitrary and unrealistic) was decided upon. In this section it would be useful to specify the recommended methods for measuring body fat. Methods utilising bioimpedance and air displacement plethysmography should be considered alongside measures of fat oxidation (indirect calorimetry).
University of Limerick	4.5. Claims on the reduction of body fat	Line 267 Qualification of change in whole body fat mass or body fat as a percentage of body mass or whole body tissue mass should be stated. Line 269 It is difficult to stipulate an "appropriate" duration of intervention if the outcome measure in substantiation of a claim is a change in body fat mass (however feined whole body, regional etc) as the "beneficial" effect, however stated, could be attained within a couple of weeks or after many years. however, should the health claim refer to a "sustained" change in fat mass, then the period related to that claim would have to be claerly stated and achieved.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	4.5. Claims on the reduction of body fat	Given that it is widely used in medicine, is the body fat measurement by Magnetic Resonance Imaging (MRI) acceptable ?
AESGP - Association	4.6. Claims on the	Would it be possible to make reference to a suitable measurement of lean body mass?

of the European Self-Medication Industry	increase of lean body mass	
Arla Foods a.m.b.a.	4.6. Claims on the increase of lean body mass	We think that a sustained increase in lean body mass may be beneficial not only for physically active persons if not a weight gain is achieved. We also think a reduced loss of lean body mass not only in overweight and obese during energy restriction, but also in normal weight persons during energy restriction/food restriction due to e.g. allergies, IBS etc, can be considered a beneficial effect.
Arla Foods a.m.b.a.	4.6. Claims on the increase of lean body mass	We think that a sustained increase in lean body mass may be beneficial not only for physically active persons if not a weight gain is achieved. We also think a reduced loss of lean body mass not only in overweight and obese during energy restriction, but also in normal weight persons during energy restriction/food restriction due to e.g. allergies, IBS etc, can be considered a beneficial effect.
BENEO Institute	4.6. Claims on the increase of lean body mass	Line 277: Clarification should be provided what is understood and accepted as "sustained increase". Line 282: The time regarded as "appropriate duration" is exemplified as "three months". Clarification should be provided that this is not meant as the "minimum" or "maximum" intervention length required. The guidance should acknowledge that periods of other than 3 months e.g. 2 or 6 months may be appropriate durations, too. Line 283: Further clarification should be included in the guidance document what is to be understood as appropriate validity and precision. The guidance document should clearly identify the different methods of lean body mass composition considered appropriate by EFSA and those which are not considered by EFSA as methods with appropriate validity and precision. Well established and generally in science accepted measures for lean body mass composition include bioelectrical impedance analysis (BIA), air displacement plethysmography (ADP), Dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT).
Danone Research	4.6. Claims on the increase of lean body mass	277-278 We would like the Panel to clarify the definition of physically active subjects. Can overweight and obese subjects be included? Could an increase of lean body mass in these populations be considered as a beneficial physiological effect? General comments Could a reduced loss of lean body mass be considered as a beneficial physiological effect in certain target populations? For instance in elderly subjects, as there is a physiological loss of lean mass due to aging process. If yes, what should the primary criteria in clinical studies be and what are the possible secondary criteria?

		Could an intervention combining the consumption of a food/constituent and a lifestyle intervention (e.g. physical activity) substantiate a claim on increase of lean body mass? If yes, what would be the appropriate design needed to distinguish the effects of the test product itself from those of the intervention including lifestyle changes? For increase of lean body mass claims, we would like to know what should the primary criteria in clinical studies be and what are the possible secondary criteria.
European Responsible Nutrition Alliance	4.6. Claims on the increase of lean body mass	Line 282. It would be helpful if EFSA could specify what methods it would judge acceptable for such measurements. EFSA states that the most obvious health benefit of reducing body weight for overweight and obese subjects is the concomitant reduction in body fat mass, and therefore concomitant reduction in body fat is considered as supportive evidence by EFSA. It would helpful if EFSA could clarify how this should be measured to be acceptable in this context? The reduction in waist circumference and waist-to-hip ratio should be considered as supportive evidence in this context as well. According to Pischon et al (2008) general adiposity and abdominal adiposity are associated with the risk of death in more than 14,000 subjects and they support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death. Line 286. See also comments for Section 4.2 and 4.5. We feel that reduction in waist circumference can provide additional supporting evidence for weight loss and reduction of body fat, also when they are not measured by imaging techniques. It would be good if EFSA could explain why a study duration of 3 months is indicated for reduction of waist circumference as a significant reduction in waist circumference is possible within 1 or 2 months, so a minimum duration of 1 month for reduction in waist circumference should be sufficient to support such claim.
HFMA	4.6. Claims on the increase of lean body mass	Line 278. Increase in lean body mass could also be a beneficial physiological effect in elderly people, and it would be helpful for the guidance to refer to this also.
ILSI Europe aisbl	4.6. Claims on the increase of lean body mass	277 What is the appropriate period of time to demonstrate the sustained effect? How it is substantiated?

		277-280 We recommend explicitly mentioning slowing or prevention of naturally-occurring lean body mass loss in older adults (e.g. over the age of 50) and inactive individuals as a physiological benefit. 283 What methods are validated to measure lean body mass? DEXA or otherwise? What is 'appropriate validity and precision'?
Kraft Foods R&D	4.6. Claims on the increase of lean body mass	- (l277) what is the appropriate period of time to demonstrate the sustained effect? How it is substantiated? - (l282) which methods would be appropriate to measure fat oxidation? What should be understood by "appropriate validity and precision"
Tate & Lyle Plc	4.6. Claims on the increase of lean body mass	283: what methods are validated to measure lean body mass? DEXA or otherwise?
Tate & Lyle Plc	4.6. Claims on the increase of lean body mass	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.6. Claims on the increase of lean body mass	Line 277. Lean body mass may not tell the whole story and it may be important to expect information about function. For example, lean loss may appear to be quite high in situations where there may be a reduction of muscle lipid and improvement in muscle function.
Unilever Research & Development	4.6. Claims on the increase of lean body mass	Lines 277-280 We recommend explicit mention of slowing or prevention of naturally-occurring lean body mass loss in older adults (e.g. over the age of 50) and inactive individuals as a physiological benefit.

University of Limerick	4.6. Claims on the increase of lean body mass	Line 277 Qualification of change in whole body lean tissue mass or fat-free mass is required. Equally, the beneficial effect of the maintenance of lean tissue mass is not exclusive to physically active subjects. This sentence needs to be revised accordingly. Line 281 It is difficult to stipulate an "appropriate" duration of intervention if the outcome measure in substantiation of a claim is a change in lean tissue mass (however defined, whole body, regional etc). However, should the health claim refer to a "sustained" change in lean tissue mass, then the period related to that claim would have to be clearly stated and achieved. The "3 month" period relates to most studies undertaken to achieve a gain in lean tissue mass and has limited relevance to "reduced" loss of lean tissue mass in studies where the primary objective has been to reduce body mass by dietary restriction.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	4.6. Claims on the increase of lean body mass	Given that it is widely used in medicine, is the body fat measurement by Magnetic Resonance Imaging (MRI) acceptable ?
Ashwell Associates Europe Ltd	4.7. Claims on the reduction of waist circumference	289Suggest that 'imaging techniques' is clarified. Otherwise it could be taken to mean computed tomography, which although recognised as the gold standard for measuring fat distribution, would be very expensive, assume imaging techniques here refers to DEXA which is a more routine measure.
Ashwell Associates Europe Ltd	4.7. Claims on the reduction of waist circumference	284 I suggest that a sustained significant reduction in waist circumference is even more important than a reduction in body weight since there is now overwhelming evidence for the benefits of reducing abdominal obesity, as opposed to total obesity . The requirement to validate these changes by other methods such as imaging techniques puts a high burden on the experimenter and is not needed when there are so many studies which have validated the change in waist circumference with the change in abdominal obesity (eg Poirier P, Despres JP. Waist circumference, visceral obesity, and cardiovascular risk. J Cardiopulm Rehabil 2003;23:161-9). It would be better guidance to say that sustained significant reduction in waist circumference is a beneficial physiological effect. At least allow it to be claimed as supporting evidence with significant weight reduction. Again , suggesting a 3 month duration even of only given as an example is too long a duration. The important point about duration is that it is over two weeks to avoid body water losses being exaggerated and that significant decreases in relevant outcome measures should be quoted. I believe that waist circumference is one of these.

		As a further point, the use of waist-to-height ratio is becoming increasingly popular and has been shown to be an even greater predictor of health risk than waist circumference(Browning L, Hsieh S and Ashwell M (2010). "A systematic review of waist-to-height ratio as screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value." Nutrition Research Reviews 23(2): 247-269). One of the reasons for this is that it is a better correlate with abdominal obesity, especially in Asian populations. Both waist circumference and waist-to-height ratio have been shown correlate well with levels of visceral fat as measured by computed tomography. Imaging techniques such as DEXA are no better. (Micklesfield LK, Evans J, Norris SA, Lambert EV, Jennings C, Joffe Y, Levitt NS and Goedecke JH (2010). "Dual-energy X-ray absorptiometry and anthropometric estimates of visceral fat in Black and White South African Women." Obesity (Silver Spring) 18(3): 619-24)
Ashwell Associates Europe Ltd	4.7. Claims on the reduction of waist circumference	284 I suggest that a sustained significant reduction in waist circumference is even more important than a reduction in body weight since there is now overwhelming evidence for the benefits of reducing abdominal obesity, as opposed to total obesity . The requirement to validate these changes by other methods such as imaging techniques puts a high burden on the experimenter and is not needed when there are so many studies which have validated the change in waist circumference with the change in abdominal obesity (eg Poirier P, Despres JP. Waist circumference, visceral obesity, and cardiovascular risk. J Cardiopulm Rehabil 2003;23:161-9). It would be better guidance to say that sustained significant reduction in waist circumference is a beneficial physiological effect. At least allow it to be claimed as supporting evidence with significant weight reduction. Again , suggesting a 3 month duration even of only given as an example is too long a duration. The important point about duration is that it is over two weeks to avoid body water losses being exaggerated and that significant decreases in relevant outcome measures should be quoted. I believe that waist circumference is one of these. As a further point, the use of waist-to-height ratio is becoming increasingly popular and has been shown to be an even greater predictor of health risk than waist circumference(Browning L, Hsieh S and Ashwell M (2010). "A systematic review of waist-to-height ratio as screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value." Nutrition Research Reviews 23(2): 247-269). One of the reasons for this is that it is a better correlate with abdominal obesity, especially in Asian populations. Both waist circumference and waist-to-height ratio have been shown correlate well with levels of visceral fat as measured by computed tomography. Imaging techniques such as DEXA are no better. (Micklesfield LK, Evans J, Norris SA, Lambert EV, Jennings C, Joffe Y, Levitt NS and Goedecke JH (2010). "Dual-energy X-ray absorptiometry and anthropometric estimates of visceral fat in Black and White South African Women." Obesity (Silver Spring) 18(3): 619-24)

BENEO Institute	4.7. Claims on the reduction of waist circumference	Line 285: Changes in waist circumference are considered by the WHO to reflect changes in risk factors for cardiovascular disease and other forms of chronic diseases. Waist circumference is also one of the criteria for the metabolic syndrome. According to the National Institutes of Health, a high Waist Circumference (WC) is associated with an increased risk for type 2 diabetes, dyslipidemia, hypertension and cardiovascular disease. Reduction of Waist Circumference should thus be considered as beneficial effect per se, without the requirement to show in parallel changes of abdominal/visceral fat with imaging techniques for the substantiation of the claimed effect.
DSM Nutritional Products	4.7. Claims on the reduction of waist circumference	LINES 286-290 "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….": See also comments for Section 4.2 and 4.5.. Reduction in waist circumference can provide additional supporting evidence for weight loss and reduction of body fat, also when they are not measured by imaging techniques. Further it is not clear why a study duration of 3 months is indicated for reduction of waist circumference as a significant reduction in waist circumference is possible within 1 or 2 months, so a minimum duration of 1 month for reduction in waist circumference should be sufficient to support such claim.
European Nutraceutical Association (ENA)	4.7. Claims on the reduction of waist circumference	Line 284-293 We feel to understand the intention behind this paragraph (that a reduction of waist circumference without a reduction of visceral fat could be achieved by short term programmes). However the statement "A reduction in waist circumference may not … be considered a beneficial physiological effect in isolation" is very critical to us. Furthermore the mandatory demand of "e.g. imaging techniques" to proof reduction of visceral fat is disproportional to us (consider the financial investment!). We have to keep in mind that waist circumference is a well-established risk factor for obesity related diseases. Therefore this parameter has to be valued accordingly. Here we ask that this paragraph be more detailed with greater attention paid to the value of waist circumference as an important biomarker.
ILSI Europe aisbl	4.7. Claims on the reduction of waist circumference	285-293 Waist circumference is recognised as a surrogate marker for abdominal obesity and also one of the 5 criteria for metabolic syndrome. Reduction of waist circumference should be considered as a beneficial effect. It can provide additional supporting evidence for weight loss and reduction of body fat, also when they are not

		measured by imaging techniques. Further it is not clear why a study duration of 3 months is indicated for reduction of waist circumference as a significant reduction in waist circumference is possible within 1 or 2 months, so a minimum duration of 1 month for reduction in waist circumference should be sufficient to support such claim
KELLOGG"S	4.7. Claims on the reduction of waist circumference	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" We would request that waist circumference data should be permitted as accompanying evidence We would request again that and appropriate duration is not specified with an example. The 3 month time frame is arbitrary and should be evaluated on a case by case basis.
Kraft Foods R&D	4.7. Claims on the reduction of waist circumference	- (l290) what is the appropriate period of time to demonstrate the sustained effect? How it is substantiated?
Tate & Lyle Plc	4.7. Claims on the reduction of waist circumference	If only the fat mass is reduced in the periphery but not visceral fat, is this considered beneficial to health?
Tate & Lyle Plc	4.7. Claims on the reduction of waist circumference	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.7. Claims on the reduction of waist	Line 285. During all weight loss studies worldwide, a reduction in waist circumference has always been mirrored by a reduction in visceral fat - it is now accepted by all obesity experts that waist reduction can be

	circumference	taken to imply reduction in visceral fat. The above requirement for measurement of visceral fat by MRI or other means should not be a prerequisite for making such claims where there is evidence of a clear reduction in waist circumference. This is similarly the case for parameters of metabolic syndrome and waist reduction and should not need to be trialled over and over again – this is "waste" of resource and contributes to the increased production of CO2.
University of Leeds	4.7. Claims on the reduction of waist circumference	Lines 286-290: The requirement to validate changes in waist circumference against changes in abdominal/visceral fat measured using imaging techniques places an expensive and unnecessary limitation on potential experiments. The literature shows that there are many examples of validation of waist circumference against abdominal obesity (e.g. Poirer and Despres 2003, J Cardiopulm Rehabil 23: 161-9). It would also be helpful if 'imaging techniques' (Line 289) could be more precisely specified.
University of Leeds, Leeds, UK	4.7. Claims on the reduction of waist circumference	Lines 286-290: The requirement to validate changes in waist circumference against changes in abdominal/visceral fat measured using imaging techniques places an expensive and unnecessary burden on experimenters since many existing studies have already validated waist circumference against abdominal obesity (e.g. Poirer and Despres 2003, J Cardiopulm Rehabil 23: 161-9). Furthermore, the term 'imaging techniques' (Line 289) needs clarification.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	4.7. Claims on the reduction of waist circumference	Given that it is widely used in medicine, is the body fat measurement by Magnetic Resonance Imaging (MRI) acceptable ?
Wrigley Science Institute	4.7. Claims on the reduction of waist circumference	Lines 285-303. It has been argued that waist circumference is a good measure of visceral fat. In addition, it has also been argued that waist circumference is a better predictor of health risk than BMI. From a practitioner's point of view, the requirement seems too strict and unpractical to have a measure of body composition by imaging to fulfill requirement to show evidence of the change in body compositions. Therefore, the panel might consider moderating its position to permit changes in waist circumference alongside weight loss and/or change in body composition or improvement in metabolic status.
Ashwell Associates Europe Ltd	4.8. Claims referring to changes in "body shape"	295 All my comments on waist circumference and waist-to-height ratio are relevant to my views on body shape. Although shape is often shorthand for effects on fat distribution, I would prefer to see claimants refer to changes in abdominal obesity or fat distribution in their submissions using changes in waist circumference and waist-to-height ratio as evidence. Perhaps mention of body shape should be restricted to the form of words suggested for the claim. In this case, it must be made clear that shape refers to fat distribution and not to loss of water.

BENEO Institute	4.8. Claims referring to changes in "body shape"	Line 301-303: Clarification should be included in the guidance document on what is understood precisely as objective and suitable measures of body shape, as well as with respect to appropriate study duration.
DSM Nutritional Products	4.8. Claims referring to changes in "body shape"	LINES 295-303 "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.": Does this mean that evidence would always need to be based on body composition measurements? LINES 297-300 "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).": A change in the ratio between FM and FFM (lean body mass) is also a favorable change in body shape, as is change in waist/hip ratio.
European Responsible Nutrition Alliance	4.8. Claims referring to changes in "body shape"	Line 302. It would be helpful if EFSA could specify what methods it would judge acceptable for such measurements.
ILSI Europe aisbl	4.8. Claims referring to changes in "body shape"	294 Is it possible to have a wording of a claim mentioning 'body shape' when the health beneficial effect is a reduction in body fat mass for example? 300-303 Does this mean claims in body shape are not valid unless accompanied by a claim in body composition? 300 What context of the claim would be acceptable? Please provide some examples to clarify. 302 What methods are validated to measure body shape? DEXA, waist-hip ration, or otherwise?
KELLOGG"S	4.8. Claims referring to changes in "body	4.8 Claims referring to changes in "body shape"

	shape"	We would request again that and appropriate duration is not specified with an example. The 3 month time frame is arbitrary and should be evaluated on a case by case basis. We can appreciate that it is only an example but when examples are provided they set a precedent.
Kraft Foods R&D	4.8. Claims referring to changes in "body shape"	- Is it possible to have a wording of a claim mentioning 'body shape' when the health beneficial effect is a reduction in body fat mass for example?
Tate & Lyle Plc	4.8. Claims referring to changes in "body shape"	If only the fat mass is reduced in the periphery but not visceral fat, is this considered beneficial to health? 300: What context of the claim would be acceptable? Please provide some examples to clarify 302: what methods are validated to measure body shape? DEXA, waist-hip ration, or otherwise?
Tate & Lyle Plc	4.8. Claims referring to changes in "body shape"	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
The European VLCD Industry Group	4.8. Claims referring to changes in "body shape"	Line 295. The Industry Group questions notes that changes in body shape as a result of changes in body water can only mean a reduction in peripheral oedema and hence is clearly beneficial to health. Losses of body water during dieting (where this is due to loss of lean body mass) are short lived and do not contribute to measureable changes in body shape. Claims for changes in body shape should be substantiated by the appropriate use of laser techniques of measuring body shape and not by measurements of hip-waist ratios.
University of Leeds, Leeds, UK	4.8. Claims referring to changes in "body shape"	Lines 301-302: Examples of objective and suitable measures of body shape should be provided. Again, it is not clear how the suggested 3 month duration (which seems a little arbitrary and unrealistic) was decided upon. Changes in body shape (e.g. shown by a reduction in waist circumference, body fat) demonstrated over a shorter period (e.g. 2-4 weeks) could still be beneficial as this would be unlikely to be attributable to loss of body water alone.

University of Limerick	4.8. Claims referring to changes in “body shape”	295 and on... Unless clearly substantiated by reference to psychological well-being, or similar scientific construct, I see no relevance to a consideration of "body shape" in this document. "Shape" is subjective and meaningless, dare I say misleading, in the scientific evaluation of a health claim. Change in body composition as previously defined encompasses "body shape"
VAB-nutrition	4.8. Claims referring to changes in “body shape”	Ln 295-303. In addition to the possible origins of body shape changes that the panel mentions, others can be imagined (such as reduction in thigh or arm circumference). These reasons for changing the body shape have probably no benefit for human health but are not either likely to pose a health threat. If the panel states that they do not correspond to or do not suggest a health benefit, but rather a “cosmetic-type” benefit, it is likely that these claims do not comply with the EC 1924/2006 regulation and should thus not been evaluated or at least should not be included in the list of authorized and rejected claims. Can the panel comment on this point?
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	4.8. Claims referring to changes in “body shape”	Given that it is widely used in medicine, is the body fat measurement by Magnetic Resonance Imaging (MRI) acceptable ?
Wrigley Science Institute	4.8. Claims referring to changes in “body shape”	Lines 295-303. In addition to the stated changes of body shape changes by body fat distribution, the panel may wish to specify changes in a particular body part shapes e.g. reduction in limb circumference and/or lean muscle mass in limbs. While these changes in the peripheral body shape may have questionable health benefits, they are unlikely to be of a health risk. If the panel considers these as cosmetic claims rather than health related claims, they should not be included in the list of authorized and rejected claims as they would not meet the EC 1924/2006 regulation.
BENEO Institute	5. Blood glucose and insulin concentrations	The draft guidance document addresses blood glucose and related claims from a rather narrow, essentially disease (diabetes) risk reduction-oriented viewpoint. With respect to postprandial effects the guidance document only addresses the reduction of postprandial blood glucose as beneficial physiological effect. To be a real guidance with respect to possible future blood glucose related claims it would be good to see the principal acknowledgement that also other postprandial blood glucose response and insulin related effects such as reduced glycemic variability and glucose fluctuations, and prevention or reduction of hypoglycemic conditions as well as reduced insulin response are of health relevance, scientifically accepted and may thus qualify as further beneficial physiological effects. Several measures with respect to these conditions are established and accepted in science. An example is the mean amplitude of glycemic excursions (MAGE).

McCORMICK France SAS	5. Blood glucose and insulin concentrations	comments regarding claims for blood glucose and insulin concentrations • The requirement to measure both postprandial blood glucose and insulin response is excellent. • The ability to use diabetic subjects being treated with life-style measures only (e.g., diet) is also excellent. • The requirement for three-month duration of studies that measure long-term blood glucose control is also reasonable and appropriate.
SYNPA	5. Blood glucose and insulin concentrations	Line 304 Elevated fasting glucose levels should also be considered as appropriate markers in long term studies as well as multiple glucose measurement of plasma glucose levels over 24 hours.
Tate & Lyle Plc	5. Blood glucose and insulin concentrations	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
TNO	5. Blood glucose and insulin concentrations	The guidance does not discuss disease reduction claims. However, we believe that some of the outcome measures available, such as insulin sensitivity or fasting blood glucose, have been shown to have an independent predictive value for the risk of developing diabetes and thus, changes in these outcome measures may provide substantiation for a disease risk reduction claim. We would like to have the Panel's opinion on this.
VAB-nutrition	5. Blood glucose and insulin concentrations	Overall comment Can the panel comment why there is no section on claims related to "(long-term) maintenance of normal blood glucose concentrations" in part 5 of the draft guidance? Indeed, this effect has been previously assessed in several already published opinions on the substantiation of health claims pursuant to Article 13(1) (e.g., opinions on chromium -EFSA Journal 2010;8(10):1732- and coffee -EFSA Journal 2011;9(4):2057-), and the panel has concluded in every cases that "long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect". Is the reason for this omission that through the effect "(long-term) blood glucose control", described in paragraph 5.2 of the draft guidance, the panel is also referring to the effect "(long-term) maintenance of normal blood glucose concentrations"? If yes, may the panel specify in the final guidance document that both health effects are equivalent and should therefore follow the same guidance for scientific substantiation? If not, may the panel add a section on the scientific substantiation for claims related to (long-term) maintenance of normal blood glucose concentrations in part 5 of the guidance

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Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	5. Blood glucose and insulin concentrations	From a clinical point of view, a diabetic detected subject will no longer stay without anti-diabetic treatment. So how can studies be conducted on un-medicated diabetics ? What about claims targeting people with metabolic syndrome ? Are they admissible in the scope of the regulatory if people with metabolic syndrome are un-medicated ?
AESGP - Association of the European Self-Medication Industry	5.1. Claims on the reduction of post-prandial blood glucose responses	Could the Panel provide a reference to the methodology accepted for the measurement of postprandial glycaemic response?
Arla Foods a.m.b.a.	5.1. Claims on the reduction of post-prandial blood glucose responses	Reduced post-prandial blood glucose responses may be considered as beneficial if the insulin response not is disproportionally increased. We would appreciate some indication on how big a disproportional insulin increase is? This paragraph says that claims have been proposed for carbohydrate containing foods or meals. What proportion of carbohydrates is needed in the food to get a claim on postprandial blood glucose reduction?
BENEO Institute	5.1. Claims on the reduction of post-prandial blood glucose responses	Line 320-325: This guidance document as well as the existing scientific opinions on blood glucose related claims lump together several means to lower postprandial blood glucose by replacing digestible, higher glycemic carbohydrates in a food or meal, irrespective of further nutritional functions associated with. According to nutritional guidelines including EFSA NDA panel's scientific opinion on DRV for carbohydrates, carbohydrate should be the major component of the diet representing 45 to 60 % of our daily energy intake. Lowering blood glucose response by replacing digestible carbohydrates with intense sweeteners, i.e. non-caloric food constituents, eventually favors a diet proportionate higher in fat energy and lower in energy coming from carbohydrate. Diets outside the reference intake ranges for carbohydrate and fat are associated to adverse short- and long-term effects, as confirmed in EFSA NDA panel's scientific opinion on DRV for carbohydrates. Hence, there is a need to differentiate in the guidance document between lowering of postprandial blood glucose by replacing digestible carbohydrates achieved a) by intense sweeteners (non-caloric, do not contribute to overall carbohydrate energy in the diet), b) by fermentable/low-digestible carbohydrates, some providing partly carbohydrate energy, or

		c) by digestible, but low-glycemic carbohydrate alternatives providing full energy from carbohydrate. If this aspect of the nutrients for which the same positive effect is granted, is not addressed, this will ultimately lead to a misinformation of the consumer: It makes a difference whether he/she gets a lower postprandial glucose together with the same energy of available carbohydrates or their reduction/replacement by dietary fibers or intense sweeteners. In addition, it needs to be addressed that in particular starches and starch derived saccharides and syrups have a high postprandial glucose response and could thus be replaced, and not only "sugars", as referred to in previous opinions. It is thus suggested to amend the examples given in brackets in line 321 to "…(e.g. digestible carbohydrates such as starches, maltodextrins, glucose or sucrose)."
Danone Research	5.1. Claims on the reduction of post-prandial blood glucose responses	306-308 We would like the Panel to clarify what is the criteria for a food or a meal rich in digestible carbohydrates? Is there a minimal amount of carbohydrates needed? Does it exclude some food categories? 310-313 We would like the panel to clarify if the food/constituent should be tested alone or within a meal. 316-319 In the case that all characteristics (e.g. energy or volume) of a test product and control product could not be the same, would it be sufficient to have both products equivalent in terms of macronutrients? General comment For reduction of post-prandial blood glucose responses claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DSM Nutritional Products	5.1. Claims on the reduction of post-prandial blood glucose responses	LINES 308-310 "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).": Clarification is sought on the interpretation of the wording "insulin responses disproportionally increased". The term is very vague and difficult to define. It is, for instance, different in subjects with impaired glucose tolerance still considered in the normal range, compared to healthy controls. On the other side, "disproportionally increased insulin responses" can also be caused by certain ingredients such as fructose or protein. LINES 316-319 "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)." Clarification is sought on the interpretation of the term "sufficiently characterised…and comparable…". Which criteria would be considered as the leading ones: amount of carbohydrates, fat, protein and energy?
ELC	5.1. Claims on the reduction of post-prandial blood glucose responses	Lines 314-19 To prove the fact that fibre or any others foods or dietary ingredients can decrease the quantity of food absorbed by the intestine (lipids or saccharides/glucose), request technically, the use of intestinal perfusion. However, such an invasive tool could only be applied on animals (in accordance with the ethical comity agreement) but is not acceptable for humans (especially as assessing the efficacy of food is considered less useful than drugs). The national ethical comity and human protection comity (named CCP and AFSSAPS in France) would refuse such a clinical trial that represent a real risk due to the invasive tools. In any case, the glycaemia and the insulin secretion would be the most accessible biological marker to evaluate the outcome of the intestinal interaction between fiber and the food ingested during the lunch or dinner.
ELC	5.1. Claims on the reduction of post-prandial blood glucose responses	Lines 308-310 EFSA should provide more details and clarify where a "disproportionally increase of insulin response" starts.
European Nutraceutical Association (ENA)	5.1. Claims on the reduction of post-prandial blood glucose responses	Line 326-332 See our comment under Section 1 (lines 143-149).
European Responsible Nutrition Alliance	5.1. Claims on the reduction of post-prandial blood glucose responses	Line 311. Could EFSA provide a reference to the methodology they accept for the measurement of postprandial glycaemic response? Line 319. The comparison with a standardized and accepted test meal (e.g. glucose solution, etc) should also be acceptable.
GlaxoSmithKline	5.1. Claims on the reduction of post-prandial blood	Section 5.1- Please provide a reference to the methodology that the panel accept for the measurement of postprandial glycaemic response

	glucose responses	
ILSI Europe aisbl	5.1. Claims on the reduction of post-prandial blood glucose responses	309-310 EFSA excludes a "disproportionally increase of insulin response" meaning a status of dys-regulation of the glycemic response without considering that a pre-diabetic status. The latest physiologic state could be related to an abnormal insulin response which is higher than normal, and need to be higher because the subject still considered as healthy, start to have an insulin-resistance (meaning higher insulin is request to decrease the glycemia in the normal range, inside minima and maxima level). Can the panel define a threshold for non-healthy insulin response? 314-319 To demonstrate reduced post-prandial blood glucose, would it be sufficient to show a) decrease of the HOMA or Quicky index (insulin and glycemia level) and also b) the decrease of the carbohydrate or lipid absorption by the intestine which request invasive methodology in humans; or would an in vitro test be sufficient for the latter? 326-327 Can we deduct that a generic criterion the Panel applies concerning extrapolation from disease to non-disease is whether or not the disease state is treated or managed with medication?
ILSI Europe aisbl	5.1. Claims on the reduction of post-prandial blood glucose responses	306 Could the Panel suggest a consumer friendly wording of the ‘reduction of post-prandial blood glucose response’ claim? 306-313 Could the panel clarify the timing of intake of the test food in relation to the food or meal rich in carbohydrates, for instance intake of the test food X-X minutes before the food or meal rich in carbohydrates and/or during the carbohydrate rich meal. 307-308 Kindly clarify ‘food or meal rich in digestible carbohydrates’ - does it exclude some food categories like dairy? 308 As the role of the food matrix (role of macronutrients per se) is recognised to affect post-prandial blood glucose response, why nutritional constraints are not proposed in the conditions of use to guarantee that the

claimed effect is due to the food constituent selected and not to others ? (i.e. Lipids which may decrease glycemic response above a certain amount, as well as insulin secretion – Normand et al. 2001, Br J Nutr 86, 3-11; Flint et al. 2004, Am J Clin Nutr. 80: 337-347.)

308-313

Epidemiological studies have clarified that there is a positive linear relationship between rises in blood glucose (either fasted or post-challenge) and the risk of disease and for outcomes such as cardiovascular disease and premature mortality; this relationship extends far below the diabetic threshold [Diabetes Care, 2003: 26; 688-696; Diabetes Care, 2006: 29; 26-31]. To clarify the position on what constitutes a beneficial physiological effect in relation to reduction in post-prandial blood glucose responses we recommend amending the current text to provide a more definitive statement i.e. "This ability is (replacing may be) considered a beneficial effect as long as insulin responses are not disproportionally increased (e.g. for subjects with impaired glucose tolerance)".

The guidance states that data on insulin concentrations are required for claim substantiation to ensure that insulin responses are not disproportionally increased. However there is ambiguity on the level of evidence required. We recommend that EFSA provides a clear view on this, stating whether supportive evidence for a (generally established) mode of action plus corroborative clinical data is sufficient to give reassurance on this point or whether this must be substantiated at the same level as the primary claim. In addition, we recommend that the "disproportional" increase in insulin which would be viewed by EFSA as unfavourable be clarified.

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Several ways can be mentioned to decrease glycemic response with a non disproportionally insulin increase. There are different ways, some with no associated health risk compared to others - ie lipid example, see above, fructose example: see below: does the Panel consider that replacing glucose units (from starch or mono or dissacharides) by fructose is relevant to decrease glycemic response, with a potential risk of triglycerides accumulation in some part of the general population (as subjects suffered from metabolic syndrome) if fructose is consumed in excess? For general population it has been shown an upper limit for fructose consumption; however, there is no consensus regarding this upper limit (Dolan et al. 2010 Critical Reviews in Food Science and Nutrition, 50: 1, 53 — 84; Sanchez-Lozada 2008 Eur J Nutr. 2010 Feb;49(1):1-9. Epub 2009 Jul 22., Laville & Nazare. obesity reviews 2009 10: Suppl. 1; 24–33). How do you define the non disproportionally insulin increase, ie do you consider that a combination of carbohydrate and proteins is relevant to decrease glycemic response? Do you consider that an emphasised early insulin secretion may be relevant to decrease the glycemic response (Schenk et al. 2003 Am J Clin Nutr 2003;78(suppl):742–8)?

		insu
Kraft Foods R&D	5.1. Claims on the reduction of post-prandial blood glucose responses	- (l308) As the role of the food matrix (role of macronutrients per se) is recognised to affect post-prandial blood glucose response, why nutritional constraints are not proposed in the conditions of use to guarantee that the claimed effect is due to the food constituent selected and not to others ? (ie. Lipids which may decrease glycemic response above a certain amount, as well as insulin secretion – Normand et al. BJN 2001 86, 3-11; Flint et al. AJCN 2004) - Ln 309: Several ways can be mentioned to decrease glycemic response with a non disproportionally insulin increase. There are different ways, some with no associated health risk compared to others - ie lipid example, see above, fructose example: see below: do you consider that replacing glucose units (from starch or mono or dissacharides) by fructose is relevant to decrease glycemic response, with a potential risk of triglycerides accumulation in some part of the general population (as subjects suffered from metabolic syndrome) if fructose is consumed in excess? For general population it has been shown an upper limit for fructose consumption. So overconsumption can provide deleterious health effects. However, there is no consensus regarding this upper limit (Dolan et al. 2010 Critical Reviews in Food Science and Nutrition, 50: 1, 53 — 84; Sanchez-Lozada 2008 Eur J Nutr. 2010 Feb;49(1):1-9. Epub 2009 Jul 22., Laville & Nazare. obesity reviews 2009 10: Suppl. 1; 24–33). How do you define the non disproportionally insulin increase, ie do you consider that a combination of carbohydrate and proteins is relevant to decrease glycemic response? Do you consider that an emphasised early insulin secretion may be relevant to decrease the glycemic response (Schenk et al. 2003 Am J Clin Nutr 2003;78(suppl):742–8)? - (l331) On which conditions can evidence from studies in diabetic subjects be used?
Nathura	5.1. Claims on the reduction of post-prandial blood glucose responses	Could studies are conducted on healthy subjects and can I measure glucose and insulin concentrations in the blood in these subjects? Is there a minimum number of healthy or diabetic subjects for studies to be conducted?
Rudolf Wild GmbH & Co. KG	5.1. Claims on the reduction of post-prandial blood glucose responses	General: the description of postprandial blood glucose measurement is, conceptually, identical with “glycemic index” measurements in combination with insulinaemic index. Why was this wording choosen? The so called “GI” does provide a certain input about the effect of a foodstuff rich in carbohydrates on the post-prandial blood glucose response. Thus, GI may have certain relevance in this health outcome due to GI may be directly related with the post-prandial blood glucose response of a test food/constituent. Concerning target groups it should be considered, that Ethical Comitees usually do not accept nutrition intervention only for people with diabetes.

		Line 309 – What does "…as long as insulin responses are not disproportionally increased…" mean? What is a disproportional increase? Line 320-325 – Can a reference be made on carbohydrates from natural sources, which induce a lower postprandial glycemic response in comparism to sucrose, due to the natural occurring spectrum of different carbohydrates, like fructose and polyols – beside glucose? Line 328-332 – Can the paragraph also be extended to diabetic subjects under nutrition intervention only?
SYNPA	5.1. Claims on the reduction of post-prandial blood glucose responses	Lines 309-310: "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)." EFSA excludes a "disproportionally increase of insulin response" meaning a status of dys-regulation of the glycemic response without considering that a pre-diabetic status is still considered as a healthy state. The latest physiologic state could be related to an abnormal insulin response which is higher than normal, and need to be higher because the subject still considered as healthy, start to have an insulin-resistance (meaning higher insulin is request to decrease the glycemia in the normal range, inside minima and maxima level). EFSA should provide more details and clarify where a "disproportionally increase of insulin response" starts. Lines 314-319:"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)." To prove the fact that fiber or any others foods or dietary ingredients can decrease the quantity of food absorbed by the intestine (lipids or saccharides/glucose), request technically, the use of intestinal perfusion. However a such invasive tool could be only applied on animals (in accordance with the ethnical comity agreement) but it 's not acceptable for Humans; especially to assess the efficacy of food considered less useful than drugs. Then the local ethical comity and human protection comity (named CCP and AFSSAPS in France) will refuse such clinical trial that represent a real risk due to the invasive tools and not for the food. Whatever, the glycemia and the insulin secretion would be the most accessible biological marker to evaluate the outcome of the intestinal interaction between fiber and the food ingested during the lunch or dinner.
Tate & Lyle Plc	5.1. Claims on the reduction of post-prandial blood glucose responses	309: Could EFSA provide clarification on where begins a "disproportionally increase of insulin response"?
Tate & Lyle Plc	5.1. Claims on the	General comments:

	reduction of post-prandial blood glucose responses	• Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
Unilever	5.1. Claims on the reduction of post-prandial blood glucose responses	Section 5.1 - Claims on reduction of post-prandial blood glucose response General Comment In general we are supportive of the proposed EFSA guidance on the scientific requirements for health claims relating to blood glucose concentrations. We have, however, identified a few areas where we think changes are warranted. For simplicity our comments have been substantiated with a few key references but if it is useful to do so or if further information is required then additional references can be supplied. Lines 308-313 • Epidemiological studies have clarified that there is a positive linear relationship between rises in blood glucose (either fasted or post-challenge) and the risk of disease and for outcomes such as cardiovascular disease and premature mortality this relationship extends far below the diabetic threshold [Diabetes Care, 2003: 26; 688-696; Diabetes Care, 2006: 29; 26-31]. To clarify the position on what constitutes a beneficial physiological effect in relation to reduction in postprandial blood glucose responses we recommend amending the current text to provide a more definitive statement i.e. "This ability is (replacing maybe) considered a beneficial effect as long as insulin responses are not disproportionally increased (e.g. for subjects with impaired glucose tolerance)". • The guidance states that data on insulin concentrations are required for claim substantiation to ensure that insulin responses are not disproportionally increased. However there is ambiguity on the level of evidence required. We recommend that EFSA provides a clear view on this, stating whether supportive evidence for a (generally established) mode of action plus corroborative clinical data is sufficient to give reassurance on this point or whether this must be substantiated at the same level as the primary claim. In addition, we recommend that the "disproportional" increase in insulin response which would be viewed by EFSA as unfavourable be clarified. We propose that a disproportional increase in insulin response should be defined as "a significant rise in plasma insulin levels in the test situation compared to the control".
University of Leeds	5.1. Claims on the reduction of post-prandial blood	Line 310-311: 'measures of both glucose and insulin in the blood..... are required' This statement presupposes that every assessment would include both substrates to be measured concomitantly and seems to contradict the statement regarding insulin assessment (5.3). Consideration should be made of the recommendation by Brouns

	glucose responses	et al., (2010) on glucose measurement. There should be some consideration too of the use of AUC measurements vs other validated measure such as continuous interstitial glucose measures which have also been validated against arterialized venous samples (Dye et al., 2010). The guidance could better reflect the developments in this field and the sensitivity of the measures possible (e.g. Yellow Springs Instruments produce highly valid glucose measurements from capillary samples which do not interfere with subjective state or appetite measures as the proposed techniques may well do. Thus it would be helpful to specify whether glucose and insulin concentrations should be measured in capillary, venous or arterialised venous blood and to recognise the value of interstitial glucose concentrations in ascertaining glycaemic response to interventions (cf. Brynes et al 2009).
University of Leeds, Leeds, UK	5.1. Claims on the reduction of post-prandial blood glucose responses	Line 311: 'Blood' – it would be helpful to specify whether glucose and insulin concentrations should be measured in capillary, venous or arterialised venous blood and if interstitial glucose concentrations should be measured.
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	5.1. Claims on the reduction of post-prandial blood glucose responses	Lines 328-332 and lines 341-345 : About blood glucose and insulin concentrations, is the extrapolation to the general population solely relies on mechanistic datas showing that there is no interaction between the food and the anti-diabetic treatment ?
BENEO Institute	5.2. Claims on (long-term) blood glucose control	Line 335: The guidance document only identifies HbA1c as appropriate outcome, while OGTT is considered as merely supportive. The guidance document appears thus clearly in contrast to international expert committees including the International Diabetes Federation (IDF) and the WHO. Both explicitly identify Fasting Plasma Glucose (FPG) and the OGTT (Plasma Glucose at two hours) as diagnostic tests to be used to define glycaemic status.Hence, the guidance document should include other well established measures which are generally accepted in science including 2-h OGTT, Fasting Glucose and fructosamine as appropriate outcomes for scientific substantiation of claims on blood glucose control.
Cargill	5.2. Claims on (long-term) blood glucose control	Line 338: As the appropriate outcome for the scientific substantiation of such claims (only) reference is made to HbA1c. Nevertheless, hyperglycaemia is the hallmark of type 2 diabetes and contributes to the pathogenesis of the disease by impairing both insulin action and secretion. Also the pre-diabetic state is characterized by higher fasting levels of blood glucose and insulin and decreasing such levels (near to normal) is associated with improved glucose homeostasis. The suggestion therefore is also to consider fasting glucose and insulin plasma

		levels as risk factors for claims substantiation on (long-term) blood glucose control.
Danone Research	5.2. Claims on (long-term) blood glucose control	337-338 In the International Diabetes Federation consensus worldwide definition of the metabolic syndrome, OGTT is defined as the "Platinum standard" for assessment of Dysglycaemia (2005). Moreover, the decrease in the area under the curve upon the Oral Glucose Tolerance Test (OGTT) reflects a beneficial physiological effect which is an improvement of glucose tolerance impairment. Taking this into consideration, could the Panel comment on why the use of OGTT is considered as only supportive to substantiate a claim on blood glucose control? General comments There is sufficient evidence that impaired blood glucose tolerance is a predictive independent factor for diabetes (World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO consultation. Geneva. 1999). Thus, if an improvement in blood glucose control is demonstrated upon OGTT, can it be used to substantiate a disease-risk reduction claim (article 14)? For (long-term) blood glucose claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DHI Water Environment Health	5.2. Claims on (long-term) blood glucose control	ln 339: It would be helpful with criteria for determining whether the study population is "diabetic", "subjects with impaired glucose control" or "healthy" in this regard.
DSM Nutritional Products	5.2. Claims on (long-term) blood glucose control	LINES 335-338 "Appropriate outcomes for the scientific substantiation of such claims include glycosylated haemoglobin (HbA1c) measured in intervention studies of appropriate duration (e.g. at least 3 months). Measurement of the area under the curve of plasma glucose concentrations after astandard oral glucose tolerance test (OGTT) is considered as supportive. ": HbA1c should not be the only outcome parameter since even in pharma trials this has caused problems in the interpretation of the outcomes. Alternatives are fructosamine but also fasting glucose or OGGT. Blood glucose control is linked to another physiological benefit, namely insulin sensitivity, while a clear 24hr glucose control should be a physiological benefit on its own. Reduction in elevated fasting glucose levels should also be considered as evidence in blood glucose control.
ELC	5.2. Claims on (long-term) blood glucose control	Lines 335-338 The appropriate outcome for the scientific substantiation of such claims reference is made to HbA1c only. Nevertheless, hyper-glycaemia is the hallmark of type 2 diabetes and contributes to the pathogenesis of the disease by impairing both insulin action and secretion. In addition, the pre-diabetic state is characterized by higher fasting levels of blood glucose and insulin and decreasing such levels (near to normal) is associated with improved glucose homeostasis. The suggestion therefore is also to consider fasting glucose and insulin plasma levels as risk factors for claims substantiation on (long-term) blood glucose control. Elevated fasting glucose levels should be considered as appropriate markers in long term studies, as well as multiple glucose measurement of plasma glucose levels over 24 hours.

ELC	5.2. Claims on (long-term) blood glucose control	Lines 334-335 Maintaining a normal blood glucose concentration and/or improving blood glucose control are supposed to be beneficial respectively for normal subjects and, subjects that start to have some blood glucose troubles without being diagnosed as diabetic (still "normal" range of glycaemia or HbA1c). Then in order to prove a direct cause and effect relationship between the consumption of a food ingredient (or food) and the reduction of glucose concentration over a time higher than 3 months, the target population could be the general population including the persons becoming diabetic in future but still healthy (normal range of blood glycaemia).
European Nutraceutical Association (ENA)	5.2. Claims on (long-term) blood glucose control	Line 339-345 See our comment under Section 1 (lines 143-149).
European Responsible Nutrition Alliance	5.2. Claims on (long-term) blood glucose control	Line 334. We believe that a reduction in elevated fasting glucose levels should also be considered as evidence in blood glucose control.
IBET	5.2. Claims on (long-term) blood glucose control	As stated in lines 334-338 "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." The present comment intends to know if other biomarkers, such as fructosamine, and/or the continuous glucose monitoring, could be considered as additional appropriated outcomes for this health claim substantiation. Fructosamine, a measure of glycated serum proteins, represents the average of glycemia over the previous 2–3 weeks, and has been considered a reliable measurement of short to medium- term changes in blood glucose concentration [1-4]. Additionally, in combination with fasting blood glucose, fructosamine has been shown to be useful as an initial screen for incident diabetes [5]. Other recent studies have shown that this biomarker strongly correlates with other measures of glycemic control, including HbA1c [3,6], fasting glucose [7,8], and the OGTT [5,9]. Within this context, fructosamine could be considered a suitable biomarker for this specific health claim, by complementing and corroborating the results of the established HbA1c biomarker. The continuous glucose monitoring could also be used as an additional tool to substantiate long term blood glucose related claims. This analysis could provide important insights regarding the effect of a specific product/substance on daily blood glucose profile. continuous glucose monitoring could be performed using appropriate devices, such as CGMS (continuous subcutaneous glucose-monitoring systems), that are capable of measuring interstitial glucose levels every 1– 5min for 3 to 7 days. Several studies have shown a good

		correlation between interstitial glucose and plasma glucose [10], even in hyperglycemia, euglycemia and hypoglycemia conditions[11–13]. [1] Armbruster DA. Clin Chem 1987;33(12):2153–63; [2] Youssef D. et al. Tenn Med 2008;101(11):31–3 [3] Sahu A. et al. Indian J Physiol Pharmacol 2008;52(4):408–12. [4] Carter AW. Diabetes Technol Ther 2002;4(5):643–4. [5] Ko G.T. et al. Diabetes Care 1998;21(8): 1221–5 [6] Innes K.E. et al. Clinical Research & Reviews 2011, in press [7] Abdel-Gayoum A.G. et al. Saudi Med J 2004;25(2):207–11. [8] Serdarevic N. et al. HealthMED 2010;4(1): 132–7. [9] Weerasekera D.S. et al. J Obstet Gynaecol 2000;20(2):136–8. [10] Sachedina M. & Pickup J.C. Diabetic Med. 2003; 20: 1012–1015. [11]. Caplin N.J. et al. Diabetic Med. 2003; 20: 238–241. [12] Weinzimer S.A. et al. Diabetes Technol. Ther. 2003; 5:375–380. [13] Tansey M.J. et al. Diabetes Technol. Ther. 2005; 7: 109–114.
ILSI Europe aisbl	5.2. Claims on (long-term) blood glucose control	334-338 The natural history of progression from normal glucose tolerance to Type 2 Diabetes may involve the development of either fasting or post-challenge hyperglycaemia (e.g. 'pre-diabetes'). These two phenotypic pathways show distinct and disparate pathophysiologies - raised hepatic glucose output and a defect in early insulin secretion are characteristic or the former and peripheral insulin resistance is most characteristic of the latter. Although these abnormalities do co-occur, concordance is relatively limited [Diabetic Med, 2002:19 (9) 708-23]. We recommend expanding the scope of claims on blood glucose control to include claims on improvement of fasting blood glucose and post-challenge glycaemic responses. Reduction in elevated fasting glucose levels should also be considered as evidence in blood glucose control. Claims in "long-term blood glucose control" noticed that "improved blood glucose control is a beneficial physiological effect for subjects with impaired blood glucose tolerance" meaning that subjects potentially

diabetic could be include in the population analysed, despite the studied population have to be healthy and not diseased?

Would 'improved blood glucose control' be an article 13 claim?

335-337

In certain situations (e.g. individuals with anaemia, accelerated red blood cell turnover due to malaria, haemoglobin abnormalities) HbA1c is not a reliable measure and fructosamine may be used as an alternative [International Diabetes Federation, 2005: Global Guideline for Type 2 Diabetes; Diabetes Care, 2011: 34 (Suppl. 1) S11-61]. Fructosamine provides an indication of average glucose control over the preceding 2-3 weeks. We recommend specifying fructosamine as an additional outcome measure for the scientific substantiation of claims relating to improvements in chronic glucose control.

Fasting glycemia and OGTT are part of the measurements for the diagnostics of impaired glucose tolerance. Therefore why those measurements are not considered for the substantiation of the blood glucose control claim? Furthermore, in the latest IDF recommendations, it has been mentioned that not only the fasting glycemia was elevated in subjects with glucose metabolic disorder, but it has been discovered that postprandial glycemic excursions were much higher than expected because of the more precise glucometer analysis (Ceriello & Colagiuri 2008 Diabet Med 25: 1151-56). So, the OGTT can be a good marker of the improvement of metabolic state.

337-338

Blood glucose homeostasis requires effective management of both the fasted and post-prandial state and as detailed above loss of long-term glucose control may result from abnormalities in either fasting or post-challenge pathways. We recommend that demonstration of improved fasting blood glucose concentrations or improved OGTT to also be considered as supportive evidence for claims on long-term blood glucose control.

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As the appropriate outcome for the scientific substantiation of such claims (only) reference is made to HbA1c. Nevertheless, hyperglycaemia is the hallmark of type 2 diabetes and contributes to the pathogenesis of the disease by impairing both insulin action and secretion. Also the pre-diabetic state is characterised by higher fasting levels of blood glucose and insulin and decreasing such levels (near to normal) is associated with improved glucose homeostasis. The suggestion therefore is also to consider fasting glucose and insulin plasma levels as risk factors for claims substantiation on (long-term) blood glucose control.

339-345

		Would an article 14 claim be possible for diabetics, based on reduced HbA1c?
Kraft Foods R&D	5.2. Claims on (long-term) blood glucose control	- Ln 336: Fasting glycemia and OGTT are part of the measurements for the diagnostics of impaired glucose tolerance. Therefore why those measurements are not considered for the substantiation of the blood glucose control claim? Furthermore, in the last IDF recommendations, it has been mentioned that not only the fasting glycemia was elevated in subjects with glucose metabolic disorder, but it has been discovered that postprandial glycemic excursions were much higher than expected because of the more precise glucometer analysis (Ceriello & Colagiuri 2008 Diabet Med 25: 1151-56). So, the OGTT can be a good marker of the improvement of metabolic state. - (l339) On which conditions can evidence from studies in diabetic subjects be used?
Rudolf Wild GmbH & Co. KG	5.2. Claims on (long-term) blood glucose control	General: The OGTT is considered as supportive, but is not an approbiate method for testing diabetic subjects, even when treated with lifestyle / diet measures only and is generally not accepted by Ethical Committees. What is the opinion of the panel related to the use of 24h continous blood glucose monitoring systems (which are inserted subcutane and report blood glucose levels every 5 minutes for >24h)?
SYNPA	5.2. Claims on (long-term) blood glucose control	Lines 334-335: "Improved blood glucose control is a beneficial physiological effect for subjects with impaired blood glucose tolerance." Maintaining a normal blood glucose concentration and /or improving blood glucose control are supposed to be beneficial respectively for normal subjects and, subjects that start to have some blood glucose troubles without being diagnosed as diabetic (still "normal" range of glycemia or HbA1c). Then in order to prove a direct cause and effect relationship between the consumption of a food ingredient (or food) and the reduction of glucose concentration over a time higher than 3 months (the new goal for population health), the target population could be the general population including the persons becoming diabetic in future but still healthy (normal range of blood glycemia). Line 338: "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." The appropriate outcome for the scientific substantiation of such claims reference is made to HbA1c only. Nevertheless, hyperglycaemia is the hallmark of type 2 diabetes and contributes to the pathogenesis of the disease by impairing both insulin action and secretion. In addition the pre-diabetic state is characterized by higher fasting levels of blood glucose and insulin and decreasing such levels (near to normal) is associated with

		improved glucose homeostasis. The suggestion therefore is also to consider fasting glucose and insulin plasma levels as risk factors for claims substantiation on (long-term) blood glucose control. Elevated fasting glucose levels should be considered as appropriate markers in long term studies, as well as multiple glucose measurement of plasma glucose levels over 24 hours. Reduction in elevated fasting glucose levels should also be considered as evidence in blood glucose control.
Tate & Lyle Plc	5.2. Claims on (long-term) blood glucose control	335: Although we agree HbA1c measurement is an appropriate outcome for the substantiation of such claim. We would suggested that elevated fasting glucose levels would be considered as appropriate markers in long term studies, as well as multiple glucose measurement of plasma glucose levels over 24 hours.
Tate & Lyle Plc	5.2. Claims on (long-term) blood glucose control	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
TNO	5.2. Claims on (long-term) blood glucose control	337-338 We agree that measuring AUC of plasma glucose after a standard OGTT is considered supportive, in studies of limited size. However, what is the Panel's Opinion on the use of glucose AUC in larger studies, based on appropriate power calculations, and preferably in combination with insulin measures? Likewise, effects on fasting blood glucose may be an adequate measure in larger studies with adequate power
Unilever	5.2. Claims on (long-term) blood glucose control	Section 5.2 - Claims on (long-term) blood glucose control General Comment In general we are supportive of the proposed EFSA guidance on the scientific requirements for health claims relating to blood glucose concentrations. We have, however, identified a few areas where we think changes are warranted. For simplicity our comments have been substantiated with a few key references but if it is useful to do so or if further information is required then additional references can be supplied. Line 333

		• The natural history of progression from normal glucose tolerance to Type 2 Diabetes may involve the development of either fasting hyperglycaemia or post-challenge hyperglycaemia (i.e. an elevated blood glucose level after a standard glucose load). These two phenotypic pathways show distinct and disparate pathophysiologies - raised hepatic glucose output and a defect in early insulin secretion are characteristic or the former and peripheral insulin resistance is most characteristic of the latter. Although these abnormalities do co-occur concordance is relatively limited [Diabetic Med, 2002:19 (9) 708-23]. We recommend expanding the scope of claims on blood glucose control to also include claims on improvement of fasting and post-challenge (e.g. standard OGTT) glucose responses. Lines 335-337 • In certain situations (e.g. individuals with anaemia, accelerated red blood cell turnover due to malaria, haemoglobin abnormalities) HbA1c is not a reliable measure and fructosamine may be used as an alternative [International Diabetes Federation, 2005: Global Guideline for Type 2 Diabetes; Diabetes Care, 2011: 34 (Suppl. 1) S11-61]. Fructosamine provides an indication of average glucose control over the preceding 2-3 weeks. We recommend specifying fructosamine as an additional outcome measure for the scientific substantiation of claims relating to improvements in chronic glucose control. Lines 337-338 • Blood glucose homeostasis requires effective management of both the fasted and postprandial state and a loss of long-term glucose control may result from abnormalities in either fasting or post-challenge pathways. This is reflected by the diagnostic criteria for Diabetes where fasting and 2h-post-glucose-load criterion have been established [Definition and diagnosis of diabetes mellitus and its complications: WHO Report, 1999 report]. Based on this we recommend that demonstration of improved blood glucose concentrations during fasting or 2 hours after a standard glucose load should be considered as supportive evidence for claims on long-term blood glucose control. This is in addition to "the measurement of area under the curve of plasma glucose concentrations after a standard OGTT" which is already described in the guidelines.
University of Tartu	5.2. Claims on (long-term) blood glucose control	Guidance on the scientific requirements for health claims related to gut and immune function 8 EFSA Journal 2011;9(4):1984 3.Gastro-intestinal tract 3.3. Function claims related to defence against pathogens Panel p. 7 For function claims related to defence against pathogens in the gastro-intestinal tract, appropriate outcome measures are gastro-intestinal infections (e.g. number of episodes and severity or duration of infection). The infectious nature of the disease should be established, e.g. by clinical diagnosis and/or the use of validated questionnaires for recording self-reported data and/or microbiological data depending on the type of the infection. Comment: This relates on the treatment of clinically diagnosed gastro-intestinal infection by probiotic. Such kinds of trials of infectious diseases without use of specific preparations, e.g. antibiotics, antisera, toxin absorbers, ORS solutions, modulators of peristalsis are not accepted by MEDICAL ETHICS

		COMMITTEES. Panel:p.7 Another appropriate …. the reduction of the presence of specific pathogens, their toxins or other virulence factors, as measured in suitable samples (e.g. stools). A relevant reduction of pathogens, measured at appropriate time-points and in appropriately controlled studies should be demonstrated. Etc. Comment: In case of combined (ordinary + probiotic) treatment, the specific response may comprise effect of both probiotic and treatment component. This is especially valid in some infectious diseases with antibiotic use (sustained impact on pathogen or probiotic bacteria) associated with putative hospital infection due to C. difficile (Plummer et al., Int. Microbiol., 2004, 7:59-62) The defence against pathogens cannot be detected by investigating the intestinal microbiota of healthy adults in clinical trials. The intestinal microbiota of healthy adults perform a well stabilised system where by probiotic treatment the increase of some groups of bacteria like lactic acid bacteria usually results in simultaneous increase of some other groups (bifidobacteria, potentially pathogenic enterobacteria) to keep the species and numerical relations stable inside microbiota (Sepp et al, MEHD,1993, 6:309-314). The healthy persons are not colonized with virulent enterobacteria or Clostridium difficile strains with high amounts of toxin (Naaber et al, J. Med. Microbiol., 2004, 53, 551-554). In traveller´s diarrhoea besides bacterial pathogens the large spectra of non-diagnosed eukaryotic pathogens or viruses might alter the effect. Panel:p.8. paragraph 2 Outcome measures such as decrease in stool pH, changes in short-chain fatty acid production and reduction of intestinal permeability, are not considered beneficial physiological effects per se, but may provide evidence on the mechanisms and the biological plausibility of a claim related to defence against pathogens. p.8 paragraph 9 in 3.5 Function claims. … The evidence available to the Panel does not establish that increasing the number of any groups of microorganisms, including lactobacilli and/or bifidobacteria, is in itself a beneficial physiological effect. For function claims related to changes in gastro-intestinal microbiota these changes should be accompanied by a beneficial physiological or clinical outcome. This applies to both adult and infant/children populations. Comment :These two paragraphs on the page 8 but far away from each other could be united for more clarity of the content and conclusion as …changes should be accompanied by a beneficial physiological or clinical outcome. Conclusive comment: It should be clearly stated that experimental data showing clear suppression of pathogen, combined with healthy human studies measuring indices suitable to detect defense again
VAB-nutrition	5.2. Claims on (long-term) blood glucose control	Ln 334-335. May the panel explain why it has been specified that “improved blood glucose control is a beneficial physiological effect for subjects with impaired blood glucose tolerance” in the draft guidance, while it has previously been recognized by the panel that the “long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect”, without any further specification (as in the opinion on chromium -EFSA Journal 2010;8(10):1732)? This clarification is of particular importance if the two effects - “improved blood glucose control” and “(long-term) maintenance of normal blood glucose concentrations” – are considered as equivalent by the panel.

		Ln 335-337. 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). Since fasting blood glucose and insulin concentrations were not mentioned here, it may be concluded that they are not considered as appropriate outcomes for these types of claims. This would be consistent with previously published opinions which stated that "fasting blood glucose and insulin concentrations are not appropriate outcome measures of long-term blood glucose control" (e.g., opinion on intense sweeteners - EFSA Journal 2011;9(6):2229). However, since fasting blood glucose and insulin concentrations are classically and routinely measured to monitor and diagnose diabetes (among other outcomes), can the panel comment on the appropriateness of these outcomes for these types of claims?
Valorial and Nutrition Health Longevity french clusters : Biomarkers working group	5.2. Claims on (long-term) blood glucose control	Lines 328-332 and lines 341-345 : About blood glucose and insulin concentrations, is the extrapolation to the general population solely relies on mechanistic datas showing that there is no interaction between the food and the anti-diabetic treatment ?
AESGP - Association of the European Self-Medication Industry	5.3. Claims on increased insulin sensitivity	Lines 347-352: It would be helpful to clarify what is meant by "short-term" and "small numbers" in line 351, so that this section can be fully understood.
Ashwell Associates Europe Ltd	5.3. Claims on increased insulin sensitivity	348 The hyperinsulinaemic-euglycaemic clamp might be an 'appropriate measure' of insulin sensitivity in human intervention studies. However, this is an invasive measure as well as being labour intensive, I suggest the panel may discuss allowing evidence from other simpler techniques for intervention studies
BENEO Institute	5.3. Claims on increased insulin sensitivity	Line 348: The hyperinsulinemic-euglycemic clamp is certainly an appropriate measure of insulin sensitivity and could be considered as the gold standard. Nevertheless, according to the chapter 2 of the draft guidance document, appropriate outcome measures of the claimed effect are those generally accepted in the relevant research fields. The homeostatic model assessment index/indices (HOMA) as well as fasting plasma insulin alone are accepted and widely applied markers for the diagnosis of insulin resistance. They should consequently also be listed as appropriate measures of insulin sensitivity not only for epidemiological but also in intervention studies. As another aspect it is still agreed among physicians that a euglycemic clamp method, in particular in diabetics is a risky procedure which can easily lead to hypoglycemia when less skilled staff is used. Thus, it should be in the interest of the NDA panel to reduce unnecessary risks to subjects as the alternative methods are usually

		without any risk other than associated with blood drawings. Secondly, they are less invasive and would thus reflect more the normal dietary situation/living condition.
Danone Research	5.3. Claims on increased insulin sensitivity	347- 351 In the International Diabetes Federation consensus worldwide definition of the metabolic syndrome, the Homeostatic Model Assessment (HOMA) is defined as the "Platinum standard" for assessment of insulin resistance (2005). Taking this into consideration, could intervention studies with a large number of subjects and appropriate duration (e.g. at least 3 months) substantiate a claim on increased insulin sensitivity based on HOMA as the primary criteria? We would like the panel to clarify the target population. What kind of subjects could be included in the study (overweight, obese, diabetics not under medication…)? General comment For increased insulin sensitivity claims, we would like to know what the primary criteria in clinical studies should be and what are the possible secondary criteria.
DSM Nutritional Products	5.3. Claims on increased insulin sensitivity	LINES 347-352 "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.": Next to Homa and Quick, OGGT and fasting glucose level may be considered as very reliable indicators of insulin sensitivity. Clamps as golden standard are very invasive and may not be justified in properly powered studies using other methods like HOMA.
ELC	5.3. Claims on increased insulin sensitivity	Lines 347-352 What does "short term" mean in this case? Is it 3 months or more? And what is the expectation for a, or the meaning of "small numbers of subjects"? The number of subjects has to be estimated and calculated based on previous studies that give some measures with its standard deviation.
European Responsible Nutrition Alliance	5.3. Claims on increased insulin sensitivity	Line 351. Could EFSA clarify what it means with "short-term and "small number"?

For Comvita Ltd	5.3. Claims on increased insulin sensitivity	Line 352 The Matsuda index (Matsuda & Defronzo, Diabetes Care 1999, 22: 1462-1470) provides a composite measure of whole body insulin sensitivity (hepatic & peripheral tissue) and considers insulin sensitivity both in the basal state and after the ingestion of a glucose load. It provides indices of insulin sensitivity from measurements of plasma glucose and insulin concentrations during the OGTT. It provides robust measures of the dynamics of insulin responsiveness to glucose challenge, key information not available from the hyperinsulinaemic-euglycaemic clamp. DeFronzo, who developed the hyperinsulinaemic-euglycaemic clamp, was the senior author on the original Matsuda paper suggesting recognition of the need to move beyond the clamp methodology. The Matsuda index has been validated against the hyperinsulinaemic-euglycaemic clamp in 153 subjects (66 men and 87 women, aged 18–71 years, BMI 20–65 kg/m2) with varying degrees of glucose tolerance (62 subjects with normal glucose tolerance, 31 subjects with impaired glucose tolerance, and 60 subjects with type 2 diabetes) (Matsuda & Defronzo, Diabetes Care 1999, 22: 1462-1470). Whole-body insulin sensitivity measured with the hyperinsulinaemic-euglycaemic clamp correlated closely with the Mastuda index in subjects with normal glucose tolerance ($r = 0.73$, $P < 0.0001$), with IGT ($r = 0.66$, $P<0.0001$) and with type 2 diabetes ($r = 0.54$, $P<0.0001$). Mastuda's index gave better correlations than the ISI(HOMA) ($r = 0.69$, $P<0.0001$), ISI(Ceder) ($r = 0.62$, $P<0 .0001$) and ISI(Bel) ($r = 0.54$, $P<0.0001$) estimates of whole-body insulin sensitivity compared with the hyperinsulinaemic-euglycaemic clamp. The correlation coefficients derived from the Cederholm ($P<0.05$) and Belfiore ($P<0.01$) estimates were significantly lower and there was no correlation between the G/I ratio during the OGTT and the hyperinsulinaemic-euglycaemic clamp ($r = 20.02$, NS) (Matsuda & Defronzo, Diabetes Care 1999, 22: 1462-1470). Lorenzo et al (J Clin Endocrinol Metab 2010, 95 (11): 5082-5090) compared surrogate indices of insulin resistance vs the hyperinsulinaemic-euglycaemic clamp. The correlation for the Matsuda index was $r = 0.77$, and was stronger than for indices derived from fasting insulin ($r = 0.72$) and HOMA ($r=0.71$). Surrogate indices were similar to directly measured insulin sensitivity in their relationships with metabolic abnormalities including definitive measures of fat distribution. The Matsuda method has also been shown to be reproducible for moderately sized clinical trials requiring repeated measurements (Maki et al, Diabetes Technology & Therapeutics, 2010, 12: 895-900), in a study that evaluated the test–retest repeatability of insulin sensitivity and secretion indices derived from liquid meal tolerance tests in subjects with normal fasting glucose. The Matsuda index also appropriately ranked categories of fasting glucose tolerance. The Matsuda index has been used in short-term studies in recent scientific literature. The methodology is safe

		and the results are reproducible and closely correlate with the hyperinsulinaemic-euglycaemic clamp. In view of the strong evidence that supports the Matsuda index as an additional appropriate and validated measure of insulin sensitivity in human intervention studies, it would be helpful for the guidance to confirm that this in an accepted method for measuring insulin sensitivity in human intervention trials, particularly for subject numbers of at least n=30 and for interventions of at least 2 weeks.
For Comvita Ltd	5.3. Claims on increased insulin sensitivity	Line 351 Though the size and time period of studies should be appropriate to the type of study and the variability of the end point, and the size of a study is dependent on a power calculation, it is nevertheless important for the guidance to give a clearer indication as to what is meant by "short-term" and "small numbers of subjects". Industry requires more specific guidance as a basis for designing appropriate trials to support claims in this important area of health. We would contend for example that double blind cross-over studies involving 6 months of nutritional supplementation and 3 periods of insulin sensitivity assessment in 50 subjects are neither short term nor small.
For Comvita Ltd	5.3. Claims on increased insulin sensitivity	Line 348 There are good scientific reasons, as well as various practical considerations, why the hyperinsulinaemic-euglycaemic clamp is no longer considered the most appropriate measure of insulin sensitivity in human intervention studies. These include: • The hyperinsulinaemic-euglycaemic clamp is an early method and requires the achievement of steady state conditions to achieve meaningful results. These may vary between groups and are not always easy to define. • Additionally the clamp utilises steady state insulin levels that may be supraphysiological and therefore less meaningful.• Also steady state insulin levels are less representative of the normal highly dynamic relationship between glucose and insulin, so clamping may not accurately reflect insulin sensitivity or insulin resistance under 'normal' physiological conditions. A key reason for this may be the secondary pathways involved in glucose and insulin metabolism which have their own control systems and may respond to prolonged infusion of insulin in an unrepresentative manner. Such pathways can operate at the level of the gut as well as peripheral tissues providing further justification for the use of oral-based dynamic challenges to insulin secretion and glucose uptake. For example the method of Matsuda (Matsuda & Defronzo, Diabetes Care 1999, 22: 1462-1470). • The main limitations of the hyperinsulinaemic-euglycaemic clamp are that it is time consuming, labour intensive, and requires medical supervision and a skilled operator to manage the technical complexity (Grulet et al, Diabetes Res Clin Pract 1993, 20: 201-7; Bastard et al, Diabetes Metab 2003, 29: 285-8; Cutfield et al, Horm Res 2005, 64 (S3): 25-31). It is unsuitable for routine screening of patients outside a hospital base

		(Akinmokun et al, Diabet Med 1992, 9: 432-7). Thus for epidemiological studies, medium to large clinical trials or monitoring interventions the clamp is considered too intensive and inappropriate.• The hyperinsulinaemic-euglycaemic clamp is an invasive technique and for several reasons subjects may be at greater risk compared to other methods, as a result firstly of the use of prolonged insulin infusions and secondly the need for multiple longitudinal blood sampling which far exceeds other methods.• The insulin infusion rate needs to be carefully matched to the study population (eg insulin resistant populations) requiring care and judgement for best results. • Equally, to achieve robust results, more than one insulin infusion rate should be used further decreasing practicality of the clamping approach. • Constant infusion of insulin also requires careful monitoring of potassium to prevent adverse affects. New methods have been developed that overcome these concerns and this is supported by current best practice advice of diabetes researchers and clinicians globally as recently summarised (Levy-Marchal C, Arslanian S, Cutfield W, Sinaiko A, Druet C, Marcovecchio ML, Chiarelli F; ESPE-LWPES-ISPAD-APPES-APEG-SLEP-JSPE; Insulin Resistance in Children Consensus Conference Group. Insulin resistance in children: consensus, perspective, and future directions. J Clin Endocrinol Metab. 2010, 95(12): 5189-98. Epub 2010 Sep 8).
GlaxoSmithKline	5.3. Claims on increased insulin sensitivity	Line 351- Please clarify “short-term” and “small number” so as this point can be fully understood.
HarlandHall Associates	5.3. Claims on increased insulin sensitivity	Line 351 What is the rationale for suggesting the use of HOMA and QUICKI assessment of insulin sensitivity is only appropriate for epidemiological studies. The hyperinsulinaemic-euglycaemic clamp is an invasive and expensive technique. In randomised controlled intervention studies of 6-8 weeks duration the above techniques could also be employed.
HFMA	5.3. Claims on increased insulin sensitivity	Line 348. The hyperinsulinaemic-euglycaemic clamp is a difficult, invasive and time consuming method. Surrogate markers of insulin resistance should be accepted provided they have been shown to correlate to determinations of insulin sensitivity e.g. using the intravenous glucose tolerance test or insulin tolerance test.
ILSI Europe aisbl	5.3. Claims on increased insulin sensitivity	347-352 Type 2 Diabetes develops as a consequence of insulin resistance in a setting of inadequate pancreatic beta-cell compensation. The first line therapy for the treatment of Type 2 Diabetes is the adoption of lifestyle measures (e.g. bodyweight reduction, increasing physical activity) largely designed to promote insulin sensitivity. With respect to the study population, we recommend that studies conducted in diabetic subjects can be used for the scientific substantiation of these claims, with the caveat that in populations under treatment

		with blood glucose lowering medications the rationale for extrapolations of results to a healthy target population should be provided and considered on a case-by-case basis. Although the hyperinsulinaemic-euglycaemic clamp represents the reference standard for directly determining metabolic insulin sensitivity in humans it is an extremely intensive technique which is impractical for use in larger studies [Am J Physiol Endocrinol Metab (2008) 294: E15-E26]. We recommend that consideration should be given on a case-by-case basis for the use of proxy measures of insulin sensitivity for claim substantiation in intervention studies where feasibility issues prevent the use of the clamp procedure. There are conditions in which the change in insulin sensitivity is evident from the data without performing a clamp. For instance, if fasting glucose remains the same and insulin decreases (thus HOMA insulin resistance decreases) it is evident that insulin sensitivity is improved. Paradoxically, this condition may be paralleled by an unchanged M-value from the clamp, as the phenomenon behind this may be improved hepatic insulin sensitivity, not detected by the clamp, which only detects improved periferal (muscle) insulin resistance. Does the panel therefore consider the use of HOMA or OGTT derived measurements of insulin resistance as appropriate parameters of improved insulin sensitivity, in case nutrition improves insulin sensitivity in tissues other than the muscles, for instance the liver or gastrointestinal tract? In which populations would the Panel consider an increase in insulin sensitivity to be beneficial? What would be considered the appropriate study population? There is no mentioning of fasting insulinemia; does the panel not consider maintenance of normal fasting insulinemia levels to be beneficial? 351 Can the Panel define "short-term" and "small numbers of subjects", or provide examples? On which criteria would epidemiological studies be accepted in a dossier?
Kraft Foods R&D	5.3. Claims on increased insulin sensitivity	- (l351) On which criteria would epidemiological studies be accepted in a dossier? - (l352) How "short-term' should be interpreted? - (l352) What is the minimal number of subjects for a study to be considered? Conclusions: Ln 353 – 362: Do you plan to organise a workshop on these topics to better determine the new guidances of EFSA and increase the dialogue opportunities between scientific community and EFSA ?
Kraft Foods R&D	5.3. Claims on increased insulin sensitivity	- (l351) On which criteria would epidemiological studies be accepted in a dossier? - (l352) How "short-term' should be interpreted? - (l352) What is the minimal number of subjects for a study to be considered?
Rudolf Wild GmbH & Co. KG	5.3. Claims on increased insulin sensitivity	Line 348 – The hyperinsulinaemic-euglycaemic clamp is considered a very invasive method and is not used on a regular basis. It might also cause ethical problems and it should be reconsidered by the Panel to use HOMA, ISI and/or QUICKI as standards also for intervention studies. Line 351 – What does "short term" mean? Less than 3 months? What does "small number of subjects" mean?
SYNPA	5.3. Claims on	Lines 347-352: "Increasing insulin sensitivity may be a beneficial physiological effect depending on the target

	increased insulin sensitivity	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." What is the meaning of "short term" in this case? Is it 3 months or more? And what is the expectation for a, or the meaning of "small numbers"? The number of subjects has to be estimated and calculated with some previous studies that give some measures with its standard deviation.
Tate & Lyle Plc	5.3. Claims on increased insulin sensitivity	348: For which target population would it be considered beneficial to health? Diabetics or metabolic syndrome, or obese with impaired glucose tolerance? 351: What would be considered as sufficiently long interventions and high enough number of subjects? Examples would be helpful.
Tate & Lyle Plc	5.3. Claims on increased insulin sensitivity	General comments: • Missing information regarding low grade inflammation and obesity/diabetes. • Is a reduction in low grade inflammation in the visceral adipose tissue considered as beneficial to health and sufficient to make a claim referring to inflammation? • Examples of acceptable claim wordings for each section would be helpful • Also nothing is mentioned about prevention of fatty liver disease (NASH) or other diseases like CVD, diabetes • Can weight gain or visceral fat be considered a validated risk factors for fatty liver disease (NASH) or other diseases like CVD, diabetes
TNO	5.3. Claims on increased insulin sensitivity	348: Indeed the hyperinsulinemic euglycemic clamp is the gold standard for measuring insulin sensitivity. Other measures of insulin sensitivity have been developed and used in studies. The guidance refers to the acceptable use of such measures in epidemiologic studies. We would like to argue that the acceptability of the use of other methods should depend on both the correlation with the gold standard and on size and duration of the studies in which they are used. In addition, a meta-analysis of (smaller) studies in which a consistent effect is seen on one of the "proxy" outcome measures, may provide valid scientific support. In addition, we would like to have the Panel's opinion on the use of FSivGTT (frequently-samples intravenous glucose tolerance test), which was mentioned in the PASSCLAIM documents as an alternative for the glucose

		clamp.
Unilever	5.3. Claims on increased insulin sensitivity	Section 5.3 - Claims on increased insulin sensitivity General Comment In general we are supportive of the proposed EFSA guidance on the scientific requirements for health claims relating to blood glucose concentrations. We have, however, identified a few areas where we think changes are warranted. For simplicity our comments have been substantiated with a few key references but if it is useful to do so or if further information is required then additional references can be supplied. Lines 347-352 • Although the hyperinsulinaemic-euglycaemic clamp represents the reference standard for directly determining metabolic insulin sensitivity in humans it is an extremely intensive technique which is impractical for use in larger studies. Furthermore, the procedure utilises supra-physiological plasma levels of insulin which may not accurately reflect insulin action and glucose dynamics under physiological conditions. Many alternative methods for assessing insulin sensitivity have been developed. As each has distinct advantages and limitations, the selection of the appropriate method is very much dependent on the size and nature of the study [Am J Physiol Endocrinol Metab (2008) 294: E15-E26]. Based on this we strongly recommend that for intervention studies where feasibility issues prevent the use of the clamp procedure consideration should be given on a case-by-case basis for the use of alternative measures of insulin sensitivity for claim substantiation. Indeed, surrogate indices (e.g. Matsuda index, Gutt index) based on information derived from an OGTT correlate well with clamp measures [Diabetes Care (1999) 22: 1462-1470; Diabetes Res Clin Pract (2000) 47: 177-184] and may reflect more closely the glucose and insulin dynamics of physiological conditions. • Type 2 Diabetes develops as a consequence of insulin resistance in a setting of inadequate pancreatic beta-cell compensation. The first line therapy for the treatment of Type 2 Diabetes is the adoption of lifestyle measures (e.g. bodyweight reduction, increasing physical activity) largely designed to promote insulin sensitivity. With respect to the study population, we recommend that studies conducted in diabetic subjects can be used for the scientific substantiation of these claims. However, in populations under treatment with blood glucose lowering medications the rationale for the extrapolations of results to a healthy target population should be provided and considered on a case-by-case basis.
University of Leeds	5.3. Claims on increased insulin sensitivity	Line 348: Although the proposal to measure insulin sensitivity via hyperinsulinaemic-euglycaemic clamp is valid. This is an invasive measure and is labour intensive. This measure along with repeated venous sampling, whether arterialized or not requires careful supervision and both strategies, in and of themselves, are likely to exert effect on subjective state and appetite response which could confound other measures. Moreover,

		insistence on these types of measures limits the research and reduces ecological validity and therefore relevance to the consumer. Evidence from other less invasive techniques should also be considered. Again, my concern is that the imposition of the use of these highly invasive techniques and their exclusive acceptance by EFSA will lead to the curtailment of research to develop and validate less invasive, more cost effective and portable techniques which would have benefits to the scientific field in toto. These restrictions limit the potential funders of research (excluding smaller companies with limited budgets) and confine the research to institutions which have the facilities to undertake these invasive or highly technological measures. Taken together the guidance as it stands would not deliver or facilitate the development of sound evidence for claims nor further academic development of the field.
University of Leeds, Leeds, UK	5.3. Claims on increased insulin sensitivity	Line 348: The hyperinsulinaemic-euglycaemic clamp measure of insulin sensitivity is an invasive and labour intensive measure. Evidence from other simpler and less expensive techniques should also be considered.
University of Limerick	5.3. Claims on increased insulin sensitivity	Line 346 and on.. fully support this section
VAB-nutrition	5.3. Claims on increased insulin sensitivity	Ln 348-352. It appears from this that the only appropriate measure of insulin sensitivity in human intervention studies is the hyperinsulinaemic-euglycaemic clamp. It is specified that 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. May the panel provide some guidance about the appropriate duration and sample size for randomized controlled trials to be entitled to use such proxy biomarkers?