



Københavns Universitet

A fixed carbohydrate:protein ratio 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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

Published in:
E F S A Journal

DOI:
[10.2903/j.efsa.2017.4839](https://doi.org/10.2903/j.efsa.2017.4839)

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Document license:
[CC BY](https://creativecommons.org/licenses/by/4.0/)

Citation for published version (APA):
EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2017). A fixed carbohydrate:protein ratio 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006: (Scientific Opinion). *E F S A Journal*, 15(6), [4839]. <https://doi.org/10.2903/j.efsa.2017.4839>

ADOPTED: 4 May 2017

doi: 10.2903/j.efsa.2017.4839

A fixed carbohydrate:protein ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA),
Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean,
Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf,
Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka,
Kristina Pentieva, Yolanda Sanz, Anders Sjödin, Martin Stern, Daniel Tomé, Henk Van Loveren,
Marco Vinceti, Peter Willatts, Ambroise Martin, John Joseph Strain and Alfonso Siani

Abstract

Following an application from Marks and Spencer PLC, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to a CHO:P ratio ≤ 1.8 on an energy basis in the context of an energy-restricted diet and body weight. The Panel considers that the food/constituent that is the subject of the health claim is sufficiently characterised. The Panel also considers that reduction of body weight in the context of an energy-restricted diet is a beneficial physiological effect. The target population proposed by the applicant is 'adults between the ages of 18 and 70 years with excess body weight'. No conclusions could be drawn from two unpublished studies investigating the effect of ready-to-eat meals with a CHO:P ratio ≤ 1.8 on body weight. The remaining 14 human intervention studies investigated the effect of diets targeting a CHO:P ratio ≤ 1.8 as compared to diets targeting a CHO:P ratio ≥ 3.0 on overweight and obese adults in the context of energy restriction. Four out of seven studies lasting < 12 weeks reported an effect of a CHO:P ratio ≤ 1.8 on body weight in overweight/obese subjects, whereas no significant effect was observed in six out of the seven studies lasting 12 weeks or more. The Panel considers that these studies do not provide evidence for a sustained effect of the food/constituent on body weight. The Panel concludes that a cause and effect relationship has not been established between the consumption of a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

© 2017 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: carbohydrate:protein ratio, energy-restricted diet, body weight, obesity, weight loss, health claim

Requestor: Competent Authority of the United Kingdom following an application by Marks and Spencer PLC

Question number: EFSA-Q-2016-00436

Correspondence: nda@efsa.europa.eu

Panel members: Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Dominique Turck, Hendrik Van Loveren, Marco Vinceti and Peter Willatts.

Acknowledgements: The Panel wishes to thank the members of the Working Group on Claims: Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Harry J McArdle, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Sean (J.J.) Strain, Hendrik Van Loveren and Peter Willatts, for the preparatory work on this scientific output.

Suggested citation: EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle HJ, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Sjödin A, Stern M, Tomé D, Van Loveren H, Vinceti M, Willatts P, Martin A, Strain JJ and Siani A, 2017. Scientific Opinion on a fixed carbohydrate:protein ratio \leq 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight: evaluation of a health claim pursuant to Article 13 (5) of Regulation (EC) No 1924/2006. *EFSA Journal* 2017;15(6):4839, 12 pp. <https://doi.org/10.2903/j.efsa.2017.4839>

ISSN: 1831-4732

© 2017 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs License](https://creativecommons.org/licenses/by/4.0/), which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.



The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.



Summary

Following an application from Marks and Spencer PLC, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The application included a request for the protection of proprietary data.

The general approach of the NDA Panel for the evaluation of health claim applications is outlined in the EFSA general guidance for stakeholders on health claim applications and the guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations.

In the application, the food proposed by the applicant as the subject of the health claim is 'a high-protein moderate-carbohydrate (HPMC) "macronutrient recipe" (used in a range of pre-prepared meals), which is a mixture of food ingredients/whole foods chosen to provide a macronutrient composition with a ratio of carbohydrate:protein (CHO:P) equal to or less than 1.8:1'.

Upon a request from the European Food Safety Authority (EFSA), the applicant acknowledged that the food/constituent that is the subject of the health claim is a CHO:P ratio < 1.8 on an energy basis in the context of an energy-restricted diet, which could be achieved by the combination of a wide range of foods belonging to several food categories in variable amounts. Foods or meals with a CHO:P ratio ≤ 1.8 on an energy basis, when consumed in the context of an energy-restricted diet, are proposed to bear the claim.

The Panel considers that the food/constituent that is the subject of the health claim, a fixed CHO:P ratio ≤ 1.8 on an energy basis to be consumed in the context of an energy-restricted diet, is sufficiently characterised.

The claimed effect proposed by the applicant is 'reduction in total body weight in overweight adults, under energy restricted conditions'. The target population proposed by the applicant is 'adults between the ages of 18 and 70 with excess body weight (BMI > 25 kg/m²)'. The Panel considers that reduction of body weight in the context of an energy restricted diet is a beneficial physiological effect.

The applicant provided a total of 16 human intervention studies for the scientific substantiation of the claim. The Panel considers that no conclusions can be drawn from two unpublished studies investigating the effect of a range of ready-to-eat meals with a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet on body weight for the scientific substantiation of the claim.

The remaining 14 human intervention studies investigated the effect of diets targeting a CHO:P ratio ≤ 1.8 on an energy basis as compared to diets targeting a CHO:P ratio ≥ 3.0 on an energy basis on overweight and obese adults (BMI > 25 kg/m²) in the context of energy restriction.

The Panel notes that four out of seven studies lasting < 12 weeks reported an effect of a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of energy restriction on body weight in overweight/obese subjects, whereas no significant effect was observed in six out of the seven studies lasting 12 weeks or more. The Panel considers that these studies do not provide evidence for a sustained effect of the food/constituent on body weight.

In the absence of evidence for a sustained effect of a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of energy restriction on body weight, the studies provided by the applicant on the proposed mechanisms by which the food/constituent could exert the claimed effect were not considered by the Panel for the scientific substantiation of the claim.

On the basis of data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

Table of contents

Abstract.....	1
Summary.....	3
1. Introduction.....	5
1.1. Background and Terms of Reference as provided by the requestor.....	5
1.2. Interpretation of the Terms of Reference.....	5
2. Data and methodologies.....	5
2.1. Data.....	5
2.2. Methodologies.....	6
3. Assessment.....	7
3.1. Characterisation of the food/constituent.....	7
3.2. Relevance of the claimed effect to human health.....	7
3.3. Scientific substantiation of the claimed effect.....	8
4. Conclusions.....	10
Steps taken by EFSA.....	11
References.....	11
Abbreviations.....	12

1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1924/2006¹ harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

1.2. Interpretation of the Terms of Reference

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: a fixed carbohydrate:protein (CHO:P) ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction in body weight.

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet, a positive assessment of its safety, nor a decision on whether a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

2. Data and methodologies

2.1. Data

Information provided by the applicant

Food/constituent as stated by the applicant

According to the applicant, the food for which the health claim is made is a high-protein medium-carbohydrate (HPMC) macronutrient blend, which comprises a mixture of food ingredients chosen to provide a macronutrient composition with a ratio of carbohydrate:protein (CHO:P) equal to or less than 1.8:1, presented in prepared recipes. The prepared recipes can be used to deliver an energy restricted diet with a total energy of between 5,021 and 8,368 kJ/day (1,200–2,000 kcal/day), a suitable energy restriction for overweight adults (body mass index (BMI) > 25) wishing to lose excess body weight. When consumed in this context, a CHO:P macronutrient ratio $\leq 1.8:1$ describes high-protein, moderate-carbohydrate meals. Each meal prepared with the HPMC recipe comprises a maximum of 50% energy from carbohydrates, a minimum of 30% of energy from protein and a maximum of 30% energy from fat. HPMC is delivered via whole foods in a balanced range of ready-to-eat meals and is not a preformulated macronutrient recipe intended for use as a meal replacement, e.g. in liquid diets.

¹ 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.

Health relationship as claimed by the applicant

According to the applicant, the claimed effect relates to: 'reduction in total body weight in overweight adults, under energy restricted conditions. The outcome measures used to assess the relationship between HPMC diet consumption and reduction in total body weight were body weight, body lean mass and body fat mass'.

Mechanism by which the food/constituent could exert the claimed effect as proposed by the applicant

According to the applicant, influences on satiety and on energy efficiency are generally accepted to underlie the significantly greater weight loss while consuming HPMC diets than when consuming standard protein (SP) diets. Protein affects feedback mechanisms linked to satiety; the combination of protein and carbohydrate in HPMC diets has been shown to affect hormone signalling in the gut, and has recently been demonstrated to interact with specific genes to modify response to weight loss.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: 'helps to achieve a reduction in body weight and body fat when consumed as part of an energy restricted diet (< 8,368 kJ/2,000 kcal/day) for a minimum of 12 weeks'.

Specific conditions of use as proposed by the applicant

According to the applicant, the target population for the health claim is adults between the ages of 18 and 70 years with excess body weight (BMI > 25 kg/m²). The HPMC macronutrient blend has been incorporated into prepared ready-to-eat meals. These meals are presented with a clear indication of their caloric value, for selection by the individual to make a daily menu which delivers a set energy intake, recommended at 5,021–8,368 kJ/day (1,200–2,000 kcal/day), suitable for overweight adults wishing to lose weight. The specific daily caloric intake is determined by considering the individual's gender, age range and level of activity. Menus can be entirely self-designed or can be selected from a range of four varied weekly menus already prepared. Daily menus selected at the set calorie intake should be consumed for a minimum of 12 weeks to achieve a clinically significant weight loss.

Data provided by the applicant

Health claim application on consumption of high-protein, medium-carbohydrate range of foods and a reduction in body weight and body fat pursuant to Article 13.5 of Regulation 1924/2006, presented in a common and structured format as outlined in the Scientific and technical guidance for the preparation and presentation of applications for authorisation of health claims.²

As outlined in the General guidance for stakeholders on health claim applications,³ it is the responsibility of the applicant to provide the totality of the available evidence.

This health claim application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006.

Data claimed to be proprietary by the applicant include: product specification and analysis, manufacturing process and quality control, stability information, manufacturing process, supplementary nutritional/compositional information.

2.2. Methodologies

The general approach of the NDA Panel for the evaluation of health claim applications is outlined in the EFSA general guidance for stakeholders on health claim applications (EFSA NDA Panel, 2016).

The scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations are outlined in a specific EFSA guidance (EFSA NDA Panel, 2012).

² EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle HJ, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Sjödin A, Stern M, Tomé D, Van Loveren H, Vinceti M, Willatts P, Martin A, Strain JJ, Heng L, Valtuena Martinez S and Siani A, 2017. Scientific and technical guidance for the preparation and presentation of a health claim application (Revision 2). EFSA Journal 2017;15(1):4680, 31 pp. <https://doi.org/10.2903/j.efsa.2017.4680>

³ EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. General scientific guidance for stakeholders on health claim applications. EFSA Journal 2016;14(1):4367, 38 pp. <https://doi.org/10.2903/j.efsa.2016.4367>

3. Assessment

3.1. Characterisation of the food/constituent

In the application, the food proposed by the applicant as the subject of the health claim is 'a high-protein moderate-carbohydrate (HPMC) "macronutrient recipe" (used in a range of pre-prepared meals), which is a mixture of food ingredients/whole foods chosen to provide a macronutrient composition with a ratio of carbohydrate:protein (CHO:P) equal to or less than 1.8:1'.

According to the applicant, the diet plan is available to consumers as a selection of ready-to-eat meals (excluding preformulated macronutrient recipes intended for use as meal replacements in, e.g. liquid diets), all with a CHO:P ratio (expressed as the energy contribution of carbohydrates/the energy contribution of protein) ≤ 1.8 . The applicant claims that this is likely to increase compliance with the proposed diet. Consumers are provided with nutrition advice to combine meals together with fresh fruit and vegetables, to achieve a total daily energy intake $< 8,368$ kJ/day (2,000 kcal/day). Menu planners and energy calculators are provided on a dedicated website. Consumers should maintain the proposed diet for a minimum period of 12 weeks.

In response to a request for clarification by EFSA during the scientific evaluation of the claim, the applicant confirmed that the subject of the health claim is a diet characterised by a CHO:P ratio ≤ 1.8 . The diet is 'energy restricted' (total energy intake $< 8,368$ kJ/day (2,000 kcal/day)), with a maximum of 50% energy from carbohydrates, a minimum of 30% energy from protein and a maximum of 30% energy from fat. The comparator diet is characterised by a CHO:P ratio > 2.0 , with $> 50\%$ energy from carbohydrates, 20–30% energy from fat and $< 20\%$ energy from protein.

Being informed that the claim on a whole diet does not comply with the requirements laid down in Regulation (EC) No 1924/2006, which defines a health claim as any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health, the applicant clarified that the subject of the application is 'a fixed combination of carbohydrate and protein, such that on consumption, the energy derived from carbohydrate is equal to or less than 1.8 times the energy derived from protein. The fixed combination of carbohydrate and protein has been incorporated into prepared meals, using a wide range of food types in specially formulated recipes'. The applicant stated that 'the composite meals should be viewed as the vehicle in which the defined food component is presented to the consumer'.

In this context, the applicant acknowledged that the food/constituent that is the subject of the health claim is a CHO:P ratio ≤ 1.8 on an energy basis in the context of an energy-restricted diet, which could be achieved by the combination of a wide range of foods belonging to several food categories in variable amounts. Foods or meals with a CHO:P ratio ≤ 1.8 on an energy basis, when consumed in the context of an energy-restricted diet, are proposed to bear the claim.

The Panel considers that the food/constituent that is the subject of the health claim, a fixed CHO:P ratio ≤ 1.8 on an energy basis to be consumed in the context of an energy-restricted diet, is sufficiently characterised.

3.2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is 'reduction in total body weight in overweight adults, under energy restricted conditions'. The target population proposed by the applicant is 'adults between the ages of 18 and 70 years with excess body weight (BMI > 25 kg/m²)'.

A reduction in body weight is 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 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 (EFSA NDA Panel, 2012).

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 (EFSA NDA Panel, 2012).

The Panel considers that reduction of body weight in the context of an energy-restricted diet is a beneficial physiological effect.

3.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in the Cochrane Central Register of Controlled Trials, PubMed and Embase databases, to find evidence in support of using an energy-restricted diet with a selected, fixed macronutrient composition for weight loss, in adults with excess body weight (BMI > 25 kg/m²). Selection criteria included: macronutrient composition of the active intervention to be carbohydrate at $> 20\%$ and $< 50\%$ total energy, fat at 20–30% total energy and protein at $> 30\%$ total energy, with a CHO:P ratio < 2.0 . The control diet was specified to contain carbohydrate at $> 50\%$ total energy, fat at 20–30% total energy and protein at $< 20\%$ as total energy, with a CHO:P ratio > 2.0 . Studies using liquid diets and meal replacements were excluded.

The applicant confirmed that the search terms used were broader than the definition of the food/constituent being the subject of the claim proposed.

Human intervention studies

The applicant provided a total of 16 human intervention studies for the scientific substantiation of the claim (Baba et al., 1999; Labayen et al., 2003; Layman et al., 2003; Johnston et al., 2004; McAuley et al., 2005; Noakes et al., 2005; Kleiner et al., 2006; Leidy et al., 2007; Clifton et al., 2008; Lasker et al., 2008; Abete et al., 2009; Evangelista et al., 2009; Layman et al., 2009; Johnstone, 2010, unpublished study report; Wycherley et al., 2012; Johnstone and Maloney, 2015, unpublished study report), of which two (Johnstone, 2010, unpublished study report; Johnstone and Maloney, 2015, unpublished study report) were conducted using the ready-to-eat meals described in the application.

The study by Johnstone (2010, unpublished study report) was a one-arm, short-term (4 weeks) pilot study which assessed the effect of a range of ready-to-eat meals with a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet on body weight in a group of overweight and obese adults (mean BMI 33.7 ± 4.0 kg/m²). The Panel considers that no conclusions can be drawn from this uncontrolled study for a scientific substantiation of the claim.

In a two-arm, parallel study by Johnstone and Maloney (2015, unpublished study report), the effect of a range of ready-to-eat meals with a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet on body weight was evaluated in a group of 34 overweight and obese adults 'with no existing medical conditions or taking medications that could influence appetite or mood'. The control group consisted of 16 subjects. No information was provided on the target CHO:P ratio, energy restriction, or macronutrient composition of the diet for this study group.

The procedures for the selection and inclusion of subjects in the study were not described. Upon a request from EFSA, the applicant clarified that 'subjects were self-selected in response to an advert shown in local press for a weight loss diet trial'. Volunteers completed a self-reported screening form to record height, body weight and medication use. A medical examination was conducted in the study centre. The Panel notes the poor reporting of the study, and that detailed inclusion and exclusion criteria were not specified in the study report or in the reply to EFSA request.

No information was provided on the primary and secondary outcomes of the study. Upon a request for clarification from EFSA, the applicant specified that the primary outcome was changes in body weight. Secondary outcomes were changes in body composition (i.e. fat mass and fat-free mass measured by air-displacement plethysmography), waist circumference, waist-to-hip ratio, indices of appetite and hunger, and changes in selected biomarkers (e.g. blood pressure, plasma lipids, fasting plasma glucose, nutrient intakes).

The applicant was requested to provide details on the allocation of subjects to the intervention and control groups, including the methods used for randomisation, if any. The applicant stated that randomisation into the study groups was overseen by the study statistician using a randomisation matrix, and that the study groups were balanced to give equal numbers of males and females in each arm. The Panel notes that this information was absent in the study report, that no more details were provided on how randomisation was conducted, and that the unequal number of subjects randomised to the intervention ($n = 34$) and control ($n = 16$) groups was not justified.

No information was provided on how the study had been powered. The applicant claims that, based on pilot studies, a reduction in body weight of 7–10 kg was expected in the intervention group relative to baseline. The applicant also claimed that, to detect a decrease in body weight of 7.0 kg with a two-sided significance level of 0.05 and a power of 0.90, 28 subjects would be needed in the intervention group. The Panel notes that the control group includes only 16 subjects, that power calculations do not appear to have been performed on a target weight loss difference at the end of

the study between the intervention and control groups, and that the baseline characteristics of the control group were not provided.

The participants in the intervention group were given, every other week, ready-to-eat meals (salads, main meals, sandwiches and soups from the range of foods characterised by high protein and low carbohydrate content) with a CHO:P ratio ≤ 1.8 on an energy basis and an energy content of 661–2,167 kJ (158–518 kcal) per portion, depending on whether the dish had been developed as a main meal or as a light lunch. The participants were given access to a range of daily menus or self-designing menus. Additionally, they selected a range of fresh fruit and vegetables to be incorporated into the diet.

The control group was assigned two types of menu. One referred to ready-to-eat meals which had not been formulated with any specific macronutrient composition. The second menu allowed self-preparation of foods from specific ingredients; daily meal suggestions were supplied. Subjects in the control group were given advice regarding healthy eating for weight loss (i.e. booklet, menu plan and recipes). The target energy intake for control group was not reported.

The intervention lasted 12 weeks. All subjects attended the centre on a biweekly basis, and body weight was recorded. Upon a request from EFSA to specify the statistical methods used for data analysis, the applicant clarified that 'all data was scrutinised for outliers and tested for normality. Changes in the various outcome variables, relative to the maintenance diet, were compared by ANOVA. Both inter-subject and intra-subject comparisons were made'. The Panel notes that the description of the statistical methods used for data analysis is insufficient for a scientific evaluation.

A total of 34 adult subjects (mean age 39.8 ± 2.2 years, BMI 32.2 ± 0.58 kg/m²) were assigned to the intervention group and 30 (15 women) completed the study. Four participants dropped-out; the reasons were not reported. The control group consisted of 16 subjects (8 females) (number of drop-outs not reported). Baseline characteristics for the control group were not provided.

The Panel notes the poor reporting of the study with respect to the methods used for the recruitment of subjects, the inclusion and exclusion criteria, the rationale for sample size calculation, the allocation of subjects to the study groups, the characterisation of the intervention (energy-restriction target) and control (macronutrient composition, energy and CHO:P ratio target) diets, and the methods used for the statistical analysis of data. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The remaining 14 human intervention studies investigated the effect of diets targeting a CHO:P ratio ≤ 1.8 on an energy basis as compared to diets targeting a CHO:P ratio ≥ 3.0 on an energy basis on overweight and obese adults (BMI > 25 kg/m²) in the context of energy restriction. The target energy restriction was similar in both the intervention and control groups. In some studies, dietary advice was given to participants (McAuley et al., 2005; Evangelista et al., 2009); in others, either fully planned daily diets (Leidy et al., 2007; Clifton et al., 2008; Lasker et al., 2008; Abete et al., 2009; Layman et al., 2009) or prepared meals were provided. Prepared meals were supplied either to replace part of the diet (Johnston et al., 2004; Noakes et al., 2005) or the whole diet (Baba et al., 1999; Layman et al., 2003; Kleiner et al., 2006; Wycherley et al., 2012).

The intervention lasted less than 12 weeks in seven studies (Baba et al., 1999; Labayen et al., 2003; Layman et al., 2003; Johnston et al., 2004; McAuley et al., 2005; Kleiner et al., 2006; Abete et al., 2009) and 12 weeks or more in seven studies (Noakes et al., 2005; Leidy et al., 2007; Clifton et al., 2008; Lasker et al., 2008; Layman et al., 2009; Evangelista et al., 2009; Wycherley et al., 2012).

In the short-term studies (lasting < 12 weeks), study duration ranged between 4 and 10 weeks and sample size between 11 and 71 subjects (about half on each study group). The target CHO:P ratio for the intervention group ranged between 0.6 and 1.4 on energy basis, and between 3.2 and 4.8 for the control group. Within each study, the targeted energy intake for the intervention and control groups was similar, although variable between studies (i.e. some targeted an energy deficit at individual level, whereas others aimed at a fixed energy intake or ranges of energy intake for the groups). Overall, diets provided between 1,200 and 1,800 kcal/day. In most cases, the target CHO:P ratio of the intervention and control diets was achieved by participants during the study. Four studies report a significant reduction in body weight in the intervention group compared to controls (Baba et al., 1999; Labayen et al., 2003; McAuley et al., 2005; Abete et al., 2009), whereas three studies report no significant differences between groups (Layman et al., 2003; Johnston et al., 2004; Kleiner et al., 2006). The Panel notes that the characteristics of the studies showing a significant effect of the intervention as compared to the control group on body weight were comparable to the characteristics of the studies not showing a significant effect.

In the long-term studies (lasting ≥ 12 weeks), study duration ranged between 12 and 52 weeks and sample size between 14 and 100 subjects (about half in each study group). The target CHO:P ratio for the intervention group ranged between 1.1 and 1.5 on energy basis, and between 3.2 and 3.8 for the control group. Within each study, the targeted energy intake for the intervention and control groups was similar. Overall, diets provided between 1,200 and 1,800 kcal/day. In most cases (except in the study by Clifton et al., 2008), the target CHO:P ratio of the intervention and control diets was achieved during the study. The Panel notes that in the study by Evangelista et al. (2009), the CHO:P ratio achieved in the study groups was not reported. Among the seven studies lasting ≥ 12 weeks, this (Evangelista et al., 2009) is the only study which reports a significant effect of the intervention on body weight as compared to 'standard protein diet' or a 'conventional diet'. The Panel notes that this is also the study with the smallest sample size (≤ 5 subjects per group). In the study by Noakes et al. (2005), a significant effect of the intervention as compared to the control was reported in the intention-to-treat (ITT) analysis in which baseline body weight for drop-outs was carried forward, whereas the effect was not significant in the ITT analysis in which the last observation for drop-outs was carried forward or in the per-protocol (PP) analysis. The Panel considers that this study does not show an effect of a CHO:P ratio ≤ 1.8 on body weight. In the remaining five studies, no significant effect of the intervention as compared to the control on body weight was reported.

The Panel notes that four (Baba et al., 1999; Labayen et al., 2003; McAuley et al., 2005; Abete et al., 2009) out of seven studies lasting < 12 weeks report an effect of a CHO:P ratio ≤ 1.8 on energy basis consumed in the context of energy restriction on body weight in overweight/obese subjects, whereas no significant effect was observed in six out of seven studies lasting 12 weeks or more as compared to the control (Noakes et al., 2005; Leidy et al., 2007; Clifton et al., 2008; Lasker et al., 2008; Layman et al., 2009; Wycherley et al., 2012). The Panel considers that these studies do not provide evidence for a sustained effect of the food/constituent on body weight.

Mechanisms of action

The applicant indicated several possible mechanisms by which the food/constituent could exert the claimed effect on body weight and body fat, including the satiating and thermogenic effect of protein, interactions of protein with leptin, luteinising hormone (LH), glucagon-like peptide-1 (GLP-1), peptide YY (PYY) and some immunoproteins.

In the absence of evidence for a sustained effect of a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of energy restriction on body weight, the studies provided by the applicant on the proposed mechanisms by which the food/constituent could exert the claimed effect were not considered by the Panel for the scientific substantiation of the claim.

Weighing of the evidence

In weighing the evidence, the Panel took into account that, among the 14 human intervention studies from which conclusions could be drawn for the substantiation of the claim, four out of the seven lasting < 12 weeks reported a significant effect of a CHO:P ratio ≤ 1.8 as compared to a CHO:P ratio > 3.2 during energy restriction on body weight, whereas six out of the seven studies lasting ≥ 12 weeks did not. In the absence of evidence for a sustained effect of a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of energy restriction on body weight, the Panel did not consider the studies provided in support of a mechanism by which the food/constituent could exert the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

4. Conclusions

On the basis of the data presented, the Panel concludes that:

- a fixed CHO:P ratio ≤ 1.8 on an energy basis to be consumed in the context of an energy-restricted diet is sufficiently characterised.
- the claimed effect proposed by the applicant is 'reduction in total body weight under energy restricted conditions'. The target population proposed by the applicant is 'adults between the ages of 18 and 70 with excess body weight (BMI > 25 kg/m²)'. Reduction of body weight in the context of an energy-restricted diet is a beneficial physiological effect.

- a cause and effect relationship has not been established between a CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

Steps taken by EFSA

Health claim application on 'In the context of a well-balanced diet and a mild caloric restriction, the addition of high-protein, medium-carbohydrate range of foods' and 'reduction in body weight and body fat' pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 000319_0449_UK). Submitted by Marks and Spencer plc (No. 214436), Waterside House, 35 North Wharf Road, London W2 1NW, United Kingdom. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The application included a request for the protection of proprietary data.

- 1) This application was received by EFSA on 6/7/2016. On 31/8/2016, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- 2) On 12/9/2016, EFSA received the missing information as submitted by the applicant.
- 3) The scientific evaluation procedure started on 6/10/2016.
- 4) On 16/11/2016, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The scientific evaluation was suspended on 8/12/2016 and was restarted on 23/12/2016, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- 5) On 6/1/2017, EFSA received the applicant's reply (which was made available to EFSA in electronic format on 6/1/2017).
- 6) On 4/4/2017, the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The scientific evaluation was suspended on 13/4/2017 and was restarted on 28/4/2017, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- 7) On 1/5/2017, EFSA received the applicant's reply.
- 8) On 4/5/2017, the NDA Panel, having evaluated the data submitted, adopted by written procedure an opinion on the scientific substantiation of a health claim related to a fixed CHO:P ratio ≤ 1.8 on an energy basis consumed in the context of an energy-restricted diet and reduction of body weight.

References

- Abete I, Parra D, De Morentin BM and Alfredo Martinez J, 2009. Effects of two energy restricted diets differing in the carbohydrate/protein ratio on weight loss and oxidative changes of obese men. *International Journal of Food Sciences and Nutrition*, 60(suppl 3), 1–13.
- Baba NH, Sawaya S, Torbay N, Habbal Z, Azar S and Hashim SA, 1999. High protein vs high carbohydrate hypoenergetic diet for the treatment of obese hyperinsulinemic subjects. *International Journal of Obesity and Related Metabolic Disorders*, 23, 1202–1206.
- Clifton PM, Keogh JB and Noakes M, 2008. Long-term effects of a high-protein weight loss diet. *American Journal of Clinical Nutrition*, 87, 23–29.
- EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2012. Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations. *EFSA Journal* 2012;10(3):2604, 11 pp. <https://doi.org/10.2903/j.efsa.2012.2604>
- EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. General scientific guidance for stakeholders on health claim applications. *EFSA Journal* 2016;14(1):4367, 38 pp. <https://doi.org/10.2903/j.efsa.2016.4367>
- Evangelista LS, Heber D, Li Z, Bowerman S, Hamilton MA and Fonarow GC, 2009. Reduced body weight and adiposity with a high-protein diet improves functional status, lipid profiles, glycemic control, and quality of life in patients with heart failure: a feasibility study. *Journal of Cardiovascular Nursing*, 24, 207–215.
- Johnston CS, Tjonn SL and Swan PD, 2004. High-protein, low-fat diets are effective for weight loss and favorably alter biomarkers in healthy adults. *Journal of Nutrition*, 134, 586–591.
- Johnstone AM, 2010. A controlled pilot trial assessing the efficacy of a 4-week hypocaloric high protein medium carbohydrate diet on reduction in body weight, motivation to eat and selected biomarkers of health in overweight and obese men and women. (unpublished study report).

- Johnstone AM and Maloney N, 2015. A randomised controlled trial assessing the efficacy of a 12-week hypocaloric high protein medium carbohydrate diet, with a further 12-week follow-up, on reduction of body weight and fat, hunger and selected other biomarkers of health in overweight and obese men and women. (unpublished study report).
- Kleiner RE, Hutchins AM, Johnston CS and Swan PD, 2006. Effects of an 8-week high-protein or high-carbohydrate diet in adults with hyperinsulinemia. *Medscape General Medicine*, 8, 39–44.
- Labayen I, Diez N, Gonzalez A, Parra D and Martinez JA, 2003. Effects of protein vs. carbohydrate-rich diets on fuel utilisation in obese women during weight loss. *Forum of Nutrition*, 56, 168–170.
- Lasker DA, Evans EM and Layman DK, 2008. Moderate carbohydrate, moderate protein weight loss diet reduces cardiovascular disease risk compared to high carbohydrate, low protein diet in obese adults: a randomized clinical trial. *Nutrition and Metabolism*, 5, 30–38.
- Layman DK, Boileau RA, Erickson DJ, Painter JE, Shiue H, Sather C and Christou DD, 2003. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. *Journal of Nutrition*, 133, 411–417.
- Layman DK, Evans EM, Erickson D, Seyler J, Weber J, Bagshaw D, Griel A, Psota T and Kris-Etherton P, 2009. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *Journal of Nutrition*, 139, 514–521.
- Leidy HJ, Carnell NS, Mattes RD and Campbell WW, 2007. Higher protein intake preserves lean mass and satiety with weight loss in pre-obese and obese women. *Obesity*, 15, 421–429.
- McAuley KA, Hopkins CM, Smith KJ, McLay RT, Williams SM, Taylor RW and Mann JI, 2005. Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia*, 48, 8–16.
- Noakes M, Keogh JB, Foster PR and Clifton PM, 2005. Effect of an energy-restricted, high-protein, low-fat diet relative to a conventional high-carbohydrate, low-fat diet on weight loss, body composition, nutritional status, and markers of cardiovascular health in obese women. *American Journal of Clinical Nutrition*, 81, 1298–1306.
- Wycherley TP, Brinkworth GD, Clifton PM and Noakes M, 2012. Comparison of the effects of 52 weeks weight loss with either a high-protein or high-carbohydrate diet on body composition and cardiometabolic risk factors in overweight and obese males. *Nutrition and Diabetes*, 2, e40. <https://doi.org/10.1038/nutd.2012.11>

Abbreviations

BMI	body mass index
CHO:P	carbohydrate:protein
GLP-1	glucagon-like Peptide-1
HPMC	high-protein medium-carbohydrate
ITT	intention-to-treat
LH	luteinising Hormone
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
PP	per protocol
PYY	peptide YY
SP	standard protein