EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2014. Scientific Opinion on the substantiation of a health claim related to Bimuno® GOS and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to Bimuno® GOS and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006[1]

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from Clasado Limited, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Malta, 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 Bimuno® GOS and reducing gastro-intestinal discomfort. The food constituent that is the subject of the health claim, Bimuno® GOS, which is a mixture of β-galacto-oligosaccharides produced through conversion of lactose by enzymes from *Bifidobacterium bifidum* NCIMB 41171, is sufficiently characterised. The claimed effect is reducing gastro-intestinal discomfort and is considered to be a beneficial physiological effect. The applicant did not provide any studies from which data could be used for the scientific substantiation of the claimed effect of reducing gastro-intestinal discomfort. A cause and effect relationship has not been established between the consumption of Bimuno® GOS and reducing gastro-intestinal discomfort.

KEY WORDS

Bimuno®, GOS, β-galacto-oligosaccharides, gastro-intestinal discomfort, health claims

[1] On request from the Competent Authority of Malta following an application by Clasado Limited, Question No EFSA-Q-2014-00022, adopted on 25 June 2014.

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[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Hildegard Przyrembel, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Sean (J.J.) Strain, Inge Tetens, Hendrik Van Loveren, Hans Verhagen and Peter Willatts for the preparatory work on this scientific opinion.

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SUMMARY

Following an application from Clasado Limited, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Malta, 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 Bimuno® GOS and reducing gastro-intestinal discomfort.

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 food constituent that is the subject of the health claim is Bimuno® GOS, a mixture of β-galacto-oligosaccharides, which is produced through conversion of lactose by enzymes from *Bifidobacterium bifidum* NCIMB 41171. The Panel considers that Bimuno® GOS is sufficiently characterised.

The claimed effect proposed by the applicant is "reduce bloating, flatulence and abdominal pain: these effects can be described collectively as abdominal discomfort". The target population proposed by the applicant is the general adult population. Symptoms such as abdominal pain, cramp, bloating, straining, borborygmi (rumbling) and sensation of incomplete evacuation are associated with gastro-intestinal discomfort. Reducing gastro-intestinal discomfort is considered an indicator of improved gastro-intestinal function. Gastro-intestinal discomfort may be measured by using validated subjective global symptom severity questionnaires such as described in consensus opinions. The Panel considers that reducing gastro-intestinal discomfort is a beneficial physiological effect.

Following a literature search in PubMed, the applicant identified four human intervention studies and one review publication as being pertinent to the health claim. The applicant also provided two unpublished human intervention studies and three non-human studies for the scientific substantiation of the claim.

All the human and non-human studies provided by the applicant for this claim were already submitted in previous applications for the same claim, and which were assessed by the Panel with unfavourable outcomes, except for one unpublished human intervention study.

This multicentre, placebo-controlled, randomised, double-blind, parallel study investigated the effect of Bimuno® GOS on symptoms related to gastro-intestinal discomfort in subjects suffering from gastro-intestinal discomfort (bloating, flatulence, abdominal pain and/or need to defecate) in the past 12 months. Subjects who had a weekly average composite score of > 10 to questions on flatulence, "bowel moments" (difficulty, urgency, straining, sense of incomplete evacuation), abdominal pain and abdominal bloating in the week prior to randomisation were randomised to consume Bimuno® GOS (1.37 g/day; n = 208) or maltodextrin (n = 200) daily for four weeks. Participants completed on-line questionnaires on "bowel movements", abdominal pain, bloating, flatulence, and stool consistency on a daily and/or weekly basis one week prior to the beginning of the study, during the four-week treatment period, and in the two-week follow-up period. At the end of the treatment and follow-up periods, participants also completed on-line "quality of life questionnaires".

Upon a request by EFSA for clarification on the validation of the questionnaires used in the study to assess changes in gastro-intestinal symptoms during an intervention, and particularly in relation to their on-line use, the applicant referred to a consensus opinion and guidelines on the design of trials for functional gastro-intestinal disorders, and to a series of clinical trials on the efficacy of Tegaserod, a partial serotonin agonist, in treating symptoms of irritable bowel syndrome. However, the Panel considers that the evidence provided by the applicant did not establish that the on-line questionnaires used in the study to assess individual gastro-intestinal symptoms (abdominal pain, abdominal bloating, flatulence and "bowel movements") have been validated to be integrated into an overall measure of functional gastro-intestinal discomfort. The Panel also notes that subjective global

assessment of symptoms used to characterise the study population (flatulence, abdominal pain, abdominal bloating and bowel movement urgency) at baseline has been recommended as the primary outcome of efficacy (on which the main results should be based) for trials investigating functional gastro-intestinal disorders in the consensus opinion provided by the applicant and others published thereafter.

The Panel notes that the effect of Bimuno® GOS on the subjective global assessment of symptoms, a combined measure of efficacy which would indicate whether the intervention provided adequate relief of symptoms of gastro-intestinal discomfort, was not assessed, and that measures of individual gastro-intestinal symptoms through validated questionnaires may only be used as supportive evidence for the scientific substantiation of health claims on the reduction of gastro-intestinal discomfort. In addition, the Panel notes the reported effects of Bimuno® GOS on three out of the five individual outcomes investigated (i.e. abdominal pain, bloating and flatulence, but not in "bowel movements" or stool consistency) did not translate into a significant improvement of the subjects' quality of life, which revels inconsistency in the results. The Panel considers that this study does not provide information about the effect of Bimuno® GOS on relieving subjects from gastro-intestinal discomfort.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Bimuno® GOS and reducing gastro-intestinal discomfort.

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BACKGROUND

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. 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).

STEPS TAKEN BY EFSA

- The application was received on 16/01/2014.
- 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.
- On 31/01/2014, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 06/02/2014, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 13/02/2014.
- On 10/04/2014, the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application and the clock was stopped on 14/04/2014 in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 23/04/2014, EFSA received the requested information and the clock was restarted.
- On 07/05/2014, the Working Group Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application and the clock was stopped on 16/05/2014.
- On 23/05/2014, EFSA received the requested information and the clock was restarted.
- During its meeting on 25/06/2014, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to Bimuno® GOS and reducing gastro-intestinal discomfort.

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: Bimuno® GOS and reducing gastro-intestinal discomfort.

[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.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of Bimuno® GOS, a positive assessment of its safety, nor a decision on whether Bimuno® GOS 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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: Clasado Limited, Regent House, Office 25, Bisazza Street, Sliema, SLM 1641, Malta.

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006 for seven published studies (Tzortzis et al., 2005a, b; Goulas et al., 2007; Depeint et al., 2008; Vulevic et al., 2008; Silk et al., 2009; Drakoularakou et al., 2010) and two unpublished studies (Vulevic et al., undated; Tzortzis et al., 2013) The application also includes a request for protection of proprietary data for analytical and stability data pertaining to the manufacturing process.

Food/constituent as stated by the applicant

According to the applicant, the food constituents that are the subject of the health claim are galacto-oligosaccharides from Bimuno® (Bimuno® GOS), which are a mixture of β-linked galacto-oligosaccharides (β-1→3, β-1→4, β-1→6) with a degree of polymerisation ranging between 2 and 5 and α-linked galacto-oligosaccharides (α-1→6) with a degree of polymerisation of 2.

Health relationship as claimed by the applicant

According to the applicant, Bimuno® GOS acts to reduce bloating, flatulence and abdominal pain. These effects can be described collectively as "abdominal discomfort".

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "Regular daily consumption of 1.37 g galacto-oligosaccharides from Bimuno® may reduce abdominal discomfort".

Specific conditions of use as proposed by the applicant

According to the applicant, 1.37 g of galacto-oligosaccharides from Bimuno® should be consumed once daily for a minimum of seven days.

The target population as proposed by the applicant is the general male and female adult population.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is Bimuno® GOS, a mixture of β-galacto-oligosaccharides, which is produced through conversion of lactose by enzymes from *Bifidobacterium bifidum* NCIMB 41171.

Based on chemical analyses that were provided on five batches, Bimuno® powder contains a mixture of β-galacto-oligosaccharides (Bimuno® GOS, 47-53 %), lactose (25-35 %), glucose (6-10 %) and galactose (4-7 %).

Bimuno® GOS comprises a mixture of β-linked galacto-oligosaccharides (β-1→3, β-1→4, β-1→6) and α-linked galacto-disaccharides (α-1→6). The ratio of β-linked galacto-oligosaccharides to α-linked galacto-disaccharides is 93:7.

The results of stability tests showed that the Bimuno® powder is stable for up to two years.

The Panel considers that the food constituent, Bimuno® GOS, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is "reduce bloating, flatulence and abdominal pain: these effects can be described collectively as abdominal discomfort". The target population proposed by the applicant is the general adult population.

Symptoms such as abdominal pain, cramp, bloating, straining, borborygmi (rumbling) and sensation of incomplete evacuation are associated with gastro-intestinal discomfort. Reducing gastro-intestinal discomfort is considered an indicator of improved gastro-intestinal function. Gastro-intestinal discomfort may be measured by using validated subjective global symptom severity questionnaires (such as described in the consensus opinions by Veldhuyzen van Zanten (1999) and Irvine et al., (2006)).

The Panel considers that reducing gastro-intestinal discomfort is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed with the following key words: abdominal pain prebiotic, bloating prebiotic, flatulence prebiotic, IBS prebiotic, galactooligosaccharide bloating, galactooligosaccharide digestion, galactooligosaccharide gastrointestinal, bloating colonic microbiota, galacto oligosaccharide, trans galactooligosaccharide, transgalactooligosaccharide, transgalacto oligosaccharide. No restrictions related to publication dates, types or languages were applied by the applicant.

The applicant identified four human intervention studies (Depeint et al., 2008; Vulevic et al., 2008; Silk et al., 2009; Drakoularakou et al., 2010) and one review publication (Tzortzis, 2009) as being pertinent to the health claim. The applicant also provided two unpublished human intervention studies (Vulevic et al., undated; Tzortzis et al., 2013) and three non-human studies (Tzortzis et al., 2005a; Searle et al., 2009, 2010) for the scientific substantiation of the claim.

Except for the unpublished human intervention study by Tzortzis et al. (2013), all the human and non-human studies provided by the applicant for this claim were already submitted in previous applications for the same claim, and which were assessed by the Panel with unfavourable outcomes (EFSA NDA Panel, 2011, 2013).

The multicentre (UK, France, Germany, Spain), placebo-controlled, randomised, double-blind, parallel study by Tzortzis et al. (unpublished, 2013) investigated the effect of Bimuno® GOS on symptoms related to gastro-intestinal discomfort in subjects (aged 18-65 years) suffering from gastro-intestinal discomfort (bloating, flatulence, abdominal pain and/or need to defecate) in the past 12 months. Participants were selected based on a composite score of abdominal symptoms (i.e. flatulence, "bowel moments", abdominal pain and abdominal bloating). Subjects were excluded if they had organic disease of the gastro-intestinal tract or malignancy in the past five years, were under medication for "gastro-intestinal conditions" or had consumed "probiotic" or "prebiotic" preparations at least three times per week in the previous two weeks.

Participants completed on-line questionnaires on their "bowel habits" on a daily and weekly basis one week prior to the beginning of the study, during the four-week treatment period and during the two-week follow-up period. At the end of the treatment and follow-up periods, participants also completed on-line "quality of life questionnaires". Upon a request by EFSA for clarification on the

questionnaires used, the applicant provided the forms that were completed on a daily and weekly basis to collect information on "bowel movements", abdominal pain, bloating, flatulence, and stool consistency (recorded only in the daily questionnaire). Different scales were used in the daily and weekly questionnaires to describe abdominal symptoms. In the daily questionnaires, number of "bowel movements" was recorded; a scale from "0 = none" to "6 = preventing normal daily activity" was used for abdominal pain, bloating, flatulence; a scale from "1 = hard" to "4 = watery" was used for stool consistency. In the weekly questionnaire, a generic indication that "0 means none" and "6 means a lot" was used to describe the difficulty experienced in relation to bowel movements, and flatulence, whereas a generic indication that "0 means not at all" and "6 means very" was used to describe the severity of symptoms for abdominal pain, and bloating. Another scale from "0 = none" to "3 = severe" was used to describe symptoms related to several factors including flatulence. The on-line forms used for the "quality of life questionnaires" were also provided.

Subjects who met the inclusion and exclusion criteria and had a weekly average composite score of > 10 to questions on flatulence, "bowel moments" (difficulty, urgency, straining, sense of incomplete evacuation), abdominal pain and abdominal bloating in the week prior to randomisation were randomised to consume Bimuno® GOS (1.37 g/day; n = 208) or maltodextrin (n = 200) daily for four weeks. At the beginning of the trial, participants were asked to choose the formulation of the study products they intended to consume, i.e. powder (2.75 g/sachet) or syrup (5.7 g/sachet). The study products were supplied to participants in white sachets (30 sachets/box) by post together with the instructions for use. During the trial, the use of antibiotics and other "colonic functional food ingredients (i.e. probiotics, prebiotics and synbiotics)" was not allowed, whereas all other medications were allowed but not monitored. The Panel notes that this study was not controlled for the use of medications (e.g. antispasmodics, pain killers, antidepressants) which may have affected the gastro-intestinal symptoms assessed or their perception by the subjects. Treatment compliance was monitored through the daily completion of the on-line questionnaires and weekly communication with participants. Upon a request by EFSA for clarification, no data on compliance with the study products for the intervention and the control groups were provided by the applicant.

In the study report, baseline characteristics of the study subjects in relation to age, gender, weight, body mass index, and "irritable bowel syndrome (IBS) medication" were provided. Upon a request by EFSA for clarification, the applicant also provided baseline characteristics in relation to "bowel movements", stool consistency, abdominal pain, bloating and flatulence, and clarified that "IBS medication" meant any medication used for the treatment or relief of gastro-intestinal discomfort.

In the study report, the applicant stated that the subjective global assessment (SGA) of symptoms (flatulence, abdominal pain, abdominal bloating, bowel movement urgency), which was assessed at weekly intervals and scored from 0 to 6 (0 = none; 6 = a lot), and the weekly average of abdominal pain, abdominal bloating, flatulence and "bowel movements" were the primary measures of efficacy. The Panel notes that a validated, combined SGA of symptoms (flatulence, abdominal pain, abdominal bloating, bowel movement urgency) may be an appropriate outcome measure of gastro-intestinal discomfort. However, the results of the SGA were not provided. Upon a request by EFSA for clarification on the primary outcome which was used for power calculations, the applicant indicated that the primary endpoints used to power the study were abdominal pain, abdominal bloating, flatulence and "bowel movements", and that for such calculations data from the study by Vulevic et al. (unpublished) were used. The applicant also indicated that the results of the SGA of symptoms (combined) with details of analysis were available in the analysis report which combined daily and weekly responder analyses. However, the Panel notes that the analyses combining the results from daily and weekly questionnaires were provided only for the individual symptoms (abdominal pain, abdominal bloating, flatulence and "bowel movements") and not for the combined SGA of symptoms.

Upon a request by EFSA for clarification on the validation of the questionnaires used in the study to assess changes in gastro-intestinal symptoms during an intervention, and particularly in relation to their on-line use, the applicant referred to a consensus opinion (Veldhuyzen van Zanten et al., 1999)

and guidelines on the design of trials for functional gastro-intestinal disorders, and to a series of clinical trials on the efficacy of Tegaserod, a partial serotonin agonist, in treating IBS symptoms, the results of which are summarised in a Cochrane systematic review and meta-analysis (Evans et al., 2007). The Panel notes that an assessment which integrates the symptoms associated with gastro-intestinal discomfort (SGA) used to characterise the study population (flatulence, abdominal pain, abdominal bloating, and bowel movement urgency in the case of Tzortzis et al., unpublished, 2013) has been recommended as the primary outcome of efficacy (on which the main results should be based) for trials investigating functional gastro-intestinal disorders in the consensus opinion provided by the applicant and others published thereafter (Veldhuyzen van Zanten et al., 1999; Irvine et al., 2006). The Panel also notes that the clinical studies quoted by the applicant on the efficacy of Tegaserod in treating IBS symptoms adhere to that recommendation. The applicant argued that the questionnaires used in the study by Tzortzis et al. (unpublished, 2013) were similar. The applicant also stated that "the questionnaires, in all four languages used, which are Likert scale-based, were validated for comprehension and accuracy during the screening period against their printed version". However, the Panel considers that the evidence provided by the applicant did not establish that the on-line questionnaires used in the study by Tzortzis et al. (unpublished, 2013) to assess individual gastro-intestinal symptoms (abdominal pain, abdominal bloating, flatulence and "bowel movements") have been validated to be integrated into an overall measure of functional gastro-intestinal discomfort.

A total of 34 subjects (n = 7 in the intervention group; n = 27 in the control group) discontinued the study for different reasons (e.g. not answering calls, not willing to continue for unspecified reasons). One subject in the control group experienced an adverse event (increased abdominal pain) which, after medical examination, was considered to be unrelated to the trial. Upon a request by EFSA for clarification, the applicant indicated that the "per protocol (PP)" population was calculated as the number of completers who filled in the questionnaires for at least four days during each week of the study. The Panel notes that the applicant's definition of "PP" population, calculated as the number of completers, did not take into account subjects' compliance with the study products, and that compliance data were not provided by the applicant. The applicant provided data on gastro-intestinal symptoms at baseline and at the end of the treatment and follow-up periods for the population of completers (n = 373 subjects, n = 172 in the control and n = 201 in the intervention groups).

For each individual outcome ("bowel movement", stool consistency, abdominal pain, bloating, and flatulence), but not for the SGA of symptoms, the means of weekly averages from the daily questionnaires and the scores from weekly questionnaires were calculated and analysed with a linear mixed model. Daily and weekly scores were analysed separately and combined. Responders' analyses for each outcome were also performed using logistic regression. Each participant was identified as being a "responder" for each endpoint if there was at least a 30 % decrease in their average response for at least two weeks on treatment compared to the average screening response (daily questionnaires), in their weekly response for at least two weeks on treatment compared to the screening response (weekly questionnaires), and if they had at least a 30 % reduction from screening in their daily responses averaged over each week and at least a two-category decrease in their weekly score compared to screening, in the same week, for at least two weeks during the treatment period (combined analyses). The Panel notes that subjects with scores 0 or 1 at baseline for a given outcome were excluded from the responders' analyses instead of considering them as non-responders. The Panel also notes that the last observation carried forward (LOCF) was used to input missing values for daily scores (up to six per week in the intention-to-treat (ITT) population, up to three per week in the population of "completers").

The Panel notes that the effect of Bimuno® GOS on the subjective global assessment (SGA) of symptoms, a combined measure of efficacy which would indicate whether the intervention provided adequate relief of symptoms of gastro-intestinal discomfort, was not assessed, and that measures of individual gastro-intestinal symptoms through validated questionnaires may be used only as supportive evidence for the scientific substantiation of health claims on the reduction of gastro-intestinal discomfort. In addition, the Panel notes the reported effects of Bimuno® GOS on

three out of the five individual outcomes investigated (i.e. abdominal pain, bloating and flatulence, but not in "bowel movements" or stool consistency) did not translate into a significant improvement of the subjects' quality of life, which revels inconsistency in the results.

The Panel also notes the methodological limitations of this study (i.e. lack of evidence that the on-line questionnaires have been validated in relation to the use of individual gastro-intestinal symptoms as primary measures of efficacy; lack of control for the use of medications such as antispasmodics, painkillers or antidepressants which may have affected the gastro-intestinal symptoms assessed or their perception by the subjects; the use of a single imputation method for the handling of missing values; the exclusion of subjects with scores 0 or 1 at baseline for a given outcome from the responders' analyses). The Panel considers that this study does not provide information about the effect of Bimuno® GOS on relieving subjects from gastro-intestinal discomfort.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Bimuno® GOS and reducing gastro-intestinal discomfort.

CONCLUSIONS

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

- The food constituent, Bimuno® GOS, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is "reduce bloating, flatulence and abdominal pain these effects can be described collectively as abdominal discomfort". The target population proposed by the applicant is the general adult population. Reducing gastro-intestinal discomfort is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of Bimuno® GOS and reducing gastro-intestinal discomfort.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Bimuno® GOS and reducing gastro-intestinal discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0406_MT). January 2014. Submitted by Clasado Limited.

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ABBREVIATIONS

GOS	galacto-oligosaccharides
IBS	irritable bowel syndrome
PP	per protocol
SGA	subjective global assessment