

SCIENTIFIC OPINION

BimunoTM and reduction of the bad bacteria that can cause travellers' diarrhoea

Scientific substantiation of a health claim related to BimunoTM and reduction of the bad bacteria that can cause travellers' diarrhoea pursuant to Article 14 of Regulation (EC) No 1924/2006¹

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2009-00232)

Adopted on 15 May 2009

PANEL MEMBERS

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SUMMARY

Following an application from Clasado Limited submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to BimunoTM and reduction of the bad bacteria that can cause travellers' diarrhoea.

The scope of the application was proposed to fall under a health claim referring to disease risk reduction.

The food supplement, BimunoTM, a β -galacto-oligosaccharide mixture, that is the subject of the health claim is sufficiently characterised.

The claimed effect is "reducing the bad bacteria that can cause travellers' diarrhoea". The target population is adults and young persons (12 years and over). The Panel considers that a decrease in bacterial, viral and parasitic enteric pathogens is beneficial to human health by reducing the risk of travellers' diarrhoea.

The applicant identified one (unpublished) double-blind, placebo-controlled, randomised clinical study including 159 adults as being pertinent to the health claim. Healthy adult

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volunteers were given Bimuno™ or placebo starting seven days prior to reaching the final travel destination. The number of episodes with diarrhoea was lower and the duration of diarrhoea and abdominal pain was significantly shorter in the study group. The Panel notes that the subjects were not sufficiently characterised and that no data on risk factors were provided. Further weaknesses of this study include the high drop-out rate and the insufficient description of statistical analyses. The Panel considers that the weaknesses of this study limit its value as a source of data to substantiate the claimed effect of Bimuno™.

One unpublished study showed that Bimuno™ can suppress *Salmonella enterica typhimurium* induced clinical and histopathological signs in a mouse model. A further combined *in vitro* and animal study indicated that Bimuno™ enhances growth of bifidobacteria *in vivo* in a pig model and can reduce adhesion of *Salmonella enterica typhimurium* to intestinal cells *in vitro*. The results from the animal and *in vitro* studies cannot be extrapolated to humans.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of Bimuno™ and reduction of the bad bacteria that can cause travellers' diarrhoea.

Key words: Bimuno™, β -galacto-oligosaccharide, travellers' diarrhoea

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BACKGROUND

Regulation (EC) No 1924/2006² 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 that Regulation and are authorised in accordance with this Regulation and included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Articles 14 to 17 of that Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to Article 15 of that Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, who will make the application and any supplementary information supplied by the applicant available to European Food Safety Authority (EFSA).

Steps taken by EFSA:

- The application was received on 30/01/2009.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction.
- The scientific evaluation procedure started on 15/03/2009.
- During the meeting on 15/05/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to Bimuno™ and reduction of the bad bacteria that can cause travellers' diarrhoea.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16 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™ and reduction of the bad bacteria that can cause travellers' diarrhoea.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of Bimuno™, a positive assessment of its safety, nor a decision on whether Bimuno™ 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 17 of Regulation (EC) No 1924/2006.

² European Parliament and Council (2006). 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. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

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1. Information provided by the applicant

Applicant's name and address: Clasado Limited, 5 Canon Hartnett Court, Wolverton Mill, Milton Keynes, MK12 5NF, United Kingdom.

1.1. Food/constituent as stated by the applicant

Bimuno (BGOS) Prebiotic.

1.2. Health relationship as claimed by the applicant

Regular consumption of Bimuno (BGOS) Prebiotic before and during a holiday can help to protect consumers by reducing the bad bacteria that can cause travellers' diarrhoea.

1.3. Wording of the health claim as proposed by the applicant

Regular consumption of Bimuno (BGOS) Prebiotic helps to protect against the bad bacteria that can cause travellers' diarrhoea.

1.4. Specific conditions of use as proposed by the applicant

Recommended daily serving for adults and young persons (12 years and over) is 5.5 g of Bimuno (BGOS) Prebiotic.

2. Assessment

2.1. Characterisation of the food/constituent

The food supplement which is the subject of the claim is a "prebiotic" β -galactooligosaccharide mixture produced through conversion of lactose by exposure to enzymes from permeabilised *Bifidobacterium bifidum* NCIMB 41171.

Bimuno™ powder contains monosaccharide 15–17%, lactose 22%, disaccharides 18–25%, trisaccharides 20–25%, tetrasaccharides 8–12% and pentasaccharides 7–10%.

The composition of the constituent has been sufficiently characterised (source, origin, purity, chemical composition).

Stability was tested in one batch:

- 1) syrup stored at 4°C: tested 6x in three samples per time point during a 12 month period;
- 2) powder (stored at 25°C): tested 8x in three samples per time point during a 2 year period;
- 3) in fruit juice (room temperature): tested 5 x in one sample per time point for 6 months.

Powder was found to be stable up to two years.

Data on batch to batch variability in composition and stability are not provided. It is unclear if monitoring of stability is included in a standardised way during the manufacturing process.

The Panel considers that the food supplement, Bimuno™, which is the subject of the health claim is sufficiently characterised.

2.2. Relevance of the claimed effect to human health

The claimed effect is “reducing the bad bacteria that can cause travellers' diarrhoea”. The target population is adults and young persons (12 years and over).

Travellers' diarrhoea (TD) mainly affects people travelling to developing countries (worldwide estimated 10 million persons per year). Despite existing recommendations for the prevention of TD, 20%–50% of international travellers are affected. The primary source of infection is ingestion of faecally contaminated food or water (WHO and Centers for Disease Control and Prevention).

Most cases are benign and resolve in 1-2 days without treatment. TD is rarely life-threatening. Treatment is mainly based on oral rehydration. Bacterial enteropathogens cause approximately 80% of TD cases. The most common causative agent isolated in countries surveyed has been enterotoxigenic *Escherichia coli*. Besides *E. coli* and other bacterial pathogens, a variety of viral and parasitic enteric pathogens are potential causative agents (WHO and Centers for Disease Control and Prevention).

The Panel considers that a decrease in bacterial, viral and parasitic enteric pathogens is beneficial to human health by reducing the risk of travellers' diarrhoea.

2.3. Scientific substantiation of the claimed effect

The applicant performed a literature search through PubMed [MEDLINE] with the following key words: galactooligosaccharides, *E. coli*, Salmonella, diarrhoea and travellers' diarrhoea. Only English language papers were included. A time frame for the search is not reported.

The applicant identified one unpublished randomised controlled human intervention study (Drakoularakou et al., claimed to be confidential by the applicant), one unpublished non-human study (Searle et al., in press, claimed to be confidential by the applicant), three published *in-vitro* studies (Sharp et al., 2001; Shoaf et al., 2006; Tzortzis et al., 2005) and one review (Cummings et al., 2004) as being pertinent to the health claim.

As Bimuno™ was not tested in the *in vitro* studies by Sharp et al. (2001) and by Shoaf et al. (2006), the Panel considers that these studies are not pertinent to the health claim.

The Panel considers that the review by Cummings et al. (2004) is not pertinent to the health claim as it provides general information on claims on gut health and immunity and on methods for the assessment of gut function, gut flora and immunity without any specific information on TD or Bimuno™.

The study by Drakoularakou et al. (unpublished) was a placebo-controlled, randomised, double blind, parallel design study to determine the potential of Bimuno™ to reduce TD in adults. Healthy volunteers, who would travel for a minimum of 14 days and a maximum of 60 days, aged 18 years or older, were enrolled in this study. The following exclusion criteria were applied: pregnancy, lactation, diabetes, gastrointestinal disorders or consumption of prebiotic or probiotic preparations, and use of ciprofloxacin or antimalaria prophylaxis. From 298 enrolled subjects, 81 in the prebiotic group (5.5 g Bimuno™/day) and 78 in the placebo group (5.5 g maltodextrin/day) completed the study. Intervention with Bimuno™ or placebo started seven days prior to reaching the respective final travel destination. Gastrointestinal symptoms were assessed with daily diaries completed by the participants. Mean ages (no age ranges given) were 38 years for the placebo group and 34 years for the Bimuno™ group. Further characteristics, except previous history of TD, such as weight, sex or race are not given. The high drop out rate (47%) was mainly due to incomplete or missing diaries (equally distributed

between groups). Subjects with “diarrhoeal incidence” were significantly more frequent in the placebo group (30/78 subjects in the placebo group versus 19/81 subjects in the Bimuno™ group), with significantly longer average duration of diarrhoea (4.6 days in the placebo group versus 2.4 days in the Bimuno™ group) and abdominal pain (3.5 days in the placebo group versus 2 days in the Bimuno™ group). Ranges of duration of diarrhoeal episodes and pain are not reported. From the legends of the tables, it is unclear which statistical test was applied to the respective data. The Panel notes that the study population was insufficiently characterised and no data on risk factors were provided. Further weaknesses of this study include the high drop-out rate and the insufficient description of statistical analyses. The Panel considers that the weaknesses of this study limit its value as a source of data to substantiate the claimed effect of Bimuno™.

In addition to the one human intervention study, a study (Searle et al., in press) describing animal and *in vitro* data was supplied. This study showed that 2.5 g Bimuno™/kg (body weight) can suppress *Salmonella enterica typhimurium* induced pathology and associated clinical signs in a mouse model. A further combined *in vitro* and animal study by Tzortzis et al. (2005) showed that colonic bifidobacterial growth can be enhanced by β -galactooligosaccharide (BGOS) *in vivo* and that BGOS can reduce binding of *E. coli* and *S. enterica typhimurium* to an intestinal epithelial cell line. The product used in this study is derived from *Bifidobacterium bifidum* NCIMB 41171 which is the same bacterial strain which is used in the production of Bimuno™. However, the disaccharide content in the studied product is lower than in Bimuno™ (9.9% in the studied product versus 18–25% in Bimuno™). The results from the animal and *in vitro* studies cannot be extrapolated to humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Bimuno™ and reduction of the bad bacteria that can cause travellers' diarrhoea.

CONCLUSIONS

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

- The food supplement which is the subject of the claim, Bimuno™, a β -galactooligosaccharide mixture, is sufficiently characterised.
- The claimed effect “reducing the bad bacteria that can cause travellers' diarrhoea” is beneficial to human health. The target population is adults and young persons (12 years and over).
- A cause and effect relationship has not been established between the consumption of Bimuno™ and reduction of the bad bacteria that can cause travellers' diarrhoea.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Bimuno™ and reduction of the bad bacteria that can cause travellers' diarrhoea pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0236_UK). January 2009. Submitted by Clasado Limited.

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GLOSSARY / ABBREVIATIONS

BGOS	β-galacto-oligosaccharide
TD	Travellers' diarrhoea