European Food Safety Authority

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SCIENTIFIC OPINION

Bimuno™ and help to maintain a healthy gastro-intestinal function

Scientific substantiation of a health claim related to Bimuno™ and help to maintain a healthy gastro-intestinal function pursuant to Article 13(5) of Regulation (EC) No 1924/2006[1]

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

(Question No EFSA-Q-2009-00231)

Adopted on 15 May 2009

PANEL MEMBERS

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SUMMARY

Following an application from Clasado Limited submitted pursuant to Article 13(5) 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 Bimuno™ and help to maintain a healthy gastro-intestinal function.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The food supplement, Bimuno™, a β-galacto-oligosaccharide mixture, which is the subject of the health claim is sufficiently characterised.

The claimed effect is "helps to maintain a healthy gastro-intestinal (GI) function by stimulating and increasing the number of bifidobacteria in the gut". The target population is the general population from the age of 3 years upwards. From the evidence provided it has not been established that increasing the number of bifidobacteria in humans is *per se* beneficial to a normal GI function. The Panel considers that a normal gastro-intestinal function is beneficial to human health.

[1] For citation purposes: Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Clasado Limited on the scientific substantiation of a health claim related to Bimuno™ and help to maintain a healthy gastro-intestinal function. *The EFSA Journal* (2009) 1107, 1-10

The applicant identified one double blind, placebo-controlled, crossover study in 30 healthy volunteers as being pertinent to the health claim. The subjects were randomised to receive one of the following supplements for seven days: 7 g sucrose/d, 7 g Bimuno™/d and 3.6 g Bimuno™ plus 3.4 g sucrose/d (to maintain osmotic characteristics) provided in a milk powder preparation. This study was conducted with an old formulation of Bimuno™, 7 g corresponding to 5.5 g of the Bimuno™ formulation which is the subject of the health claim. The primary outcome was the count of faecal bifidobacteria. The study demonstrated a bifidogenic effect of Bimuno™.

The applicant provided another study in patients with Rome II positive irritable bowel syndrome. The patients were randomised to receive either 3.5 g Bimuno™/d, 7 g Bimuno™/d or 7 g maltodextrin/d (placebo). This study was conducted with an old formulation of Bimuno™, 7 g corresponding to 5.5 g of the Bimuno™ formulation which is the subject of the health claim. This study supports the effects seen in other studies with respect to an increase in the number of faecal bifidobacteria after the consumption of Bimuno™. However, as the study was not powered adequately to detect changes in IBS symptoms, the Panel could not draw a conclusion on the effect of Bimuno™ on any other outcome measures.

A third human randomised controlled trial used a dose of Bimuno™ which was double the amount of Bimuno™ proposed to obtain the claimed effect and thus it is not relevant for the substantiation of the health claim.

From *in vitro* and animals studies provided by the applicant, only one used Bimuno™. This study showed a bifidogenic effect of Bimuno™ *in vitro* and in a pig model. Gut function parameters were not addressed.

The Panel considers that the studies provided by the applicant demonstrate that the consumption of Bimuno™, corresponding to doses between 2.75 g/d and 5.5 g/d, significantly increases the number of bifidobacteria in the gut. However, the results do not show that the changes in the number of bifidobacteria are beneficial for the gut function.

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 maintenance of a normal gastro-intestinal function.

Key words: Bimuno™, β-galacto-oligosaccharide, gastro-intestinal function

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BACKGROUND

Regulation (EC) No 1924/2006[2] 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, Article 13(5) of that Regulation lays down provisions for 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 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 that Regulation, an application for inclusion in the Community list of permitted claims referred to in Art 13(3) 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 based on newly developed scientific evidence.
- The scientific evaluation procedure started on 30/01/2009.
- 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 help to maintain a healthy gastro-intestinal function.

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™ and help to maintain a healthy gastro-intestinal function.

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 18(4) 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.

ACKNOWLEDGEMENTS

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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

Bimuno (BGOS) Prebiotic selectively stimulates and increases the number of bifidobacteria in the gut of regular consumers. Bifidobacteria are recognised as health promoting bacteria that support the general well-being of the host.

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

Helps maintain a healthy gastro-intestinal (GI) function.

1.4. Specific conditions of use as proposed by the applicant

Bimuno (BGOS) Prebiotic is recommended for all people from the age of 3 years and upwards. Recommended daily serving for adults and young persons is 2.75 g of Bimuno™ (BGOS) Prebiotic.

2. Assessment

2.1. Characterisation of the food/constituent

The food supplement that is subject of the claim is a "prebiotic" β-galacto-oligosaccharide 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 "helps to maintain a healthy GI function by stimulating and increasing the number of bifidobacteria in the gut". The target population is individuals from the age of 3 years and upwards.

The gastro-intestinal tract is populated with a large number of micro-organisms, and acts as an effective barrier against opportunistic and pathogenic infections. Many different groups of bacteria are present and the numbers and proportions of bacteria from these groups vary widely in healthy subjects. However, increasing the number of bifidobacteria does not constitute *per se* a beneficial effect in the gastro-intestinal (GI) tract. The Panel notes that from the evidence provided by the applicant it has not been established that increasing the number of bifidobacteria in humans is *per se* beneficial to a normal GI function.

The Panel considers that a normal gastro-intestinal function is beneficial to human health.

2.3. Scientific substantiation of the claimed effect

The applicant performed a literature search through PubMed [MEDLINE] with the following key words: galacto-oligosaccharides, and prebiotic. Only English language papers were included. A time frame for the search is not reported.

Based on the search criteria the applicant identified three human intervention studies, two published (Depeint et al., 2008; Vulevic et al., 2008) and one unpublished at the time of the submission (Silk et al., 2009, claimed to be confidential by the applicant), and 11 non-human studies (Rabiu et al., 2001; Rycroft et al., 2001; Tzortzis et al., 2004 and 2005; Rada et al., 2008; Palframan et al., 2002; Mountzouris et al., 2006; Cummings et al., 2004; MacFarlane et al., 2006; Gibson et al., 2004; Roberfroid, 2007). Furthermore, an unpublished meta-analysis of human studies by Tzortzis (claimed to be confidential by the applicant) was considered as pertinent to the claim.

As Bimuno™ was not tested in the non-human studies by Rabiu et al., 2001; Rycroft et al., 2001; Tzortzis et al., 2004; Rada et al., 2008; Palframan et al., 2002; Mountzouris et al., 2006, the Panel considers that these studies are not pertinent to the health claim.

The Panel considers that the reviews by Cummings et al. (2004), MacFarlane et al. (2006), Gibson et al. (2004) and Roberfroid (2007) are not pertinent to the health claim as they do not provide specific information on Bimuno™.

The studies by Depeint et al. (2008) and Silk et al. (2009) were conducted with an old formulation of Bimuno™, 7 g corresponding to 5.5 g of the Bimuno™ formulation which is the subject of the health claim.

In the double blind, placebo-controlled, crossover study by Depeint et al. (2008) 30 healthy volunteers (mean age 36.3 years; age range 21–59 years) were randomised to receive successively one of three supplements for seven days with seven day washout periods between supplement changes. Supplements were a) 7 g sucrose/d, b) 7 g Bimuno™/d, c) 3.6 g Bimuno™ plus 3.4 g sucrose/d (to maintain osmotic characteristics) provided in a milk powder preparation. The primary outcome was the count of faecal bifidobacteria. Details of blinding are not reported. It is unclear if/how adherence to the protocol was controlled. Bifidobacteria were counted (FISH) and related to total bacterial counts in faecal samples. Baseline counts did not differ among the groups. Supplementation with Bimuno™ was associated with significantly increased bifidobacteria in a dose dependent way for doses corresponding to 2.8 and 5.5g/d of the Bimuno™ formulation which is the subject of the health claim.

The applicant provided a 12 week single centre parallel sequential clinical trial (Silk et al., 2009) involving 44 patients with Rome II positive irritable bowel syndrome (IBS). The patients were randomised to receive either 3.5 g Bimuno™/d, 7 g Bimuno™/d or 7 g maltodextrin/d (placebo). Only patients were blinded. The study supports the effects seen in other studies with respect to an increase in the number of faecal bifidobacteria after the consumption of Bimuno™. However as the study was not powered adequately to detect changes in IBS symptoms, the Panel could not draw a conclusion on the effect of Bimuno™ on any other outcome measures.

In a double blind controlled intervention trial by Vulevic et al. (2008) 44 elderly, healthy subjects (mean age 69.3 years; range 64–79 years) were randomised to receive 5.5 g Bimuno™/d or 5.5 g maltodextrin/d for 10 weeks followed by a 4 weeks wash-out period and a 10 weeks crossover period. Primary outcome was the concentration of faecal bifidobacteria. Compared with baseline and placebo, Bimuno™ supplementation was associated with a significant increase of faecal bifidobacteria. The Panel notes that the dose of Bimuno™ used in this study is double the amount of Bimuno™ proposed to obtain the claimed effect.

The three human intervention studies described above (Depeint et al., 2008; Silk et al., 2009; Vulevic et al., 2008) were subjected to a meta-analysis using the methodology of Roberfroid (2007) (Tzortzis, unpublished). This meta-analysis confirms the significant increase in number of faecal bifidobacteria after Bimuno™ consumption.

From the non-human studies provided, only the study by Tzortzis et al. (2005) used Bimuno™ in an *in vitro* model and in a parallel continuous randomised pig trial. The *in vitro* model of proximal, transverse and distal colon that was inoculated with human faecal homogenates with or without Bimuno™ (1% wt/v) showed that Bimuno™ did not affect numbers of total bacteria, lactobacilli, bacteroides or clostridia, while bifidobacteria were increased significantly ($p < 0.01$) as assessed by FISH. In the animal model four groups of pigs (each n = 10) received a standardised diet alone or supplemented with Bimuno™ (1.6% or 4% by weight) or with inulin (1.6% by weight). Animals receiving 4% Bimuno™ had significantly more colonic bifidobacteria than animals receiving 1.6% Bimuno™ or standard chow. Faecal bifidobacteria were highest in groups receiving inulin or 4% Bimuno™ followed by 1.6% Bimuno™. The non-human studies support the bifidogenic effect of Bimuno™.

The Panel considers that the studies provided by the applicant demonstrate that the consumption of Bimuno™, corresponding to doses between 2.75 g/d and 5.5 g/d significantly increases the number of bifidobacteria in the gut. However, the results do not show that the changes in the number of bifidobacteria are beneficial for the gut function.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Bimuno™ and maintenance of a normal gastro-intestinal function.

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-galacto-oligosaccharide mixture, is sufficiently characterised.
- The claimed effect is "helps to maintain a healthy GI function by stimulating and increasing the number of bifidobacteria in the gut". The target population is the general population from the age of 3 years upwards. From the evidence provided it has not been established that increasing the number of bifidobacteria in humans is *per se* beneficial

to a normal GI function. The Panel considers that a normal gastro-intestinal function is beneficial to human health.

- A cause and effect relationship has not been established between the consumption of Bimuno™ and maintenance of a normal gastro-intestinal function.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Bimuno™ and help to maintain a healthy gastro-intestinal function pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0238_UK). January 2009. Submitted by Clasado Limited.

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GLOSSARY / ABBREVIATIONS

GI	Gastro-intestinal
FISH	Fluorescence in situ hybridisation
IBS	Irritable bowel syndrome