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SCIENTIFIC OPINION

Follow-on formulae with bioactive constituents and intestinal ailments

Scientific substantiation of a health claim related to "Follow-on formulae with fixed combination of short-chain galacto-oligosaccharides (GOS), acidified milk, nucleotides and beta-palmitate" and intestinal ailments pursuant to Article 14 of Regulation (EC) No 1924/2006[1]

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

(Question No EFSA-Q-2008-270)

Adopted on 22 January 2009

PANEL MEMBERS

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SUMMARY

Following an application from Plada Industriale Srl submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Italy, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate" and intestinal ailments.

The scope of the application was proposed to fall under a health claim referring to children's development and health.

The food that is the subject of the claim is a follow-on formula containing a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate.

The Panel considers that the food that is the subject of the claimed effect is sufficiently characterised.

[1] For citation purposes: Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Plada Industriale Srl on the scientific substantiation of a health claim related to "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate" and intestinal ailments. *The EFSA Journal* (2009) 939, 1-10

The claimed effect is "aids minor intestinal ailments" (as colic, constipation, digestive symptoms). The target population is infants aged 6 to 12 months, who are not, or are not anymore breast-fed.

Reduction of intestinal symptoms (e.g. constipation, colic) is beneficial for children's health.

Only one study used a formula with a composition proposed by the applicant. The study compared the effect of the formula as proposed in the application to a standard formula in a double-blind, randomised, placebo-controlled trial including 58 newborn babies observed for 135 days. The rates of abdominal distension, cramps, gas production, diarrhoea and constipation (which were the secondary outcome of the study) were lower in the study group, but statistical analysis of the differences was not performed. The Panel considers this study as having limited relevance for the proposed claim.

Most studies were performed in an infant population which is not relevant to the target population. The only study involving infants of an age range closer to that of the target population, used a formula differing in composition from the proposed formula that is the subject of the claim and did not result in a significantly different outcome.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate" and the claimed effect (i.e. "aids minor intestinal ailments").

Key words: Follow-on formulae, short-chain galacto-oligosaccharides, GOS, acidified milk, nucleotides, beta-palmitate, intestinal, ailments, constipation, colic, infants

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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, 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 07/04/2008.
- The scope of the application was proposed to fall under a health claim referring to children's development and health.
- During the check for completeness[3] of the application, the applicant was requested to provide missing information on 16/05/2008.
- The applicant provided the missing information on 05/09/2008.
- The scientific evaluation procedure started on 15/10/2008.
- During the meeting on 22/01/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides (GOS), acidified milk, nucleotides and beta-palmitate" and intestinal ailments.

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: "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate" and intestinal ailments.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate", a positive assessment of its safety, nor a decision on whether "follow-on formulae with a fixed combination of short-chain

[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.

[3] In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim"

galacto-oligosaccharides (GOS), acidified milk, nucleotides and beta-palmitate" 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.

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1. Information provided by the applicant

Applicant's name and address: Plada Industriale Srl., Via Cascina bel Casule n° 7, Milan 20141, Italy.

1.1. Food/constituent as stated by the applicant

The claim is made for follow-on formulae with a fixed combination of the following bio-active ingredients: short-chain galacto-oligosaccharides (hereafter GOS), acidified milk, nucleotides and beta-palmitate (structured vegetable oils with high content of palmitic acid in sn-2 position of the triglyceride structure).

1.2. Health relationship as claimed by the applicant

According to the applicant, "the use of milk formulae integrated with galacto-oligosaccharides, nucleotides, palmitic acid at the sn-2 position and acidified milk could produce a favourable modification of the intestinal microflora, a change in the metabolism of fatty acids and absorption of electrolytes, possibly leading to a minor gastrointestinal discomfort. The use of the afore-mentioned formula may in a measurable way favourably influence gastrointestinal symptoms (such as constipation, infant colic, abdominal malabsorption and discomfort)".

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

"Aids minor intestinal ailments (as colic, constipation, digestive symptoms)" and equivalent wording.

1.4. Specific conditions of use as proposed by the applicant

The follow-on formulae contains the following fixed combination of the bioactive constituents:

a) Galacto-oligosaccharides (0,7g/100mL of reconstituted follow-on formula);

b) Nucleotides (3,1 mg/100mL of reconstituted follow-on formula);

c) Beta-palmitate: structured vegetable oils (40% of total fat amount of reconstituted follow-on formula) with high content of palmitic acid in sn-2 position of the triglyceride structure (43% of the total palmitic acid which is 21-24% of the structured vegetable oils);

d) Acidified skim milk (50% of total milk added in final product).

The follow-on formulae for which the health claim is made complies with the compositional criteria set out in Annex II of Directive 2006/141/EC taking into account the specifications set out in Annex V of the same Directive. The quantity of GOS and nucleotides are in compliance with the Directive.

2. Assessment

2.1. Characterisation of the food/constituent

The food that is the subject of the claim is a follow-on formula containing a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate.

Galacto-oligosaccharides, nucleotides and triglycerides containing β-palmitic acid are well defined constituents and their concentrations can be measured by established methods.

The Panel considers that the food that is the subject of the claimed effect (i.e. "follow-on formulae containing a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate") is sufficiently characterised.

2.2. Relevance of the claimed effect to human health

The claimed effect is "aids minor intestinal ailments" (as colic, constipation, digestive symptoms). The target population is infants aged 6 to 12 months, who are not, or are not anymore breast-fed.

The Panel considers that reduction of intestinal symptoms (e.g. constipation, colic) is beneficial for children's health.

2.3. Scientific substantiation of the claimed effect

The applicant used the following sources to identify the pertinent studies: Medline database (1990 – Jan 2008) with adding references found in reviewed articles, publications of ESPHGAN, SCF and EFSA and a hand search in a dozen of journals subscribed by the applicant. Main criteria were as follows: galacto-oligosaccharide and/or acidified/fermented milk and/or nucleotides and/or palmitic acid/fatty acid soap and infant or follow-on milk formulae in term healthy infants. Additional criteria were also used and they consist of: primary and secondary study outcomes dealing with the influence on minor intestinal aliments in infants (i.e. colic, constipation, diarrhoea, stool consistency). Studies with only other outcomes than described above, published in other languages than English, studies with formulae not cow milk based (i.e. soy), and studies on preterm infants were excluded.

The applicant found 27 relevant publications (including 9 reviews) out of the 58 identified. The applicant selected 16 intervention studies and 2 observational studies, which were considered pertinent to the claim by the applicant. The results of 17 of them have been published and one is unpublished, as yet.

Only one study used a formula with a composition proposed by the applicant (Castelazzi et *al*., 2008, unpublished). The study compared the effect of the formula as proposed in the application to a standard formula in a double-blind, randomised, placebo-controlled trial including 58 newborn babies observed for 135 days. The rates of abdominal distension, cramps, gas production, diarrhoea and constipation (which were the secondary outcome of the study) were lower in the study group, but statistical analysis of the differences was not performed. The Panel considers this study to provide limited relevance for the claim under consideration.

Most studies were performed in infants younger than 6 months of age. Indeed, 4 interventions were carried out between 0 and 3 months of age (Quinlan et *al.*, 1995; Carnielli et *al.*, 1996; Moro et *al*., 2002, 2003; Costalos et *al*., 2008) and 11 between 0 and 6 months of age (Brunser et *al*., 1994; Kennedy et *al*., 1999; Savino et *al*., 2003, 2005, 2006; Schmelzle et *al*., 2003; Xiao-Ming et *al*., 2004; Bongers et *al*., 2007; Ziegler et *al*., 2007; Singhal et *al*., 2008; Castellazzi et *al*., unpublished). Thus, 15 studies have been carried out in infants younger (0-6 months) than the target population (6-12 months) of the proposed claim.

Data from younger infants (0-6 months) cannot be generalised to older infants or young children because these populations differ by the level of maturation of digestive functions and the introduction of solid foods in children over 6 months.

Moreover, several studies indicate that the beneficial effects of the constituents decrease or vanish with time (Kennedy et al., 1999; Tsou et *al*., 2003; Ziegler et *al*., 2007; Singhal et *al*., 2008; Pickering et *al*., 1998; Thibault et *al*., 2004). Besides, the primary endpoints of two

studies involving infants between 1 week and 1 year of age were either not relevant to the proposed claim or not significant in the appropriate age range (Pickering et *al*., 1998; Tsou et *al*., 2003).

Only one study (Thibault et *al*., 2004) enrolled 4-6 month old infants in a randomised, double-blind, placebo controlled trial. This 5-month study compared the number and duration of diarrhoea episodes in infants fed a control or a study formula. However, the primary endpoint (incidence of diarrhoea) did not differ between groups, and the study did not use the formulation including the bioactive constituents that is subject of the claimed effect.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between consumption of "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides (GOS), acidified milk, nucleotides and beta-palmitate" and intestinal ailments.

CONCLUSIONS

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

- The food that is the subject of the claimed effect (i.e. "follow-on formulae containing a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate") is sufficiently characterised.
- The claimed effect is "aids minor intestinal ailments (as colic, constipation, digestive symptoms). The target population is infants aged 6 to 12 months, who are not, or are not anymore breast-fed.
- Reduction of intestinal symptoms (e.g. constipation, colic) is beneficial for children's health.
- A cause and effect relationship has not been established between consumption of "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides, acidified milk, nucleotides and beta-palmitate" and the claimed effect (i.e. "aids minor intestinal ailments".

DOCUMENTATION PROVIDED TO EFSA

Health claim application on "follow-on formulae with a fixed combination of short-chain galacto-oligosaccharides (GOS), acidified milk, nucleotides and beta-palmitate" and intestinal ailments, pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0141-IT). September 2008. Submitted by Plada Industriale Srl.

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GLOSSARY / ABBREVIATIONS

GOS	galacto-oligosaccharides