

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) (ID 1010, 1011, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

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ABSTRACT

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on health claims pursuant to Article 13.1 of Regulation (EC) No 1924/2006 in the framework of further assessment related to *Saccharomyces boulardii* ATY-SB-101 and the following claimed effects: "maintains and restores the natural flora" and "modulating both innate and adaptive host immunity to respond against pathogen infection". The food constituent that is the subject of the claims, *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837), is not sufficiently characterised. On the basis of the data presented, the Panel concludes that a cause and effect relationship cannot be established between the consumption of *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) and the proposed claimed effects.

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KEY WORDS

Saccharomyces boulardii, ATY-SB-101, microorganisms, health claims.

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SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. This opinion addresses the scientific substantiation of health claims in relation to *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) and the following claimed effects: "maintains and restores the natural flora" and "modulating both innate and adaptive host immunity to respond against pathogen infection". The scientific substantiation is based on the information provided by the competent Authority of Belgium for further assessment of this claim.

The food constituent that is the subject of the health claims is *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) related to the following claimed effects: "maintains and restores the natural flora" and "modulating both innate and adaptive host immunity to respond against pathogen infection".

The Panel notes that the information provided did not allow concluding that the strain that is the subject of the claims (ATY-SB-101) can be identified as *S. cerevisiae* var *boulardii*. The Panel considers that *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) is not sufficiently characterised.

On the basis of the data presented, the Panel concludes that a cause and effect relationship cannot be established between the consumption of *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) and the proposed claimed effects.

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INTRODUCTION

The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. These claims include already assessed claims related to micro-organisms which the Panel considered to be not sufficiently characterised and claims for which the NDA Panel concluded that there was insufficient evidence to establish a cause and effect relationship between the consumption of the food and the claimed effect.

Following an opinion of the NDA Panel on a health claim pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ in which the Panel concluded that the data available were not sufficient to characterise *Saccharomyces boulardii* ATY-SB-101 (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009), EFSA received additional information from the competent Authority of Belgium for further assessment of these claims. The information provided in the framework of further assessment for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

The approach used in the evaluation of Article 13(1) health claims is explained in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims⁵.

In assessing each specific food/health relationship that forms the basis of a health claim the NDA Panel considers the extent to which:

1. the food/constituent is defined and characterised;
2. the claimed effect is defined and is a beneficial physiological effect ("beneficial to human health");
3. a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use).

Substantiation of the claim is dependent on a favourable outcome of the assessment of 1, 2 and 3 above. Thus, a cause and effect relationship is considered not to be established if the outcome of any one of these assessments is unfavourable.

For a claim, each relationship between a food/constituent and a claimed effect is assessed separately, and individual assessments are combined, as appropriate, to form coherent opinions.

1. Characterisation of the food/constituent (ID 1010, 1011)

The food constituent that is the subject of the health claims is *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) related to the following claimed effects: "maintains and restores the natural flora" and "modulating both innate and adaptive host immunity to respond against pathogen infection".

A culture collection number from the Belgian Co-ordinated Collections of (Agro) Industrial Fungi and Yeast Collection (BCCM/MUCL) is provided (MUCL 53837). The BCCM/MUCL is an internationally recognised culture collection, which has the status of an International Depository

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.

⁵ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

Authority under the Budapest Treaty. In the MUCL, cultures can be deposited in a restricted-access collection for safe deposit or for patent purposes.

The identification of the strain ATY-SB-101, which is the subject of the claim, at species level (as *S. cerevisiae*) was based on phylogenetic analyses of rDNA sequences (the D1/D2 region and the 5.8S rDNA internal transcribe spacer [ITS] region) and the mitochondrial CytC gene sequence. The Panel notes that these analyses allow the identification of the strain ATY-SB-101 with the species *S. cerevisiae* but not the discrimination between *S. cerevisiae* and *S. cerevisiae* var. *boulardii*.

The characterisation of *S. cerevisiae* var. *boulardii* ATY-SB-101 at strain level was based on restriction analyses of two rDNA regions (ITS and 18S). The restriction analysis of the ITS region resulted in a unique DNA band, and that of the 18S rDNA in two bands. The Panel notes that comparative analysis of the DNA band profiles with those of a reference strain identified as *S. cerevisiae* var. *boulardii*, or references to publications showing the expected DNA profiles, were not provided, and therefore, it is not possible to conclude that the strain that is the subject of the claims (ATY-SB-101) can be identified as *S. cerevisiae* var. *boulardii*.

Three references were provided in the application related to the use of phenotypic and genotypic techniques for the identification of *S. cerevisiae* strains (Fietto et al., 2004; van der Aa Kuhle and Jespersen, 2003; van der Aa Kuhle et al., 2005), but none of these included data related to the strain that is the subject of the health claims (ATY-SB-101).

The Panel considers that the food constituent, *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837), which is the subject of the health claims, is not sufficiently characterised.

The Panel concludes that a cause and effect relationship cannot be established between the consumption of *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) and the proposed claimed effects.

CONCLUSIONS

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

- The food constituent, *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837), which is the subject of the health claims, is not sufficiently characterised.
- A cause and effect relationship cannot be established between the consumption of *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837) and the proposed claimed effects.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 for further assessment (No: EFSA-Q-2012-00156, EFSA-Q-2012-00157). The scientific substantiation is based on the information provided by the competent Authority of Belgium for further assessment of this claim (available at: <http://www.efsa.europa.eu/en/topics/topic/article13.htm>).

REFERENCES

EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009. Scientific opinion on the substantiation of health claims related to non-characterised microorganisms pursuant to Article 13 of Regulation (EC) No 1924/2006 on request from the European Commission. EFSA Journal 2009; 7(9):1247, 64 pp.

- Fietto JL, Araujo RS, Valadao FN, Fietto LG, Brandao RL, Neves MJ, Gomes FC, Nicoli JR and Castro IM, 2004. Molecular and physiological comparisons between *Saccharomyces cerevisiae* and *Saccharomyces boulardii*. *Canadian Journal of Microbiology*, 50, 615-621.
- van der Aa Kuhle A and Jespersen L, 2003. The taxonomic position of *Saccharomyces boulardii* as evaluated by sequence analysis of the D1/D2 domain of 26S rDNA, the ITS1-5.8S rDNA-ITS2 region and the mitochondrial cytochrome-c oxidase II gene. *Systematic and Applied Microbiology*, 26, 564-571.
- van der Aa Kuhle A, Skovgaard K and Jespersen L, 2005. In vitro screening of probiotic properties of *Saccharomyces cerevisiae* var. *boulardii* and food-borne *Saccharomyces cerevisiae* strains. *International Journal of Food Microbiology*, 101, 29-39.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁶ (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined 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".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

- a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- b) psychological and behavioural functions; or
- c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

- (i) based on generally accepted scientific evidence; and
- (ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD⁷

Foods are commonly involved in many different functions⁸ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

⁶ OJ L12, 18/01/2007

⁷ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁸ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

- (a) the claimed effect of the food is beneficial for human health,
- (b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),
- (c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,
- (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. 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 wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Health claims related to *Saccharomyces boulardii* ATY-SB-101 (BCCM/MUCL 53837), including conditions of use, as proposed in the framework of further assessment.

ID	Food or Food constituent	Health Relationship	Proposed wording
1010	<i>Saccharomyces boulardii</i> ATY-SB-101 (=MUCL 53837)	<p><i>Saccharomyces boulardii</i> is yeast closely related to <i>Saccharomyces cerevisiae</i> able to grow at 37°C. It was isolated for the first time by Henri Boulard in 1923 from tropical fruits. <i>S. boulardii</i> has been shown to be non-pathogenic, non-systemic remaining in the gastrointestinal tract. It has been demonstrated that its consumption brings many beneficial effects for intestinal tract and was classified as a probiotic .</p> <p>The beneficial effect of <i>Saccharomyces boulardii</i> has been demonstrated by several clinical. So, Centina-Sauri et al. (1994) and Kurugöl et al. (2005) has demonstrated that <i>S. boulardii</i> maintains and restores the natural flora in the large and small intestine especially in the case of acute gastroenteritis.</p> <p>The beneficial effect has been also demonstrated in much other gastrointestinal affections such as (i) in recurrent <i>Clostridium difficile</i> infection, (ii) in irritable bowel syndrome, (iii) in inflammatory bowel disease, (iv) in travelers' diarrhea, and (v) in antibiotic-associated diarrhea.</p>	<ul style="list-style-type: none"> • Maintains intestinal microflora's balance; • probiotic regulates intestinal transit; • balances intestinal flora; • supports healthy digestive system.
	Conditions of use At least 10 E+8 CFU/day. The target population is the normal population and person with digestive troubles. It can be used to promote intestinal comfort/health.		
ID	Food or Food constituent	Health Relationship	Proposed wording
1011	<i>Saccharomyces boulardii</i> ATY-SB-101 (=MUCL 53837)	<p><i>Saccharomyces boulardii</i> is yeast closely related to <i>Saccharomyces cerevisiae</i> able to grow at 37°C. It was isolated for the first time by Henri Boulard in 1923 from tropical fruits. <i>S. boulardii</i> has been shown to be non-pathogenic, non-systemic remaining in the gastrointestinal tract. It has been demonstrated that its consumption brings many beneficial effects for health and immune system and was classified as a probiotic.</p> <p>Several studies demonstrated that <i>S. boulardii</i> might induces a protective effect in modulating both innate and adaptive host immunity to respond against pathogen infection.</p>	<ul style="list-style-type: none"> • Helps to reinforce the natural defenses; • Stimulates the immune system; • Modulates the immune response;
	Conditions of use At least 10 E+8 CFU/day. The target population is the normal persons		

GLOSSARY AND ABBREVIATIONS

BCCM	Belgian Co-ordinated Collections of Micro-organisms
CytC	Cytochrome complex
DNA	Deoxyribonucleic acid
ITS	Internal transcribe spacer
MUCL	Mycothèque de l'Université catholique de Louvain
rDNA	Ribosomal DNA