ehpm
European Federation of Associations of Health Product Manufacturers

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EHPM Probiotics guidelines

The objective of this document is to define guidelines for a practical, reliable and safe use of probiotics in food supplements (FS). It provides recommendations on what constitutes probiotic microorganisms: strain characterisation, safety, viability, manufacturing practices and labelling of FS containing probiotics.

This document is not intended to be legal in nature but consists in recommendations for operators in the FS sector (strain suppliers, manufacturers, distributors, etc.) for the control of their formulations and manufacturing conditions of their products.

Definitions

Food supplement (FS)
"foodstuffs the purpose of which is to supplement the normal diet, and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination"[1].

Strain(s) manufacturer
company that produces probiotics strains. The obtained ingredient corresponding to one strain or a mix of strains is ready for use by the FS Manufacturer.

FS manufacturer
company that undertakes the food supplement production on an industrial scale.

Food business Operator
company which affixes its name on the label, and which is responsible for the declaration of the food supplement.

Distributor
company that will distribute the food supplement.

1 - Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements.

1 - Probiotics strains

Definition as recommended by FAO/WHO (2001/2002)[2]
"Live microorganisms which, when administered in adequate amounts confer a health benefit on the host."

Probiotics are classified as per reference nomenclature, at the species level: genus, species, and sometimes subspecies (subsp). A strain is the genetic variant of a species or subspecies.

Probiotic strains are required to be deposited in a recognised culture collection having an international depositary authority status in accordance with the Budapest Treaty of April 28, 1977.

Probiotics can be used in food supplements as ingredients with nutritional or physiological effect[3]. It is the responsibility of the person placing the product on the market to justify the authorisation for use of the selected strains in order to guarantee a safe and wholesome product to the consumer.

The use of a probiotic strain must be justified by the characterisation of the strain(s), their safety, as well as the non-novel food aspect (microorganisms justifying a consumption history prior to May 15, 1997) or a novel food authorisation according to Regulation (EU) 2015/2283[4].

2 - Guidelines for the Evaluation of Probiotics in food. Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. London, Ontario, Canada, April 30 and May 1, 2002.

3 - Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements.

4 - Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) 258/97 of the European Parliament and of the Council and Commission Regulation (EC) 1852/2001.

(1) CHARACTERISATION OF THE PROBIOTIC STRAIN(S)

The probiotic strains are specific strains that must be characterised at the phenotypic and genotypic level, in order to justify their identification by using the most current, valid and internationally accepted techniques. Sequencing and annotation of the genome are essential for characterisation.

(2) SAFETY

Each probiotic strain manufacturer must be able to guarantee that it is safe for human consumption.

In 2007, EFSA published a list of species of microorganisms based on the concept of recognised presumption of harmlessness, for use by food and feed manufacturers: "Qualified Presumption of Safety / QPS"[5] [6].

This QPS inventory lists species which are known to be safe for human consumption and specifies that any strain whose identity could be unambiguously established and meets the qualification conditions are presumed to be safe for human consumption, thus exempt from full safety assessment. An antibiotic resistance screening must be carried out to demonstrate the absence of transferable resistance to antibiotics:

- If there is no atypical resistance, the strain is considered safe;
- If there is atypical resistance, then the absence of transferability of the gene or genes responsible for this resistance must be demonstrated.

For additional details, refer to the EFSA Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA 2018)[7].

Strains that do not belong to a QPS – listed species require full safety assessment to be performed based on the QPS assessment criteria.

Understanding the realities of confidentiality and data ownership, the applicant is not obliged to hold all the information. In such case, he must obtain the commitment of the strain manufacturer to make the relevant information available to the authorities when needed.

5 - Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. Opinion of the Scientific Committee. EFSA Journal (2007) 587, 1-16.

6 - EFSA. Update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 15: suitability of taxonomic units notified to EFSA until September 2021. EFSA Journal 2022;20(1) :7045.

7 - https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5206.

(3) VIABILITY

The viability of strains must be ensured until the end of their shelf life.

The survival capacity of probiotics during the manufacturing process and during the digestion is really dependent on the microorganism (genus, species, strain).

Common practices to demonstrate these aspects are to generate data from stability studies and from some in vitro tests, such as resistance to gastric acid and bile acids, or during clinical investigation by strain recovery evaluation in the feces.

(4) SCIENTIFICALLY DOCUMENTED

According to FAO/WHO documents (2001/2002)[8] [9], microorganisms are considered probiotics if they are scientifically documented. The level of scientific documentation, at the species or strain level, is depending on the demonstrated benefits.

A comprehensive literature review of the species used and ideally of the strains used will support their nutritional and physiological effects.

8 - FAO/OMS Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. Córdoba, Argentina, 1-4 October 2001.

9 - Guidelines for the Evaluation of Probiotics in food. Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. London, Ontario, Canada, April 30 and May 1, 2002.

2 - Formulation of FS with probiotics strains

In order to guarantee the quality of the finished product, any FS manufacturer must control all aspects of the formulation and manufacturing process. This includes the quality control of the final product (aspect, concentration, contaminants, microbiological contaminants) as per the applicable regulation to food.

(1) COMPATIBILITY WITHIN THE FORMULATION

To ensure that the addition of other ingredients has no effect on the viability of the probiotic strain(s), compatibility tests must be performed prior to manufacturing. This involves bringing the strain into contact with the mixture and, if necessary, with individual ingredients and test the viability.

(2) CONTROL OF TEMPERATURE AND HUMIDITY CONDITIONS

Probiotics are sensitive to environmental conditions such as humidity, temperature, and especially to variations in external conditions in time.

In order to guarantee the total quantity of strains labelled on the finished product until the end of shelf life, the FS manufacturers must comply with the storage conditions specific to the strains used. The temperature and humidity suitable for the formulation must be determined and monitored between the strain(s) incorporation until delivery of the finished product to the customer. Throughout, the production chain cold storage is typically recommended to maximise the viability of probiotic strains.

Storage recommendations must be established and indicated on the technical sheets of the FS, on the delivery documents and on the final packaging so that at the points of sale and consumers are informed and able to comply with these storage conditions.

(3) DURATION AND CONDITIONS OF STORAGE

In the absence of real-time stability data on the finished product, the duration and storage conditions of probiotic-based FS can be initially established on the basis of (1) the stability data available for the strains, (2) the stability data available for similar products, (3) results of compatibility tests, and (4) of the overage possibly applied. This may be sufficient for placing the product on the market. It is recommended to run real-time stability tests on the finished product according to market conditions in parallel.

(4) PROBIOTIC CONCENTRATION

As for any ingredient used for nutritional or physiological purposes, the intake must be determined based on the available data related to the nutritional or physiological effects, as per regulations.

Based on scientific data and probiotics regulations already implemented[10] [11] [12] [13], it is recommended that a food supplement provides a minimum of 10^7 to 10^9 live microbial cells of at least one strain/blend of strains per day. Lower concentrations should be justified by scientific data, especially by clinical data.

No upper limit has been scientifically established or agreed for probiotics, but based on existing probiotics guidelines[10] [12] [14], there is no upper limit for safety when the strain is deemed safe to be administered to the healthy general population. An overage is necessary to ensure the total labelled amount of the probiotics strain(s) until the indicated date of minimum durability. As stated above, there is no fixed limit for overage, and the overage does not pose any additional safety risk.

Regarding labelled amounts, a tolerance of +/- 0.5 log is recommended for the measurement uncertainty[10].

10 - Linee Guida Su Probiotici e Prebiotici. Ministero della Salute Revisione marzo 2018.

11 - Effets des probiotiques et prébiotiques sur la flore et l'immunité de l'homme adulte. AFSSA Février 2005.

12 - Natural Health Product Probiotics. Heath Canada, 25 March 2019.

13 - Ordinance of the Federal Department of Home Affairs (DFI) on Dietary Supplements (DietSO; SR 817.022.14), Article 3.

14 - EFSA. Update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 15: suitability of taxonomic units notified to EFSA until September 2021. EFSA Journal 2022;20(1) :7045.

(5) METHOD OF ANALYSIS

To the quantification of probiotics, the conventional method used is the enumeration of colonies following incubation on specific culture medium according to a scientifically valid and appropriate method, or other scientifically valid method.

(6) LABELLING

Without prejudice to Regulation (EU) 1169/2011[15], and the Directive 2002/46/CE[16], the following labelling specificities should be applied for probiotic-based FS:

- **Category name**
  If these guidelines are followed, the category name "probiotics" should be used on the labelling of the finished product to provide information to the consumer.

- **Ingredients list**
  The designation of the genus and species is mentioned in italics in the list of ingredients. The reference of the strain must also be specified therein.

- **Quantity of microorganisms**

  - The quantity of microorganisms is expressed in colony forming units (CFU) per recommended daily intake (or other scientifically valid unit according to the analytical method used);

  - The labelled quantity corresponds to the minimum guaranteed quantity on the date of minimum durability indicated.

    The indication of the amount of microorganisms can represent the total amount of probiotics, all of the strains combined, with any constituent strain listed in descending order according to the ratio determined at the time of manufacturing.

- **Storage recommendations**
  Storage conditions should be included on the labelling in order to allow good preservation of the product throughout the distribution chain and for the consumer.

15 - Regulation (EU) 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) 1924/2006 and (EC) 1925/2006 of the European Parliament and of the council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) 608/2004.

16 - Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements.

Conclusion

Adherence to these guidelines will ensure the quality and safety of probiotic-based FS.

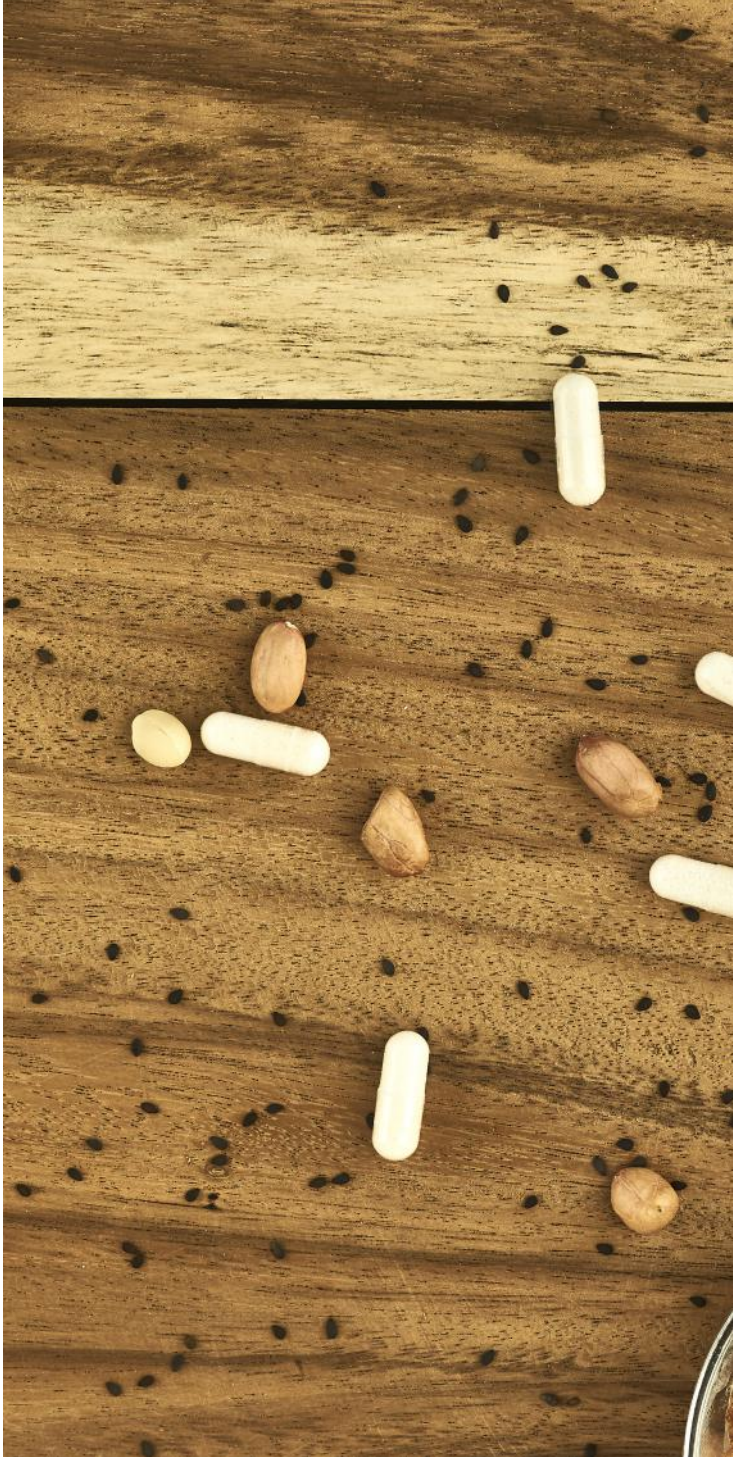
Responsibility is shared between the various stakeholders considering their specialty and their level of intervention.

About the EHPM

EHPM was created in 1975 and represents and supports approximately 1,600 health-product manufacturers, distributors and suppliers in 14 European Countries, the majority of which are Small and Medium Size Enterprises (SMEs).

As the EU trade association for the food supplement sector, EHPM proactively and constructively engages with the EU Institutions to contribute to the development of a fair European regulatory framework for the sector.

Through our member associations EHPM aims to provide consumers with safe, science-based, high-quality products as well as accurate and helpful information about their nutritional value and use.



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