

## **COLLEGIATE BOARD RESOLUTION – RDC NO. 241 OF 26 JULY 2018**

Provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 15, items III and IV, and Article 7, items III and IV of Law no. 9,782 of 26 January 1999, and item V, paragraphs 1 and 3 of Article 53 of the Internal Regulation approved in the terms of Annex I of the Collegiate Board Resolution – RDC no. 61 of 3 February 2016, adopts the following Collegiate Board Resolution, as decided upon in a meeting held on 17 July 2018, and I, Deputy Director-President, determine its publication.

### **CHAPTER I**

#### **INITIAL PROVISIONS**

##### **Section I**

###### Scope of Application

Article 1. This Resolution provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods.

Article 2. In a complementary way, this Resolution applies to the provisions in:

I – Resolution no. 17 of 30 April 1999, which approves the technical regulation that establishes the basic directives for food risk and safety assessment; and

II – Resolution no. 18 of 30 April 1999, which approves the technical regulation that establishes the basic directives for analysis and confirmation of functional and/ or health properties claimed in food labeling.

##### **Section II**

###### Definitions

Article 3. For the purposes of this Resolution, the following definitions shall apply:

I – probiotic: live microorganism that, when administered in adequate quantities, confers a benefit to one's health; and

II – lineage: subpopulation of cells from the same species that present the same characteristics and are identified by numbers, letters, or names following the specific epithet.

### **CHAPTER II**

## **REQUIREMENTS TO CONFIRM THE SAFETY OF AND THE HEALTH BENEFITS FROM PROBIOTICS FOR USE IN FOODS**

### **Section I**

#### General Principles

Article 4. The use of probiotics in foods requires the confirmation of their safety and health benefits.

Paragraph 1. The confirmation referred to in the caption of this article must be requested through the submission of a petition for safety and efficacy assessment.

Paragraph 2. The result of the petition referred to in Paragraph 1 shall be published through a Resolution (RE).

Article 5. The confirmation of safety and health benefits from probiotics does not exempt the foods added with probiotics from the compliance with the other requirements needed for their regularization, in the terms of Resolution no. 23 of 15 March 2000, which provides for the manual of basic procedures for marketing authorization and the exemption from marketing authorization for food products.

Article 6. The decisions on petitions for marketing authorization for foods containing probiotics, submitted from the date this Resolution is published, shall be bound to the previous decision on the safety and efficacy assessment petition, according to the procedure provided for in Article 4.

### **Section II**

#### Identity of Probiotics

Article 7. The confirmation of the safety of probiotics and their health benefits requires the unequivocal microorganism lineage characterization and identification, through the presentation of technical documents or scientific studies that:

- I – identify the species, in accordance with the latest binomial nomenclature;
- II – identify and characterize the lineage, through genotypic and phenotypic methods;
- III – specify the lineage origin; and
- IV – confirm the lineage deposit in a culture collection acknowledged internationally.

### **Section III**

#### Safety of Probiotics

Article 8. Safety confirmation must be given through technical documents or scientific studies that present:

- I – safe use history;

II – absence of relevant adverse event reports obtained from clinical trials or post-use vigilance;

III – absence of virulence and pathogenicity factors relevant to human health;

IV – absence of production of substances or metabolites that represent risk to human health;

V – absence of resistance potentially transferrable to antibiotics relevant to human health; and

VI – susceptibility to, at least, two antibiotics.

Article 9. Without prejudice to the provisions in Article 8 of this Resolution, when probiotics are not isolated from foods or from the human endogenous microbiota, and do not have their safety established at gender or species level, safety must be confirmed through the following studies:

I – genotoxicity and mutagenicity;

II – acute toxicity;

III – subchronic toxicity;

IV – long term toxicity; and

V – reproductive and development toxicity, when the lineage is indicated for children under three years old and pregnant women.

Article 10. Without prejudice to the provisions in Articles 8 and 9 of this Resolution, when probiotics are indicated for pregnant women or children under three years old, the lineage safety must be confirmed through clinical trials that assess the occurrence of adverse effects and growth and development parameters.

Article 11. In the case of probiotic associations, the lineages used must have their safety confirmed individually.

#### **Section IV**

##### **Benefits from Probiotics**

Article 12. The health benefit associated to the use of probiotics must be clearly identified and reflect the set of evidences presented, in the most appropriate way.

Sole paragraph. In the products added with probiotics, the benefit must be declared through a functional or health property claim approved for the lineage, except when there are contrary provisions in a specific technical regulation.

Article 13. The benefit claimed may have a general or specific nature, considering the totality and the level of evidence available.

Article 14. The confirmation of benefits from probiotics requires the demonstration of survival against human digestive tract conditions and evidence of effect on humans obtained from studies that:

I – are conducted with the microorganism lineage;

II – involve a representative group from the population of interest, or the results from which can be extrapolated to the population of interest;

III – consider the minimum amount suggested to obtain the benefit;

IV – assess relevant outcomes to the claimed benefit; and

V – minimize biases and confounding factors.

Sole paragraph. In addition to the evidences in humans referred to in the caption of this article, other types of studies and references that help explain the biological plausibility of the claimed effect may be presented.

Article 15. When the benefit to be confirmed is associated to a mixture of lineages, human studies must be conducted using the same mixture with which the claimed effect is intended to be presented.

Sole paragraph. The health benefit confirmation referred to in the caption of this article is not necessary for the association of probiotics where all lineages used already have a confirmed benefit.

### **CHAPTER III**

#### **FINAL AND TRANSITIONAL PROVISIONS**

Article 16. If the evidence presented is inconclusive or there are uncertainties to confirm the safety of or the benefit from the lineage, additional studies or information may be required.

Article 17. The period of up to 60 (sixty) months is established for the adequacy of foods containing probiotics that are regularized with the competent organization on the date this Resolution is published.

Article 18. The companies responsible for marketing authorization petitions for foods containing probiotics and for safety and efficacy assessment petitions for probiotics, pending Anvisa's decision on the date this Resolution is published, shall be duly notified to expressly state, in the period of 30 (thirty) days from the date of the notification, their interest in:

I – withdraw the petition;

II – amend the petition, in accordance with the provisions approved in this Resolution;

III – inform that the documents related to the safety and efficacy assessment of the probiotic present in the product that is the object of the marketing authorization petition will be submitted in a specific safety and efficacy assessment petition.

Paragraph 1. The amendment referred to in item II must be effected in the period of up to three hundred sixty-five days from the date this Resolution is published, in a single act.

Paragraph 2. The safety and efficacy assessment petition for the probiotic, provided for in item III, must be submitted in the period of up to three hundred sixty-five days from the date this Resolution is published.

Paragraph 3. For the companies that choose the situation provided for in item III, the decision on the marketing authorization petition shall be bound to the previous decision on the safety and efficacy assessment petition.

Paragraph 4. After the period established in paragraphs 1 and 2, the petition shall be analyzed regardless of the submission of safety and efficacy assessment petitions or the addition of complementary information to the marketing authorization.

Article 19. The transitional provisions established in Articles 17 and 18 do not apply to dietary supplements containing probiotics, which must comply with the provisions in Resolution – RDC no. 243 of 26 July 2018, which provides for the health requirements for dietary supplements.

Article 20. The failure to comply with the provisions in this Resolution constitutes a health infraction, in the terms of Law no. 6,437 of 20 August 1977 and its updates, without prejudice to the applicable civil, administrative, and criminal liabilities.

Article 21. Administrative Rule SVS/MS no. 36 of 13 January 1998, which approves the technical regulation on cereal-based foods for infant feeding, comes into force with the addition of the following subitem:

"4.1.8.1. In the case of probiotics, the provisions in Resolution – RDC no. 241 of 26 July 2018, which provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods, must be complied with." (new wording)

Article 22. Item V of Article 22 of Resolution – RDC no. 43 of 19 September 2011, which provides for the technical regulation for infant formulas, comes into force with the addition of the following letter:

"d) in the case of probiotics, the provisions in Resolution – RDC no. 241 of 26 July 2018, which provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods, must be complied with." (new wording)

Article 23. Item V of Article 22 of Resolution – RDC no. 44 of 19 September 2011, which provides for the technical regulation for follow-up infant formulas for infants and young children, comes into force with the addition of the following letter:

"d) in the case of probiotics, the provisions in Resolution – RDC no. 241 of 26 July 2018, which provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods, must be complied with." (new wording)

Article 24. Article 4 of Resolution – RDC no. 22 of 13 May 2015, which provides for the technical regulation of nutrient compounds and other substances for enteral nutrition formulas and gives other provisions, enters into force with the following wording:

"Article 4. The use in formulas for enteral nutrition of probiotics, nutrient compounds, and other substances not provided for in this Resolution must be requested by the companies through a specific petition, including documentation that confirms the following requirements are complied with:

I – in the case of nutrients and other substances, constituents must:

a) be confirmedly safe for human consumption, in accordance with Resolution no. 17 of 30 April 1999, which approves the technical regulation that establishes the basic directives for food risk and safety assessment;

b) be bioavailable, based on evidence from studies with animals or humans; and

c) comply with the provisions in item II of Article 3 of this Resolution.

“II – in the case of probiotics, the provisions in Resolution – RDC no. 241 of 26 July 2018, which provides for the requirements to confirm the safety of and the health benefits from probiotics for use in foods, must be complied with.” (new wording)

Article 25. This Resolution enters into force on the date of its publication.

**FERNANDO MENDES GARCIA NETO**

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