CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 11 **CX/NFSDU 18/40/12**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

Fortieth Session

Berlin, Germany
26 – 30 November 2018

DISCUSSION PAPER ON HARMONIZED PROBIOTIC GUIDELINES FOR USE IN FOODS AND DIETARY SUPPLEMENTS

(*Prepared by Argentina*)

BACKGROUND

1. At the thirty-ninth Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) in 2017 the Committee adopted the Agenda with the following addition under item 11 - Other business: iii. Harmonized probiotic guidelines for use in foods and dietary/food supplements (International Probiotics Association).

2. The observer of the International Probiotics Association (IPA) introduced that item and proposed to develop guidelines with a harmonized framework for probiotics to ensure and sustain the quality of probiotic products on a global scale and presented a “Proposal for New Work on Harmonized Probiotic Guidelines for Use in Foods and Dietary Supplements” (NFSDU/39 CRD/3).

3. Argentina expressed their support to the proposal and their willingness to lead this work.

4. In view of the late receipt of the document, delegations were not in a position to fully discuss the proposal in order to make an informed decision on starting new work.

5. The Committee agreed that Argentina would prepare a discussion paper together with a project document for consideration at its next session.

SCOPE

6. The purpose of the work is to establish guidance to assist competent national authorities in their evaluation of ‘probiotics’ in order to authorize a strain as a probiotic strain.

7. The scope of the discussion paper, applies exclusively on the development of standard/guidelines on probiotics used as food ingredient, including dietary/food supplements.

8. The scope of this document will include live microorganisms recognized to convey a health benefit to humans in appropriate, efficacious amounts. Only live microorganisms intended to be added to foods or used to supplement the diet where scientific data has demonstrated a health benefit will be discussed.

9. This document is not intended for use in any aspects of production of biologics or pharmaceutical products or animal feeds.

10. The discussion paper includes definitions of ‘probiotics’ and ‘food with probiotics’, requirements for the evaluation of a probiotic as a food ingredient, requirements for the evaluation of a food with probiotics, aspects of production, contaminants, hygiene, labelling and methods of analysis and sampling.

11. The scope of this discussion paper only refers to probiotics and food with probiotics that are produced in food manufacturing facilities and traded internationally.

INTRODUCTION

12. A joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria was held in 2001 to evaluate many aspects of the use of probiotic foods. The importance of probiotic microorganisms to the health of the human population was recognized in addition to the growth of probiotic food and drinks that market health benefits. With a lack of international agreement of the assessment of safety and efficacy, the FAO/WHO Consultation intended to address methodologies for assessment of safety and efficacy and promote general guidelines.

13. Subsequently, an Expert Working Group was assembled to create a methodology for evaluation of probiotics and criteria for substantiating health claims for probiotic foods.

14. The outcome of the Consultation and the Working Group both provided very general guidance where a global regulatory landscape was lacking. The scope of these meetings did not include probiotics not used in food.

15. With the goal of enhancement of the overall safety and quality of food with probiotics for consumers, these previous documents laid the groundwork for building guidelines or standards for probiotics. Due to technological advances, the probiotics industry now requires a broader scope that includes advancements in technology.

UNDERLYING PRINCIPLE

16. Today, more than a decade later, the lack of harmonization in industry practice and legislation remains and often leads to issues and concerns for the probiotics regulators, industry, and even consumers in regard of quality, safety and labelling.

17. Despite the widely recognized FAO/WHO definition (2001), revised by Hill et al. (2014), as “Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”, there is global occurrence of products sold as ‘probiotics’ that do not meet this definition. As such, the countries recognize the need and opportunity for development of a Codex Alimentarius guidance or standard to more clearly define the required characteristics of safe and efficacious probiotics, and to ensure the same level of quality and manufacturing requirements for all operators on the market. The ultimate goal is to establish eligibility criteria to ensure consistent application at national and international levels by Codex member countries, available to promote human health and well-being.

18. The establishment of eligibility criteria and an organized framework for probiotic products will provide a guideline for global regulatory agencies to build probiotics-focused regulations. The establishment of global requirements will satisfy the triumvirate of authorities, consumers and industry, and will certainly lead to better consumer satisfaction, health and well-being.

PROBIOTIC PRODUCTION

19. At present, according to information provided by the International Probiotics Association (IPA), IPA membership currently is at 105 member companies which are involved only in Probiotics.

These companies are from 29 countries from around the world and are based in the following regions; North and South America, Europe, Asia and Australia.

IPA member category breakdown is as follows:

Finished Products and/or Marketers	37
Bacteria Producers/Fermenters	22
Manufacturer, Formulators and/or Ingredients	34
Services and/or Institutions	12
Total	105

Ingredients Market:

a) Fermentation and Bacteria Production:

Known fermentation capabilities and production facilities are based in many countries across the globe. Some of these are in the following countries:

USA, Canada, Pan EU including UK, Brazil, Argentina, Chile, Japan, China, South Korea, India, Australia, South Africa, to name but a few. Fermentation capacity of these facilities range from 20 metric tons to 500 metric tons capacity.

b) Ingredient Market Revenue:

The global probiotics ingredient market was valued at $1.5 billion USD in 2016 and is expected to be valued at $2.15 billion USD by the year 2021. (Source IPA).

The split of the revenue in 2016 was Functional Food and Beverages 58%, Dietary Suplements 29%, Other Human Nutrition 3%, Animal Feed & Others 10%. (Source IPA).

PROBIOTIC DISTRIBUTION AND TRADE

20. Probiotics are distributed in 63 countries and probiotic dairy based yoghurts are distributed in 196 countries. (Source IPA).

i. North America (USA, Canada, Mexico),

ii. Latin America and Caribbean (Argentina, Colombia, Peru, Brazil, Venezuela, Chile, Ecuador, Guatemala, Cuba, Bolivia, Haiti, Dominican Republic, Honduras, Paraguay, Nicaragua, El Salvador, Costa Rica, Panama, Puerto Rico, Uruguay, Jamaica, French Guiana, Guadeloupe, Martinique, Bahamas, Belize, Barbados, Curaçao, Aruba, British Virgin Islands, Grenada, Dominica, Bermuda, Saint Kitts, Sint Maarten, Anguilla, Antigua),

iii. Europe (France, Spain, Sweden, Norway, Germany, Finland, Poland, Italy, United Kingdom, Denmark, Belgium, Switzerland, Ireland, Portugal, Austria, Netherlands, Greece, Iceland, Luxembourg, Monaco, Georgia, Andorra, Malta, Liechtenstein, Albania, Turkey, Czech Republic, Serbia, Hungary, Bulgaria, Romania, Belarus, Cyprus, Montenegro, Kosovo, Russia, Azerbaijan, Lithuania, Latvia, Croatia, Ukraine, Bosnia and Herzegovina, Macedonia, Slovakia, Slovenia, Estonia, Kazakhstan, Moldova),

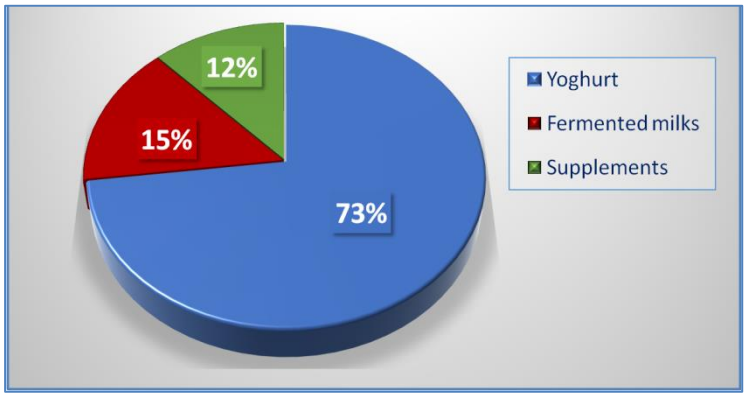
iv. Asia (Afghanistan, Armenia, Bahrain, Brunei, Cambodia, China, India, Indonesia, Iran, Iraq, Israel, Japan, Jordan, Kuwait, Kyrgyzstan, Laos, Lebanon, Malaysia, Myanmar, Mongolia, North Korea, Oman, Philippines, Qatar, Saudi Arabia, Singapore, South Korea, Syria, Taiwan, Tajikistan, Thailand, Turkmenistan, Uzbekistan, Vietnam, Yemen, Macau),

vi. Australasia (Australia, New Zeland, French Polynesia, Papua New Guinea, Fiji, New Caledonia, Kiribati, Vanuatu, Nauru, Tonga, Tuvalu, Solomon Islands, Samoa

vii. Africa (Argeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cape Verde, Cameroon, Central African Republic, Chad, Comoros, Democratic Republic of the Congo, Congo-Brazzaville, Côte d'Ivoire, Djibouti, Egypt, Equatorial Guinea, Eritrea, Swaziland, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Libya, Madagascar, Malawi, Mali, Mauritania, Mauritius, Morocco, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tomé e Príncipe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Tanzania, Togo, Tunisia, Uganda, Zambia, Zimbabwe, Réunion).

PROBIOTIC CONSUMER CONSUMPTION

21. Probiotics are consumed in foods, beverages and dietary/food supplements. Foods include mainly dairy products as yoghurts and other fermented milks as represented in graph 1 and in table 1.



Graph 1: 2017 Global Retail Value (Source IPA)

World Retail Value (2017)	$45,300,000,000.00
Yoghurt	$30,900,000,000.00
Fermented milks	$8,900,000,000.00
Supplements	$5,500,000,000.00

Table 1: 2017 Global Retail Value (Source IPA)

PROBIOTICS TRADE EXCHANGE

22. Data and information for this item will be request to Codex member countries.

NEED FOR PROBIOTIC STANDARD / GUIDELINES

23. Given the wide acceptance of the importance of probiotic microorganisms to the health of the human population in addition to the growth of probiotic food and drinks that market health benefits, governments have raised questions about appropriate regulatory framework to apply to probiotics and foods with probiotics, to facilitate its appropriate regulation on their national market.

24. The proposed work is to address the current lack of harmonization through the development of a Codex Standard or Guidelines in order to harmonize framework that includes essential requirements for 'probiotics', as justified in paragraph 16.

PRODUCTS APPLICABLE FOR THE CODEX STANDARD / GUIDELINES

25. There are two kinds of products, probiotic microorganisms and foods with probiotics. Both kinds of products are applicable for the proposed Codex standard/guidelines.

26. Probiotic microorganisms are used as a food ingredient in a wide range of products, including dietary/food supplements.

REQUIREMENTS FOR THE EVALUATION OF A PROBIOTIC

27. The following minimum requirements should be accomplished in order to authorize a strain as a probiotic strain as a food ingredient, including dietary/food supplements: taxonomic characterization of the microorganism; characterization of the strain (in vivo e in vitro); demonstration of functional properties of the strain; and demonstration of safety of the microorganism for the intended use.

28. The food with probiotics should accomplish the following minimum requirements: amount of probiotic microorganism(s); the probiotic microorganism(s) should be alive when consumed; demonstration of health benefits of the food. Additionally, it should be proved that the strain keeps its functional properties in the food by in vivo and in vitro tests, and by at least one human clinical study with the aim of getting scientific support to establish the health effects of the strain.

SAFETY

29. Establishment of safety criteria is essential for public health. A safety assessment specific for probiotics as live microorganisms will be proposed.

ASPECTS OF PRODUCTION

30. The main aspects of production would be addressed to indicate the most appropriate phases of probiotic production within a closed, controlled system to provide utmost purity, quality and efficacy. Quality control and quality assurance will be addressed in addition to a stability program.

CONTAMINANTS

31. The products covered by the standard/guidelines shall comply with the maximum levels for contaminants that are specified by the *General Standard for Contaminants and Toxins in Food and Feed* (CXS 193-1995).

HYGIENE

32. The products covered by the provisions of the standard/guidelines should be prepared and handled in accordance with the *General Principles of Food Hygiene* (CXC 1-1969), and other relevant Codex texts such as Codes of Hygienic Practice and Codes of Practice.

LABELLING

33. It is proposed that, in addition to the *General Standard for Labelling of Prepackaged Foods* (CXS 1-1985), it should be applied the following specific provisions: name of the microorganism(s) (genus, species and strain) mentioned in the list of ingredients; amount of viable cells of each microorganism (CFU/g); name of the food; serving size and storage conditions.

METHODS OF ANALYSIS AND SAMPLING

34. The analyses should be carried out by laboratories recognized by competent national authorities or by internationally recognized laboratories. Methods used for determinations should be validated and calibrated against a certified reference material, if available.

35. The strain typing shall be based on molecular techniques.

36. Activity of microorganisms should be based on plating methods or other standardized method for the evaluation of total lactic bacteria.

CONCLUSIONS

37. Development of a standard or guidelines, and a harmonized framework for probiotics, including general specifications and considerations is necessary to ensure and sustain quality probiotic products on a global scale. This objective is in line with the Core Values of Codex, promoting collaboration, inclusiveness, consensus building and transparency, and follows the principles set as the Scientific Basis of Codex, listed within the Codex Alimentarius Commission Strategic Plan 2014-2019, Goal 1: To establish international food standards that address current and emerging food issues and its corresponding objectives.

38. Development of a Codex standard will provide:

a. a harmonized definition of probiotics among Codex member countries.

b. agreed essential requirements and specifications for probiotics that contribute to protecting the health of consumers, and ensuring fair practices in food trade.

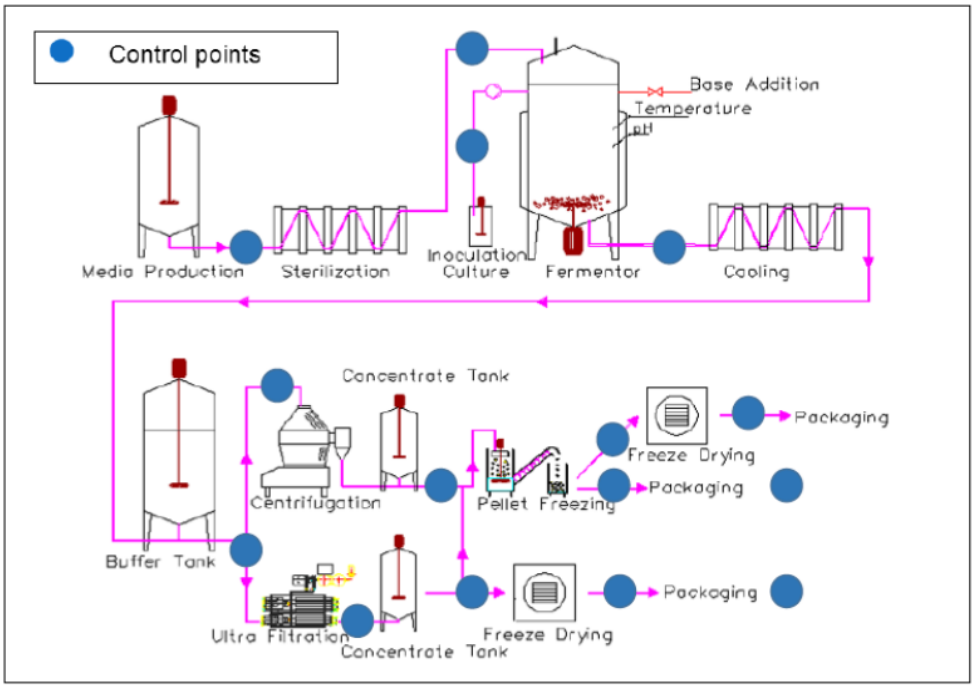
39. The term probiotic should be used only on products that deliver live microorganisms with suitable viable count of well-defined strains with a reasonable expectation of delivering benefits for the wellbeing of the host.

RECOMMENDATION

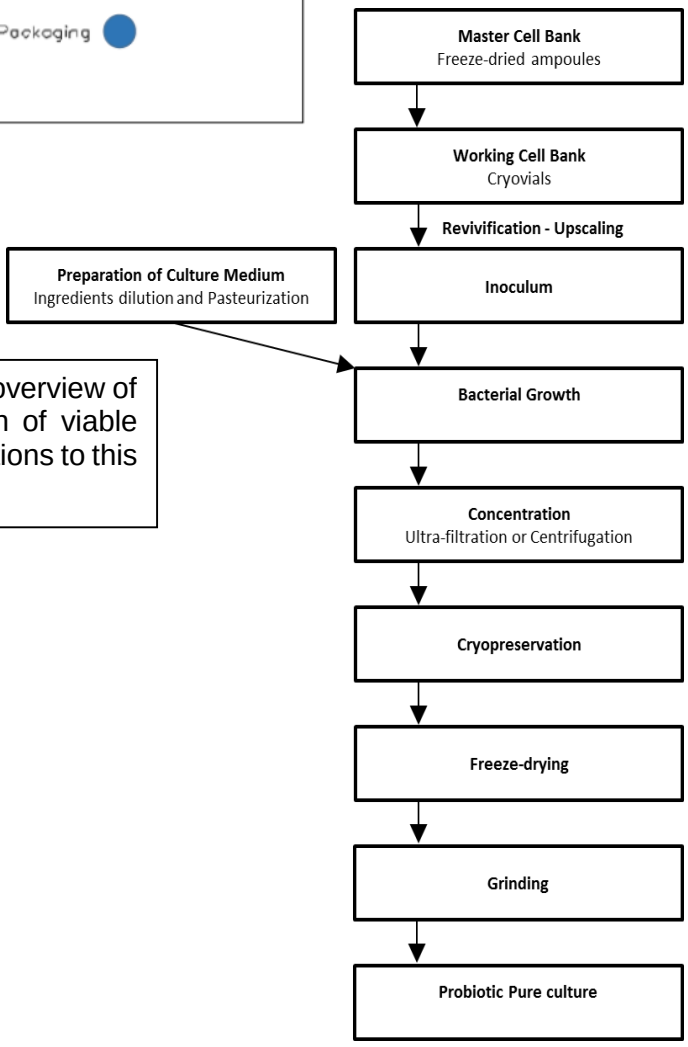
40. The Committee is invited to consider development of a standard or guidelines for probiotics. A project document is presented in Appendix 5 and a proposal for a standard/guideline is attached in Appendix 6

Appendix 1

Bacteria Production Flow Diagram



This process is included to provide a general overview of the most widely used process for production of viable probiotic strains in a freeze-dried format, variations to this process are allowed.



Appendix 2

Applicable Codex Standards

i. *General Principles of Food Hygiene* (CXC 1-1969)

ii. *General Methods of Analysis for Contaminants* (CXS 228-2001)

iii. Recommended Methods of Analysis and Sampling (CXS 234-1999)

iv. *General Standard for Contaminants and Toxins in Food and Feed* (CXS 193-1995)

v. *General Standard for the Labelling of Pre-packaged Foods* (CXS 1-1985)

vi. Guidelines for Use of Nutrition and Health Claims (CXG 23-1997)

Appendix 3

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Appendix 4

Glossary of terms

Active Fluorescent Units	AFU
Codex Alimentarius Commission	CAC
Codex Committee on Nutrition and Foods for Special Dietary Uses	CCNFSDU
Colony forming unit	CFU
Conference room document	CRD
Food and Agricultural Organization	FAO
International Code of Nomenclature	ICNB
International Committee on Systematics of Prokaryotes	ICSP
International Probiotic Association	IPA
List of Prokaryotic Names with Standing in Nomenclature	LPSN
World Health Organization	WHO

Appendix 5

PROJECT DOCUMENT

1. PURPOSE AND SCOPE OF THE STANDARD / GUIDELINES

At the present time, there is no internationally adopted definition for 'probiotics' although some countries have included regulations on 'probiotics' in their food legislation as an intervention to fill a legal gap in this area.

The proposed work is to address the current lack of harmonization which leads to issues and concerns for the regulators, probiotics industry, and even consumers, with regard to quality, safety and labelling of 'probiotics' through the development of a standard or guidelines for probiotics and food with probiotics in order to harmonize framework that includes essential requirements for 'probiotics'.

In accordance with the Food and Agriculture Organization of the United Nations and World Health Organization (FAO/WHO) guidelines, the scope of the standard/guidelines is limited to the use of probiotics in food, including dietary/food supplements. Drug applications and animal feeds are excluded from the scope of this work.

Therefore, it is essential that the industry have specifications for probiotics in foods, in order to ensure the proper use of the term without contradicting national requirements or health claim provisions.

2. RELEVANCE AND TIMELINESS

There has been growing interest in the concept of probiotics and its role in human nutrition. Probiotics are used in a variety of foods, the main category being dairy products, but they are also present as dietary/food supplements. Also they are found in other foods for infants, young children and adults. By definition, probiotics should convey physiological and/or nutritional benefits for consumers. The general population is increasingly interested in maintenance of health and self-care and this may explain the consumers' interest in probiotics. The establishment of a probiotic guideline is supporting the United Nations sustainable development goal 3: "*Good health and well-being",* ensure health lives and promote well-being for all at all ages.

The scientific and clinical evidence have progressed rapidly, as has the development of a number of probiotic foods. Unfortunately, misuse of the term probiotic has also become an important issue, with many foods using the term without meeting the requirements criteria. At the same time, probiotic foods have received the legitimate attention of regulatory authorities with an interest in protecting consumers from misleading claims.

Regulations on 'probiotics' are now under discussion in some countries while other countries have already established criteria and an organized framework for 'probiotics'. With no international guideline, standard or reference harmonized, many different approaches would be taken.

Currently, probiotics are distributed in 63 countries and probiotic dairy-based yoghurts are distributed in 196 countries. (Source IPA).

3. MAIN ASPECTS TO BE COVERED

i. The main aspect to be covered is the establishment of a harmonized definition of 'probiotics'. It will be necessary to ensure that the definition is sufficiently broad to cover vegetative microorganisms, spores, inactivated microorganisms, etc. Dead microorganisms, or other microbial-based, nonviable products has potential, however, these should not fall under the probiotic definition.

ii. Establishment of a definition of 'food with probiotics'.

iii. Requirements for the evaluation of a "probiotic" as a food ingredient.

The requirements should include the following aspects:

a) *Taxonomic characterization of the microorganism*: the assessment of the taxonomic classification is an important point to guarantee the safety of the used microorganism, because it allows recognizing the bacterial specie with a long history of safe use.

b) *Characterization of the strain:* the studies of characterization of the strain must show that the strain resists the passage through the body's main chemical and biological barriers, and it reaches the gut alive.

c) *Demonstration of functional properties of the strain:* the functional properties of the strain must be demonstrated by in vivo and in vitro tests, and by at least one human clinical study with the aim of getting scientific support to establish the health effects of the strain.

d) *Safety of the microorganism for the intended use:* Establishment of safety criteria is essential for public health.

The safety of a probiotic strain must be demonstrated by in vivo and in vitro tests with the objective of getting scientific endorsement to ensure the safety of the strain.

Gut translocation of bacteria is considered one of the most important safety tests.

iv. Requirements for the evaluation of a 'food with probiotics'.

The requirements should include the following aspects:

a) *Demonstration of health benefits of the food*: the health benefit of the food must be documented by scientific substantiation by at least one human clinical study according to generally accepted scientific standards.

v. Provisions for hygienic practice for production, handling, processing, storage and distribution of probiotics and foods with probiotics with reference to the General Principles of Food Hygiene and other relevant codex texts.

vi. Provisions for chemical contaminants with reference to the *General Standard for Contaminants and Toxins in Food and Feed*.

vii. Provisions for labelling in accordance with the *General Standard for Labelling of Prepackaged Foods* (CXS 1-1985).

viii. Reference Methods of Analysis and Sampling.

The applicable methodology of analysis for the typing of strains and the counting of microorganisms will be considered.

Traditionally, plating has been used and endorsed as the "standard way" to evaluate microbial viability and it has been determined through counting "colony forming units", CFU. The plate count method is based on the premise that a single bacterium can grow and divide to give an entire colony. This method is historically and currently, the most broadly used method to demonstrate the activity of the microorganisms.

Now, other methods such as flow cytometry (ISO 19344 IDF 232) are coming to be used widely and a standardized method has been developed and used as the way to evaluate total lactic acid bacteria.

All work will be coordinated with the applicable general subject Codex Committee to ensure the appropriate application of Codex expertise and resources.

4. ASSESSMENT AGAINST THE CRITERIA FOR THE ESTABLISHMENT OF WORK PRIORITIES

General criteria

The Codex Alimentarius Commission has a mandate of protecting consumer's health and ensuring fair practices in food trade. The proposed new standard/guidelines will meet this criterion by promoting consumer protection from the point of view of health, food safety and ensuring fair practices in the food trade and in particular:

i. *Fair practices in food trade:*

Despite the widely recognized FAO/WHO definition (2001), revised by Hill et al. (2014), which states that "*Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host*" there is no clear harmonization regarding the use of the term 'probiotic'. On a global level, there are a number of products sold as 'probiotics' that do not comply with this definition.

In the absence of an internationally accepted standard and guidelines, trading practices can become disordered and non-compliant.

ii. *Food safety:*

Establishment of safety criteria is essential for public health. It will be proposed that the safety of probiotics as live microorganisms be demonstrated. In first place, a scientific approach for those genera and species with an established safe history of use in foods, and for those newly recognized as probiotics, an *in-vitro* evidence-based approach, genomic mining and phenotypic analysis shall all be utilized to demonstrate safety.

Criteria applicable to general subjects

(a) *Diversification of national legislations and apparent result or potential impediments to international trade*

The lack of a harmonized definition for probiotics and probiotic food could result in many different definitions being developed for the purposes of inclusion in national regulations. The lack of a harmonized could result in unnecessary barriers to trade.

Also there could be misuse by manufacturers of the "probiotic" denomination and the misinterpretation of the probiotic concept by consumers.

In addition, a harmonized definition for the term 'probiotics' could prevent its misuse on products labels, communications or advertising.

(b) *Scope of work and establishment of priorities between the various sections of the work*

The scope of work is limited to develop probiotic criteria that address the following:

1. Definitions: ‘probiotics’, ‘food with probiotics’ and the aspects of ‘live microorganisms’, ‘adequate amounts’ and ‘a health benefit on the host’ could be individually defined and addressed, as they are equally important requirements for all probiotic products.

It could be considered that health benefit refers to physiological and/or nutritional benefits.

2. Requirements for the evaluation of a probiotic as a food ingredient.

(c) *Work already undertaken by other international organizations in this field and/or suggested by the relevant international intergovernmental body (ies)*

In 2001, scientific community and experts convened by FAO/WHO provided a scientific opinion on ‘probiotics’ agreed on the following definition (later amended by an expert consensus group): "*live microorganisms that, when administered in adequate amounts, confer a health benefit on the host*".

This report was followed by the "Guidelines for the Evaluation of Probiotics in Food" where the FAO/WHO experts made several recommendations. One of these was to officially adopt the definition as well as more specific criteria as a prerequisite to qualify a microbial strain as a "probiotic".

While the definition of probiotics has been widely acknowledged by the scientific community and key players in the field of probiotics, the FAO/WHO guidelines have not been implemented.

Only a few countries have regulations on probiotics. Those countries that have developed legislation have different views on probiotics in food, beverages and dietary/food supplements and their labelling.

In 2011, Argentina incorporated into its food regulatory framework a definition of probiotics, a guide for the evaluation of a probiotic as food ingredient and a definition of food with probiotics.

Brazil, Colombia and Ecuador have adopted a definition of probiotics that is aligned with the definition proposed by FAO/WHO. In addition, Brazil has a protocol for the evaluation of a probiotic as a food ingredient.

The Southern Cone and Caribbean countries include requirements for "probiotic" microorganisms on food labelling.

In Europe, there is neither regulatory status nor guidelines defining the probiotics category, nor a commonly acknowledged list of individual probiotic strains and/or species.

EU Member States, such as Italy, have developed certain requirements for qualifying specific strains as probiotics.

Canada has developed a Guidance Document in order to clarify the acceptable use of health claims about microorganisms represented as ‘probiotics’ on food labels and in advertising.

Australia and New Zealand have not neither specific regulations on probiotics nor a definition of probiotics. Microorganisms, including probiotics are considered “novel food”.

(d) *Amenability of the subject of the proposal to standardization*

The aspects that are essential for the identity of the product are: a harmonized definition, requirements for the evaluation of a probiotic and the amount of viable cells of each microorganism in the product.

There are many similarities in approaches in those countries that have developed regulation on probiotics suggesting that development of Codex guidance would be timely.

(e) *Consideration of the global magnitude of the problem or issue*

There have traditionally been many products available in the marketplace carrying the label 'probiotic'. However, there are currently no defined criteria or guidelines internationally accepted on what constitutes a 'probiotic' microorganism. The term ‘probiotic’ should only be used to describe microorganisms when certain requirements are met.

The establishment of eligibility criteria and an organized framework for the production of probiotic products will provide proper guidance for global regulatory agencies, enabling them to prepare probiotics specific regulations, and also will benefit consumers and industry.

5. RELEVANCE TO THE CODEX STRATEGIC OBJECTIVES

Development of guidelines and a harmonized framework for probiotics, including general specifications and considerations is necessary to ensure and sustain quality probiotic products on a global scale. The development of international standards, guidelines and other recommendations contributes to protect the health of consumers and to ensure fair practices in food trade.

This objective is in line with Core Values of Codex, promoting collaboration, inclusiveness, consensus building and transparency, and follows the principles set as the Scientific Basis of Codex, listed within the Codex Alimentarius Commission Strategic Plan 2014-2019.

The new work proposal will contribute to:

Strategic goal 1: *"Establish international food standards that address current and emerging food issues":*

1.2 Proactively identify emerging issues and Member needs and, where appropriate, develop relevant food standards.

The lack of harmonized regulations on probiotics has been clearly identified as an emerging issue related to food safety, nutrition, and fair practices in the food trade.

1.3.2 Promote cooperation with other international governmental and non-governmental standard setting organizations to support development of relevant Codex standards and to enhance awareness, understanding and use of Codex standards.

In order to optimize the development of the standard/guidelines will be very important facilitate the effective participation of organizations and all Codex Members.

Strategic goal 2: *"Ensure the application of risk analysis principles in the development of Codex Standards"*

6. INFORMATION ON THE RELATION BETWEEN THE PROPOSAL AND OTHER EXISTING CODEX DOCUMENTS

The standard / guidelines, once adopted, would be available for use as appropriate in future amendments of specific commodity standards and/or general standards.

The proposed work will make reference to relevant standards and related texts in particular of the following:

- *General Principles of Food Hygiene* (CXC 1:1969).
- *General Standard for Labelling of Prepackaged Foods (CXS 1-1985)*
- *General Standard for Contaminants and Toxins in Food and Feed* (CXS 193-1995*)*.
- *Guidelines for Use of Nutrition and Health Claims*, which refer to the use of health claims in food labelling and, where required by the authorities having jurisdiction, in advertising of foods. The guidelines are applied with the aim of assisting competent national authorities in their evaluation of health claims in order to determine their acceptability for use by the industry (CAC/GL 23-1997).

7. IDENTIFICATION OF ANY REQUIREMENT FOR AND AVAILABILITY OF EXPERT SCIENTIFIC ADVICE

No expert advice other than which is to be found in the CCNFSDU is required at this time.

8. IDENTIFICATION OF ANY NEED FOR TECHNICAL INPUT TO THE STANDARD FROM EXTERNAL BODIES SO THAT THIS CAN BE PLANNED FOR

No technical input other than which is to be found in the CCNFSDU is required at this time.

9. PROPOSED TIME-LINE FOR COMPLETION OF THE NEW WORK

Subject to approval by the Codex Alimentarius Commission in 2019. The draft standard / guidelines will be submitted for consideration by CCNFSDU in 2019 and the work is expected to take at least three sessions of the Committee.

Appendix 6

PROPOSED DRAFT STANDARD / GUIDELINES ON PROBIOTICS

1. PURPOSE

To establish guidance to assist competent national authorities in their evaluation of 'probiotics' in order to authorize a strain as a probiotic strain.

The recommendations focus on the criteria for substantiating that a microorganism addresses the minimum requirements to be considered probiotic microorganism and the general principles for the systematic review of the scientific evidence.

These recommendations include considerations of safety within the evaluation of a probiotic strain, but are not intended for the complete evaluation of the safety and the quality of a food, for which relevant provisions are laid out by other Codex Standards and Guidelines or general rules of existing national legislations.

2. SCOPE

This standard applies exclusively to probiotics used as ingredient in the manufacture of food, including dietary/food supplements. Drug applications and animal feeds are excluded from the scope of the standard/guidelines.

3. DESCRIPTION

3.1. Probiotics means live microorganisms that, when administered in adequate amounts, confer physiological and/or nutritional benefits on the host.

3.2. Food "with probiotics" means a food which has a content of probiotics microorganisms' viable cells of 10^9 CFU/ per daily portion throughout the end of its shelf-life.

4. REQUIREMENTS FOR THE EVALUATION OF A PROBIOTIC

4.1. PROBIOTICS MICROORGANISMS AS A FOOD INGREDIENT

The following minimum requirements should be accomplished in order to authorize the strain as a probiotic strain, and it should be labelled in accordance with item 8.1.

4.1.1. Minimum requirements

4.1.1.1. Taxonomic characterization of the microorganism

The microorganism should be identified at strain level, by using validated and internationally accepted techniques. This would require using a combination of the most appropriate molecular techniques, according to the List of Prokaryotic Names with Standing in Nomenclature (LPSN) or the International Committee on Systematics of Prokaryotes (ICSP).

Probiotics should be classified, as per reference nomenclature, at species level (genus, species and strain). The probiotic should be named according to the International Code of Nomenclature (ICNB).

Probiotic strains should be deposited in an internationally recognized culture collection.

4.1.1.2. Characterization of the strain (*in vivo e in vitro*)

The characterization of a probiotic strain should be demonstrated by *in vivo* and *in vitro* tests (human or animals studies) with the objective of getting scientific endorsement to demonstrate the survival of the microorganism through the gastrointestinal tract.

Minimum required tests should demonstrate: resistance to gastric acidity; bile acid resistance and lysozyme resistance.

Optionally tests that demonstrate: adherence to mucus and/or epithelial cells or cell lines; antimicrobial activity against pathogenic bacteria; ability to reduce pathogen adhesion to surfaces and/or bile salt hydrolase activity.

4.1.1.3. Demonstration of functional properties of the strain

The physiological and/or nutritional benefits of the microorganism should be documented by scientific substantiation by at least one human clinical study, statistically supported, according to internationally recognized scientific standards.

Microorganisms described as 'probiotic' should, for example, facilitate a beneficial balance of the intestinal microbiota and/or support desirable gastrointestinal function, among others.

All the studies to screen the potential probiotics, including human trials, should be conducted by institutions accepted by competent national authorities or by institutions with wide international recognition, following international standards.

4.1.1.4. Safety of the microorganism for the intended use

The strain should be safe for the intended use (i.e. for the targeted consumer and in the conditions of recommended use).

The safety of a probiotic strain should be demonstrated by *in vivo* and *in vitro* tests with the objective of getting scientific endorsement to ensure the safety of the strain.

Bacterial translocation should be researched in the probiotic concentrations intended to be used in foods. The microorganism should not induce bacterial translocation from the gut in the conditions of recommended use.

Minimum required tests should demonstrate that: the microorganisms do not have specific antibiotic resistance genes; they do not have virulence factor which causes hemolytic activity and they do not produce toxins.

Optionally tests that demonstrate: lactate production; bile salt deconjugation; side-effect during human studies and adverse incidents in consumers.

4.2. FOOD WITH PROBIOTICS

The manufacturer should prove that the strain keeps its functional properties in the food by in vivo and in vitro tests, and by at least one human clinical study with the aim of getting scientific support to establish the benefits of the strain. Then, the food can be authorized as a food “with probiotics”, and it should be labelled in accordance with the item 8.2.

4.2.1. Minimum requirements

4.2.1.1. Amount of probiotic microorganisms

The content of live cells in the portion of the food recommended for daily consumption should be 10^9 CFU/ daily portion until the end of the product shelf-life, at the specified storage conditions, with uncertainty of 0,5 log.

The use of different amount of microorganism could be accepted if substantiated by studies that have shown the probiotic strain is effective in smaller amounts.

The amount of live probiotic strain in the food should be consistent with the scientifically demonstrated amount required to achieve the desired effect up to the end of shelf-life.

4.2.1.2. The probiotic microorganism should be alive when consumed

Probiotic strains should be alive (including in freeze-dried form) in the food throughout shelf life.

4.2.1.3. Demonstration of physiological and/or nutritional benefits of the food

The benefit of the food should be documented by scientific substantiation by at least one human clinical study, statistically supported, according to internationally recognized scientific standards.

Animal and in vitro studies are considered supportive evidence. Supportive evidence refers to studies/data which, on their own, are not sufficient for the scientific substantiation of a benefit and that may be part of the totality of the evidence only if pertinent human studies showing an effect of the food/ingredient are available.

All the studies to screen the potential benefits, including human trials, should be carried out with the food as it is consumed. Those studies should be conducted by institutions accepted by competent national authorities or by institutions with wide international recognition.

4.2.1.3.1. Strains with probiotic activity demonstrated

In case the probiotic strain is already known to have probiotic properties, it is safe for human consumption and, it has an established safe history of use in foods, it should only be demonstrated that the probiotic keeps its functionality/efficacy in the food where it is added, within the proposed end use of the food.

Efficacy study refers to an intervention study (in humans, in animals) which investigates the relationship between the food/ingredient and the claimed effect.

4.2.1.3.2. A new strain without probiotic activity demonstrated

In case the strain is a new strain, without probiotic activity demonstrated, it should prove that the microorganism presents probiotic activity and that it accomplishes with the minimum requirements established in item 4.1.1.

Also, it should be demonstrated that the probiotic keeps its functionality/efficacy in the food where it is added, within the proposed end use of the food.

4.2.1.3.3. A change in food matrix of an authorized ‘food with probiotics’

When the food producer changes the composition of a food that has been already authorized as ‘food with probiotics’, he should demonstrate the adequate survival of the probiotic in the food throughout its shelf live (i.e. fermented milks and drinks based on fermented milk, plains, flavored and with fruit juice, fruit pulp, cereals, etc.).

4.2.2. Mixture of two or more strains with probiotic activity

If a combination of two or more probiotic strains is added, each of the microorganisms in the mixture should be proved to have probiotic activity and to meet the minimum requirements set out in 4.1.1.

In addition, it should be demonstrated that the combination of probiotic microorganisms maintains its functionality/efficacy in the food in which it is added, as it is to be consumed.

5. ASPECTS OF PRODUCTION

Probiotics and food with probiotics should be prepared, processed, packaged, transported and stored within a closed and controlled system to provide utmost quality and purity, and to address quality control aspects and quality assurance aspects.

6. CONTAMINANTS

The products covered by these Guidelines shall comply with the maximum levels of the General Standard for Contaminants and Toxins in Food and Feed (CXS 193-1995).

7. HYGIENE

It is recommended that the products covered by the provisions of this standard / guidelines be prepared and handled in accordance with the General Principles of Food Hygiene (CXC 1-1969), and other relevant Codex texts such as Codes of Hygienic Practice and Codes of Practice.

8. LABELLING

In addition to the *General Standard for Labelling of Prepackaged Foods* (CXS 1-1985) the following specific provisions apply:

8.1. Name of the microorganism(s)

8.1.1. Genus, species and strain classification of the microorganism(s) should be mentioned in the list of ingredients.

8.1.2. The amount of viable cells of each microorganism (CFU/g) should be mentioned in or in close proximity to the list of ingredients.

8.2. Name of the food

The product should be labelled as “*Name of the food* _____”, the blank being filled in with the wording: “*Contain probiotics*” or *“With Probiotics”*.

8.3. List of ingredients

8.3.1. Genus, species and strain designation of the microorganism(s) should be mentioned in the list of ingredients.

8.3.2. The amount of viable cells of each microorganism (CFU/g) should be mentioned in or in close proximity to the list of ingredients.

8.3.3 The amount of microorganisms could be expressed in Colony Forming Units (CFU), Active Fluorescent Units (AFU) or any other validated alternative method to indicate the number of live cells in the product.

The CFU listed should be expressed in numbers of cells/100ml or 100g. In addition to the expression of the numbers of cells/100ml or 100g the number of cells per portion could be mentioned.

8.4. Serving size

The serving size that needs to be consumed daily to obtain the documented physiological and/or nutritional effects, which should be equal to the daily amount tested in human studies, should be mentioned.

8.5. Storage conditions

The storage conditions of the product to maintain its quality should be specified.

9. METHODS OF ANALYSIS AND SAMPLING

The analyses should be carried out by laboratories recognized by competent national authorities or by internationally recognized laboratories. Methods used for determinations should be validated and calibrated against a certified reference material, if available.

9.1. Strain typing

9.1.1. The strain typing shall be based on molecular techniques.

9.1.2. The strain typing could be performed by the use of DNA sequences encoding 16S rDNA. Sambrook, J. and D. W. Russell. 2001. Molecular Cloning: A Laboratory Manual, Third ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY", or other method providing at least equal sensitivity and specificity.

9.2. Activity of microorganisms

9.2.1. Activity of microorganisms shall be based on plating methods or other standardized method for the evaluation of total lactic bacteria.

9.2.2. Activity of the microorganisms could be determined by flow cytometry (ISO 19344 IDF 232); Yogurt-Enumeration of characteristic microorganisms - Colony-count technique at 37 degrees C (IDF 7889:2003), or other standardized method for the evaluation of total lactic bacteria.