PUBLIC MEETING: RESPONSIBLE INNOVATION IN DIETARY SUPPLEMENTS

COMBINED COMMENTS FROM IPA AND IFAC

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THE SCOPE OF THE DIETARY INGREDIENTS UNDER DSHEA

PROBIOTICS: AN IMPORTANT SECTOR
How do we take our probiotics

Consumer Consumption - World

World Retail Value
US$43.8 billion in 2018

World Retail Value
US$38 billion in 2013

* Euromonitor International
The fastest Growing Supplement Globally

**Market Overview**

**Probiotic Market Trend (Mil/USD)**

<table>
<thead>
<tr>
<th>Year</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series1</td>
<td>$3,400</td>
<td>$4,300</td>
<td>$5,100</td>
<td>$5,700</td>
<td>$7,000</td>
</tr>
</tbody>
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*Euromonitor International*
Definitions

“Live microorganisms which when administered in adequate amounts confer a health benefit on the host”

FDA - ODSP (NDI guidance, 2016):

“Live microbial dietary ingredient: A single celled prokaryotic or eukaryotic microorganism that is intended to be viable at the point of ingestion”
So where do probiotics fall?
Probiotics fit under 201 (ff) E

(E) a **dietary substance** for use **by man** to **supplement** the diet **by increasing** the total dietary intake

This statement implies:
1) Need to increase the intake and to supplement the diet with that particular substance to help the maintenance of health & normal body functions
2) Is a dietary substance
What if we did not ingest probiotic microorganisms?

Benefits and role:

“The panel further considered two common general benefits often associated with probiotics: supporting a healthy digestive tract and a healthy immune system”

Hill C. et al. 2004

- Humans are made of bacteria
- Beneficial to gut
- Allow better digestion of nutrients
- Bacteria in gut have multi functional roles
- Aging process decline the bacteria in the gut possibly shifting the function of the body
- Immune supporting role
- Skin, Gut-Brain axis and more

Necessary like vitamins & minerals!
So why did DSHEA not include...

(A) a vitamin;
(B) a mineral;
(C) an herb or other botanical;
(D) an amino acid;
(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E).

They were prevalent prior to 1994!
OLD DIETARY INGREDIENT LIST

Adiantum limadatum –
Adiantum pedatum L. –
adipec acid –
Adonis venus –
Adonis majus –
Aftin ipomoea –
Aesculus hippocastanum L. +
Adscension megepeta (Roscac) K. Schumann –
ag gar –
Aegle marmelos (Fisch. # Mees) D. Kuru –

Microorganisms & Microbial-Derived Ingredients Used in Food (Partial List)

Probiotics- History and Evolution
Elie Mechnikoff (1845-1916)
Longevity without Ageing
“The prolongation of life” (1908)

Prior sanctions were granted for the use of harmless lactic acid producing bacteria, such as Lactobacillus acidophilus, as optional ingredients in specified standardized foods. These bacteria are permitted for use in cultured milk (which includes buttermilk) (§ 131.112), sour cream (§ 131.100), cottage cheese (§ 133.128), and yogurt (§ 131.200), provided that the mandatory cultures of Lactobacillus bulgaricus and Streptococcus thermophilus are also used in the yogurt.
Probiotics fit under 201 (ff) E

(E) a **dietary substance** for use by man to supplement the diet by increasing the total dietary intake

This statement implies:

1) Need to increase the intake and to supplement the diet with that particular substance to help the maintenance of health & normal body functions

2) Is a dietary substance
International Probiotics Association

- NHP Probiotics
- FDA Partial List of Microorganisms
- Customs Union Prohibited micro-organisms List
- Probiotic Korea
- Malaysia permitted and prohibited list
- Thailand list
- South Africa list
- Complementary medicines list

IFAC List (FCC)
Probiotics fit under 201 (ff) E because

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake;

- Probiotics have been in the food supply for thousands of years as dietary substances.
- Like vitamins and minerals, there is health benefit to “increase the total dietary intake” of probiotics above and beyond what can be easily consumed in food alone.
- Probiotics were prevalent in “dietary supplements” in the USA prior to 1994 but not taken into account in a clearer manner does not make them fall outside of the definition.
- Advancements in science should not prohibit new strains from being included in this definition as they are still in the general category of “dietary substances” (i.e. changes in vitamins and minerals could trigger NDI issues, it does not take them out of the definition of “dietary ingredient”).
How to be Practical -

1. Proposed grandfathered / exempted list

- A list of species with a safe history of use
- Manufacturers of strains within these species, intended to be used as dietary ingredients, have the onus to establish safety based on an abbreviated criteria of safety and identity
- Similar to the requirements of global regulatory agencies which allow strains within each listed species to be anticipated as safe
- Safety assessments would not be foregone in the grandfathering process
  - Strains within the species list would not require a NDIN
  - Minimum safety assessments should be conducted
How to be Practical –

2. Master Files

- Make information accessible to the FDA while avoiding unnecessary notifications
- To include but not limited to:
  - Whole Genome Sequencing for Identification
    - align with well-characterized strain and explain differences in the genome
  - Genome Mining the lack of genetic regions responsible for the production of virulence factors characteristic of the Genus
  - Genome Mining to demonstrate the lack of genetic regions responsible for the production of toxins characteristic of the Genus
  - Appropriate toxicological studies when necessary - novel bacteria
  - Genomic Analysis for the presence of biogenic amine genetic regions
  - Antibiotic Resistance profile targeting clinically relevant antibiotics
  - Genomic Analysis for evidence of lack of antibiotic resistance transfer potential
Hence MF + grandfathered/ exempted list is the logical way forward

But as...

Science evolves

Innovation continues

New strains on the horizon:

- NDI to be filed
IPA and I FAC are here to help
We want to be part of the WG
The International Probiotics Association (IPA) is a global non-profit organization bringing together through its membership, the probiotic sector’s stakeholders including but not limited to academia, scientists, health care professionals, consumers, industry and regulators. The IPA’s mission is to promote the safe and efficacious use of probiotics throughout the world. Holding NGO status before Codex Alimentarius, the IPA is also recognized as the unified Global Voice of Probiotics® around the world.

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The International Food Additives Council (IFAC) is a global association representing manufacturers of food ingredients, including food additives and GRAS substances. IFAC strives to promote science-based regulations, standards and specifications for food ingredients worldwide.

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The research from Euromonitor International is part of a global strategic intelligence that offers a complete picture of the commercial environment including but not limited to: market analysis, market share, distribution channels, forecasting and much more.