Probiotics and Categories of FDA Regulated Products

Francis B Palumbo, PhD, Esq.
University of Maryland
School of Pharmacy
Center on Drugs & Public Policy
Probiotics

• Live microorganisms that when administered in adequate amounts confer a health benefit on the host.
Claims

• The claims made for a particular regulated product generally control where that product fits into the definitions.
Drug

- (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and
- (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and
- (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and
- (D) articles intended for use as a component of any article specified in clause (A), (B), or (C)
The term 'biological product' means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

42 U.S.C. §262(i)
Food

- articles used for food or drink for man or other animals
- chewing gum, and
- articles used for components of any such article.
Food Additive

any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use),

- if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures to be safe under the conditions of its intended use
- or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food to be safe under the conditions of its intended use
Medical Food

- a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation. 21USC §360ee(b)(3)

- Claims must not be false or misleading.
- FDA approval for marketing is not required
Dietary Supplement

a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(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);
“Functional Food” and “Nutraceutical”

• Not officially recognized in law or regulation

• Generally used to describe foods that have particular health related benefits.
Device

- an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is--
  (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
  (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  (3) intended to affect the structure or any function of the body of man or other animals, and

- does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and is not dependent upon being metabolized for the achievement of its primary intended purposes.
Cosmetic

- (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and
- (2) articles intended for use as a component of any such articles; except that such term shall not include soap.
Probiotics and Drugs?

• Encouraging evidence for use:
  – To treat diarrhea (this is the strongest area of evidence, especially for diarrhea from rotavirus)
  – To prevent and treat infections of the urinary tract or female genital tract
  – To treat irritable bowel syndrome
  – To reduce recurrence of bladder cancer
  – To shorten how long an intestinal infection lasts that is caused by a bacterium called *Clostridium difficile*
  – To prevent and treat pouchitis (a condition that can follow surgery to remove the colon)
  – To prevent and manage atopic dermatitis (eczema) in children

Source*: http://nccam.nih.gov/health/probiotics/
# Clinical Trials

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Condition</th>
<th>Intervention</th>
<th>Sponsor</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety and Clinical Effectiveness of Oral Probiotic MIYA-BM to Prevent Recurrent Clostridium Difficile Infections</td>
<td>Clostridium Difficile Infection</td>
<td>MIYA-BM Fine Granules (CBM588) v. Placebo Fine Granules (without CBM588)</td>
<td>Osel, Inc.</td>
<td>Phase II</td>
</tr>
<tr>
<td>Intravaginal LACTIN-V for Prevention of Recurrent Urinary Tract Infection</td>
<td>Urinary Tract Infection</td>
<td>LACTIN-V v. placebo</td>
<td>National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); Osel, Inc.</td>
<td>Phase II</td>
</tr>
<tr>
<td>Safety and Efficacy Study of Lactobacillus Administered Vaginally in Women With Bacterial Vaginosis</td>
<td>Bacterial Vaginosis</td>
<td>LACTIN-V v. placebo controlled substance</td>
<td>Osel, Inc.; University of California, San Francisco</td>
<td>Phase II</td>
</tr>
</tbody>
</table>
# Clinical Trials

<table>
<thead>
<tr>
<th>Study Title:</th>
<th>Condition:</th>
<th>Intervention:</th>
<th>Sponsor:</th>
<th>Phase:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probiotic Lactobacillus GG (LGG) in Patients With Minimal Hepatic Encephalopathy</td>
<td>Minimal Hepatic Encephalopathy</td>
<td>Lactobacillus GG v. placebo</td>
<td>Virginia Commonwealth University; National Center for Complementary and Alternative Medicine (NCCAM)</td>
<td>Phase I</td>
</tr>
<tr>
<td>Safety Study of Probiotics in Adults With Irritable Bowel Syndrome</td>
<td>Irritable Bowel Syndrome</td>
<td>Probiotic</td>
<td>Baylor College of Medicine; National Institute of Nursing Research (NINR); University of Washington</td>
<td>Phase I</td>
</tr>
<tr>
<td>Safety of Lactobacillus Reuteri (L. Reuteri) in Healthy Adults</td>
<td>Colic; Gastrointestinal Tract Infections</td>
<td>L. reuteri v. Sunflower Oil</td>
<td>The University of Texas Health Science Center, Houston; National Center for Complementary and Alternative Medicine (NCCAM)</td>
<td>Phase I</td>
</tr>
<tr>
<td>Lactobacillus GG in Pediatric Ulcerative Colitis (UC)</td>
<td>Ulcerative Colitis</td>
<td>Lactobacillus GG</td>
<td>Children's Hospital Medical Center, Cincinnati</td>
<td>Phase II</td>
</tr>
</tbody>
</table>
Food Claims
Nutrient Content Claims

• Characterizes the level of a nutrient such as Vitamin C
  • The food is a good source of----
    – FDA must have issued a regulation authorizing certain nutrient content claims
    – Exception: if based on authoritative statement by a scientific body, it need not have FDA approval.
Health Claims

• Health Claim: Claim that characterizes relationship to a disease or health related condition must be approved by FDA.
  – Must be supported by significant scientific agreement among qualified experts
  – “Use of calcium in the diet on a regular basis may help to reduce the risk of osteoporosis”
Structure/Function Claims
Foods & Dietary Supplements

Examples

• Calcium and strong bones
• Describe general well being from DS
• Helps support a healthy immune system

Must be truthful & not misleading
Probiotics and Food?

- **Yogurt**
  - Activia (Bifidus Regularis™) contains Bifidus Regularis, a natural probiotic culture that can help regulate your digestive system by helping reduce long intestinal transit time
Probiotics and Food?

- **Beverages**
  - Kefir (milk), Naked Juice Probiotic Juice Smoothie, WildWood Probiotic Soymilk™, Bi Okay (soft drink)
  - Naked Juice Probiotic Juice Smoothie; beneficial active cultures that help promote a healthy digestive and immune system.

- **Granola and Chocolate bars**
  - Attune Strawberry Bliss, Attune Chocolate Probiotic Wellness Bar (Bifidobacterium Lactis, Lactobacillus Acidophilus, Lactobacillus Casein
  - Each Attune wellness bar is packed with probiotics that help rebalance your digestive system, so your whole body can work better.
Probiotics and Food?

• **Breakfast cereals**
  - Kashi Vive Probiotic Digestive Wellness Cereal (Lactobacillus Acidophilus.
  - Balance ~ Active probiotic cultures & ginger
  - Probiotics help break down foods and maintain digestive balance, crowding out the bad bacteria.

• **Infant formula**
  - GERBER® GOOD START® Protect PLUS® Formula (BIFIDUS BL)
  - The first infant formula with BIFIDUS BL™—beneficial cultures like those found in breastmilk to help support Baby's healthy immune system. One way these beneficial cultures can help support Baby's healthy immune system is by increasing levels of key antibodies.
Probiotics and Medical Food?

• VSL#3: Self described by manufacturer as intended for use under medical supervision:
  o Each packet of VSL#3® contains 450 billion live lactic acid bacteria, which collectively act as a Living Shield™ in the gastrointestinal (GI) tract
DS and Nutritional Support

• Statements of “nutritional support” are allowed without prior FDA approval
Probiotic and Dietary Supplement?

- Align Daily Probiotic Supplement Capsules (Bifantis)
  - When taken daily, Align promotes a healthy digestive system, helping to restore your natural balance and giving you an ongoing natural defense against these occasional episodes of digestive upsets that can interrupt your life.
Super 5 Probiotic Lozenges (Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus bulgaricus, Streptococcus thermophilus, Lactobacillus salivarius)
- Protects against thrush, gum conditions, tooth decay, inflamed mouth tissue, and bad breath
Probiotics and Device?

- Ellen Probiotic Tampon (Lactobacillus fermentum, Lactobacillus gasseri, Lactobacillus casei) – Swedish product
  - combination of patented benevolent lactic acid bacteria that can strengthen women's defence against infections

- Drug delivery devices:
  - BioGaia Probiotic Straw - The inside of the straw is lined with probiotic organisms which are consumed when straw is used (L. reuteri)
    - Give your child (or yourself!) a BioGaia Probiotic Straw daily for sickness prevention, boosting immune health, and good gut health
Probiotics and Device?

- Ganeden quick dissolving, thin strip probiotic product delivers significant probiotic doses (Bacillus coagulans)
  - It is a Gram-positive spore-forming bacterium that, once germinated, produces L+ lactic acid, supporting good bacteria in the gut, displacing non-beneficial bacteria.
Probiotics and Cosmetic?

- **Shampoo**
  - Natural Active Hair Loss Prevention Shampoo (lactobacillus ferment, lactococcus ferment)

- **Lotion**
  - Dr. Ohhira’s Probiotic Magoroku Skin Care Lotion (E. faecalis TH10 strain of lactic acid bacteria)- May be used on bedsores, prickly heat, skin parasites, ringworm, toenail fungus, rosacea, athlete’s foot, and other skin conditions

- **Bar Soap**
  - Candida Freedom Probiotic Soap (Bacillus coagulans)- encourage beautiful skin

- **Toothpastes**
  - PerioBiotic Probiotic Toothpaste by Designs for Health (Lactobacillus paracasei)- prevent caries!
Probiotics and Food Additive?

- GRAS notification of *Carnobacterium maltaromaticum* strains CB1, CB2, CB3, LV17, UAL26, ATCC 35586 and ATCC43225 for use in ready-to-eat (RTE) and fresh comminuted', processed meat products, for use as an inhibitor of *Listeria monocytogenes*; October 2004.
Conclusion

• There are many different products regulated by FDA and each has its own definition.
• But there is often a fine distinction among product categories based on claims made.