The Path to U.S. Market for Functional Food Ingredients

American College of Nutrition Symposium

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Topics

- Statutory Bans
  - Prohibition of “drugs” in foods
  - Dietary supplement exclusionary clause
- Functional Food Ingredients
  - Food additives
  - GRAS substances
  - Dietary ingredients in dietary supplements
- Health-related Claims
  - Drug claims vs. health claims vs. structure/function claims vs. medical food claims
Prohibition of “Drugs” in Foods

- FDCA § 301(II) Prohibition
  - Prohibits addition of approved new drug or a licensed biologic to food.
  - Prohibits addition of drug or biological product for which:
    - substantial clinical investigations of drug/biological were instituted, and
    - existence of the substantial clinical investigations made public
  - Unless first marketed in food or qualify for other limited exceptions
  - Example: stevia CP
Dietary Supplement Exclusionary Clause

- FDCA § 201(ff)(3)(B) Exclusion
  - Excludes article approved as new drug or licensed as biologic
  - Excludes article:
    - authorized for investigation as new drug or biological, and
    - substantial clinical investigations have been instituted, and
    - existence of such investigations made public
  - Unless first marketed as dietary supplement or as a food or FDA authorizes use by regulation
  - Examples: pyridoxal 5’-phosphate (CP pending); pyridoxamine
Functional Foods

- Conventional Foods
  - Consumed primarily for taste, aroma or nutritive value
  - Includes medical foods
    - for dietary management of patient
    - who has special medically-determined nutrient requirements that can’t be met by modifying the normal diet alone, and
    - intended for use under medical supervision

- Dietary Supplements
Functional Food Ingredients

- Food additives
- Color additives
- Pesticide chemicals/residues
- Animal drugs
- Prior-sanctioned substances
- Generally recognized as safe (GRAS) substances (for conventional foods/medical foods)
- Dietary ingredients in dietary supplements
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 … if such substance is not generally recognized, among experts … to be safe under the conditions of its intended use…”

- Exemptions include substances that are generally recognized as safe under conditions of intended use, subject to a prior-sanction for food use, or used as dietary ingredients in dietary supplements.
Generally Recognized as Safe (GRAS) Substances

- [A] substance is . . . generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (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 . . . .
Dietary Ingredients in Dietary Supplements

- Dietary Supplements may contain the following dietary ingredients:
  - a vitamin;
  - a mineral;
  - an herb or other botanical;
  - an amino acid;
  - a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
  - a concentrate, metabolite, constituent, extract, or combination of any of the above.
New Dietary Ingredients

- A Dietary Ingredient marketed in U.S. before 15 October 1994 (pre-DSHEA) is a grandfathered/old dietary ingredient.
- A Dietary Ingredient marketed in U.S. post-DSHEA is a New Dietary Ingredient (NDI) and must either:
  - have been present in the food supply as an article used for food in a form in which the food has not been chemically altered, OR
  - have history of use or other evidence of safety establishing that use as recommended or labeled will reasonably be expected to be safe, and manufacturer or distributor submits a 75-day premarket notification (NDIN) to FDA providing information that is the basis for concluding there is a reasonable expectation of safety.
FDA’s NDIN Guidance – Industry Concerns

- Narrows “dietary ingredient” and grandfathered/old dietary ingredient categories
- Shifts burden of proof for grandfather status from FDA to manufacturer/distributor
- Narrows NDIN exemption
  - “Presence in food supply” limited to conventional foods (no supplements)
  - “Article used for food” excludes components of foods
  - “Chemically altered” extended beyond breakage of chemical bonds, change in chemical structure, and change in chemical properties
  - Suggests NDIN requirement is manufacturer and dietary supplement specific rather than ingredient specific
Critical Factors to Consider Before Launching Functional Food/Nutraceutical in U.S.

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<th>FACTORS TO CONSIDER</th>
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<th>DIETARY SUPPLEMENT</th>
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<td>FOOD ADDITIVE</td>
<td>GRAS SUBSTANCE</td>
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<tr>
<td>STATUTORY BAN?</td>
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<td>FDCA 301(ll) Prohibition?</td>
<td>FDCA 201(ff)((3)(B) Exclusion?</td>
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<td>ROUTE TO MARKET</td>
<td>Food Additive Petition</td>
<td>Self-Determination</td>
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<td>Voluntary GRAS Notice</td>
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<tr>
<td>PRIOR FDA APPROVAL</td>
<td>Yes</td>
<td>No</td>
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<td></td>
<td>No</td>
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<td></td>
<td></td>
<td>No (FDA Notice may be required)</td>
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<td>FDA REVIEW</td>
<td>At least 24 months</td>
<td>Self-Determination: N/A</td>
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<td>GRAS Notice: 180 days</td>
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<tr>
<td>SAFETY STANDARD</td>
<td>Reasonable certainty by competent scientists that substance is not harmful under conditions of intended use. Delaney Clause applies</td>
<td>General recognition among qualified experts that substance is safe under conditions of intended use, based on scientific procedures or common use prior to 1958</td>
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<td>Substance does not present a significant or unreasonable risk of illness or injury, under conditions of use</td>
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<td>EVIDENCE OF SAFETY</td>
<td>Technical evidence of safety under conditions of intended use</td>
<td>Documented common use or technical evidence of safety under conditions of intended use, and general recognition</td>
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<td></td>
<td>History of use and/or technical evidence of safety</td>
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<tr>
<td>PIVOTAL SAFETY DATA</td>
<td>Unpublished or published</td>
<td>Published or otherwise generally available to scientific community</td>
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HEALTH-RELATED CLAIMS FOR FOODS

- Therapeutic Drug Claims
  - Safety and Efficacy
    - FDA Approved
- Approved Health Claims
  - Significant Scientific Agreement
    - FDA Approved
- Notified Health Claims
  - Authoritative Statement of U.S. Gov’t Scientific Body
    - FDA Notified – supplements ineligible
- Qualified Health Claims
  - Weight of Scientific Evidence, tempered by Credible Evidence
    - FDA enforcement discretion
- Structure/Function Claims
  - Competent and Reliable Scientific Evidence
    - FDA notice applies to supplements only

STOP
Health-related Claims for Functional Foods

- **Approved health claim** describes relationship between ingredient and disease, damage or dysfunction of body based on significant scientific agreement
  - “25 g soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. Each serving of [food] provides [X] g soy protein.”

- **Qualified health claim** describes same relationship but notes that data is “limited and not conclusive,” or even “highly unlikely.”
  - “Limited and not conclusive scientific evidence suggests that eating about 2 tablespoons of olive oil daily may reduce the risk of coronary heart disease due to the monounsaturated-fat in olive oil.”

- **Notified health claim** is based on statement of authoritative governmental scientific body
  - “Diets containing foods that are a good source of potassium and low in sodium may reduce the risk of high blood pressure and stroke.”
Health-related Claims for Functional Foods

- **Structure/function claim** describe the effect on normal healthy structure or function of the body.
  - “Calcium helps maintain strong bones and teeth.”

- **Nutrient content claim** characterizes the level of certain nutrients in the food.
  - “High in antioxidant vitamins C and E.”

- **Medical food claim** describes role of the food in dietary management of a condition/disease for which there are distinctive nutritional requirements that cannot be met by modification of normal diet.
  - “Oral rehydration solution for dietary management of acute diarrhea.”
## Critical Distinctions for Health-related Claims

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<tr>
<td>FDA Approved Health Claim</td>
<td>Petition shows “significant scientific agreement.” FDA rulemaking: 18-24 months.</td>
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<tr>
<td>FDA Approved Qualified Health Claim</td>
<td>Petition based on credible scientific evidence &amp; use of labeling disclaimer; Evidence ranked per interim guidance; FDA rulemaking: 18 months (FDA evaluating ANPR comments).</td>
<td></td>
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<tr>
<td>FDA Notified Health Claim</td>
<td>Based on authoritative statement of U.S. scientific governmental body; Notify FDA 120 days prior to use</td>
<td>Currently not permitted</td>
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<tr>
<td>FDA Approved Nutrient Content Claim</td>
<td>Petition shows why presence or absence of substance in food is important in human nutrition; FDA rulemaking: 18 months.</td>
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<tr>
<td>FDA Notified Nutrient Content Claim</td>
<td>Based on authoritative statement of U.S. scientific governmental body; Notify FDA 120 days prior to use.</td>
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<tr>
<td>Structure/Function Claim</td>
<td>No notice to FDA; Derives from “nutritive value.” Notify FDA within 30 days of use; labeling disclaimer; Nutritive value not required.</td>
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<tr>
<td>Third Party Literature</td>
<td>No “labeling” exemption. Eligible for “labeling” exemption.</td>
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