



Centurion
UNIVERSITY

REGULATION OF DIETARY SUPPLEMENTS

WHAT WE WILL COVER ON DIETARY SUPPLEMENTS

- ◆ Basics
- ◆ New Dietary Ingredients
- ◆ Claims Allowed
- ◆ GMPs and Other Regulatory Requirements
- ◆ Adverse Events



THE BASICS

- Pre-1994 – dietary supplements regulated as foods
- 1994 – Dietary Supplement Health Education Act (DSHEA)
 - Defined “dietary supplement” (D.S.)
 - Defined “dietary ingredient”
 - Required ingredient and nutrition labeling
 - Delineated the claims and nutritional support statements that could be made
 - Gave FDA power to promulgate D.S. GMP regulations
 - Required that any D.S. ingredient that was not on the market on the date of enactment (October 15, 1994) had to be subject to a New Dietary Ingredient (NDI) notification



DEFINITION OF D.S. – PART 1

- Section 201(ff) of the Act -- The term "dietary supplement" -
 - (1) means 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);

AND ...



DEFINITION OF D.S. – PART 2

- Section 201(ff)(2):
 - ...means a product that -
 - **(A)(i)** is intended for ingestion in a form described in section 411(c)(1)(B)(i); or
 - "(ii) complies with section 411(c)(1)(B)(ii);
 - **(B)** is not represented for use as a conventional food or as a sole item of a meal or the diet; and
 - **(C)** is labeled as a dietary supplement;
 - **411(c)(1)(B)(i)** -- is intended for ingestion in tablet, capsule, powder, softgel, gelcap, or liquid form
 - **411(c)(1)(B)(ii)** -- if not intended for ingestion in such a form, is not represented as conventional food and is not represented for use as a sole item of a meal or of the diet.

AND ...



DEFINITION OF D.S. – PART 3(A)

- Section 201(ff)(3)
 - does -
 - (A) include an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351 of the Public Health Service Act (42 U.S.C. 262) and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 402(f);

AND ...

DEFINITION OF D.S. – PART 3(B)

- Section 201(ff)(3)
 - *B) does not include* -
 - (i) an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351 of the Public Health Service Act (42 U.S.C. 262), or
 - (ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,
- which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this Act.

THE BASICS

- Except for purposes of section 201(g), a dietary supplement shall be deemed to be a food within the meaning of this Act.
 - *In other words*, it can be a drug also if it meets the drug definition
- Premarket approval/clearance – not required, unless “new dietary ingredient” ...

NEW DIETARY INGREDIENTS (NDI)

- If a dietary ingredient was not marketed before October 15, 1994, must notify FDA before marketing
- Notice:
 - Goes to Office of Nutritional Products, Labeling & Dietary Supplements (ONPLDS)
 - At least 75 days before introducing NDI into interstate commerce

NDI NOTICE -- CONTENTS

- Name and address of manufacturer or distributor
- NDI name, including Latin binomial name of any herb or other botanical
- Description of products that contain the NDI + level of NDI in the product
- History of use or other evidence NDI is safe
- Process
 - Get a filing date from FDA
 - 75 days after filing date, can go to market – BUT, that does not mean FDA agrees the NDI is safe
 - FDA can object
- New draft guidance – July 2011 – for comment

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm257563.htm>

LABELS AND LABELING

- Basics
 - Statement of identity
 - Net quantity of contents
 - Ingredient list
 - Address of mfr., packer or distributor
 - Nutritional facts box



LABELING CLAIMS

- **Nutrient content claims**
 - 21 CFR 101.13 – General Principles
 - Types of claims governed:
 - “Good source,” “More” and “High Potency”
 - “Light” or “Lite”
 - Caloric claims
 - Sodium content
 - Fat, Fatty Acid and Cholesterol content



HEALTH CLAIMS

- Possible for dietary supplements
- Petition process – for an allowable health claim – 21 CFR 101.70
- Standard for allowable claim: “significant scientific agreement”
- Examples:
 - Calcium and osteoporosis
 - Sodium and hypertension
 - Fiber and cancer
 - Folate and neural tube defects (e.g., spina bifida)



HEALTH CLAIMS -- FDAMA

- ***Basis*** – a published authoritative statement of a “scientific body of the United States with official responsibility for public health protection or research directly related to human nutrition ...”
 - National Academy of Sciences
 - NIH
 - CDC
- ***Process***
 - 120 days notice – then can make claim



HEALTH CLAIMS – “QUALIFIED”

- **Result of Pearson v. Shalala** – lawsuit over First Amendment right to make truthful commercial speech
 - FDA cannot reject a health claim that *might* be misleading unless agency *also* finds that no disclaimer would eliminate the potential misconception
 - Examples:
 - “supportive but not conclusive data” shows omega-3 fatty acids may reduce risk of coronary heart disease
 - Antioxidants and cancer
 - Nuts and heart disease



NUTRIENT CONTENT CLAIMS

- These are “quasi-health” (my term) claims
- Can apply to claims relating to how the D.S:
 - helps address a classical nutrient deficiency disease (e.g., Vitamin C and scurvy); or
 - helps affect or maintain the normal, healthy structure or function of human body
 - but can't be disease claim – or it's a drug
 - FDA -- regulations and guidance on acceptable structure/function claims
 - helps with the “general well-being” supported by consumption
- **Must bear disclaimer:** “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”



LIMITS ON STRUCTURE/FUNCTION CLAIMS

- 21 CFR 101.93(g)(2) – ten criteria that are barred; include
 - Effects a specific disease or disease class
 - Effects the characteristic signs or symptoms of a specific disease
 - Effects an abnormal condition linked to a natural state if the abnormal condition is uncommon or can cause significant harm
 - Effects a disease via:
 - Name
 - Contains a non-dietary ingredient that is a drug
 - Citation to articles that refer to diseases
 - Using “disease” unless general statement on disease prevention
 - Treats, prevents or mitigates an adverse event linked to disease therapy



SUPPORTING STRUCTURE/FUNCTION CLAIMS

- Must have data to substantiate the claim
- Don't have to submit data to FDA, but you do have to inform FDA 30 days before making any nutritional support claims
- Must meet FTC standard – “*competent and reliable scientific evidence*”
 - “tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.”
- Literature reprints – if done in their entirety, are not considered “labeling”



OTHER D.S. REGULATORY REQUIREMENTS

- Registration – mandatory -- with FDA – 21 CFR 1.232
- GMPs
 - June 2007 – Final Rule published; codified at 21 CFR 111
 - Examples of requirements
 - facility cleaning and pest control
 - maintaining, cleaning and sanitizing equipment
 - QC operations, including material review and disposition decisions
 - Lab operations
 - Manufacturing operations
 - Complaints
 - Guidance issued
 - Failure to meet GMPs – product is adulterated under § 402(g) of Federal Food, Drug, and Cosmetic Act



ADVERSE EVENTS

- Labeled maker, distributor or packer must submit serious adverse events to FDA within 15 business days of learning
 - Adverse event – “any health-related event associated with the use of a dietary supplement that is adverse”
 - Serious – an event that results in:
 - Death
 - Inpatient hospitalization
 - Persistent or significant disability
 - Incapacity
 - Congenital anomaly or birth defect
 - Medical or surgical intervention ... to prevent one of the above results
- “At a Glance” on AEs – just issued –

