FDLI ANNUAL CONFERENCE
May 4, 2018

DIETARY SUPPLEMENTS
RETAILER ISSUES AND LIABILITY

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FDA Concern is Safety Only
DHSEA Act of 1994

- Know what is in your products, especially your own brand
- Rigorous specifications for manufacturing and periodic lab testing; 21 CFR Part 111 requires scientific testing to ensure identity, strength and composition
- Third party suppliers –check claims and periodic testing

Indemnification

- Supplier agreements need to be carefully reviewed for: indemnification provisions; insurance coverage; legal defense; reputation for quality based products, etc.
- Have systems for regulatory review third-party products

Major Legal Issues

- Class action suits-False Advertising, Misbranding, Consumer Fraud
- FDA and FTC Enforcement
- Defense- Assure evidence for “competent and reliable scientific evidence”.

Other Enforcement

- State Attorney's General
- More recent Vitamin Shoppe litigation involving BMPEA and DMAA
- "Unlawful ingredients" and reliable testing for the ingredients
- Monetary and non-monetary settlements

Summation

- Where is the industry going?
- Take away for defending enforcement
- Questions?

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Reading the Tea Leaves for Dietary Supplements

Current Challenges Facing How a Dietary Supplement is Defined

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Megan Olsen, Assistant General Counsel, Council for Responsible Nutrition

Dietary Supplement Definition: Overview

- A product intended to supplement the diet that contains one or more of the following ingredients:
  - A vitamin or mineral
  - An herb or other botanical
  - An amino acid
  - Another dietary substances used to supplement the diet by increasing total dietary intake
  - Or extracts, metabolites, concentrates, or combinations of the above
- Must be intended for ingestion
- Cannot be represented as a conventional food or sole item of a meal or the diet
- Must be labeled as a dietary supplement

FD&C Act Sec. 201(ff)

IND Exclusionary Clause

- Excludes ingredients from the dietary supplement definition if:
  - The ingredient was subject to substantial clinical investigations;
  - The existence of these clinical investigations has been made public; and
  - The ingredient was not first marketed as a dietary supplement or food.

FD&C Act Sec. 201(ff)(3)(B)

IND Exclusionary Clause

- FDA can issue a regulation authorizing a substance as a dietary supplement
- Scope of IND Exclusionary Clause
  - Does an authorization as an IND permanently exclude an ingredient from being a dietary supplement (absent FDA regulation)?
  - Pyridoxamine Citizen Petition

Amarin Pharma, Inc. Litigation

- Involves use of certain esterified fish oil substances in dietary supplements
- Amarin alleged importation violated ITC rules
- ITC declined to investigate, citing to FDA's primary jurisdiction over dietary supplements
- Amarin appealed ITC decision to Federal Circuit

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READING THE TEA LEAVES FOR DIETARY SUPPLEMENTS *ENFORCEMENT TRENDS*

Suzie Trigg, Partner
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What Leads to Enforcement?

- Significant threats to public health
  - Active Pharmaceutical Ingredients
  - Contamination
  - Other dangerous ingredients or dosage forms
- Claims that cause the product to be classified as a drug, not a dietary supplement
- Failure to adhere to cGMPs

Significant Public Health Threat: Highly Concentrated Caffeine

- Products consisting of only or primarily pure or highly concentrated caffeine and sold as dietary supplements
- Significant public health threat
  - At least 2 deaths
- FDA guidance to firms that manufacture, market, or distribute dietary supplement products that contain pure or highly concentrated caffeine, or are considering doing so, to help such parties determine whether their products are or would be adulterated under section 402(f)(1)(A) of the FD&C Act

Significant Public Health Threat: Highly Concentrated Caffeine

- Often sold in packages containing enough powder or liquid for hundreds or thousands of recommended servings – potentially lethal doses
- Even if a measuring device is included, consumers could easily measure incorrectly and ingest a toxic amount of caffeine (*e.g.*, a heaping scoop instead of a level scoop can increase the amount of caffeine by 200%)
- A warning cannot remedy the adulteration
- If it is a bulk package with potentially lethal amounts of caffeine and the consumer is required to separate out a safe serving from a potentially lethal amount, the product is likely adulterated

Significant Public Health Threat: Highly Concentrated Caffeine

- What would not be adulterated?
  - Tablets or capsules that do not provide an excessive amount of caffeine per item and eliminate the need for a consumer to measure a serving
  - Powdered or liquid caffeine in premeasured units that do not provide an excessive amount of caffeine and eliminate the need for the consumer to measure a serving
  - Bulk powdered or liquid caffeine dietary supplements that are diluted to low enough concentrations of caffeine such that a foreseeable error, misreading of directions, or misunderstanding about the product would not normally be expected to lead to toxic or life-threatening symptoms

Significant Public Health Threat: Kratom

- **Not a new problem**

FDA Import Alert 54-15:

"[B]ased on FDA's review of the publicly available information regarding kratom, **there does not appear to be a history of use or other evidence of safety establishing that kratom will reasonably be expected to be safe as a dietary ingredient**. In fact, the scientific literature disclosed serious concerns regarding the toxicity of kratom in multiple organ systems. **Consumption of kratom can lead to a number of health impacts**, including respiratory depression, nervousness, agitation, aggression, sleeplessness, hallucinations, delusions, tremors, loss of libido, constipation, skin hyperpigmentation, nausea, vomiting, and severe withdrawal signs and symptoms. In the absence of a history of use or other evidence of safety establishing that kratom will reasonably be expected to be safe as a dietary ingredient, **kratom and kratom-containing dietary supplements and bulk dietary ingredients are adulterated** under section 402(f)(1)(B) of the Act [21 U.S.C. 342(f)(1)(B)], because they contain a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury."

Significant Public Health Threat: Kratom

- November 2017 Public Health Advisory
- February 2018 Statement from Commissioner Gottlieb, following up to 44 deaths:

We have been especially concerned about the use of kratom to treat opioid withdrawal symptoms, as there is no reliable evidence to support the use of kratom as a treatment for opioid use disorder and significant safety issues exist. We recognize the need and desire for alternative treatments for both the treatment of opioid addiction, as well as the treatment of chronic pain. The FDA stands ready to evaluate evidence that could demonstrate a medicinal purpose for kratom. However, to date, we have received no such submissions and are not aware of any evidence that would meet the agency's standard for approval.

Problematic Claims: FDA/FTC Joint Warning Letters

- 11 companies received warning letters for promoting products as useful for treating opioid addiction
- "[U]nsubstantiated claims may prevent those addicted to opioids from seeking approved treatments that have been demonstrated to be safe and effective, delay their path to recovery, and put them at greater risk of death."
- Companies were making claims that the products could cure, treat, or prevent a disease. Examples of claims made include:
  - "#1 Selling Opiate Withdrawal Brand"
  - "Imagine a life without the irritability, cravings, restlessness, excitability, exhaustion and discomfort associated with the nightmare of addiction and withdrawal symptoms"
  - "Safe and effective natural supplements that work to ease many physical symptoms of opiate withdrawal"
  - "Break the pain killer habit"
  - "Relieve Your Symptoms…addiction, withdrawal, cravings"

Problematic Claims: Post-Inspection Website Review

- April 4th Warning Letter to Amerigo Laboratories LLC

"On November 2, 2017 through November 13, 2017, investigators from the U.S. Food and Drug Administration (FDA) conducted an inspection …. **After the close of the inspection, this is to advise you that FDA reviewed your website … in March 2018 … The claims on your website establish that the products are drugs** under section 201(g)(1)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 321(g)(1)(B)] because they are intended for use in the cure, mitigation, treatment, or prevention of disease."

- Claims related to treatment of narcolepsy and ADHD

Lawful Claims

- Types of acceptable claims:
  - Structure/function claims
  - General well-being claims
  - Nutrient deficiency disease claims
- Must be truthful, substantiated, not misleading, and made in accordance with applicable FD&C Act provisions and FDA regulations
- Include FDA disclaimer statement
- Notify FDA as required under Section 403(r)(6) of the FD&C Act

Current Good Manufacturing Practices (cGMPs)

2017 cGMP Inspection Observations by Subpart
[Total observations: 1,795]

Dietary Supplement cGMP Subpart	% of Observations
B—Personnel	3.0
C—Physical Plant and Grounds	4.3
D—Equipment and Utensils	4.6
E—Requirement to Establish a Production and Process Control System (PPCS)	33.9
F—PPCS: Requirements for Quality Control	10.8
G—PPCS: Requirements for Components, Packaging, and Labels and for Product That You Receive for Packaging or Labeling as a Dietary Supplement	3.4
H—PPCS: Requirements for the Master Manufacturing Record	8.9
I—PPCS: Requirements for the Batch Production Record	8.1
J—PPCS: Requirements for Laboratory Operations	1.6
K—PPCS: Requirements for Manufacturing Operations	1.4
L—PPCS: Requirements for Packaging and Labeling Operations	2.2
M—Holding and Distributing	6.5
N—Returned Dietary Supplements	4.6
O—Product Complaints	6.1
P—Records and Recordkeeping	0.6

Almost half of all observations related to failures to meet the requirements of:

- Subpart E—Requirement to Establish a Production and Process Control System; and
- Subpart F—Production and Process Control System: Requirements for Quality Control

Natural Products Insider, available at: https://www.naturalproductsinsider.com/regulatory/gmp-violations-production-quality-control-plague-supplement-makers

Current Good Manufacturing Practices (cGMPs)

Sampling of 2018 Inspection Observations:

- You did not implement a system of production and process controls that covers all stages of manufacturing, packaging, labeling, and holding of dietary supplements to ensure the quality of the dietary supplement. (21 C.F.R. 111.55)
- You did not establish product specifications for the identity, purity, strength and composition of the finished dietary supplement. (21 C.F.R. 111.70(e))
- You did not establish an identity specification for each component. (21 C.F.R. 111.70(b))
- You did not establish label and packaging specifications. (21 C.F.R. 111.70(d))

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