Session 2:
Direct-to-Consumer Neurotechnology:
Dietary Supplements – Dietary Ingredients

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US Regulation

Food Categories

- Conventional foods
- Dietary supplements
- “Foods for special dietary uses” (e.g., infant formulas, etc.)
- Medical Foods (rare conditions)
A Dietary Supplement is a product (other than tobacco):

- vitamin, mineral, herb or other botanical, amino acid, dietary substance or concentrate, metabolite, constituent, extract, or combination of these ingredients
- includes *drugs and biologics*, if marketed as a dietary supplement or food prior to approval as a drug or biologic
- *intended to supplement the diet*

*Dietary Supplement Health & Education Act - 1994*
US Dietary Supplement Industry

- $11.5 B USD annual sales (2012) [Package Facts -2012]
  - Botanicals / Herbals ~ $5.6 billion [American Botanical Council – 2012]

- Sold direct to consumer – *any* consumer
- ~50% US population has used dietary supplements

- Manufacturers, distributors have access to US consumers through:
  - Groceries/Markets
  - Pharmacies
  - Health food stores
  - Internet
  - Electronic and print media
  - Celebrity endorsements
Neuro-Pysch Indications

Types of DS Products

◆ **Single ingredient**
  - Vitamins (choline)
  - Nootropics (“smart” drugs) – “improve brain function and memory”; used for concentration – all kinds of chemicals
  - Energy ingredients (caffeine, other stimulants)

◆ **Complex (heterogeneous) natural ingredient**
  - Botanicals (herbals) (e.g., St Johns Wort)
  - Lipids (e.g., fish oils, etc.)

◆ **Combinations of multiple ingredients**
  - Mixtures of the above
Dietary Ingredients

Neuro-Psych Indications

- **Mood/Depression**
  - Fish oil; omega-3s
  - L-phenylalanine
  - Rhodiola Rosea
  - St Johns Wort

- **Anxiety/Insomnia**
  - 5-HTP
  - Inositol
  - Kava
  - Melatonin
  - Passion Flower
  - L-tryptophan
  - Valerian Root
  - Winter Cherry

- **Seizures**
  - Bu-yang-huan-wu-tang
  - Gelsemium
  - Ginkgo
  - Jimson Weed
  - Skullcap

- **Alzheimer’s/Cognitive Function /ADHD**
  - *Bacopa monnieri*
  - CDP -choline
  - Curcumin
  - Gingko
  - Huperzine A
  - Methyl xanthines (caffeine, theobromine, etc.)
  - *Sceletium tortuosum*
  - Vicamine/Vinposetine
Dietary Supplements: Label Claims

- Nutrient content claims ("good source of ---")
- Nutrient deficiency claims ("vitamin C prevents scurvy")
- Claims of general "well-being"
- Health claims - unqualified/qualified ("reduce the risk of colon cancer")
- Structure or function claims ("-- maintains bowel regularity"; "antioxidants maintain cell integrity")

*FDA controls the label* ----

*FTC reviews the advertising and promotion*
Health or Nutrient Content Claims

Substantiation

authoritative statements from

“a scientific body of the US
with official responsibility for
public health protection or research directly
related to human nutrition.”

(e.g., National Academy of Sciences, National Institutes of Health, Centers for Disease Control & Prevention, etc.)

CFSAN - Guidance for Industry [7-11-98]
FDAMA ‘97
“Structure/Function” Claims

Dietary supplements are intended to supplement the diet AND to affect the structure or function of the body

DSHEA -1994
Dietary Supplement

“Structure / Function” Claims

- Authorized by the *Dietary Supplement Health and Education Act (DSHEA) - 1994*
- Manufacturer is responsible for assuring truthfulness of claim
- Not pre-approved or authorized by FDA
- No direct or implied disease claims
- Label must include disclaimer:

“This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease“
“Structure/Function” Claims

Drugs are intended for use in the diagnosis, mitigation, treatment, cure or prevention of disease and to affect the structure or function of the body.

FD & C Act Sec. 201(g)
Legal Assumptions:

Dietary Supplements vs Drugs

**Dietary supplements** are intended to supplement the diet of *healthy (normal) individuals for which no risk is tolerable.*

**Drugs** are intended for use by a population for which the *benefit has been proven to outweigh the risk.*
SAFETY

Foods <<<<<<<< >>>>>> Drugs

Opposing Legal Premises
Legal Assumption: Foods

“generally recognized as safe”

OR

contain ingredients with

“a history of use or other evidence of safety”

which

“will reasonably be expected to be safe…..”
Legal Assumption:

Drugs

not generally recognized as safe & effective
under the conditions prescribed, recommended or suggested in the labeling

[Definition of “new” drug: Section 201p FD&C Act]
Legal Assumptions: Assessing Risk

**No Risk**
Safe for the general population

**Benefit to Risk**
Safe, relative to efficacy for specific indication in a target population

**SAME Evidence**

**FOODS**
- **SAFETY**
- **UNSAFETY**

**Healthy**
- **SAFE**
- **UNSAFE**

**DRUGS**
- **SAFE**
- **UNSAFE**

**Patients**
Regardless of a product’s current market channel, when the Labeling shows that it is intended to be used to diagnose, mitigate, treat, cure or prevent disease and affect the structure or function of the body....

It becomes a “drug”

Food, Drug &Cosmetic Act Sec. 201(g)
Dietary Supplements

Bioethical Considerations

- *Are Dietary Supplements adequately regulated for DTC use for neuro-psych conditions?*
- *Do consumers have adequate information to make decisions to use this products for their medical conditions?*
- *What role should Dietary Supplements have in the management of neuro-psych conditions?*
US Regulation of DSs

Good Manufacturing Practices (GMPs)

- Applies to manufacturers, packaging, labeling, holding of facilities, (not DTC retailers)
- Identity, purity, quality, strength, composition of dietary supplements
  - Food GMP compliance
  - Hazard Analysis & Critical Control Points (HACCP)
  - QA, QC and Lab Operations
  - Self-inspections
  - Production / process controls (batch records, SOPs,)
  - Training
  - Complaint files, records retention, etc.

Not inspected, pre-approved, or tested by FDA.
No requirement for lot-to-lot consistency, stability
US Regulation of DSs

Labeling

- Must bear SUPPLEMENT FACTS
- Must meet FDA requirements, depending upon the type of Claim
  - Health Claims – FDA preapproved
  - Nutrient Content Claims – meet the requirements
  - Nutrient Deficiency Claims – meet requirements OR pre-approved
  - Well-being – not approved
  - Structure-Function- 30 day Notice to FDA; must bear disclaimer

Not labeled for specific populations or clinical indications. No description of warnings, risks, precautions, contraindications, interactions, dose-modifications, etc.
Dietary Supplements

Ingredient Safety

◆ “Safe” for the general (healthy) population.

◆ DS Ingredients:
  – Grandfathered (sold in US as Foods, or DS prior to Oct 15, 1994)
  – GRAS (“generally recognized as safe”) - found safe by a panel of experts based on published data
  – “New Dietary Ingredient” notification: determined safe by the manufacturer, and reviewed by FDA the manufacturer 75 days prior to the expected date of marketing (interstate commerce).

◆ Adverse event reporting = OTC (monographed) drugs
No testing in specific populations or for specific medical conditions.
Clinical study protocols/data are not reviewed/audited.
“Dietary Ingredients can treat or prevent disease.”

- **Sold direct to consumer** - anyone can purchase; no restrictions (e.g., age or patients)

- **“Practice of Medicine”** - Licensed practitioners can prescribe dietary supplements/ingredients to their own patients.

- **Self-medication** - Consumers can use DSs as they wish, without a “learned intermediary”

- **Some DS ingredients/DS products can also be drugs** (e.g., psyllium husk, calcium carbonate, etc.)
Thank you!

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