PROPOSED CGMPs FOR DIETARY SUPPLEMENTS: RATIONALE AND IMPLICATIONS FOR PRODUCT DEVELOPMENT

NIDA CONFERENCE ON NATURCEUTICALS, NUTRACEUTICALS, HERBAL BOTANICALS AND PSCHOACTIVES: DRUG DISCOVERY AND DRUG-DRUG INTERACTIONS NOVEMBER 5-7, BALTIMORE, MD

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OUTLINE

1. INTRODUCTION
2. DIETARY SUPPLEMENT EDUCATION AND HEALTH ACT (DSHEA), OCTOBER 25, 1994
3. PROPOSED CGMP RULES (March 13, 2003)
   a. Rationale
   b. Specifics

4. FDA Enforcement of DSHEA
5. Opportunities for Scientists (at the Regulatory interface)

INTRODUCTION

Lawyers and Scientists do not communicate effectively "[b]ecause there is a general lack of understanding of each culture, [and] these interactions often lead to a cognitive friction that is both disturbing and costly to society"

(A Convergence of Science and Law, National Academy Press, 2001).

DSHEA

Purpose?

“[T]he purpose of this legislation is straightforward: To bring some much needed sanity and order to the regulation of the dietary supplement industry. We need to establish a regulatory structure that will encourage good health through the use of nutritional supplements while, at the same time, protecting consumers from unsafe products.”

Sen. Orrin Hatch

April 7, 1993 (introducing S. 784 on the Senate floor)

PROPOSED RULES

- Why are CGMPS needed?
- How will CGMP regulations take into account technical feasibility?
- How can FDA help industry achieve compliance with CGMPs?

CGMP COMPONENTS

- General provisions
- Personnel
- Physical plant
- Equipment and Utensils
- Production and process controls
- Holding and distributing
- Consumer complaints
- Records and recordkeeping

EXAMPLES (cont'd)

- **SUPERPOTENT DS (RECALLED)**
  - **VITAMINS A, D and B6**
  - **Selenium**
  - **NIACIN**
    - **452 mg (Upper Limit: 25 mg, IOM)**

Why CGMPs?

- **To promote and protect public health by ensuring product quality**

EXAMPLES

- **Contamination:**
  - » **Botanicals with Digitalis Lanata (raw material labeled “plantain”)**
    - **183 manufacturers had used this contaminated material**

EXAMPLES (cont'd)

- SUBPOTENT DS (RECALLED)
  - Folic acid (reducing neural tube defects)
    - contained 34% of labeled amount

- UNDECLARED INGREDIENTS
  - color additives, lactose, sulfites

EXAMPLES (cont'd)

- **LOT TO LOT VARIABILITY IN CONTENT**
  - **20 EPHEDRA CONTAINING HERBAL DS**
  - **ALKALOID CONTENT**
    - **180, 250 AND 1000%, IN ONE EXAMPLE FOR EPHEDRINE, PSEUDOEPHEDRINE AND METHYLEPHEDRINE**

PROPOSED RULES

- Why are CGMPS needed? √
- How will CGMP regulations take into account technical feasibility?
- How can FDA help industry achieve compliance with CGMPS?

Legal Authority - § 402 (g)

Only Congress can make laws, but can delegate

TO:

- Prescribe GMPs for DS
- Shall be modeled after CGMPs for food
- May not impose standards for which there are no current and generally available analytical methodology
- Notice and Comment

Technical feasibility?

- Will not propose rules that are not technically feasible
  - **No requirements for:**
    - Disintegration
    - Dissolution
    - Bioavailability
    - Expiration Dating
    - Defect Action Levels (DALs)

DAL

- **LEVELS OF NATURAL OR UNAVOIDABLE DEFECTS IN FOODS THAT PRESENT NO HEALTH HAZARDS FOR HUMANS**

Definition of Microorganisms

- 1. Includes viruses
  - **Animal tissues are used in the manufacture of DS**

- 2. **FDA "recognize[s] that there are few effective virus detection methods and that industry may be incapable of showing the presence and absence of specific viruses in its products"**

HERBALIST

- **NOT EXCLUDED FROM CGMP REGULATION**

FDA ENFORCEMENT OF DSHEA

- January 2000 DS Enforcement Strategy
  - To develop a " science-based regulatory program that fully implements [DSHEA] . . ."

Enforcement Activities

- Traditional
  - Inspections of DS Manufacturers(80 in 2001-02)
    - Voluntary Compliance
      - Noni Fresh Juice: To treat diseases ranging from immune system disorders to arthritis, malaria, and alcohol addiction
        - » Company president removed impermissible claims from Web site and learning about DS Claims

Enforcement Activities (cont'd)

- Traditional
  - Voluntary Compliance
    - Miracle Bust
      - » Destruction of Inventory
      - » Affidavit to voluntarily stop selling and distributing product

Enforcement Activities

- Traditional
  - Warning Letters
    - Violations and corrective actions needed to prevent further agency action
      - Synthetic ephedrine (17 letters)
        - » Compliance (with one exemption)
      - Calm Focus (Better Way Kids)
        - » To treat ADHD
        - » “Natural alternative to Ritalin”
        - » “Formulated to energize neurotransmitters in the brain”
      - Company correcting claims

Enforcement Activities

- Traditional
  - Seizures and Injunctions
    - Court action to seize and destroy and enjoin future violations
      - Brain Nutrient Capsule
        - » To treat mental retardation, cerebral palsy and epilepsy
        - » Claims it “has the function of increasing the intelligence, elevating the IQ and promoting growth”
      - FDA: claims are baseless; move to condemn seized products

Enforcement Activities

- Traditional
  - Seizures and Injunctions (cont'd)
  - Street Drug Alternatives
  - FDA seized the product and sought destruction
    - misbranded and unapproved drug
    - Court agreed with the FDA

Enforcement Activities

- Traditional
  - Criminal Enforcement
    - Company sold DSs: colloidal gold, silver and titanium
    - Claimed cures for cancer and rheumatoid arthritis and heart disease
    - Company founder convicted of “ introducing unapproved” new drugs into interstate commerce and sentenced for 4 months in a “community correctional center”
  - –

USA v. Lane-Labs, Inc.
(decided July 9, 2004)

FACTS:

LANE LABS MARKETED:

BENEFIN: SHARK CARTILAGE (POWDER/CAPLET)

MGN-3:POLYSACCAHARIDE DIETARY FIBER (ARABINOXYLAN) (CAPSULE)

SkinAnswer: GLYCOALKALOID (SAND BRIER EXTRACT) SKIN CREAM

USA v. Lane-Labs, INC.

(decided July 9, 2004)

FDA CASE AGAINST LANE LAB

MARKETING THESE 3 PRODUCTS FOR "THE CURE, MITIGATION OR TREATMENT OF DISEASE" ?

TREATMENT OF CANCER, SKIN CANCER AND HIV/AIDS

Conclusion

- CGMPS should improve DS quality
- Will increase cost of production

YOUR SCIENTIFIC CONCLUSIONS CAN APPEAR ON A DS PRODUCT NEAR YOU