

Medical Device & Dietary Supplement Development

Pharm 309
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1

Objectives

- Continued from ...
- Understand the differences between the developmental demands and regulatory requirements for
 - Drugs & biologics
 - Medical devices
 - Dietary supplements

2

More Disasters ... Medical Device Amendments of 1976

- 1969 HEW survey: 10 years 10,000 injuries & 751 fatalities
- FDA survey: 858 deaths
- Independent survey 36,000 complications in one year

3

FDA History - Medical Device Amendments of 1976

- Dalkon Shield, an IUD, marketed w/o proper testing:
 - removal rate of 26.4%
 - an infection rate of 5%
 - 25 miscarriages, 16 deaths
- Cardiac pacemakers defects necessitated 30 recalls involving 23,000 units
- May 28, 1976

4

Differentiate drug & device Food, Drug & Cosmetic Act

- Drug/biologic 21USC201(g)(1)
 - USP/NF
 - **INTENDED** for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and
 - intended to affect the structure or any function of the body of man or other animals;
 - Component
 - Not food or dietary supplement
- Medical device 21USC201(h)(1)
 - USP/NF
 - **INTENDED** for use in the diagnosis of disease or other conditions ..., or
 - intended to affect the structure or any function ...,
 - does not achieve its primary intended purposes through chemical action within or on the body ... and which is not dependent upon being metabolized

5

FDA History - Medical Device Amendments of 1976

- **Key features of the 1976 Amendments**
 - Classification for regulatory purposes
 - Pre-market approval: implanted & life supporting devices
 - Interstate commerce is presumed in all cases
 - Authority to issue GMP's, Access to industry records
 - Registration and list, Authority to ban devices

6

Basis for Classification of Devices

- Amount of information known about device *for intended use & indications for use*
 - Scalpel: intended use - cut tissue. Indication in labeling "for making incisions in the cornea".
- What level of controls are necessary to assure Safety & Effectiveness of device
- Support or sustain human life OR important in preventing impairment of human health
- Risk of causing illness or injury

7

Medical Device Classification & Regulatory Requirements

- Class I - General Controls (with & w/o exemptions)
- Class II – General Controls and Special Controls (with & w/o exemptions)
- Class III – General Controls and Premarket Approval

8

Class I - General Controls

- Known information provides reasonable assurance of safety & effectiveness using General Controls

OR

- Known information does not assure S & E, BUT the device
 - Does not support or sustain human life, OR
 - Is not used to prevent impairment of human health AND
 - No unreasonable risk of illness or injury

9

Examples of Class I Devices

- Examination Gloves [21CFR880.6250](#)
- Dental Hand Instrument [21CFR872.4565](#)
- Elastic Bandages [21CFR880.5075](#)
- Pacemaker Charger [21CFR870.3670](#)
- Ultrasonic Cleaner for Medical Instruments [21CFR880.6150](#)
- Hand-held (Manual) Surgical Instruments [21CFR878.4800](#)

10

Class II - Special Controls

- General Controls alone are insufficient to provide assurance of Safety & Effectiveness
 - BUT
- Information exists to establish Special Controls

11

Special Controls

- General Controls +
 - Special Labeling Requirements
 - Performance Standards
 - Postmarket Surveillance
 - Patient Registries
 - Guidelines, Recommendations
 - Any other appropriate actions

12

Examples of Class II Devices

- Cardiac Monitor [21CFR870.2300](#)
- Elbow Joint Metal/Polymer Constrained Cemented Prosthesis [21CFR888.3150](#)
- Pediatric hospital bed [21CFR880.5140](#)
- Infusion Pump [21CFR880.5725](#)
- Powered Wheelchair [21CFR890.3860](#)
- Surgical Drapes [21CFR878.4370](#)
- TENS device [21CFR882.5890](#)

13

Class III - Premarket Approval

- Not enough information to classify as either Class I or II
- Device usually supports/sustains life,
- is of substantial importance in preventing impairment of human health or
- presents a potential, unreasonable risk of illness or injury

14

Premarket Approval (PMA)

- Extensive submission including data showing Safety & Effectiveness
- Conditions of Approval
- Annual Reports

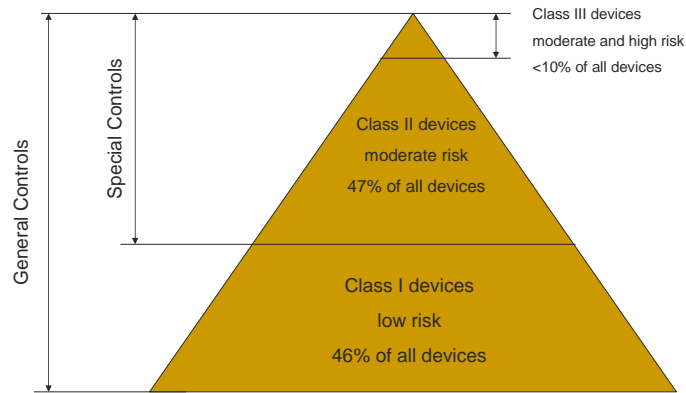
15

Examples of Class III Devices

- Implantable pacemaker pulse generator [21CFR870.3610](#)
- Replacement heart valve [21CFR870.3925](#)
- Cranial electrotherapy [21CFR882.5800](#)
- Implanted electrical urinary continence device [21CFR876.5270](#)
- Silicone gel-filled breast implant [21CFR878.3540](#)
- Implanted cerebella stimulator [21CFR882.5820](#)

16

Device Pyramid (Classification)

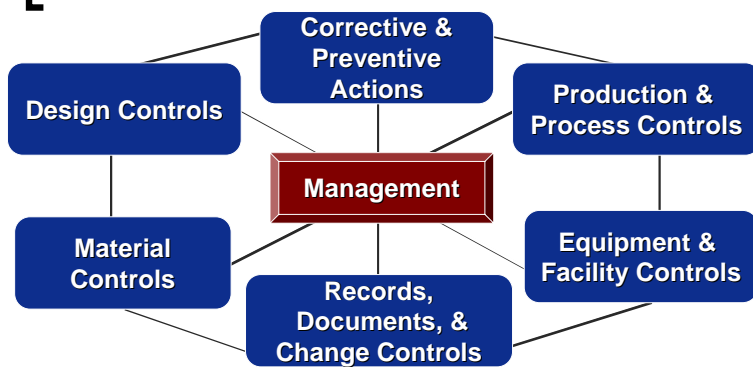


QSIT Quality System Inspection Technique

- Management Controls
- Design Controls
- Corrective and Preventive Actions (CAPA)
- Production and Process Controls
- Risk Analysis
- Design & Process
 - Verification
 - Validation

18

Subsystems of a Quality System



19

More history; different kind of disaster Dietary Supplement & Health Education Act of 1994

- 1976 VITAMINS AND MINERALS AMENDMENTS
 - "Proxmire Amendments" stop FDA from establishing standards limiting potency of vitamins and minerals in food supplements or regulating them as drugs based solely on potency.
- 1989 FDA issued a nationwide recall of all over-the-counter dietary supplements providing 100 milligrams or more of L-TRYPTOPHAN.
- 1990 NUTRITION LABELING AND EDUCATION ACT
- 1994 DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT (DSHEA)
 - specific labeling requirements,
 - provides a regulatory framework,
 - good manufacturing practice regulations
 - commission to recommend how to regulate claims.

20

Dietary Supplement Food, Drug & Cosmetic Act – 21USC201(ff)

- 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 [but no other animals] 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);

21

DSHEA-2

- intended for ingestion in pill, capsule, tablet, or liquid form.
- not represented for use as a conventional food or as the sole item of a meal or diet.
- is labeled as a "dietary supplement."

22

Dietary Supplement Regulatory Requirements

- No pre-market notification except for "new dietary ingredient"
 - Grandfathered all ingredients available through 10/15/94
 - Vetting for "new dietary ingredients"
 - Demonstration that product is **unsafe** for regulatory action
- Manufacturer/distributor responsible for safety and claims/representations made on label or in labeling
- No manufacturer/distributor registration

23

DSHEA Labeling Requirements

- Descriptive name, including "supplement"
- Place of manufacture, etc.
- Complete list of ingredients
- Net quantity of contents
- NLEA-compliant "supplement facts" panel
- Certain "structure/function" claims permitted
 - Vitamin C – scurvy
 - Calcium – osteoporosis
- Otherwise, disclaimer required when claim is made
 - "This claim has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease"

<http://vm.cfsan.fda.gov/~dms/supplmnt.html>

24

[Is Something Missing?]

- Medical Products?
- Dietary Supplements?

25

[Summing Up]

- where was the science?
- phases of drug, device, dietary supplement development
- major regulatory events
- questions

26