

FDA Laws & Pharmacy Practice

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Objectives

- Be able to discuss the evolution of food and drug law in the United States
- Be able to discuss the ways in which pharmacists and other health care practitioners may violate these laws
- Be able to explain the significance of “adulterated” and “misbranded” in the context of pharmacy practice
- Be able to describe
 - the use of the “Orange Book” and its significance in pharmacy practice in Washington
 - expiration date meaning
 - National Drug Code and its usefulness and liabilities
 - FDA “voluntary” recalls

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History Review

- Review Pharmacy 309 Notes (posted on web site)
- Review Chapters 2 & 3 in Abood – optional
- Check out FDA web site
 - www.fda.gov
 - Do Drugs, Biologics; look over “From Test Tube to Patient”, etc.

<http://www.fda.gov/fdac/special/testtubetopatient/default.htm>

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Food, Drug & Cosmetic Act, *as amended*

- Statutory authority (Title 21 United States Code) to promulgate regulations (Title 21 Code of Federal Regulations)
 - [Laws Enforced by FDA](#)
- Centers for
 - Drug Evaluation & Research (CDER)
 - Biologics Evaluation & Research (CBER)
 - Devices & Radiological Health (CDRH)
 - Food Safety & Applied Nutrition (CFSAN)
 - Veterinary Medicine (CVM)

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What makes a drug a “drug”

- 4 things
 - recognized in an “official compendium”
 - USP / NF
 - Homeopathic Pharmacopeia of the United States
 - **intended** for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals
 - intended to affect the structure or function of the body of man or other animals, but not food
 - components

section 201(g)(1)

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device

- Same as “drug”, except
 - “... does not achieve any of its principal **intended** purposes through chemical action ... **and** is not dependent upon being metabolized”

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cosmetic

- **Intended** to be [applied, smeared, squished about ...] for cleaning, beautifying, promoting attractiveness, altering appearance
- components
- not soap
- man or any other beast?

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food

- ... used for food or drink for man or other animals
- components
- *cf.* dietary supplements;
 - DSHEA – Dietary Supplement & Health Education Act
 - Proxmire Amendment

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biologic

- Parallel evolution -- Public Health Service (see Public Health Service Act of 1945, regulations at 21CFR600 *et seq.*)
- any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man; “biotechnology-derived therapeutic”
- big administrative differences; some similarities
- “cats marching ...”; and again; transfer of “well characterized biologicals” to CDER

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Durham-Humphrey Amendment & Prescription Drugs, etc.

- **Intended** for use by man, and
 - is a habit-forming drug, or
 - because of its toxicity or other potentiality for harmful effect ... method of use ... collateral measures necessary to its use
- is not safe except under the supervision of a practitioner licensed to administer ...
- *Plan B* issues

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DH2

- Limited by an approved application
- violations → “misbranded”
- exemption from § 502 requirements
- requirement for federal “Caution” [legend]

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FD&C Act’s 2 big sticks

- Adulteration
- Misbranding
- Penalties: notifications (including a “warning letter”), seizure, injunction, fine, criminal prosecution
 - what kind of legal action is this?
- Most FDA regulatory actions linked to A or D, somehow

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Thou shalt not -- prohibitions

- “Introduce” or deliver into inter~~er~~state commerce any [stuff] that is adulterated or misbranded
- adulterate or misbrand
- “receive” stuff that’s A’d or M’d
- refuse to permit inspection by an authorized person
- counterfeit (placebo?)
- alter labeling in a way that would result in the product being A’d or M’d

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Adulteration

- Made from bad stuff (“filthy, putrid ...”)
- made in a place or way that could result in (“whereby”) A
- container/closure system could permit A
- strength/quality differs from claim; official compendium or otherwise
- parrot in the pharmacy ...
- note burden of proof

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A-word 2

- Current Good Manufacturing Practices
- International Commission on Harmonisation
- Product tampering; tamper-resistant packaging (*cf.* child-resistant packaging)

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21 CFR Part 1.3 Definitions

- (a) **Labeling** includes all written, printed, or graphic matter accompanying an article at any time while such article is in inter~~er~~state commerce or held for sale after shipment or delivery in interstate commerce.
- (b) **Label** means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.

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Misbranding

- “Labeling” is false or misleading in any particular
- place of business (manufacturer, packer or distributor)
- understandability by ordinary person under customary conditions of purchase/use
- warning for habit-forming

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M-word 2

- Size of type
- active ingredients specified; inactives in (descending order of predominance) **alpha order**; alcohol
- established name (USAN – United States Adopted Names)
- adequate directions for use & warnings
- packaging per compendial standards
- misleading packaging; imitation

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M-word 3

- Following labeling could result in health hazard
- if subject to deterioration; packaging, precautions in labeling
- **adequate information** for use (MedGuide)

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Other FDA - Pharmacy Practice Items

- Orange Book
- Expiration Dates
- Recalls
- NDC

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Orange Book

- ... some inconvenient terminology
- “therapeutic equivalence” vs. “generic substitution”, “therapeutic interchange” (aka therapeutic substitution)
- Electronic Orange Book -- Approved Products with Therapeutic Equivalence Evaluations
 - <http://www.fda.gov/cder/orange/default.htm>

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OB3 – WA issues

- **WAC 246-899-030 Product selection responsibilities.**
 - (1) The **determination** of the drug product to be dispensed on a prescription is a **professional responsibility of the pharmacist**, and the pharmacist shall not dispense any product that in his/her professional opinion does not meet adequate standards.
 - (2) Pharmacists may utilize as the basis for their decisions on therapeutically equivalent drug products:
 - (a) Available drug product information from federal and state agencies, official compendia, and drug manufacturers, or
 - (b) Other scientific or professional resources, or
 - (c) The **federal food and drug administration "approved drug products"** as a board approved reference for a positive formulary of therapeutically equivalent products within the limitations stipulated in that publication.

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OB4 – WA Issues

- Importance of definitions
- RCW 69.41.110 Definitions. As used in RCW 69.41.100 through 69.41.180, the following words shall have the following meanings:
 - (3) "Substitute" means to dispense, with the practitioner's authorization, a "therapeutically equivalent" drug product of the **identical base or salt** as the specific drug product prescribed: PROVIDED, That with the practitioner's prior consent, therapeutically equivalent drugs other than the identical base or salt may be dispensed;
 - (4) "Therapeutically equivalent" means essentially the same efficacy and toxicity when administered to an individual in the same dosage regimen;

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Expiration Date

- All OTC and prescription drugs have expiration dates, but ...
- Drug expires on ... the last day of the month
- Misbranding to sell after expiration
- Watch computer assignment of expiration date; patient confusion when pharmacy and printed label differ

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Expiration Date 2

- cGMP regulations, drug products are labeled with an expiration date determined by appropriate stability testing (21CFR211.137 and 166)
- ... evaluated over time, in same container-closure system, conditions of storage, transportation
- accelerated stability studies to support tentative expiration dates; firm liability
- new studies required for packaging changes

Expiration Date 3

21CFR137 Expiration Dating (excerpts)

- (e) Homeopathic drug products are exempt
- (f) Allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt
- (g) New drug products for investigational use are exempt ... provided that they meet appropriate standards ...
- (h) Pending consideration of a proposed exemption, published in the Federal Register of September 29, 1978, the requirements in this section shall not be enforced for human OTC drug products if their labeling does not bear dosage limitations and they are stable for at least 3 years as supported by appropriate stability data.

"FDA" Recalls

- Product is subject to FDA legal action
 - threat or potential threat to humans or animals
 - adulteration
 - misbranding
 - materially misleading (fraud/deception)
- Voluntary, **NOT** government action
- FDA can only get injunctions or seizures

Types of Recalls

- Class I - use or exposure can cause serious health consequences or death
- Class II - use may cause temporary medically reversible health consequences
- Class III - use not likely to cause adverse health consequences

Levels of Recalls

- 1 consumer or patient level (pharmacy cooperation in identifying patients)
- 2 retail level
- 3 wholesale level

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Recalls 3

- Where do you hear about recalls?
 - news media (FDA media release); FDA listserve
 - Manufacturer / wholesaler
 - National publications (i.e., *ASHP Newsletter*)
 - Pharmacy "hot lines"

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Drug and Device Listing and Establishment Registration

- FD&C Act and FDA regulations require registration of establishments and products in 4 major categories:
 - "low acid" canned foods
 - acidified foods
 - drugs
 - medical devices
- Failure to register facility a crime and renders the products misbranded
- Cosmetic firms (formulas) may register voluntarily

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FDA Registration 2

- Applicable to **bulk** and **finished** dosage forms, and to imported and exported commodities
- Establishment registration must be updated annually
- Product listings updated January & June, if material changes have occurred

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National Drug Code (NDC)

- 21CFR207.35(b)(3) FDA **requests** but does not require that the NDC number appear on all drug labels and in other drug labeling, including the label of any prescription drug container furnished to a consumer.
- The NDC is one of the following configurations:
4-4-2, 5-3-2, or 5-4-1: labeler, product, packaging
- 10 vs. 11 digits
- Who cares?

<http://www.fda.gov/cder/ndc/>

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NDC Examples

- "Labeler" code
 - 0002 ELI LILLY AND CO
- "Labeler", "product" and "package" code
 - STRATTERA CAPSULES 18MG 0002 - 3238 - 01 BLPK 1 X 4
 - STRATTERA CAPSULES 18MG 0002 - 3238 - 07 BOT 1 X 7
 - STRATTERA CAPSULES 18MG 0002 - 3238 - 30 BOT 30

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More NDC Examples

Labeler Code	Firm Name	Trade Name	Strength
54868	PHYSICIANS TOTAL CARE INC	ACCOLATE TABLETS	20MG
54868	PHYSICIANS TOTAL CARE INC	ACCUPRIL TABLETS	5MG
54868	PHYSICIANS TOTAL CARE INC	ACCUPRIL TABLETS	40MG
54868	PHYSICIANS TOTAL CARE INC	ACCUPRIL TABLETS	10MG
54868	PHYSICIANS TOTAL CARE INC	ACCUPRIL TABLETS	20MG
54868	PHYSICIANS TOTAL CARE INC	ACCUTANE CAPSULES	40MG
54868	PHYSICIANS TOTAL CARE INC	ACETAMINOPHEN AND CODEINE PHOSPHATE SOLUTION COMBO	

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Summing Up

- What makes a drug a drug
- What is FDA's jurisdiction
- Distinguish between adulteration and misbranding
- Expiration dates
- FDA registration
- Recalls
- NDC

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