PPTA
Plasma Protein Therapeutics Association

Global Regulatory Landscape

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Shanghai, China
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Why Pharmaceutical Regulation?

- Protect citizens from dangerous drugs
- Prevent marketing of ineffective therapies
- Ensure quality of marketed drugs
- Maintain confidence in:
  - Health systems
  - Health professionals
  - Pharmaceutical manufacturers

Why so different?

- Regulation is based on law
  - Legal structures of nations differ
  - Granted authorities
    1. Degree of regulation
    2. Function of regulation
  - Focus
    1. Public health
    2. Consumer protection
    3. Sanitation
  - Evolution over time
    1. Triggers for regulation
    2. Risk perception/acceptance

Effect of Globalization

- World is smaller
  - Transportation
  - Communications
  - Cold storage
- Improved medical care
  - Diagnosis
  - Treatment options
- Allow for global resource
  - Plasma for fractionation
  - Plasma protein therapies

Efforts to foster global “harmonization”

- Trade agreements
  - Regulatory restrictions
  - Trade restrictions
- International Conference on Harmonization
  - Few players at first
  - Limited biotechnology application
  - Expanding
- World Health Organization
  - Standards
  - Guidelines

PIC/S

- Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S)
  - two international instruments between countries and pharmaceutical inspection authorities
  - provide together co-operation (harmonization) in the field of GMP
  - GMP standards/guidance documents; training competent authorities/inspectors; assessing inspectorates
  - 46 participating authorities

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Overview of US Regulatory System

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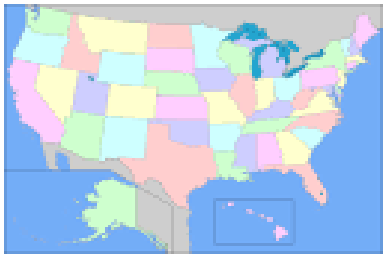
Authority for drug regulation

- United States of America
  - Federal government
    1. Centralized regulation of drugs
    2. Commerce clause of US Constitution
    3. US Congress: Laws



  - 50 individual States
    1. Each self-governed
    2. Retain some powers over drugs, eg., wholesale licenses

Relevant Laws

- Federal Food, Drug and Cosmetic Act (21 USC 302 et. seq.) [consumer protection]
  - Manufacturers must prove a drug is safe and effective before marketing
  - Prohibits interstate commerce of misbranded and adulterated drugs, foods, cosmetics and therapeutic devices
  - Provides penalties for violations, including court injunction
  - Requires manufacturing facility registration (x-US also plus name US agent)
  - Authorizes manufacturing facility inspections

Relevant Laws

- Public Health Service Act (42 USC 262 et. seq.) [public health and hygiene]
  - Regulation of biological products and control of communicable diseases
  - Defines biological product to include blood, blood components and derivatives
  - Section 351—stipulates requirements for licensure; Secretary establishes requirements for approval, suspension and revocation of a biologics license; Allows interstate commerce of approved products
  - Section 361—requires control of communicable diseases

Agency tasked with enforcement

- Food and Drug Administration
  - FDA is an agency within the Department of Health and Human Services.
  - The FDA's organization consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency: Medical Products and Tobacco, Foods, Global Regulatory Operations and Policy, and Operations.

- Operational Centers
  - Center for Biologics Evaluation and Research
  - Center for Drugs Evaluation and Research
  - Center for Devices and Radiological Health
  - Center for Veterinary Medicine
  - Center for Food Science and Applied Nutrition
  - Center for Tobacco Products

FDA Requirements/Resources

- FDA promulgates regulations to implement the PHS and FDC Acts
- Codified in the Code of Federal Regulations (CFR)
- Once promulgated, have the force of law
- FDA regulations are found in Title 21 of CFR
  - Drug regulations 21 CFR 200 et. seq.
  - Biologics regulations 21 CFR 600 et. seq.
- Regulations include both addt. Product standards and cGMP requirements

cGMP requirements

- Manufacturers must have systems in place to control the manufacturing process
- cGMP regulations provide direction for control and include concepts of:
  - Quality assurance
  - Quality control
  - Process validation
- Drug cGMPs—21 CFR 210 -211
- Blood component cGMPs 21 CFR 606.3 – 606.171 (include Source Plasma and recovered plasma for manufacturing)

Additional Resources for Biologics

- Guidance documents
  - Contain FDA's recommendations (current considerations) on how to comply with statutes and regulations
  - Describe new policies and procedures
  - Do not bind FDA or industry
  - Alternative approaches can be used if they satisfy the requirements in applicable statutes and regulations
  - Found on FDA/CBER's website

Summary

THANK YOU

Blood is local. Plasma is global.

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