Global Clinical Trial Regulations

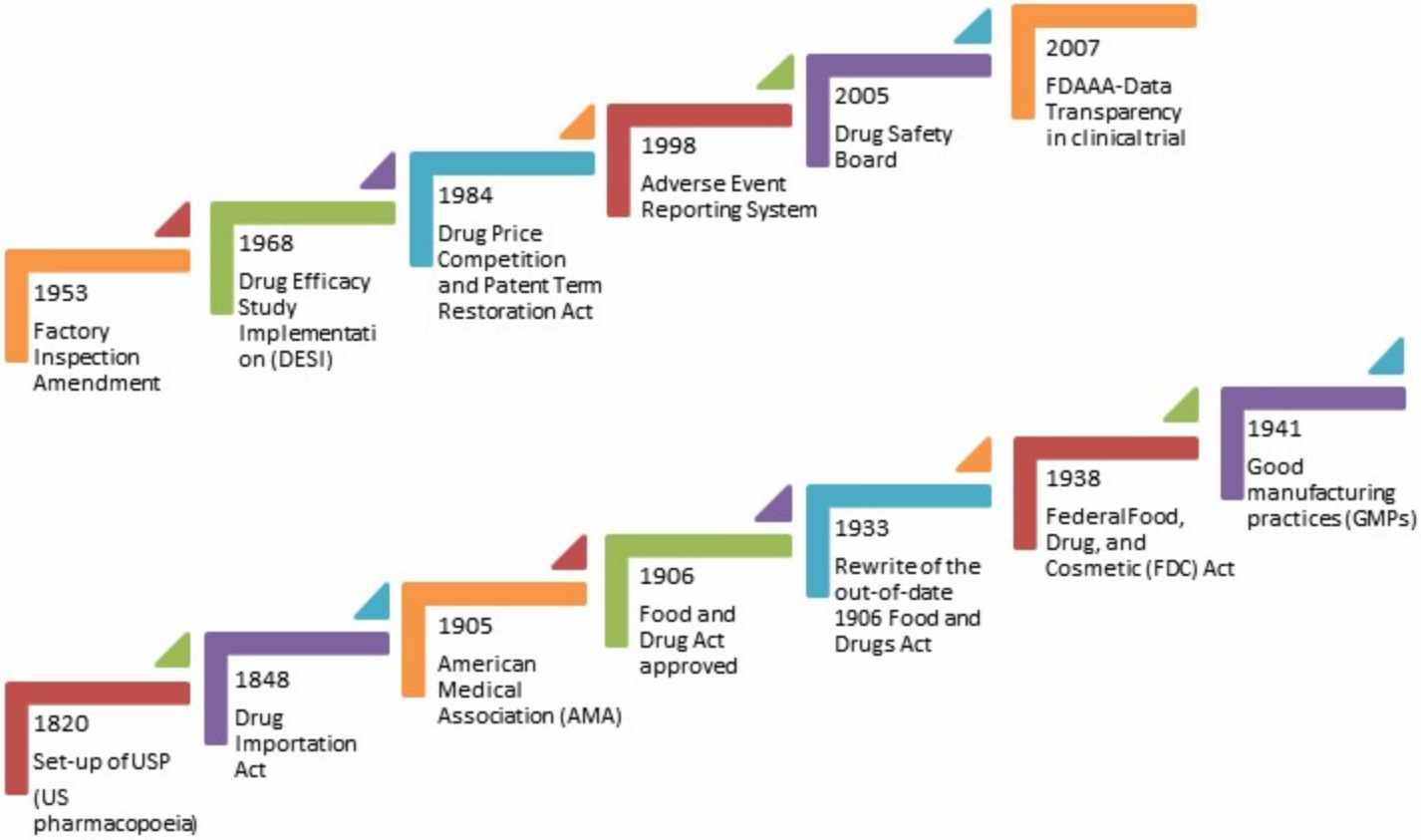
Module 5 Topic 1_1

History of USFDA

- FDA can trace its origins back to the creation of the Agricultural Division in the Patent Office in 1848, its origins as a federal consumer protection agency began with the passage of the 1906 Pure Food and Drugs Act.

- This law was the culmination of about 100 bills over a quarter-century that aimed to rein in long-standing, serious abuses in the consumer product marketplace.

Laws and Amendments: Shaped USFDA



Structure of USFDA

- The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services
- It consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency:
  - Medical Products and Tobacco
  - Foods and Veterinary Medicine
  - Global Regulatory Operations and Policy
  - Operations

Structure of USFDA

Office of the Commissioner

- Leadership of the agency's
  - Scientific activities
  - Communication
  - Legislative liaison
  - Policy and planning
  - Women's and minority health initiatives
  - Agency operations
  - Toxicological research

Reference: https://www.fda.gov/AboutFDA/CentersOffices/default.html

Structure of USFDA

Office of Foods and Veterinary Medicine

- Leads a functionally unified FDA Foods Program that addresses
  - Food and feed safety
  - Nutrition
  - Other critical areas to achieve public health goals

Structure of USFDA

Office of Global Regulatory Operations and Policy

- Provides leadership for FDA's domestic and international product quality and safety efforts
  - Office of Global Regulatory Operations and Policy (GO)
    - Comprises the Office of Regulatory Affairs and the Office of International Programs.
    - The Deputy Commissioner for GO provides executive oversight, strategic leadership, and policy direction to FDA's domestic and international product quality and safety efforts, including global collaboration, global data-sharing, development and harmonization of standards, field operations, compliance, and enforcement activities.

Structure of USFDA

Office of Medical Products and Tobacco

- Provides advice and counsel to the Commissioner on all medical product and tobacco-related programs and issues
- Provides high-level coordination and leadership across the centers for drug, biologics, medical devices, and tobacco products. The office also oversees the agency's special medical programs.

Structure of USFDA

Office of Operations

- Mission
  - To ensure the timely and effective delivery of high quality and cost effective mission support services across the FDA and its centers, and coordinate emergency preparedness and response activities for incidents involving FDA-regulated products across FDA and its stakeholders.
- Vision
  - Excellence and innovation in delivering mission support services and emergency preparedness and response, exceeding stakeholder expectations.

Responsibilities of USFDA

- Protection of the public health by assuring that foods (except for meat from livestock, poultry and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary and properly labeled
- Ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective

Responsibilities of USFDA

- Protecting the public from electronic product radiation
- Assuring cosmetics and dietary supplements are safe and properly labeled
- Regulating tobacco products
- Advancing the public health by helping to speed product innovations

Code of Federal Regulation

- The Code of Federal Regulations (CFR) is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal Government
- Title 21 of the CFR is reserved for rules of the Food and Drug Administration.
- CFR 21 was received from the Government Printing Office (GPO) and contains the most recently received revision.
- Food and Drugs: Parts 1 to 1499 different types of parts to food, drug , cosmetic and medical devices and etc.

Code of Federal Regulation
Parts of 21 CFR

- 21 CFR part 11- Electronic submission and Electronic signature
- 21 CFR part 50- Protection of human subjects
- 21 CFR part 54- Financial Disclosure by Clinical Investigators
- 21 CFR part 56- Institutional Review Board
- 21 CFR part 101-Food Labeling
- 21 CFR part 104-Nutritional quality guidelines for foods
- 21 CFR part 106- Infant Formula Quality Control Procedures

Code of Federal Regulation
Parts of 21 CFR

- 21 CFR part 110- CGMP Practices in manufacturing packing or holding human food
- 21 CFR part 210- CGMP Practices in manufacturing, packing or holding of Drugs
- 21 CFR part 211- CGMP Practices for finished pharmaceuticals
- 21 CFR part 225- CGMP Practices for medicated feeds
- 21 CFR part 312- Investigational new drug application
- 21 CFR part 314- Application for FDA Approval to Market a New Drug
- 21 CFR part 600 to 680- For biological products

FDA regulatory approaches to marketing Approval

- The Food and Drug Administration's regulatory approaches to marketing approval of the products it regulates are as varied as the products themselves
- These differences are dictated by the laws FDA enforces and the relative risks that the products pose to consumers
- Some products - such as new drugs and complex medical devices must be proven safe and effective before companies can put them on the market

FDA regulatory approaches to marketing Approval (contd)

- The agency also must approve new food additives before they can be used in foods
- Other products such as x-ray machines must measure up to performance standards
- Some products such as cosmetics and dietary supplements can generally be marketed with no prior approval

Approval process for a new drug

- Drug companies seeking FDA approval to sell a new prescription drug in the United States must test it in various ways
- First are laboratory and animal tests
- Next are tests in humans to see if the drug is safe and effective when used to treat or diagnose a disease
- After testing the drug, the company then sends FDA an application called a New Drug Application (NDA)
- Some drugs are made out of biologic materials. Instead of an NDA, new biologic drugs are approved using a Biologics License Application (BLA)

NDA or BLA application

- The application includes:
  - The drug's test results
  - Manufacturing information to demonstrate the company can properly manufacture the drug
  - The company's proposed label for the drug
- The label provides necessary information about the drug, including uses for which it has been shown to be effective, possible risks, and how to use it
- If a review by FDA physicians and scientists shows the drug's benefits outweigh its known risks and the drug can be manufactured in a way that ensures a quality product, the drug is approved and can be marketed in the United States

FDA Drug Review

- If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug
- The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it

New Drug Application

- A New Drug Application (NDA) tells the full story of a drug. Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied
- A drug developer must include everything about a drug - from preclinical data to Phase 3 trial data - in an NDA. Developers must include reports on all studies, data, and analyses. Along with clinical results, developers must include:
- Proposed labeling
- Safety updates
- Drug abuse information

New Drug Application (contd)

- Patent information
- Any data from studies that may have been conducted outside the United States
- Institutional review board compliance information
- Directions for use

New Drug Application Review

- Once FDA receives an NDA, the review team decides if it is complete. If it is not complete, the review team can refuse to file the NDA. If it is complete, the review team has 6 to 10 months to make a decision on whether to approve the drug. The process includes the following:
- Each member of the review team conducts a full review of his or her section of the application. For example, the medical officer and the statistician review clinical data, while a pharmacologist reviews the data from animal studies. Within each technical discipline represented on the team, there is also a supervisory review

New Drug Application Review (contd)

- FDA inspectors travel to clinical study sites to conduct a routine inspection. The Agency looks for evidence of fabrication, manipulation, or withholding of data
- The project manager assembles all individual reviews and other documents, such as the inspection report, into an “action package.” This document becomes the record for FDA review. The review team issues a recommendation, and a senior FDA official makes a decision

New Drug Application Approval

- In cases where FDA determines that a drug has been shown to be safe and effective for its intended use, it is then necessary to work with the applicant to develop and refine prescribing information
- This is referred to as “labeling.” Labeling accurately and objectively describes the basis for approval and how best to use the drug

New Drug Application Approval (contd)

- Often, though, remaining issues need to be resolved before the drug can be approved for marketing. Sometimes FDA requires the developer to address questions based on existing data. In other cases, FDA requires additional studies
- At this point, the developer can decide whether or not to continue further development
- If a developer disagrees with an FDA decision, there are mechanisms for formal appeal

FDA Advisory Committees

- Often, the NDA contains sufficient data for FDA to determine the safety and effectiveness of a drug. Sometimes, though, questions arise that require additional consideration.
- In these cases, FDA may organize a meeting of one of its Advisory Committees to get independent, expert advice and to permit the public to make comments.
- These Advisory Committees include a Patient Representative that provides input from the patient perspective. Learn more about FDA Advisory Committees.

References

- https://www.fda.gov/Drugs/default.html
- https://www.fda.gov/downloads/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandingover-the-countermedicines/ucm093550.pdf