

# Origins and Organizational Structure of FDA Overview of Regulation of Biological Products

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# Biologics Regulation— Where we start...

It started with  
a horse...

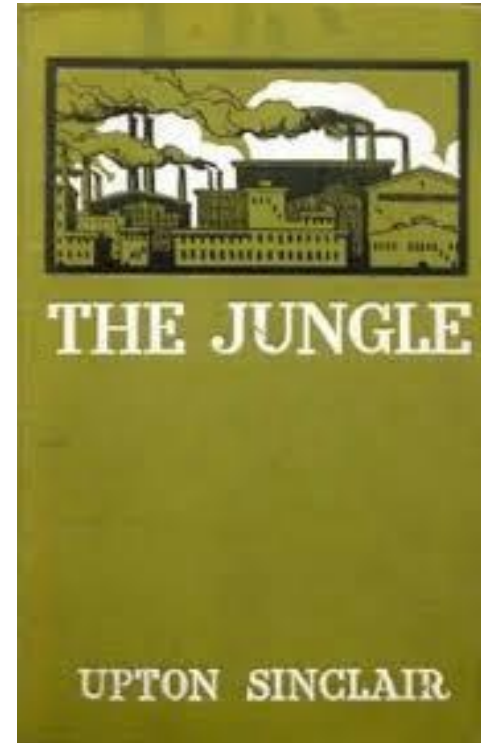


## 1902 Biologics Control Act:

In 1901, a 5-year-old girl died of tetanus in St. Louis, Missouri after being given a diphtheria anti-toxin. Investigations found that the St. Louis Board of Health produced the contaminated vaccine using the blood of a horse infected with tetanus. While the infected horse, Jim, was killed, the Board of Health continued to use the serum to treat diphtheria. It was later discovered that 12 other children had died from the same contaminated vaccines in St. Louis.

# Biologics Regulation— Where we start...

- 1906 Food and Drugs Act
  - Banned adulterated or misbranded food and drugs
  - Regulated product labeling
  - No pre-market approval yet
    - Safety
    - Efficacy



# Landmark Legislation— How did we get here...

- 1902—Biologics Control Act
- 1906—Pure Food and Drug Act
- 1938—Federal Food Drug and Cosmetic Act
- 1944—Public Health Service Act
- 2007—Food and Drug Administration Modernization Act (FDAMA)
- 2010—Biologics Price Competition and Innovation Act (BPCIA)
- 2012—Food and Drug Administration Safety and Innovation Act (FDASIA)
- 2016—21st Century Cures Act

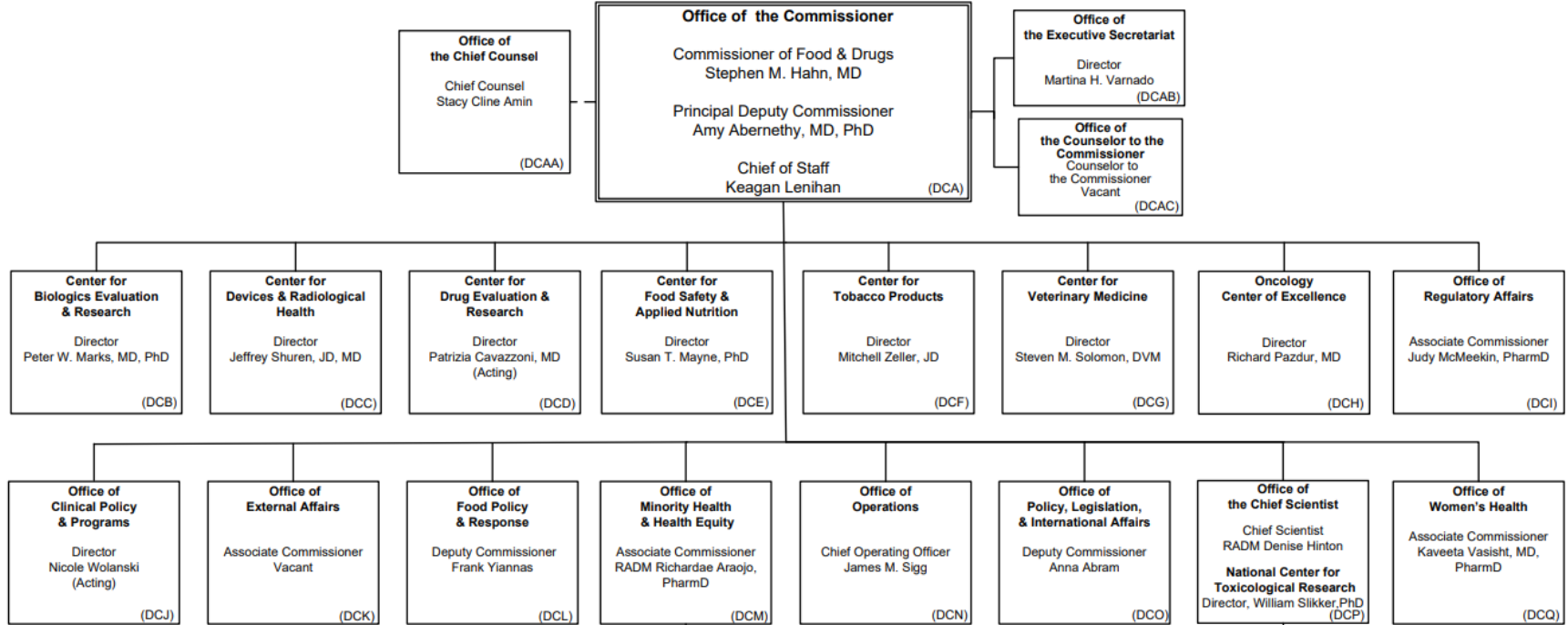
# Food and Drug Administration

- FDA Mission
  - ...**protecting** the public **health** by ensuring the **safety**, **efficacy**, and **security** of human and veterinary drugs, **biological products**, and medical devices; ...



**Department of Health and Human Services  
Food and Drug Administration**

September 2020

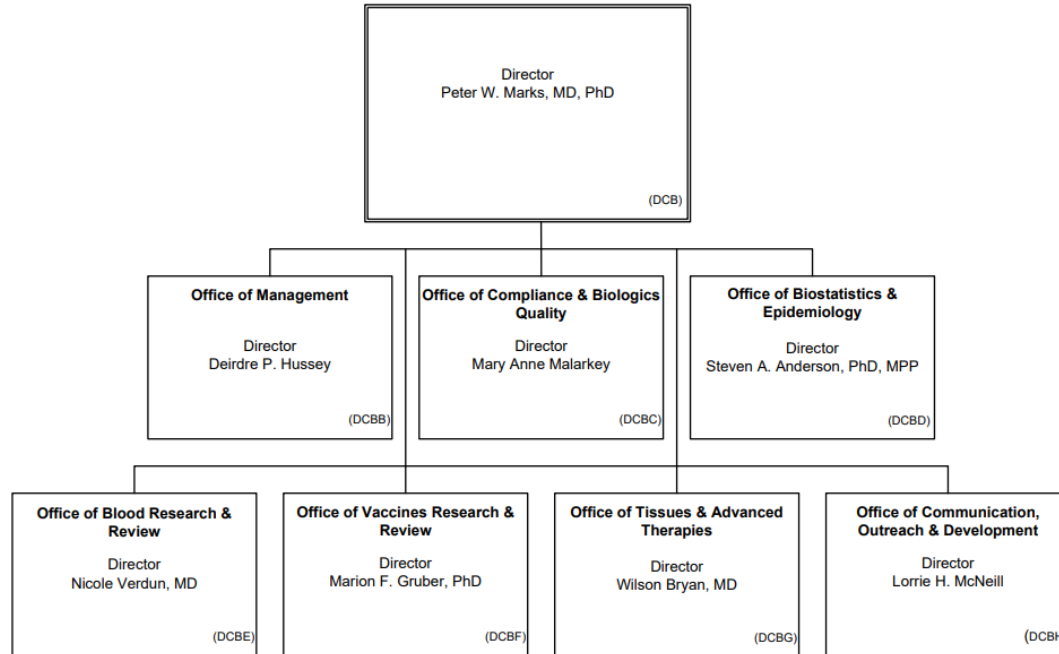


**Legend:**

- — Direct report to DHHS General Counsel
- ..... Direct report to the FDA Commissioner with operational oversight from the Office of the Chief Scientist

Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research

September 2020



# Other agencies “regulating” biologics

- Center for Medicare and Medicaid Services (CMS)
- HHS Office of Inspector General (OIG)
- National Institutes of Health (NIH)
- Centers for Disease Control and Prevention (CDC)
- Animal and Plant Health Inspection Service (APHIS)

# **FDA's Regulation of Biologics From Policy to Action**

# What is a Biologic?

In this Section:

- The term “**biological product**” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, **protein** (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the **prevention, treatment, or cure of a disease or condition of human beings.**

42 U.S.C 262(i)(1)

# What is a Biologic? (cont.)

- “Protein” definition changed by Further Consolidated Appropriations Act, 2020.
- BPCI Act amended biologics definition: a “protein (except any chemically synthesized polypeptide).”
- FCA Act removed “(except any chemically synthesized polypeptide)”
- FDA Final Rule (Feb 2020) - the term protein means any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size.
- See <https://www.govinfo.gov/content/pkg/FR-2020-02-21/pdf/2020-03505.pdf>

# Is a Biologic a Drug?

Yes.

- The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) **articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals**; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). ...

21 U.S.C 321(g)(1)

# FDA Legal Source of Authority to Regulate Biologics

- Acts of Congress (FDA Doesn't Write the Law)
  - Federal Food Drug and Cosmetic Act (FDCA)
    - New Drug Approval (NDA) (Section 505)
    - Abbreviated New Drug Application (ANDA) (Section 505(j))
  - Public Health Service Act (PHS Act)
    - Biologic License Application (BLA) (Section 351)
    - Abbreviated Biologic License Application (aBLA) (Section 351(k))

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# March 23, 2020

- Biologics Price Competition and Innovation Act turns 10 years old
- **Biological Products** approved under Section 505 of the FDCA “shall be deemed” to be licensed under Section 351 of the PHS Act. (Licensed BLA)
- All biologics must go through the BLA pathway.

# Implementation of governing statute

- **Code of Federal Regulations**
  - Notice and Comment procedure
  - Must implement governing statute
- **Guidance documents**
  - Guidance for Industry (FDA's current thinking)
- **Compliance Policy Guides (CPGs)**
  - Guidance for FDA staff

# Industry Participation in Shaping Policy

- 1) **Lobbying Congress**—new statute
- 2) **Comment** on proposed regulations (proposed guidance documents)
- 3) **FDA public meetings**
- 4) **Citizen Petitions**—seeking definite FDA action in a specific situation
- 5) **Judicial Review**
- 6) **Application Process**—e.g. Biosimilar Product Development (BPD) Program

# Mechanisms in which FDA Regulatory Requirements are Solidified

- 1) **Enforcement Actions and letters**
- 2) **Citizen Petition Responses**
- 3) **Informal statements and advice**
- 4) **Miscellaneous publications**
- 5) **Product specific proceedings**

**Policy in Action—Moving from Theory to Practice**

# Standards—Global harmonization and acceptance

## 1) International Conference on Harmonization (ICH)

- ICH's mission is to achieve greater harmonization worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.

## 2) United States Pharmacopeia (USP)

- 1906 Pure Food and Drug Act designated USP and National Formulary (NF) as official compendia.
- Close collaboration of FDA and USP

# Freedom of Information Act (FOIA)

- Allows member of public to request access to records not normally prepared for public distribution
- Exceptions
  - Nine exemptions (created by Congress)
  - **No. 4-Trade secret or confidential commercial or financial information**
  - No. 5-Privileged inter- or intra- agency communication
  - No. 6-Individual Personal Privacy

# Freedom of Information Act (FOIA)

Preventing disclosure of information submitted to FDA

- Under 21 CFR 20.61 FDA must notify a party of a FOIA request.
- 5 days to object to disclosure.
- If FDA decides to disclose, it must give notice to party.
- Party may then bring a reverse FOIA case in district court to seek relief from disclosure

# What is an Emergency Use Authorization (EUA)

- Authorization of the emergency use of certain medical products under sections 564, 564A, and 564B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as amended or added by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)
- Enacted to sustain and strengthen national preparedness for public health, military, and domestic emergencies involving chemical, biological, radiological, and nuclear (CBRN) agents, including emerging infectious disease threats such as pandemic influenza

# EUA Authorizations

- Commissioner can authorize the emergency use of an unapproved medical product or an unapproved use of an approved medical product for certain emergency circumstances after the HHS Secretary has made a declaration of emergency or threat justifying authorization of emergency use
- The Commissioner may issue an EUA to allow an medical counter measures (MCM) to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by a CBRN agent when there are no adequate, approved, and available alternatives.

# Eligible FDA-approved Medical Products

- Empower FDA to extend the expiration date of an eligible FDA-approved MCM stockpiled for use in a CBRN emergency and to establish appropriate conditions relating to such extensions, such as appropriate storage, sampling, and labeling;
- Permit FDA to waive otherwise-applicable current good manufacturing practice (CGMP) requirements (e.g., storage or handling) to accommodate emergency response needs;
- Allow emergency dispensing of MCMs during an actual CBRN emergency event without requiring an individual prescription for each recipient of the MCM or all of the information otherwise required or by responders who may not otherwise be licensed to dispense, if permitted by state law in the state where such dispensing occurs or if in accordance with an order issued by FDA; and
- Permit the Centers for Disease Control and Prevention (CDC) to create and issue “emergency use instructions” (EUI) concerning the FDA-approved conditions of use for eligible product