Overview of U.S. FDA Center for Biologics Evaluation and Research

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US Food and Drug Administration

Application of Pharmacovigilance to U.S. FDA Regulatory Decisions for Vaccines

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Outline

- FDA: a regulatory agency granted the authority to ensure that U.S. licensed vaccines are safe and effective

- Structure of FDA and the Center for Biologics Evaluation and Research

- Historical timeline of the expansion of vaccine regulation in the United States (optional topic)
FDA Legal Framework

Statutes
(enacted by Congress, signed by President)

Regulations
(FDA)
Main Statutes Pertinent to Vaccine Safety

- Federal Food, Drug and Cosmetic Act
  - Amended by the Food and Drug Administration Amendments Act of 2007

- Public Health Service Act

- National Childhood Vaccine Injury Act
US Code of Federal Regulations (CFR)

FDA implements statutes through regulations

- 21 CFR 600-680 Biological Product Standards
- 21 CFR 314.126 Adequate and well-controlled trials
- 21 CFR 312 Investigational New Drug Application
- 21 CFR 210-211 Good Manufacturing Practices
- 21 CFR 58 Good Laboratory Practices
- 21 CFR 56 Institutional Review Boards
- 21 CFR 50 Protection of Human Subjects
National Childhood Vaccine Injury Act

- Designed to stabilize supply and cost of vaccines by addressing liability
  - Created a “no fault” compensation system
  - The vaccine injury table lists conditions presumed to be caused by vaccines within specific timeframes
  - Financed through excise tax on recommended vaccine products

- Created additional U.S. vaccine safety infrastructure
  - National Vaccine Program Office to coordinate HRSA, CDC, FDA, NIH
  - Vaccine Information Statements
  - Institute of Medicine review
  - Vaccine adverse event reporting system (VAERS)

http://www.hrsa.gov/vaccinecompensation/index.html
Regulatory Definition of Safety

21 CFR 600.3

“relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time”
Unique Safety Considerations for Preventive Vaccines

Safety “in relation to the condition of the recipient. . .”

- Millions of healthy people, including young infants and children, receive vaccines each year
- State governments mandate many vaccines for children attending public schools or day care centers
- Individual risk for disease prevented by vaccination may be low (e.g., diphtheria, polio)

...thus, low tolerance for vaccine-associated risks
Safety throughout the product lifecycle

- Characterization of product and manufacturing processes
- Review of safety data from toxicological studies and clinical trials
- Inspection of manufacturing, laboratory, and clinical research facilities
- Post licensure safety surveillance
- Enforcement
Executive Authority

President of the United States

Secretary of Health and Human Services

Commissioner of Food and Drugs
The Office of Medical Products and Tobacco also includes the Office of Special Medical Programs, Office of Combination Products, and the Office of Good Clinical Practice.
How many people are employed by FDA and in what areas do they work?

As of Oct. 1, 2009, FDA employs the following numbers* of people in its centers/offices:

<table>
<thead>
<tr>
<th>Center Name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center for Biologics Evaluation and Research (CBER)</td>
<td>946</td>
</tr>
<tr>
<td>Center for Drug Evaluation and Research (CDER)</td>
<td>2,889</td>
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<tr>
<td>Center for Devices and Radiological Health (CDRH)</td>
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<tr>
<td>Center for Food Safety and Applied Nutrition (CFSAN)</td>
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<tr>
<td>Center for Tobacco Products (CTP)**</td>
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<tr>
<td>Center for Veterinary Medicine (CVM)</td>
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<tr>
<td>National Center for Toxicological Research (NCTR)</td>
<td>217</td>
</tr>
<tr>
<td>Office of the Commissioner (OC)</td>
<td>859</td>
</tr>
<tr>
<td>Office of Regulatory Affairs (ORA)</td>
<td>3,895</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11,516</td>
</tr>
</tbody>
</table>

*Full time equivalents  **Estimate based on the budget enacted by Congress for the fiscal year ending Sept. 30, 2010
Pharmacovigilance/epi at CBER

Office of Biostatistics and Epidemiology
Robert Ball

Division of Biostatistics
Research Group (ADR)
Risk Assessment Group

Division of Epidemiology
David Martin
Craig Zinderman (acting)

Analytic Epidemiology Branch (AEB)
Wei Hua (acting)

Pharmacovigilance Branch (PVB)
Michael Nguyen (acting)

Postmarketing surveillance

Slide courtesy Michael Nguyen
Summary

- FDA derives its authority to regulate vaccines from statutes enacted by Congress and signed by the President.

- Vaccines are currently regulated by the Center for Biologics Evaluation and Research.

- Expansion of regulatory authority for vaccines and other medical products has often followed disasters which gained the attention of the public.
The Cow Pox or the Wonderful Effects of the New Inoculation

Anti-Vaccine Society / J. Gilray, 1802
Milestones (1798 – 1930)

Marine Hospital Service
(1st US public health agency)

Biologics Control Act
(inspections, manufacturer license)

Laboratory of Hygiene
(1st bacteriologic lab)

National Institutes of Health

1798
1887
1902
1930

1884
1901
1906

Koch’s Postulates

Food and Drugs Act
(misbranded, adulterated)

13 deaths (tetanus from diphtheria antitoxin)
9 deaths (tetanus from smallpox vaccine)
Milestones (1930 – Present)

**Cutter Incident**
(40,000 cases abortive polio, 51 paralyzed)

**Elixir of Sulfanilamide**
(107 deaths)

**Food, Drug and Cosmetic Act**
(proof of safety, advertising)

**Thalidomide**
**Kefauver-Harris Drug Amendments**
(proof of efficacy)
Milestones (1930 – Present)

1937
- Elixir of Sulfanilamide (107 deaths)

1938
- Cutter Incident
- Division of Biologics (NIH) (40,000 cases abortive polio, 51 paralyzed)

1955
- Kefauver-Harris Drug Amendments (proof of efficacy)

1958
- Thalidomide
- Bureau of Biologics (FDA)

1972
- Food and Drug Administration Modernization Act (fast-track approval, market exclusivity)

1992
- Prescription Drug User Fee Act

1997
- Food, Drug and Cosmetic Act (proof of safety, advertising)

2004
- FDAAA

2006
- Vioxx Withdrawn

1997
- Prescription Drug User Fee Act

2006
- FDAAA