Drug Review and Related Activities in the United States

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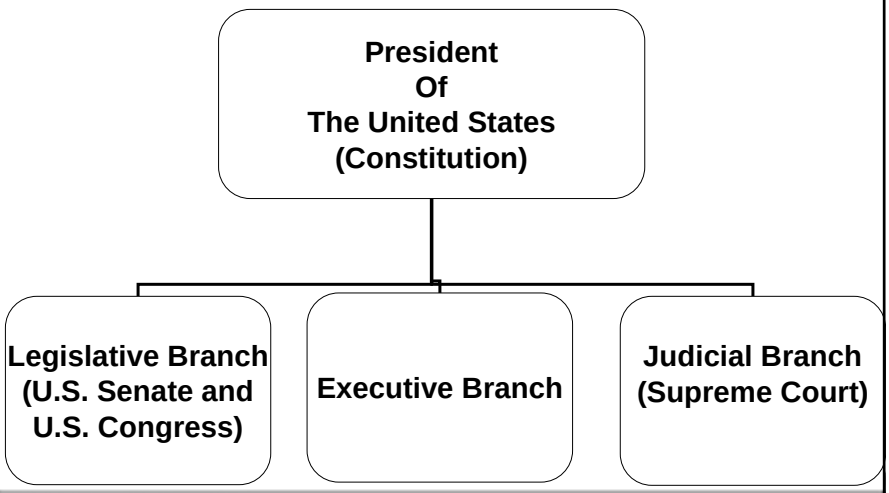
Deputy Director
Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration

Session Overview

- Organizational structure
- Laws and regulations
- Investigational New Drugs (INDs)
- New Drug Application (NDA) Reviews
- Postmarketing Activities

CDER Forum for International Drug Regulatory Authorities

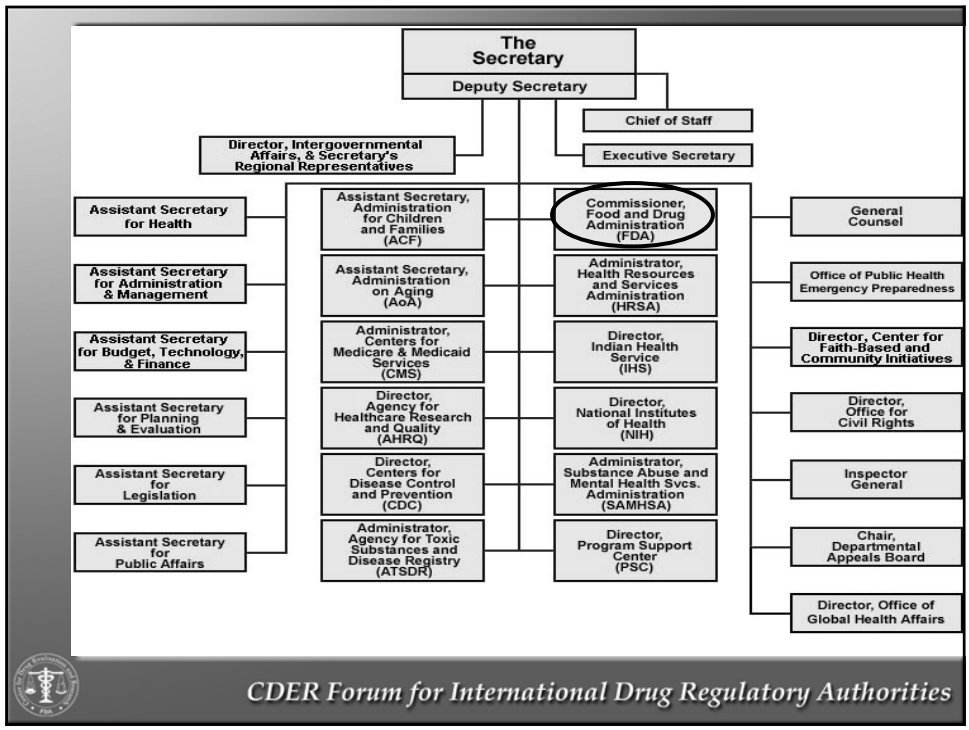
U.S. Government Framework

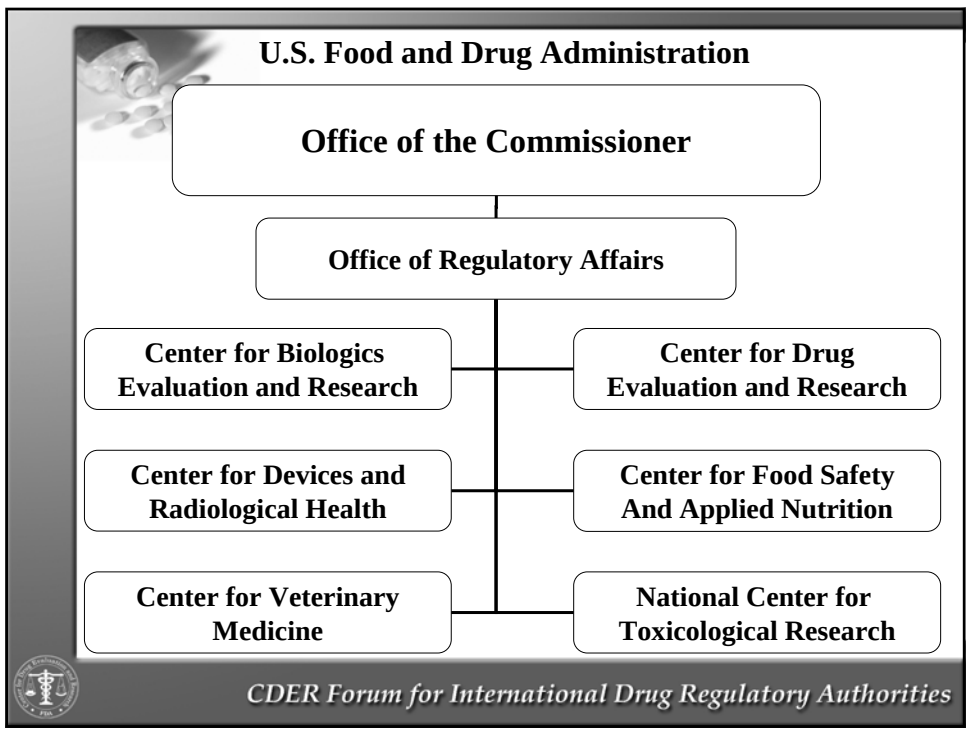


Executive Branch

The President's Cabinet

- Department of Agriculture
- Department of Commerce
- Department of Defense
- Department of Education
- Department of Energy
- ***Department of Health and Human Services –***
  - **Secretary Michael O. Leavitt**
- Department of Homeland Security
- Department of Housing and Urban Development
- Department of the Interior
- Department of Justice
- Department of Labor
- Department of State
- Department of Transportation
- Department of the Treasury
- Department of Veterans Affairs


The Secretary
Deputy Secretary
Chief of Staff
Executive Secretary
Director, Intergovernmental Affairs, & Secretary's Regional Representatives
Assistant Secretary for Health
Assistant Secretary for Administration & Management
Assistant Secretary for Budget, Technology, & Finance
Assistant Secretary for Planning & Evaluation
Assistant Secretary for Legislation
Assistant Secretary for Public Affairs
Assistant Secretary, Administration for Children and Families (ACF)
Assistant Secretary, Administration on Aging (AoA)
Administrator, Centers for Medicare & Medicaid Services (CMS)
Director, Agency for Healthcare Research and Quality (AHRQ)
Director, Centers for Disease Control and Prevention (CDC)
Administrator, Agency for Toxic Substances and Disease Registry (ATSDR)
Commissioner, Food and Drug Administration (FDA)
Administrator, Health Resources and Services Administration (HRSA)
Director, Indian Health Service (IHS)
Director, National Institutes of Health (NIH)
Administrator, Substance Abuse and Mental Health Svcs. Administration (SAMHSA)
Director, Program Support Center (PSC)
General Counsel
Office of Public Health Emergency Preparedness
Director, Center for Faith-Based and Community Initiatives
Director, Office for Civil Rights
Inspector General
Chair, Departmental Appeals Board
Director, Office of Global Health Affairs
CDER Forum for International Drug Regulatory Authorities


U.S. Food and Drug Administration
Office of the Commissioner
Office of Regulatory Affairs
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Center for Devices and Radiological Health
Center for Food Safety And Applied Nutrition
Center for Veterinary Medicine
National Center for Toxicological Research
CDER Forum for International Drug Regulatory Authorities

Mission

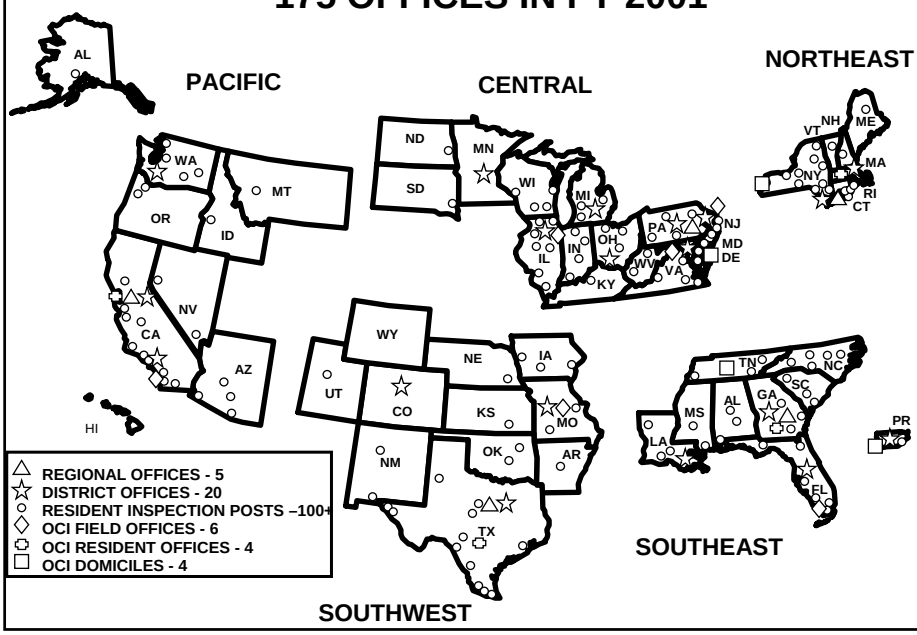
1. Promote public health

2. Protect public health

3. Participate with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements;

4. Carry out (1) through (3) in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors and retailers of regulated products.

OFFICE OF REGULATORY AFFAIRS
175 OFFICES IN FY 2001



Industry
Guidance

http://www.access.gpo.gov/nara/cfr/

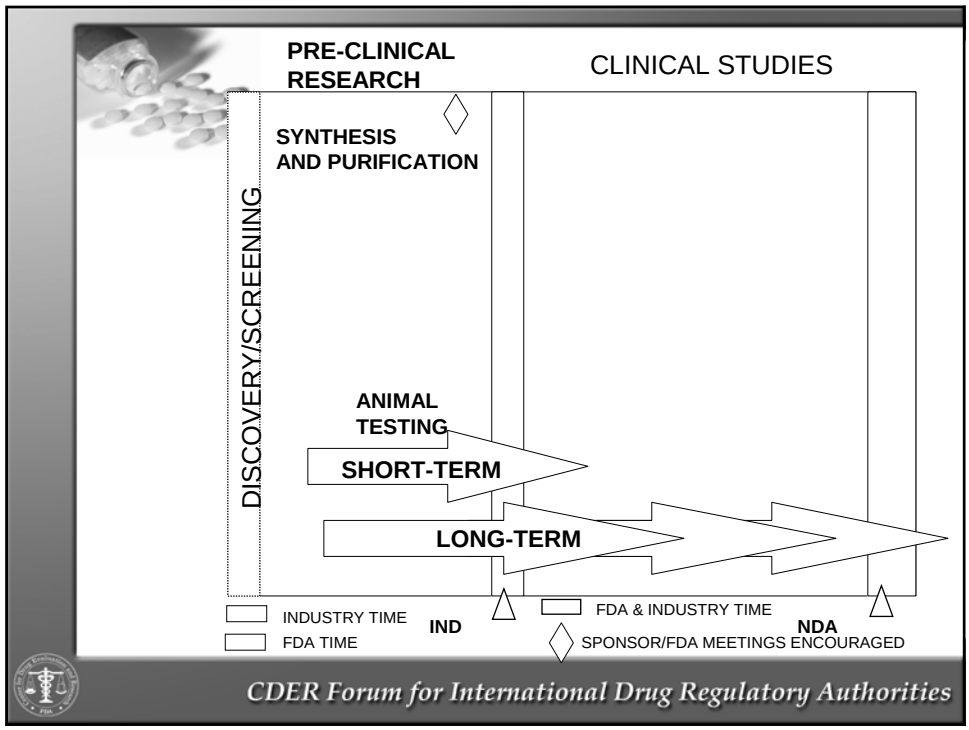
PRE-CLINICAL RESEARCH

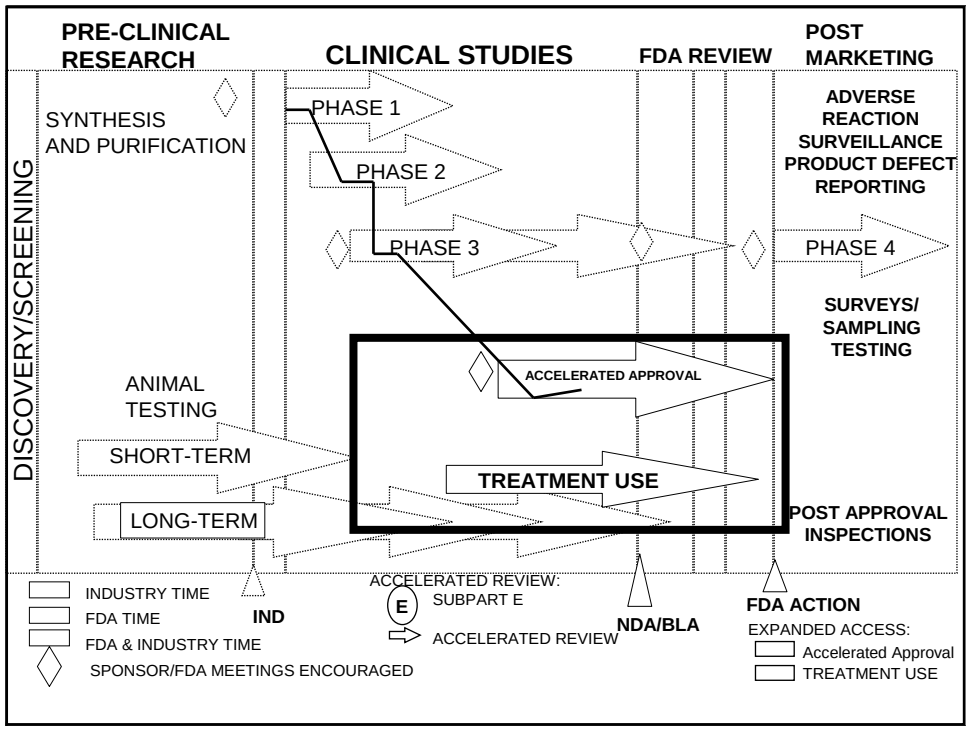
DISCOVERY/SCREENING

SYNTHESIS AND PURIFICATION ◇

▭ INDUSTRY TIME ▭ FDA & INDUSTRY TIME

▭ FDA TIME ◇ SPONSOR/FDA MEETINGS ENCOURAGED

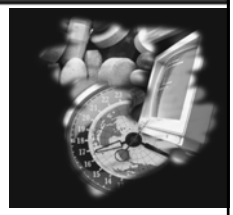

PRE-CLINICAL
RESEARCH
CLINICAL STUDIES
SYNTHESIS
AND PURIFICATION
DISCOVERY/SCREENING
ANIMAL
TESTING
SHORT-TERM
LONG-TERM
INDUSTRY TIME
FDA TIME
IND
FDA & INDUSTRY TIME
SPONSOR/FDA MEETINGS ENCOURAGED
NDA
CDER Forum for International Drug Regulatory Authorities



New Drug Application (NDA) or Biologic License Application (BLA) contains the following:

- **Pre-clinical studies**
- **Human clinical studies**
- **Manufacturing details**
- **Labeling**
- **Additional information**

Prescription Drug User Fee Act (PDUFA)



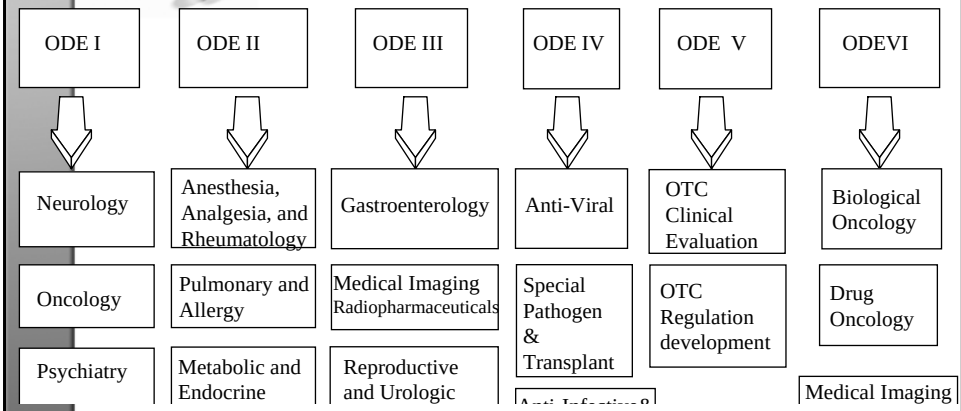
http://www.fda.gov/oc/pdufa/default.htm

- Permits CDER/CBER to charge pharmaceutical manufacturers a fee to review drug applications
- These fees provide appropriate resources to accelerate the review of applications
- Not the only source of funds for CDER/CBER
- Funds go directly to CDER/CBER, not individuals

The NDA Review Process in CDER

- Submitted to Central Document Room
  - paper or electronic
- Processed and sent to appropriate review Division
- Priority status determined
  - Standard: 10 months
  - Priority: 6 months
  - try to determine at time of acknowledgement letter, MUST be determined by filing date

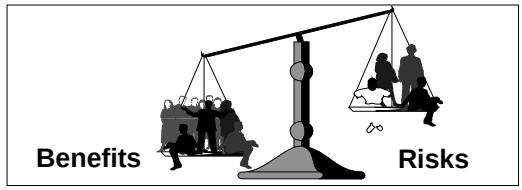
Drug Product Divisions



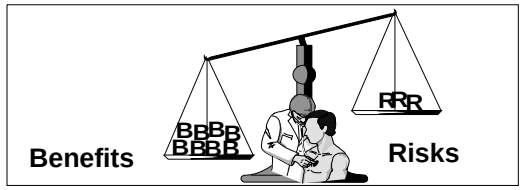
Review Team

- Project Manager
- Medical Officer
- Chemist
- Microbiologist
- Statistician
- Pharmacologist
- Establishment/Facility Reviewer
- Support Personnel

FDA
evaluates benefits/risks for the population



Provider
evaluates benefits/risks for a patient



Patient
evaluates benefits/risks in terms of personal values

NDA Review in CDER: Interactions Throughout the Process

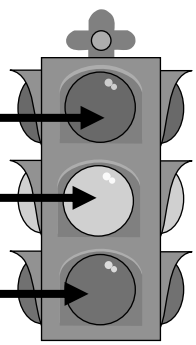
- Meetings and Tcons
  - advice is free of charge (unlike other regulatory agencies)
  - several allowable in regulations
    - status (usually tcon)
    - labeling
- Advisory Committee Meetings
  - "controversial" products
  - most NMEs

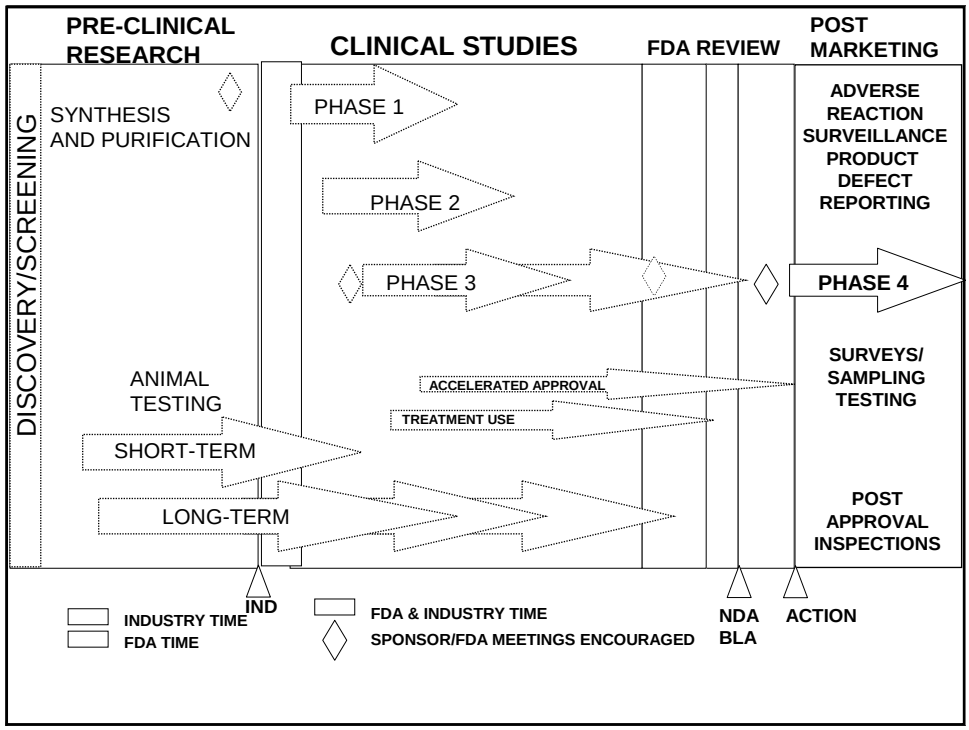
Advisory Committee

- Panel of OUTSIDE experts
- Provide advice and opinions to the FDA drug review team
- FDA advisory committee Information:
  http://www.fda.gov/oc/advisory/default

NDA Review in CDER: The Final Action(s)

- Not approvable (NA)
- Approvable (AE)
- Approval (AP)

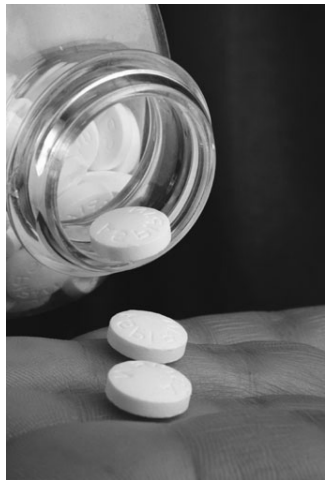




Post-market Surveillance

Office of Drug Safety

- Division of Drug Risk Evaluation
- Division of Medication Errors and Technical Support
- Division of Surveillance, Research, and Communication Support



AERS

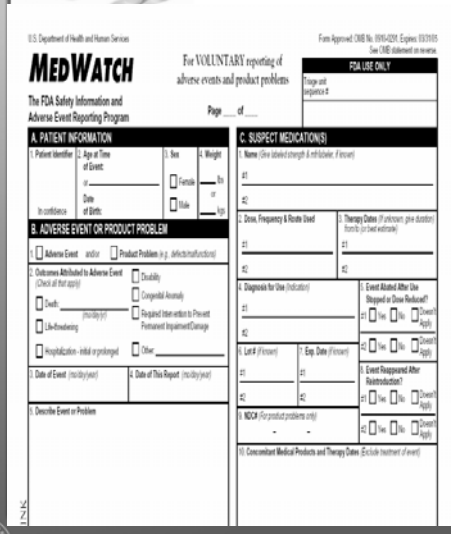
Adverse Event Reporting System (AERS)

- Database
- Internationally compatible

Office of Drug Safety (ODS) uses AERS to:

- Triage
- Review
- Assess risk

Post-marketing surveillance


U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events and product problems

FDA USE ONLY

A. PATIENT INFORMATION

B. ADVERSE EVENT OR PRODUCT PROBLEM

C. SUSPECT MEDICATION(S)

- Limited power of Phase 3 trials to detect rare events
  - Rule of 3 – To detect event with incidence of 1/1000, need 3000 patients
  - Restricted patient population in clinical trials
- Passive voluntary reporting via Medwatch ----- most events not reported (numerator)

  - total exposure not known (denominator)
- Post-marketing events reported to manufacturer or directly to FDA

Potential Regulatory Action for Postmarketing Safety Issues

- Labeling Change
- "Dear Doctor" letter (for specific warnings)
- Restricted use
- Restricted distribution
- Patient Medication guide
- Product withdrawal

MedWatch Website

- Safety Information Retrieval
- Reporting for Drugs,Devices, Biologics and Dietary Supplements

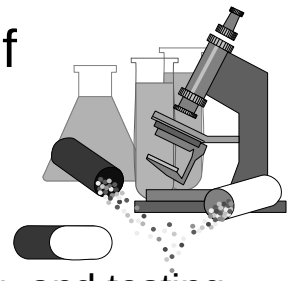
www.fda.gov/medwatch

DDMAC
(Division of Drug Marketing Advertising and Communications)

Promotion of Prescription Drug Products

- Promotional Materials Review
  Guidance and policy development
- Research
- Surveillance and enforcement

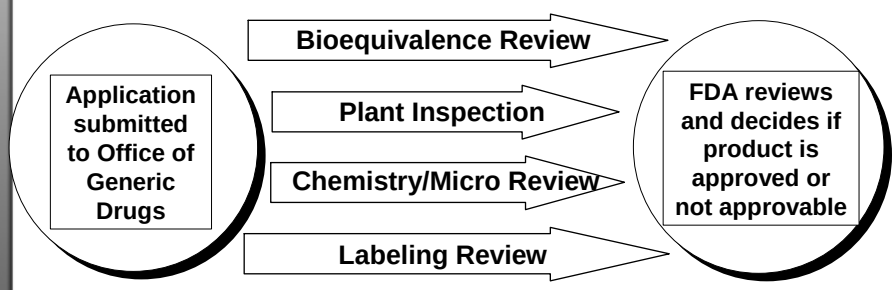
CDER's Office of Compliance



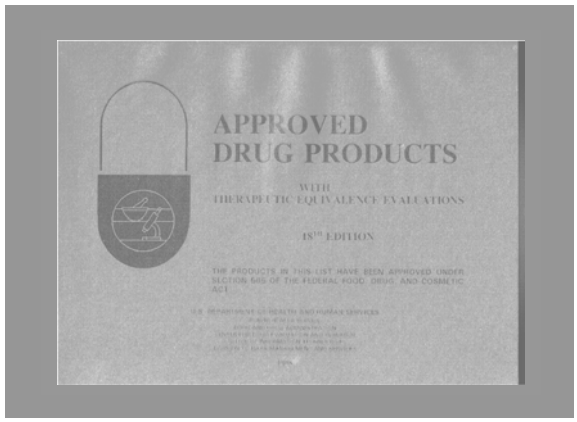
- Sets labeling, manufacturing, and testing standards
- Monitors the quality of marketed drugs
- Evaluates, classifies, and recommends human drug recalls

Generic Drug Review Process

Determine if application is acceptable



Approved Drug Products with Therapeutic Equivalence Evaluations "Orange Book"



http://cdsmlweb1/ob/index.htm

New OTC drug

The sponsor/manufacturer submits a new drug application (NDA) as an OTC drug.

Prescription to OTC Switch

The drug company submits a supplement to the new drug application NDA to "switch" to OTC.

OTC Drug Review Process

FDA reviews active ingredients and finds they are safe and effective.

http://www.fda.gov/cder/Offices/OTC/industry.htm.

FDA Priorities

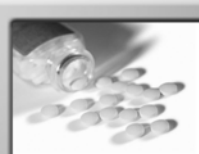
Risk Management

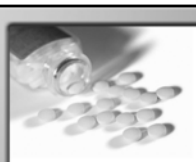
Better Consumer Information

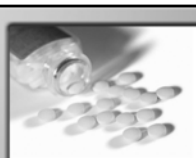
Postmarketing Safety

Counterterrorism

Effective Regulation/ Strong Science







CDER's Internet Home Page

http://www.fda.gov/cder

http://www.fda.cder/offices/ddi/pathfinder

Drug Information Contacts

888.INFO FDA

301 827 4573

druginfo@cder.fda.gov