BIOE 301

Lecture Twenty-Two

FDA

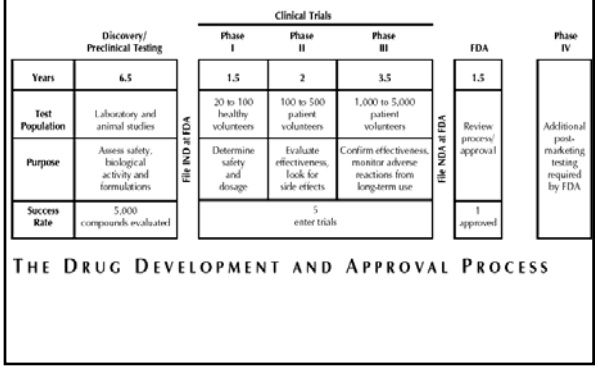
- Regulates products whose annual sales account for ¼ of consumer spending in US
- Responsible for ensuring SAFETY and EFFICACY of CHEMICAL, BIOLOGICAL agents and sophisticated medical DEVICES
- Safe:
  - Probable benefits to health for intended use outweigh any probable risk of harm
- Effective:
  - Device does what it is supposed to do in a reliable fashion

History of Regulation

- 1906
  - Food and Drug Act
  - Can't lie on label
- 1938
  - Food, Drug and Cosmetic Act
  - Premarket notification
- 1962
  - Drug amendments to FD&C Act
  - Premarket approval
- 1976
  - Medical Device Amendments to FD&C Act
- 1994
  - Dietary Supplement Health Education Act

Today

- CANNOT mention disease
- CAN make claims that food can affect structure of function of body
- Examples:
  - CANNOT say that a product reduced cholesterol but CAN say it maintains healthy cholesterol levels
  - CANNOT say echinacea cures disease, but CAN say it has natural antibiotic activities and is considered an excellent herb for infections of all kinds



THE DRUG DEVELOPMENT AND APPROVAL PROCESS

Post-Marketing Surveillance

- Vioxx – withdrawn from market
- Celebrex – black box warning
- Bextra – sales suspended
- http://www.fda.gov/medwatch/
- http://www.npr.org/templates/story/story.php?storyId=4500447
- http://www.npr.org/templates/story/story.php?storyId=5229443
- http://www.npr.org/templates/story/story.php?storyId=5336272

Regulation of Medical Devices

- FDA did not regulate devices before 1938
- 1938:
  - FDA could only challenge sale of products it believed were unsafe
  - Could only remove them from the market after patient injuries
- 1960s:
  - Rapid innovation in medical technology
  - Tried to regulate many as drugs: contact lenses, IUDs
  - Catastrophic failures of heart valves and pacemakers
- 1970s:
  - Broad recognition that different rules were needed to regulate devices

1976

- Device amendments to FD&C Act:
  - No single policy would work for all devices
    - Tongue depressor
    - Artificial heart

1976: Device amendments to FD&C Act

- Three classes of devices:
  - Class I:
    - Pose least risk to patient
    - Not life sustaining
    - GMP, proper record keeping required
    - 30% of devices
    - X-ray film, tongue depressors, stethoscopes
  - Class II:
    - Not life sustaining, but must meet performance standards
    - Blood pressure monitors, Catheter guide wires
    - 60% of devices
  - Class III:
    - Pose greatest risk to patient
    - For use in supporting or sustaining human life
    - 10% of devices
    - Stents, heart valves, LVADs
    - Require GMP, failure modes analysis, animal tests, human clinical studies under IDE

Role of CDRH

- Ensure that products coming to market have more benefit than risk
- Ensure that products are labeled so that practitioners and patients know what to expect from their use
- Regulates 1,700 types of devices
- 23,000 registered manufacturers
- 1996: received 20,236 device related submissions

Device Approval Process

- Device + intended use considered together
- Manufacturer submits request for marketing approval
- Advisory panel:
  - One consumer representative (non-voting)
  - One industry representative (non-voting)
  - Physicians and scientists
- FDA not required to follow recommendations of panel, although they usually do

IDE

- Investigational Device Exemption
  - Enables experimental use of high risk device
  - Must have positive engineering and animal data
  - First give approval for feasibility studies with small number of patients
  - Then proceed to multi-center trials
  - Larger data sets frequently show results from small sample sets are not true

Humanitarian Use Exemption

- Device designed to treat or diagnose condition that affects <4,000 patients/year
- Device would not otherwise be available without exemption
- No comparable device is available
- Patients will not be exposed to unreasonable or significant risk of injury or illness by device

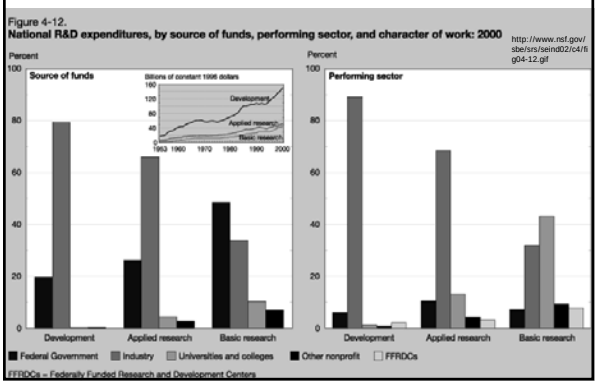
Medical Device Reporting

- System to detect device related problems in a timely manner
- Serious injuries or deaths that may have been caused by or related to a a medical device must be reported to the manufacturer of the device within 10 days
- Must be reported to the FDA within 10 days

Recently Approved Devices

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/MDA/mda-list.cfm?list=1
- NIRflex Stent System
  - http://www.fda.gov/cdrh/mda/docs/p020040.html
  - http://www.medinol.com/nirflex.html
  - http://www.fda.gov/cdrh/PDF2/P020040a.pdf
  - http://www.fda.gov/cdrh/PDF2/P020040.html

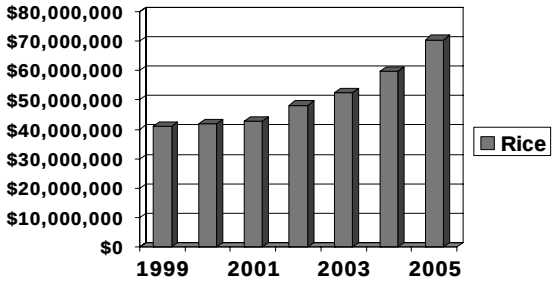
Who Funds R&D? Who Does R&D?



Types of Universities

- Carnegie Classification
  - Taxonomy of colleges and universities
    - Doctorate-Granting Institutions
      - Research Universities /Very High Research Activity ← Rice
      - Research Universities/ High Research Activity
      - Doctoral/Research Universities
    - Master's Colleges & Universities
    - Baccalaureate Colleges
  - http://www.carnegieclassification-preview.org/index.aspx

Total Research Expenditures @ Rice



R&D Funding for Biomedical Research

- Federal government:
  - Funds ~ 36% of all medical research in US
- Mostly funded through NIH:
  - Current NIH budget: $28 billion/year
  - NIH budget doubled from 1998-2003
  - This year: 0% increase
  - Focus is on basic research

US Senate Report – May, 2000

- 21 drugs introduced between 1965 and 1992:
  - Considered by experts to have had highest therapeutic impact on society
  - Public funding of research was instrumental in development of 15 of the 21 drugs (71%)
  - Three-captopril (Capoten), fluoxetine (Prozac), and acyclovir (Zovirax)-had more than $1 billion in sales in 1994 and 1995
  - Others, including AZT, acyclovir, fluconazole (Diflucan), foscarnet (Foscavir), and ketoconazole (Nizoral), had NIH funding and research to help in clinical trials

NIH

- National Cancer Institute
- National Eye Institute
- National Heart, Lung, and Blood Institute
- National Human Genome Research Institute
- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Allergy and Infectious Diseases
- National Institute of Arthritis and Musculoskeletal and Skin Diseases
- National Institute of Biomedical Imaging and Bioengineering
- National Institute of Child Health and Human Development
- National Institute on Deafness and Other Communication Disorders
- National Institute of Dental and Craniofacial Research
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute on Drug Abuse
- National Institute of Environmental Health Sciences
- National Institute of General Medical Sciences
- National Institute of Neurological Disorders and Stroke
- National Institute of Nursing Research
- National Library of Medicine

The Funding Process

- NIH → Issues request for proposals
- Investigator → Writes a proposal
  - Hypothesis
  - Background & Significance
  - Preliminary Results
  - Research Design and Methods
  - Protection of Animals and Human Subjects
- Peer-Review
  - Score
  - Comments
- Institutional Review
- Funding Decision