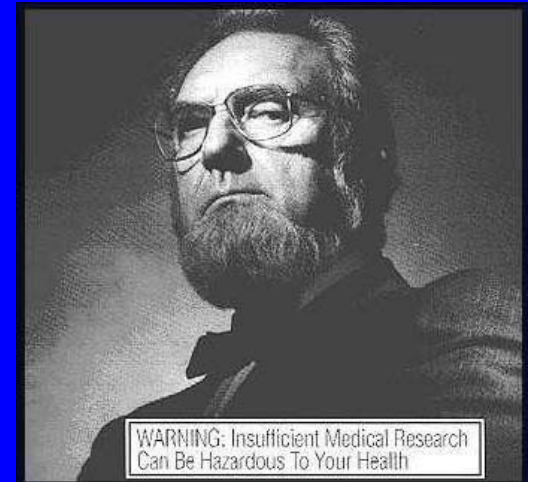


BIOE 301

Lecture Twenty-Two



FDA

- Regulates products whose annual sales account for $\frac{1}{4}$ 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

		Clinical Trials				
Discovery/ Preclinical Testing		Phase I	Phase II	Phase III	FDA	Phase IV
Years	6.5	1.5	2	3.5	1.5	Additional post- marketing testing required by FDA
Test Population	Laboratory and animal studies	20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers	Review process/ approval	
Purpose	Assess safety, biological activity and formulations	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use		
Success Rate	5,000 compounds evaluated	5 enter trials			1 approved	

File IND at FDA

File NDA at FDA

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- Vioxx – withdrawn from market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

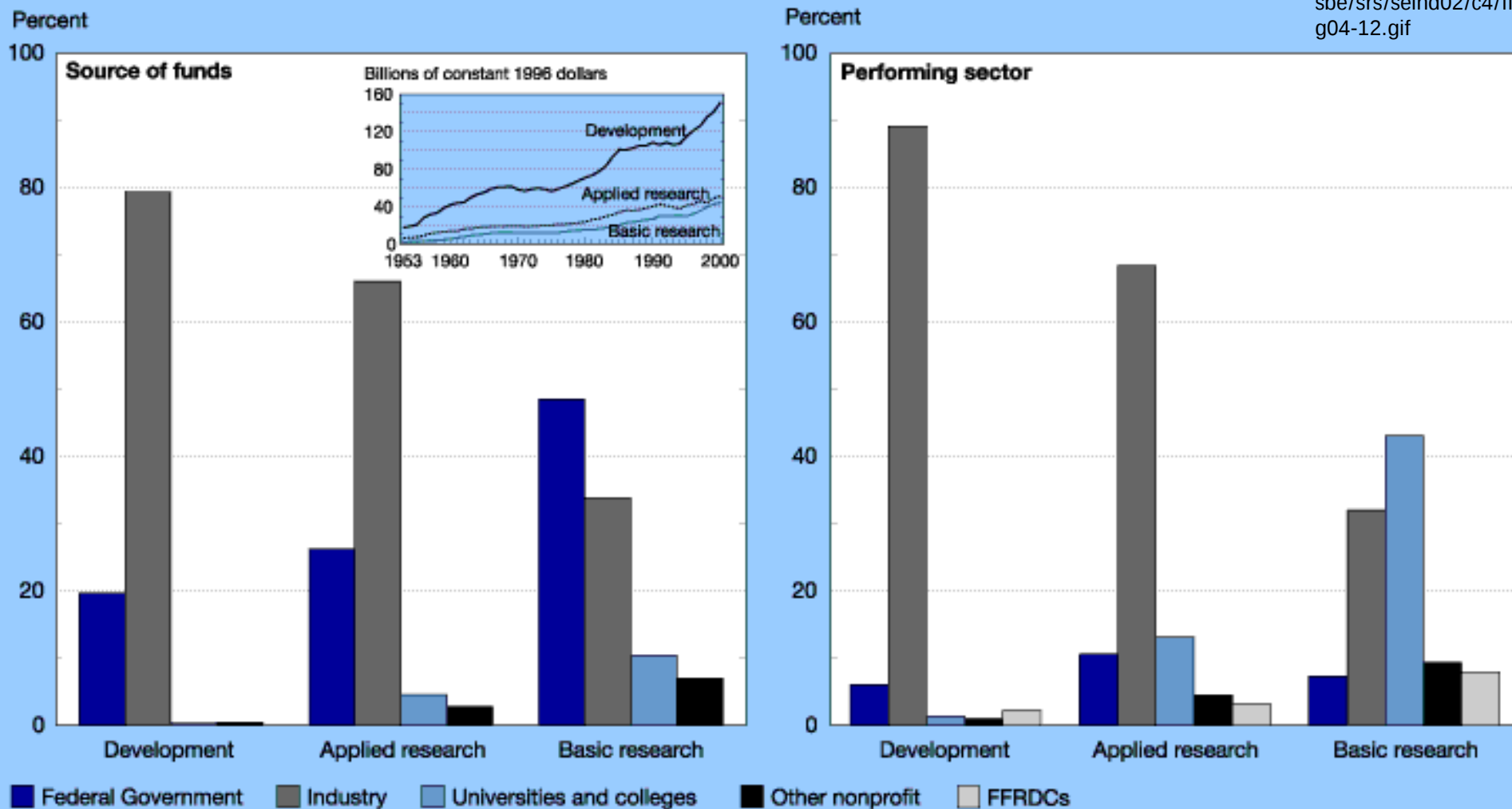
- <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/MDA/mda-list.cfm?list=1>
- **NIRflex Stent System**
 - <http://www.fda.gov/cdrh/mda/docs/p020040.html>
 - <http://www.medinol.com/nirflex.html>
 - <http://www.fda.gov/cdrh/PDF2/P020040a.pdf>
 - <http://www.fda.gov/cdrh/PDF2/P020040.html>

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

Figure 4-12.

National R&D expenditures, by source of funds, performing sector, and character of work: 2000

<http://www.nsf.gov/sbe/srs/seind02/c4/fig04-12.gif>



FFRDCs = Federally Funded Research and Development Centers

Types of Universities

■ Carnegie Classification

■ Taxonomy of colleges and universities

■ Doctorate-Granting Institutions

- Research Universities /Very High Research Activity
- Research Universities/ High Research Activity
- Doctoral/Research Universities

Rice

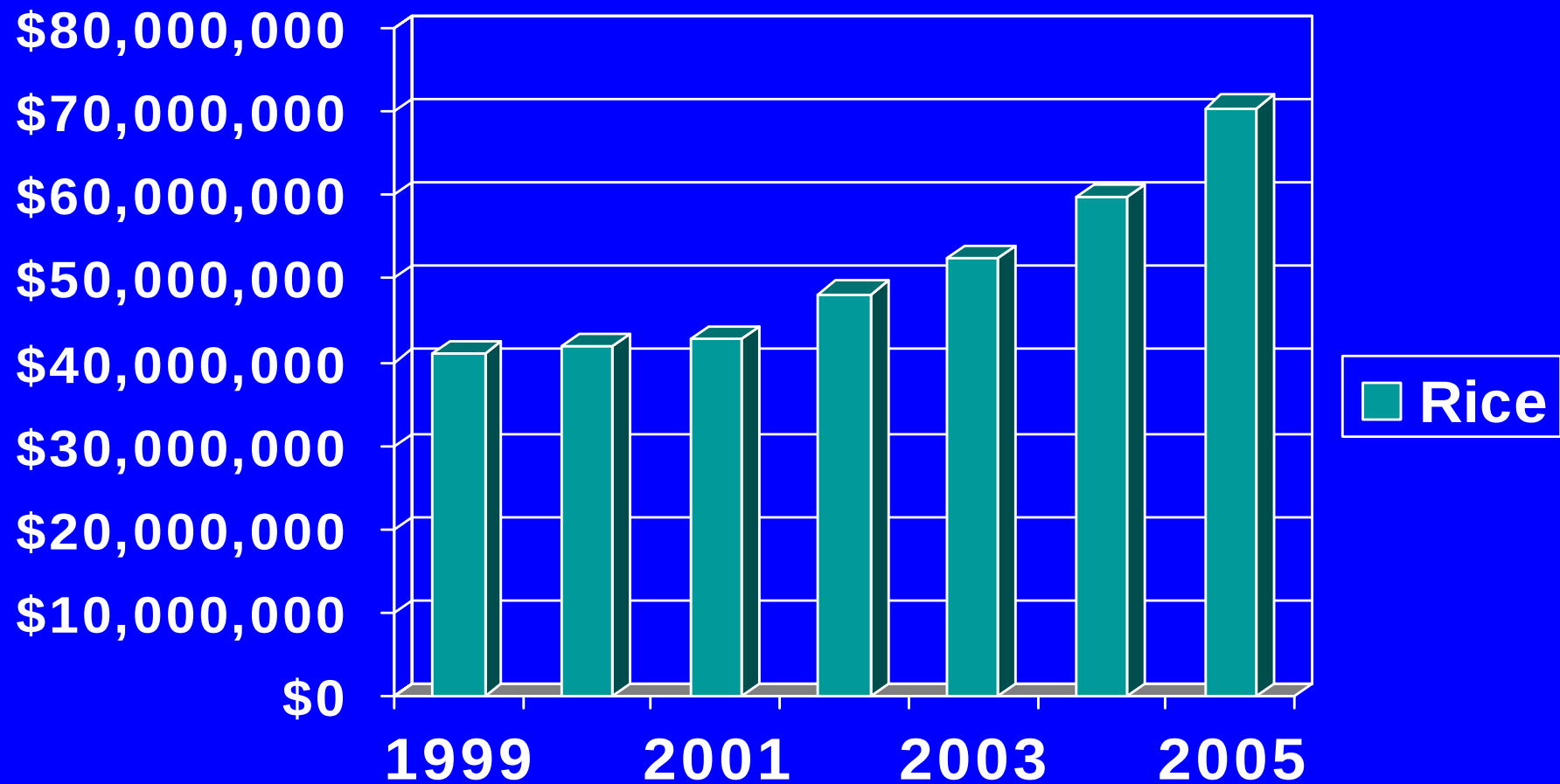


■ Master's Colleges & Universities

■ 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