



FDA Success Stories in Clinton Administration

- Tobacco
- Drug Approval
- Food Safety/Seafood HACCP
- Biotechnology
- AIDS (drugs, blood, test kits, vaccines)
- REGO
- Pediatric Labeling
- Mammography
- High Profile Food Additives (BST, Olestra, Sucralose, Meat Irradiation)
- BSE



Crushing New Responsibilities

- Soaring Workload Increases for each of last 5 years
 - 12% Annual Increase in Product Applications
 - 24% Annual Increase in Imports
 - 25% Annual Increase in Injury Reports
 - 5% Annual Increase in Regulated Firms
- Complex New Products/Technologies
 - Genetic Testing
 - Gene Therapy
 - Tissue Transplantation (Human and Xeno)
 - Cloning
 - Anti-Viral Drugs
 - Computerized Devices/Manufacturing Processes
 - Novel Foods
 - Biotechnology

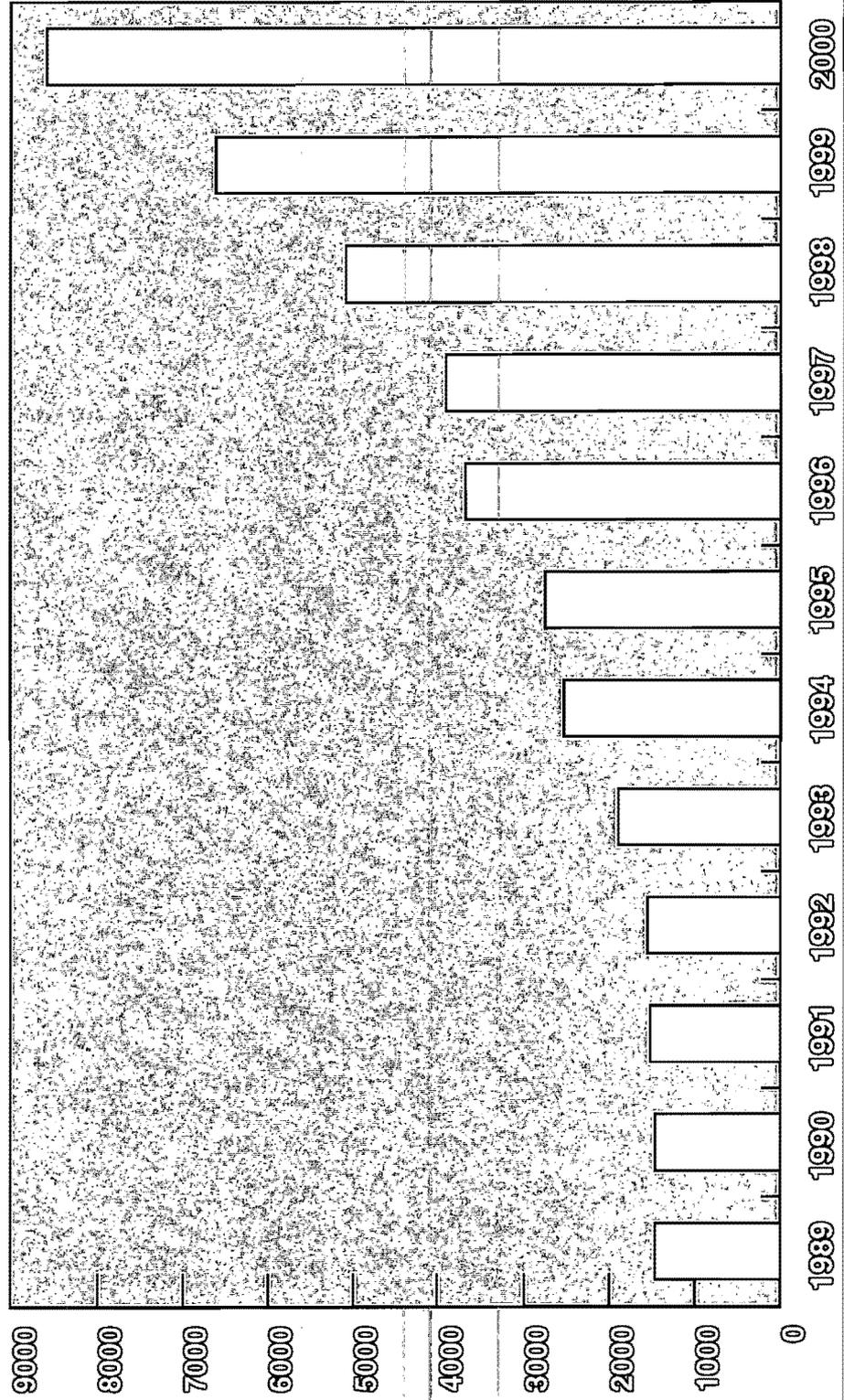


Crushing New Responsibilities

- **New Challenges**
 - Blood Safety
 - New Diseases (AIDS, BSE, HUS, CJD)
 - Emerging Pathogens
 - Counterfeiting
 - Tampering
 - Dietary Supplements
 - Drug Promotion in Managed Care/On Internet
 - International Harmonization
 - Home Test Kits
- **New Statutory Responsibilities**
 - 10 Major New Laws Since 1990
- **FDA Modernization Act**
 - 100 new regs, guidances, etc.
- **Presidential Initiatives**
 - Tobacco
 - Food Safety
 - REGO
- Bioterrorism



FDA Import Entries

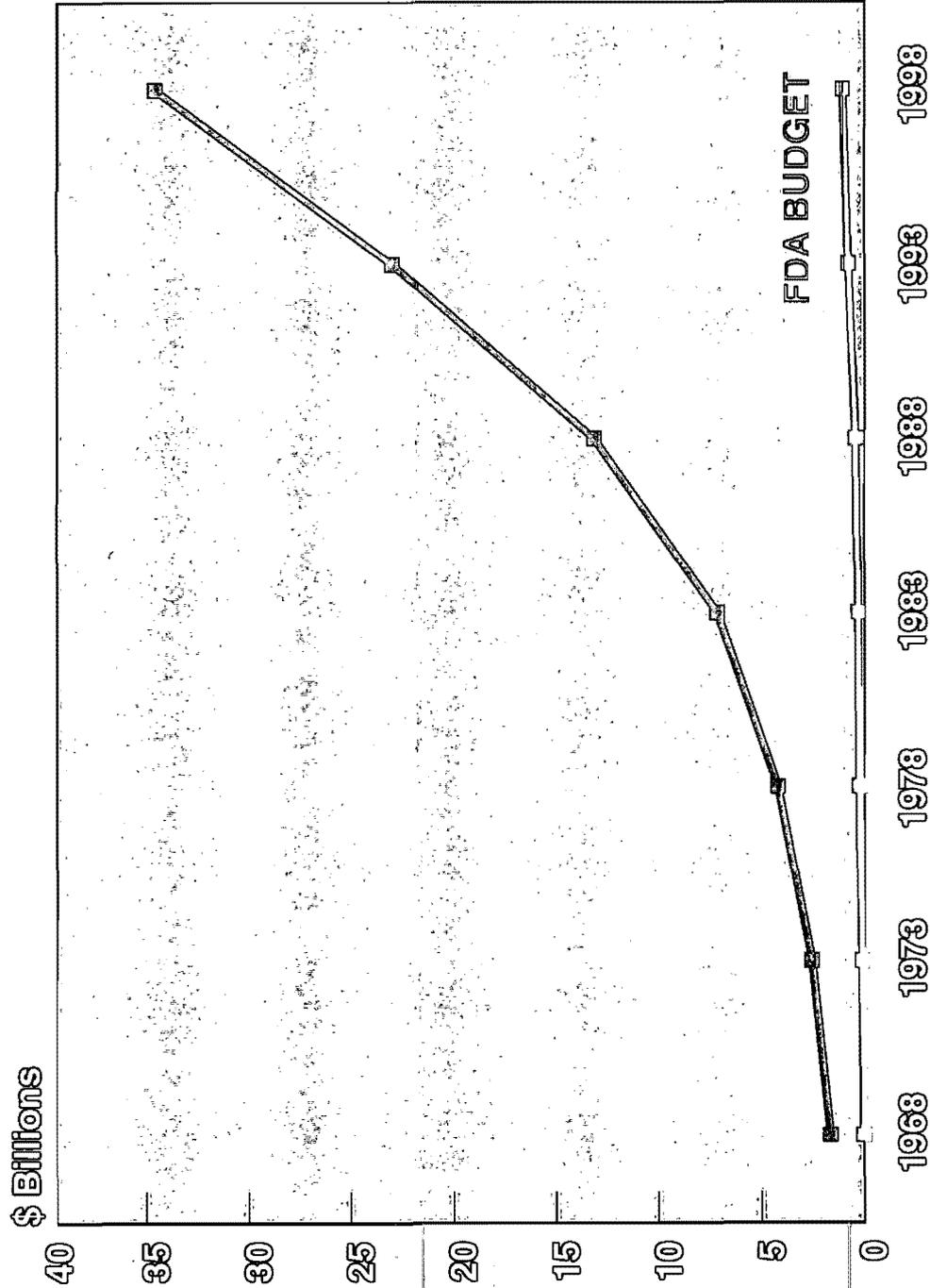


Note: The numbers for the years 1998, 1999 and 2000 are projected



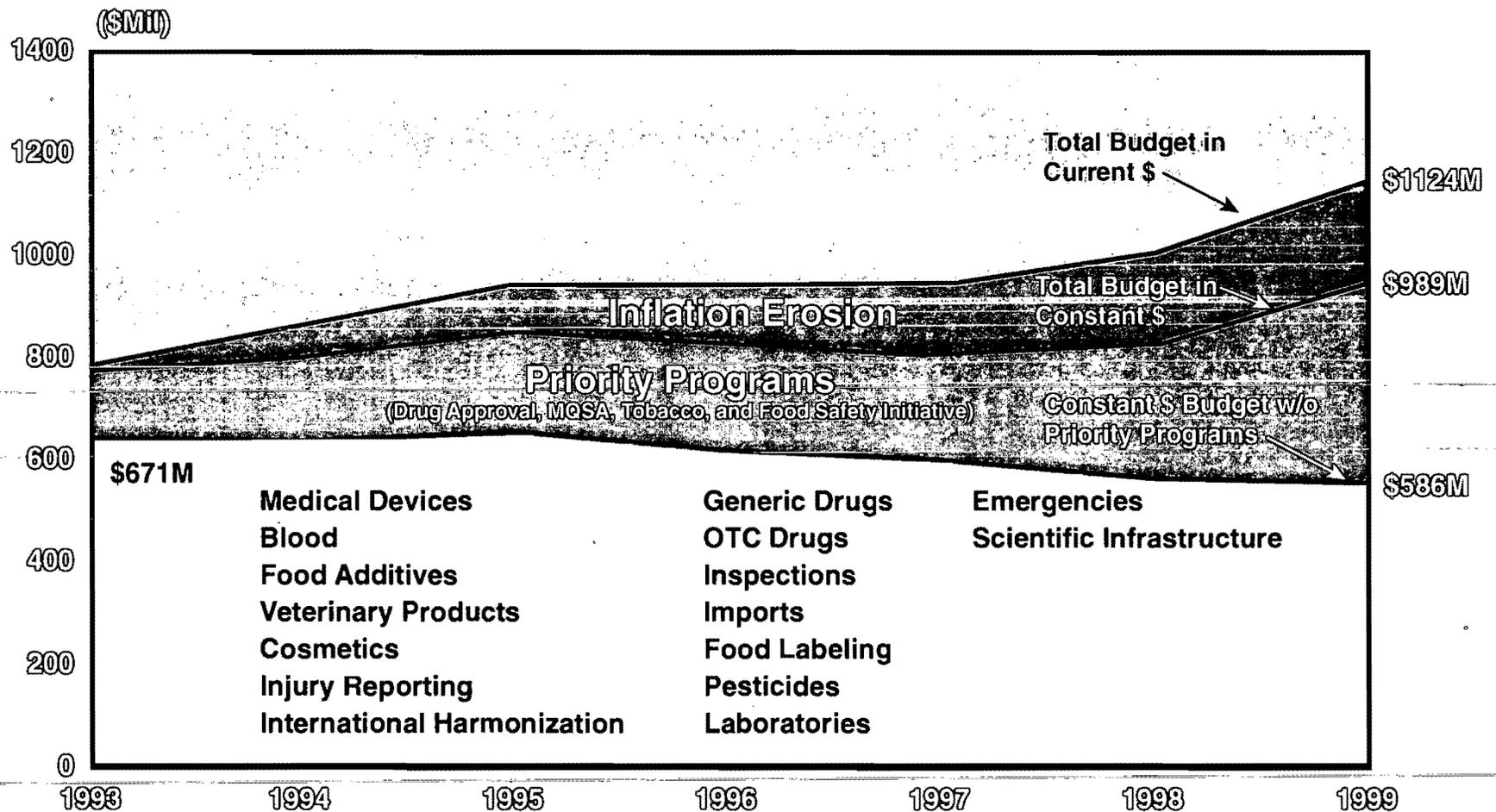
US Biomedical R&D Expenditures

Public (NIH) + Private (PhRMA)





The Shrinking FDA





What Does This Mean?

- Failure of Import Program
 - Will inspect less than 1% by 2000
- Inspections at Historically Low Levels
 - General food inspections (filth) no longer done
 - Food inspections down to 5,000 (vs. 21,000 in 1981)
 - Only 10% of foreign drug firms inspected annually
 - Only 50% of highest risk device manufacturers inspected within statutory interval (virtually no low risk)
 - Only 33% of veterinary drug manufacturers inspected within statutory interval
 - Tissue and organ banks rarely inspected
- Product Recalls Doubled in Recent Years



What Does This Mean?

- Many Products Virtually Unregulated
 - Dietary supplements
 - Cosmetics
 - Medical products purchased overseas
 - Elimination of foreign pesticide monitoring/phase out of U.S. field sampling
- Health fraud and economic fraud enforced only for outrageous violations
- New products/technologies slowed to market
- Adverse event reports 250,000/year and increasing
- Citizen petition backlog of 600 petitions



What Can Be Done?

Focus FY 2000 Budget Priorities to Strengthen Four Critical Areas

- **Adverse Event/Injury Reporting**
(Lower the enormous cost in dollars and lives)
 - reduce injuries and healthcare costs by 15%
- **Product Safety Assurance**
 - meet 95% of statutory inspection obligation; reduce rising industry recall rates
- **Product Review**
(Speed products to consumers; enhance industry competitiveness)
 - review 90% of product applications in statutory time frames
- **Food Safety**
 - achieve a 50% reduction in food borne illness



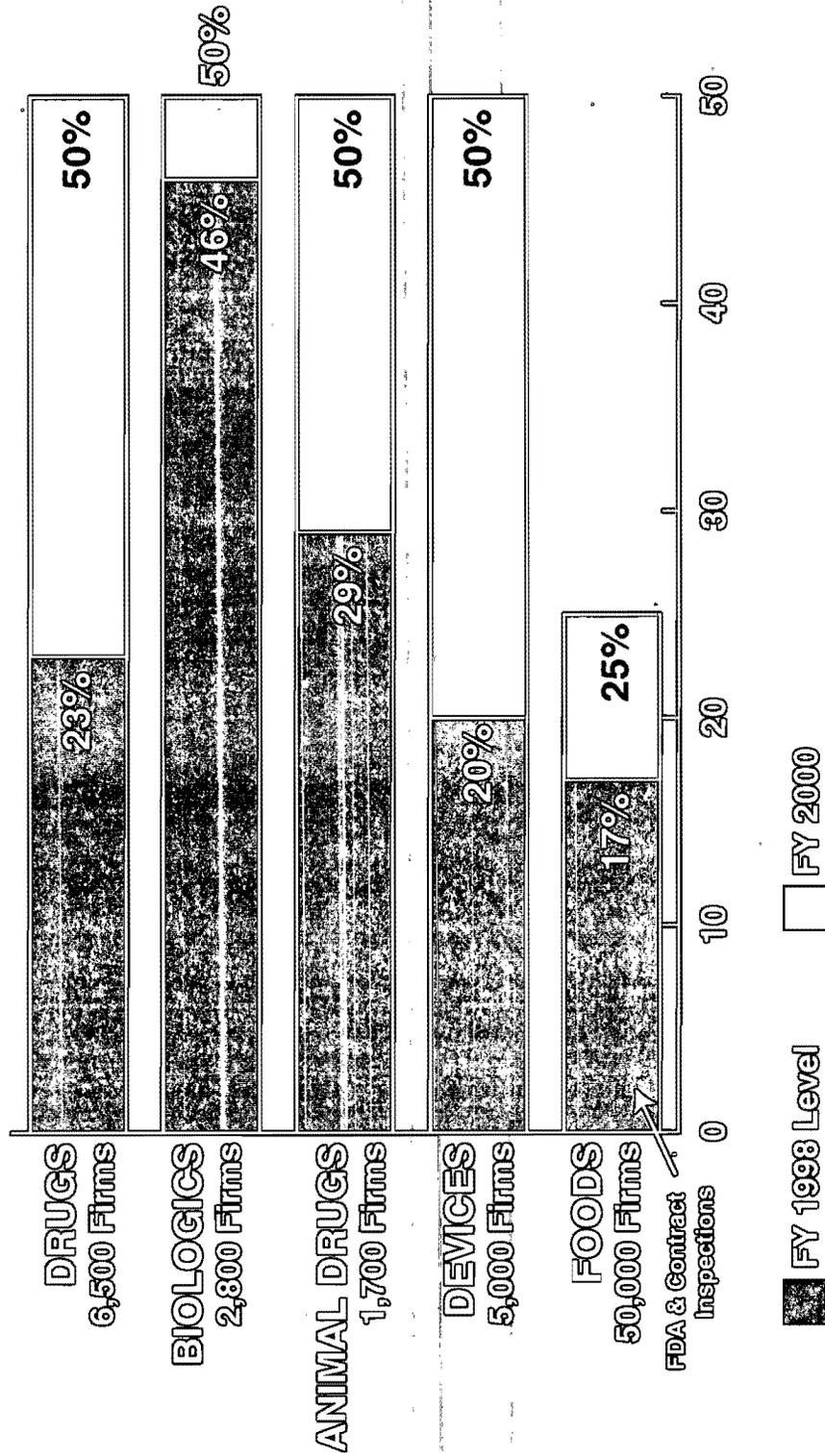
Injury Reporting:

What is the Problem?

- Estimated > 100,000 deaths and 1.3 million serious injuries/year in the U.S. (one of the top 6 causes of death)
- 10% of all hospital admissions from drug-related problems
- Drug-related illness and death in the U.S. cost approximately \$80 billion annually
- Drug-related illness and death costs U.S. government approximately \$26 billion annually



Inspection Coverage

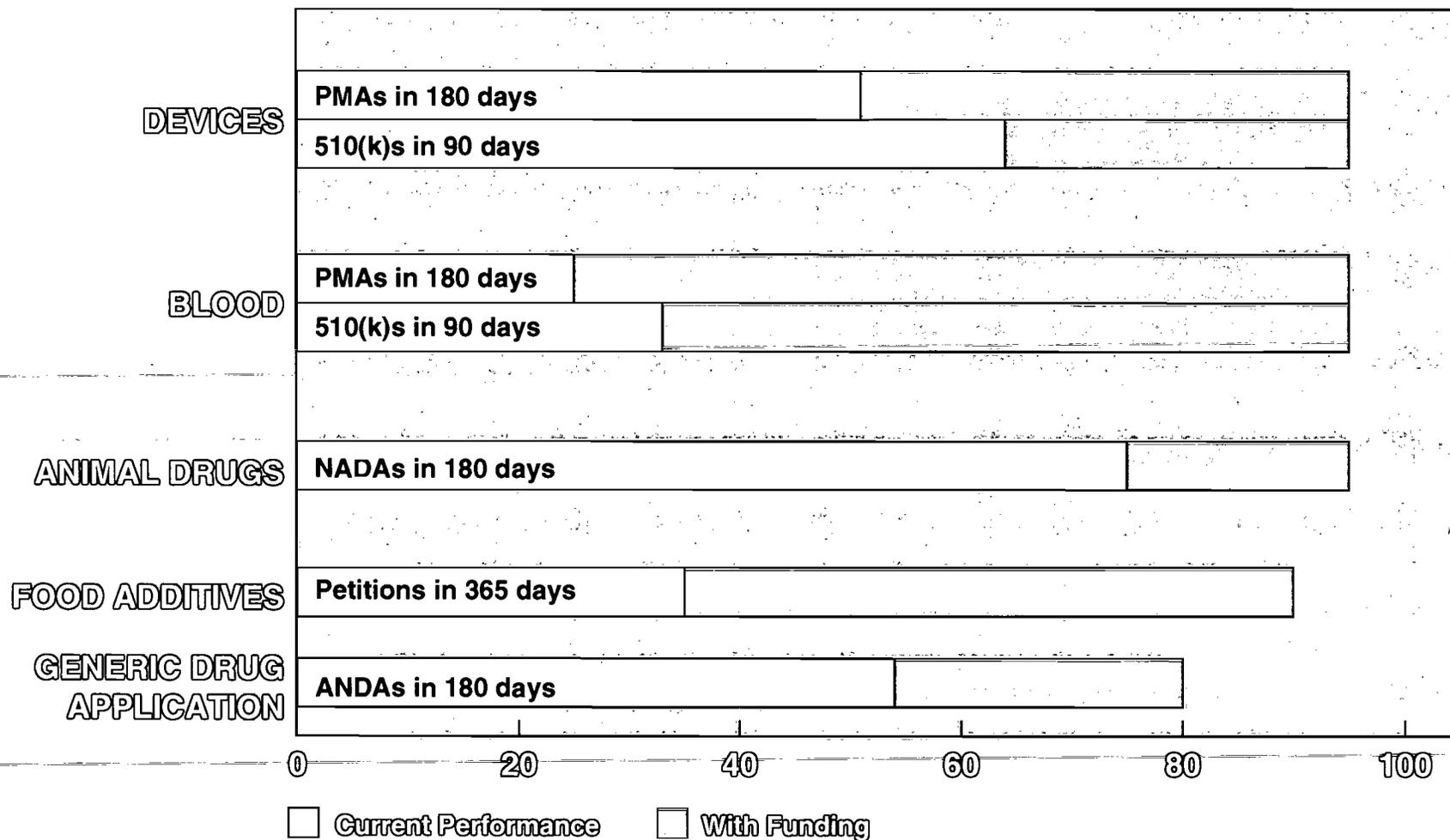


Percent of Inventory Inspected Annually



New Product Approvals

Filling the Public Health Need





12A • THURSDAY, AUGUST 6, 1998 • USA TODAY

FDA's high standards continue to save lives

Patients are deeply concerned about the USA TODAY front-page story and editorial on July 10 ("Rush to judgment? Critics say the Food and Drug Administration is approving drugs too quickly," Cover Story, News; "Fast-track drug approvals cut corners on safety," Debate: Prescription drug dangers).

In recent years, the Food and Drug Administration (FDA) has been able to hire additional employees to review drug applications, and the agency has approved new medicines more quickly as a result. But the FDA has not compromised its world-class standards for the safety and effectiveness of new medicines.

The patients we represent have benefited greatly from new medicines that have become available more quickly. We fear that in overreaction to a small number of recent drug withdrawals, policymakers may decide to slow down the drug approval process. This would hurt public health and harm the patients we represent by denying them the new treatments and cures they are so anxious to receive.

This letter also represents the views of the American Cancer Society, the Cystic Fibrosis Foundation, the National Mental Health Association, the Alliance for Aging Research, the American Liver Foundation, the National Psoriasis Foundation, the American Autoimmune Related Diseases Association, the Sickle Cell Disease Association of America Inc., the Asthma and Allergy Foundation of America, the Crohn's and Colitis Foundation of America, the American Parkinson's Disease Association, the National Multiple Sclerosis Society, the Cancer Research Foundation of America, the International Patient Advocacy Association, the American Menopause Foundation, the National Burn Victim Foundation, the Cancer Research Institute, the Log Cabin Republicans AIDS Policy Group, the National Tuberculosis Association and the National Black Nurse's Association.

Carl F. Dixon, president and
executive director
National Kidney Cancer Association
Evanston, Ill.

Report to the FDA Commissioner

Managing the risks from Medical Product Use

**An Assessment of FDA's Approach and a look to the
21st Century**

FDA FIG

Impetus for Report

- **Concerns that speed of review under PDUFA is compromising safety.**
- **Allegations of “a record number of drug withdrawals”**
- **Allegations (Public Citizen survey) that there is pressure on reviewers to recommend approval.**

Dr. Henney's request: concentrate evaluation in three areas:

- 1. Does the Agency have adequate quality assurance (QA) and quality control (QC) over its premarket review decisions? (Dr. Burlington)**
- 2. What is the status of FDA's postmarketing surveillance and risk assessment program, and what are the strengths and weaknesses? (Dr. Zoon)**
- 3. How should the Agency relate to practitioners as they make decisions about medical products? How can the Agency partner with other groups who work to ensure the safe use of medical products? (Dr. Woodcock)**

Frequency of Adverse Events: Conclusions

- Rate of drug withdrawals has gone down slightly in the PDUFA era compared to the 1980's
- Rate of significant postapproval label changes has decreased from
 - 51.5% in 1976 - 1985 to
 - 30.3% in 1994 - 1997

Postapproval Label Changes

- **GAO study published in 1990. Looked at Postapproval risks in 198 drugs approved 1976 - 1985.**
- **Slightly over half had postapproval labeling changes adding risk information.**
- **We used the same definitions and evaluated a cohort of 142 drugs approved 1994 - 1997.**
- **30.3% had changes**

Results of QA/QC Evaluation

- **Premarket reviews are subject to 100% quality control via supervisory review**
- **Majority of ISO required elements are in place - a few are in the process of implementation:**
 - **Establishing, administering & documenting explicit training requirements for review staff**
 - **Explicit, detailed standards for review (Good Review Practices effort)**

Limitations in drug development: It is not possible to identify all risks before marketing

- **Trials expose a relatively small number of people to the product, compared to marketing**
- **Patients in clinical trials are not like all patients who will take the marketed drug**
- **Clinical trial patients are selected (in part) for a good chance of a positive response**
- **Clinical trial patients are closely monitored for toxicity - which can prevent serious problems**

Market “Rollout” factors in risk

- **Rapid massive exposure increases risk liability if a major unrecognized risk exists**
- **Marketing rollout may target a broad population - i.e., to displace existing, equally effective products that have a safe track record**
- **Economic incentives push marketers to maximize use of product**

Postmarket Surveillance: Goals of FDA Systems

- 1. Detect Adverse events not previously known**
- 2. Detect changes in event severity**
- 3. Detect events arising from drug-drug interactions**
- 4. Assess potential for causal relationships**

Risk Assessment Approaches: Spontaneous Reporting Systems

- **MedWatch** - **Outreach system for direct reports from health professionals**
- **AERS** - **Adverse Event Reporting System for drugs and biologics**
- **VAERS** - **Vaccine Adverse Event Reporting System**
- **MAUDE** - **Manufacturer and User Device Experience Database**
- **Medication Errors** - **Reported through a variety of sources**

Conclusions

- **FDA systems are working well to rapidly detect serious unexpected adverse events postmarketing**
- **However, continuing investment is needed to modernize**
 - **Expand use of automated systems**
 - **Develop sentinel site network**
 - **Improve access to large healthcare databases**
 - **Develop registries**

The System of Medical Product Risk Management

- **FDA not the only player**
 - **FDA is primary risk manager until marketing decision**
 - **Practitioner is primary risk manager for marketed drugs**
- **Systems approach to drug safety is needed**

Injuries and Deaths from Drugs:

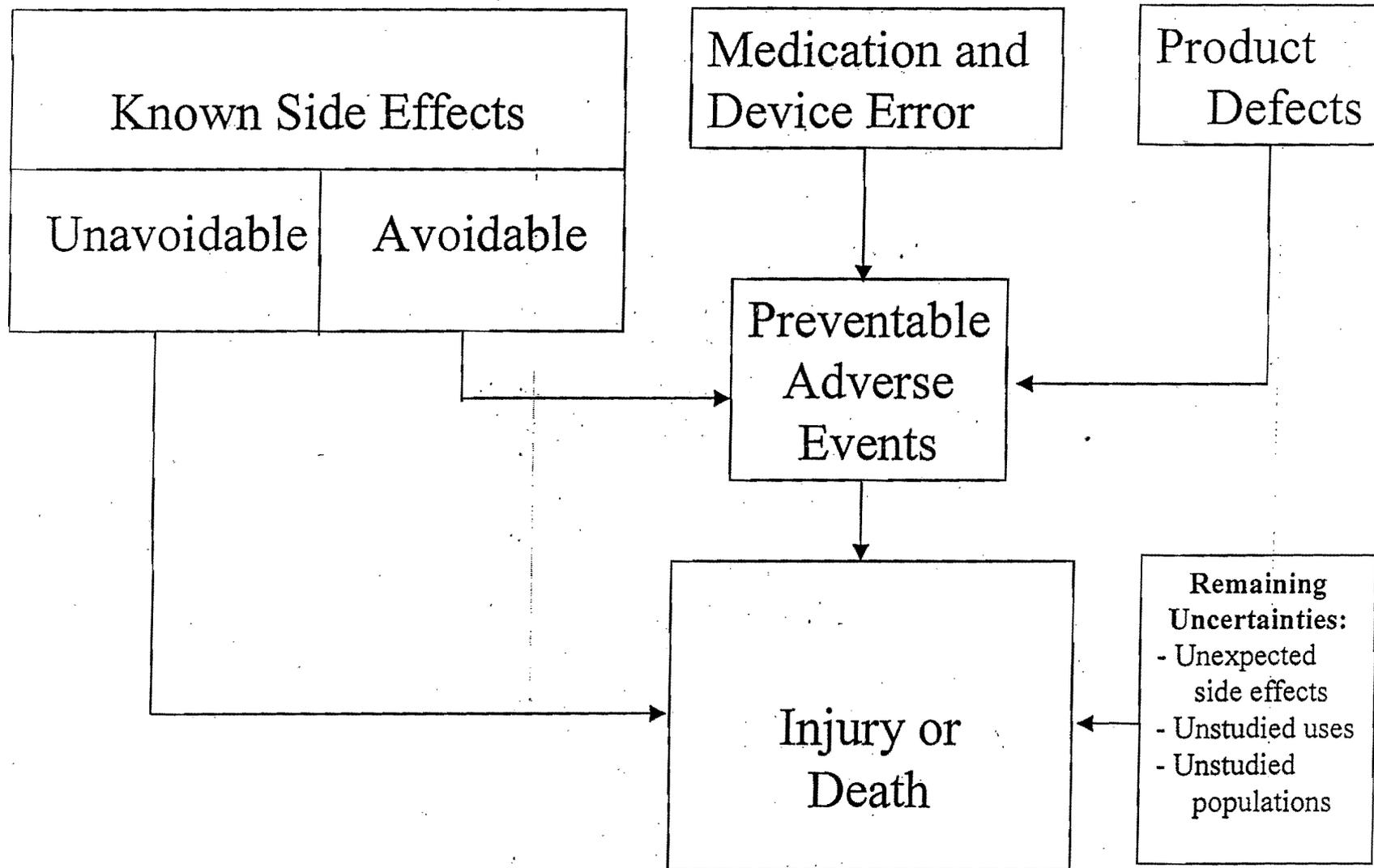
Is it New?

Is it Worse?

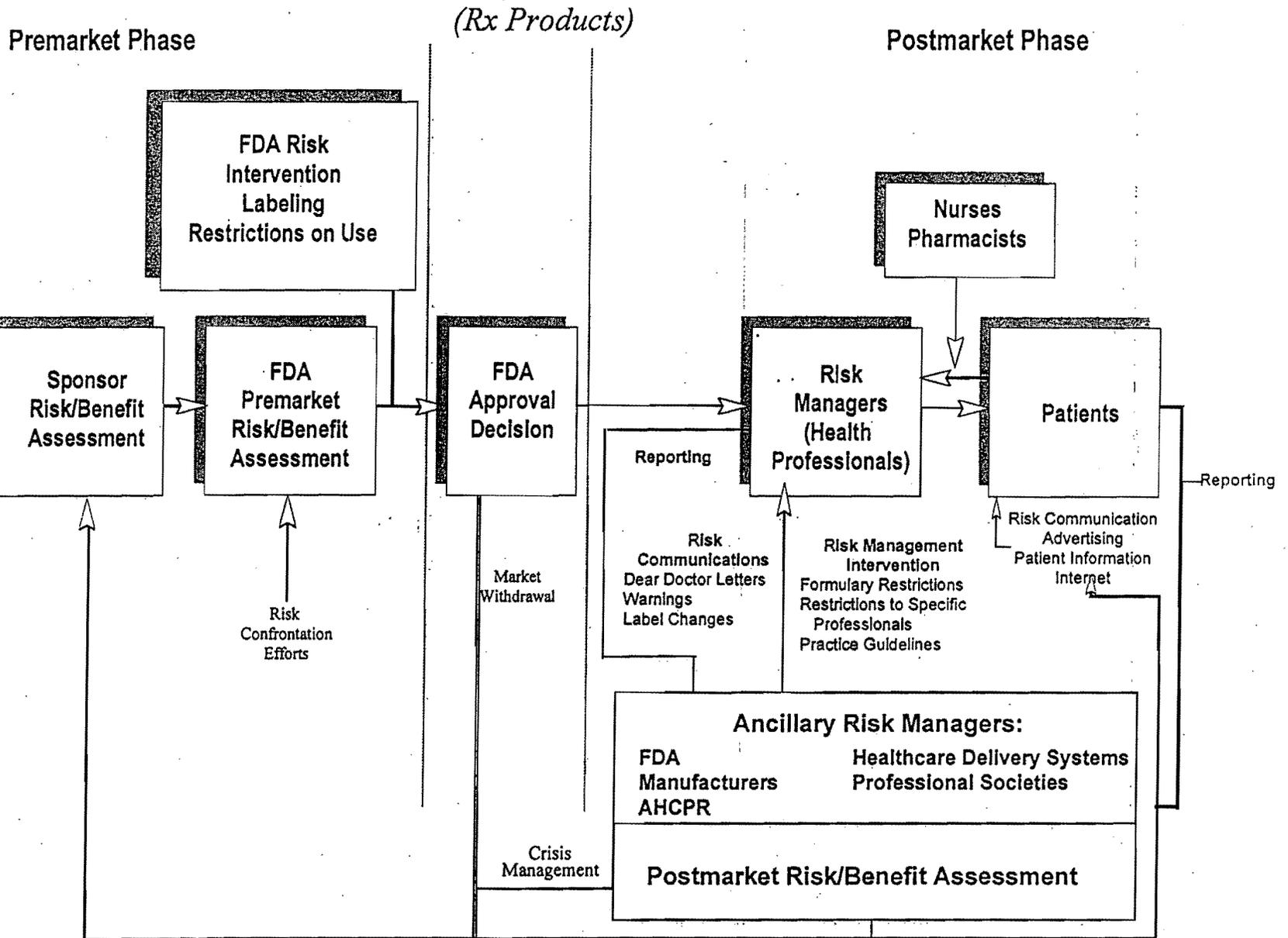
How bad is it?

- 1974 30% Hospitalized Patients
 have drug reactions
- 1977 Estimated 140,000 deaths annually
- 1991 Iatrogenic injury
 180,000 deaths annually
 69% preventable
- 1995 >\$1000,000,000 annual estimated costs
- 1997 Estimate > 100,000 deaths annually

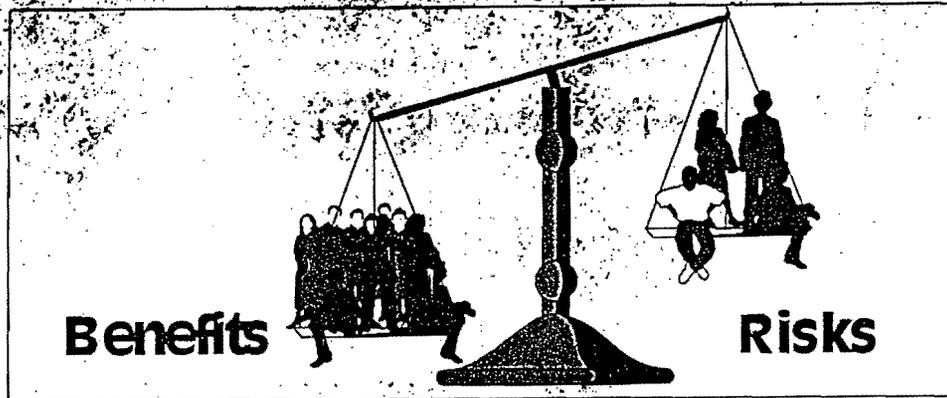
Sources of Risk From Medical Products



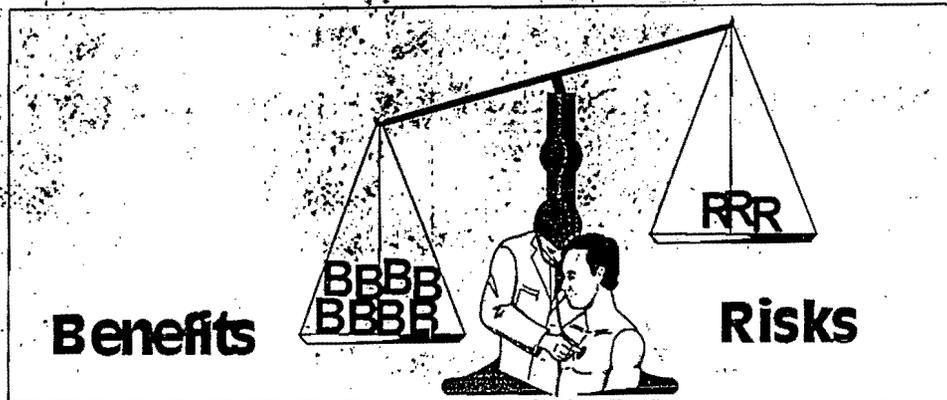
Complex System for Managing the Risks of Medical Products



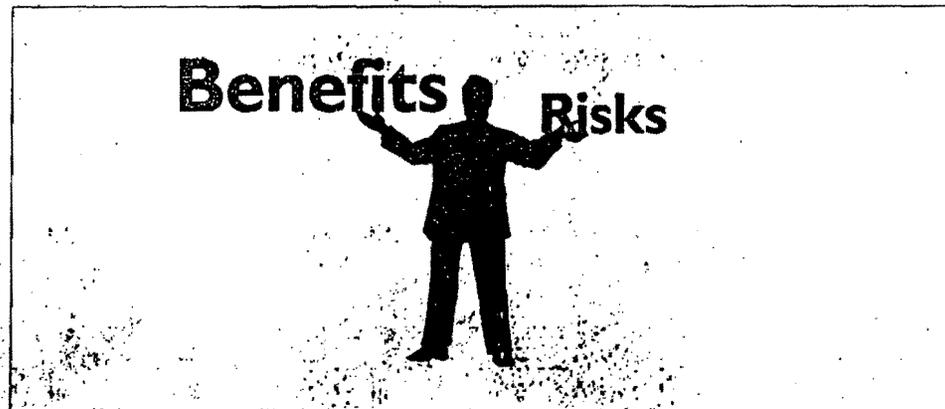
FDA
evaluates
benefits/risks
for the population



Provider
evaluates
benefits/risks
for a patient



Patient
evaluates
benefits/risks
in terms of
personal values



Recommendation: Systemic risk Confrontation

Convene public meeting with public agencies and nongovernmental groups involved in healthcare to examine the current system of managing the risks of use of medical products

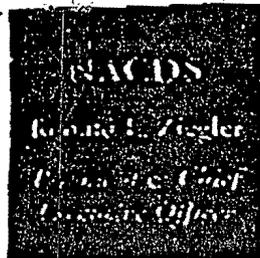
- **Roles and responsibilities**
- **Need for better data**
- **How can we improve outcomes?**

Options for FDA

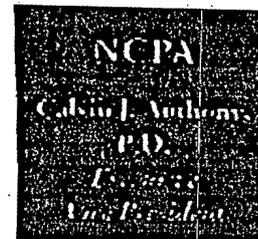
- **Improve risk confrontation**
 - **Advisory committees**
 - **State of the armamentarium**
 - **Postmarketing safety discussions**
- **Consider risk interventions for specific products**
 - **Restrictions on use**
 - **Mandatory educational programs**
 - **Special identification of risky products**
 - **Partnerships with payors to encourage appropriate use and monitoring**

Options for FDA

- **Improve direct risk communication**
 - **To health professionals**
 - » **Drug - drug interactions**
 - » **Package insert**
 - **To patients**
- **Improve system evaluation**
 - **Annual report card for newly approved drugs**
 - **Survey patients and health professionals**



COMMUNITY RETAIL PHARMACY COALITION



August 25, 1998

Chris Jennings
Assistant to the President for Health
The White House
Old Executive Office Building, Room 216
Washington, D.C.

Dear Chris:

On behalf of the Community Retail Pharmacy Coalition, we are writing to express our serious concerns with FDA's stated intent to finalize part of the original MedGuide regulation. The agency indicated that it was moving forward with this action as part of its recent "unified agenda", which was published in the Federal Register.

We strongly believe that consumers should be provided with useful information - both written and oral - about their prescriptions. However, we are surprised that the agency is moving forward with this action. We believe that the language included in the FY 97 Agriculture Appropriations bill regarding MedGuide specifically prohibits the Secretary of HHS from finalizing any part of the proposed rule, not just the voluntary part, as the agency states. This prohibition is lifted in 2001 if certain specific statutory goals are not achieved.

We believe that this comprehensive prohibition was written to prevent this very action by the agency. Congress was concerned then, as we are now, that finalizing even part of the rule would result in a uniform, government-mandated format for all written prescription information. We do not believe that patients are served by such an outcome. Moreover, we believe that the agency can continue to mandate under its existing authority that written information be distributed with certain prescription medications. This new regulation, however, would give it much broader authority, which we believe is contrary to Congressional intent.

Should the regulation be finalized it would, in our opinion, represent a breach of the understanding that community retail pharmacy entered into with the Congress and the Secretary regarding this issue. Pharmacy committed to a voluntary process to increase the quality and quantity of written prescription information being provided to consumers. We

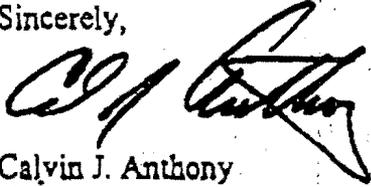
National Association of Chain Drug Stores
413 N. Lee Street, Alexandria, Virginia 22314
Tel: (703) 549-3001, Fax: (703) 836-4869

National Community Pharmacists Association
(formerly NARD)
205 Daingerfield Road, Alexandria, Virginia 22314
Tel: (703) 683-8200, Fax: (703) 683-3619

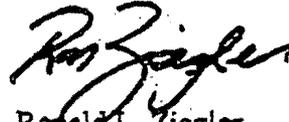
believe that we are well on our way to achieving these goals for all prescription drugs, not just those that could result in serious and significant side effects.

We ask that the Secretary respect the intent of the law and the spirit of the agreement which pharmacy and many other affected parties entered into regarding the provision of written information to consumers. Thank you for your interest and concern with this matter.

Sincerely,



Calvin J. Anthony
Executive Vice President
NCPA
National Community Pharmacists Association



Ronald L. Ziegler
President and CEO
NACDS
National Association of Chain Drug Stores