DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year 2001

Food and Drug Administration

FY 2001 Performance Plan, FY 2000 Final Performance Plan, and FY 1999 Performance Report

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Glossary Of Acronyms

Part 1: Agency Context for Performance Measurement

WELCOME TO FDA'S FY 2001 PERFORMANCE PLAN AND REPORT!

This document is the culmination of a comprehensive strategic and performance planning process led by the Commissioner and her strategic management team. The Plan outlines FDA's long-range 'corporate' goals, strategies and performance goals for FY 2001 as well as the report on FY 1999 Performance.

The Plan is divided into two Parts.

Part One describes:

- an overview of FDA, its mission and long term goals,
- strategies for achieving the goals,
- how FDA will work with partners to carry out the strategies; and
- performance highlights for FY 1999 through FY 2001.

Part Two presents FY 2000 and 2001 performance goals for each of FDA's programs; and a report on FY 1999 performance results. Each program section includes the following information:

- Program funding for FY 1999
- A broad description of program activities
- Strategic goals
- Approaches for achieving goals
- A performance goal summary table; and
- A goal-by-goal explanation of performance, including FY 1999 results

FDA: An Overview

The U.S. Food and Drug Administration is a scientific regulatory agency that touches the lives of virtually every American every day. It is FDA's job to see that the food we eat is safe and wholesome, that the cosmetics we use won't harm us, and that medicines, medical devices, and radiation-emitting consumer products such as microwave ovens are safe and effective. FDA also oversees feed and drugs for pets and farm animals. Authorized by Congress to enforce the Federal Food, Drug, and Cosmetic Act and several other public health laws, the agency monitors the manufacture, import, transport, storage, and sale of $1 trillion worth of goods annually, at a cost to taxpayers of about $4 a person. All of FDA's effort is focused on protecting the health and safety of Americans.

This Performance Plan and the Agency budget are companion documents. Performance goals in the Summary Tables are cross-referenced to their corresponding sections in the budget document.

1.1 Agency Mission and Strategic Goals

What Is FDA's Mission?

FDA's current mission, as adopted in the 1997 Food and Drug Administration Modernization Act, sets forth the following responsibilities for the Agency:

1. To promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;

2. With respect to such products, to protect the public health by ensuring that--

- foods are safe, wholesome, sanitary, and properly labeled;
- human and veterinary drugs are safe and effective;
- there is reasonable assurance of the safety and effectiveness of devices intended for human use;
- cosmetics are safe and properly labeled; and,
- public health and safety are protected from electronic product radiation.

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

4. As determined to be appropriate by the Secretary, to carry out paragraphs (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.

What Strategic Goals Will Sustain the Mission?

FDA pursues two strategic goals that support and sustain its public health and safety mission:

- **To help safe and effective new products enter the market rapidly, thus greatly enhancing the Nation's health.** Achievement of this goal requires FDA to incorporate the scientific information developed through research and surveillance efforts to bolster sound review decisions. FDA reviewer-scientists who have a solid understanding of the complex scientific issues at hand will be in a better position to make timely and informed decisions on sponsors' applications.
- **To assure that products already on the market are safe.** To achieve this goal FDA must monitor well over a trillion dollars worth of products that are essential to the health and well being of every U.S. citizen. FDA must be able to: judge the suitability of sources of domestic and international production; operate an integrated system of reporting and correcting problems associated with product use; and check advertising and labeling, particularly on the internet.

These goals are intended to create a comprehensive safety assurance system that monitors FDA-regulated products throughout their life span--from conception through consumption. Each of FDA's programs has established the same two goals, thus aligning the programs with the overall mission and goals of the Agency.

1.2 Strategies and Programs

1.2.1 Agency Strategies Essential for Achieving FDA's Strategic Goals

Although timely pre-market review and post-market safety assurance are perennial Agency goals, their successful pursuit in the 21st Century will be seriously challenged by a much more complex technological, economic and social environment. FDA, at the turn of the Century, operates in a far different world than they did twenty years ago. The table below illustrates a quantum shift in the factors that will shape the Agency's future responses.

In 1980	At the Turn of the 21st Century
• Less than 1 million FDA-regulated import shipments entered the U.S. • Public & private sector drug research expenditures under $5 billion • Medical device technology--x-ray machines, CAT scans	• Almost 6 million shipments entered, from a significantly more diverse set of countries. • $35 billion spent in drug research - a seven-fold increase. • Medical device technology - biomaterials, robotic surgery, implantable health monitoring devices made possible by miniaturization
• Drug discovery based primarily on chemical and pharmacological understanding	• At threshold of microchip screening, and human genome-driven discovery of new drugs
• Food standards based on chemical understanding of ingredients, additives • FDA 'gold standard' guided majority of domestic and international commerce	• Proliferation of genetically-modified foods
• Most consumers learned about new drugs from their doctors; health professionals learned through print media	• International collaborative standards emerging as primary driver of global trade • Internet, Rx advertising on television directed to consumers and health professionals

The above table provides just a flavor of the forces contributing to the challenges of this Millennium. FDA will not be able to address such complexity in the future by working independently, by relying on its current level of scientific understanding, or by attempting

to protect the public from all risk situations. The task is simply too daunting. The key courses of action for FY 2001 and beyond will be to:

- Keep pace with proliferating science and technology by continually accessing the science necessary to manage this revolution;
- amplify FDA's capabilities through effective collaboration with allies; and
- focus on the highest priority risks.

As the graphic below depicts, these strategies will work together to assure safety in a significantly more complex 21st Century environment.

In addition to carrying out strategies to manage complexity, FDA must continue to be responsive to the statutory review and inspection requirements mandated by the Pure Food and Drug Act, and reinforced by the FDA Modernization Act of 1997. The Performance Plan identifies goals for meeting these statutes within each program section.

Each of the strategies are described briefly below:

Strengthen the Science of the Agency

In order for FDA to achieve its safety goals in the 21st Century, it must develop the capability to regulate products of much greater complexity and sophistication than ever before. Sound science is essential for making timely and crucial regulatory decisions that impact every American citizen. A strong science capability is crucial for:

- Making sound pre-market review decisions;
- Assessing and managing risks of products in the market place; and
- Buttressing the standards that engender world-wide confidence in FDA-backed products, methods and processes.

FDA must be able to apply state-of-the-art science at the point where it is absolutely essential to steward life-saving, health-enhancing products to the market. FDA is the regulatory gateway through which an estimated $50 billion in annual biomedical research and development investment must pass and be judged. If FDA cannot apply the necessary science capability at the time that products are ready to enter the market, then these products must wait.

FDA science is also critical in understanding and managing product risk in the market place. Each year hundreds of thousands of adverse experiences are reported in association with foods, drugs and medical devices. Estimated health care costs to treat these illnesses and injuries exceed $100 billion annually. Timely application of cutting-edge science will allow FDA, working with its health and regulatory partners, to quickly identify the significant risks and minimize them. This targeted action will have major health as well as economic impacts.

The FDA standard for safe and effective products, methods and processes will continue to represent the hallmark for worldwide industry, consumer and patient confidence in the 21st Century. But the Agency must assure that the intellectual capital which underpins these standards can keep pace with increasing product, method and process complexity. To illustrate:

- *Standards for new product technology*--FDA will work with industry to develop standards for coronary artery stents, which will be used widely, and could reduce hospital stays and lower health care costs for as many as 250,000 patients.
- *Standards for detection methods*--FDA will apply research to develop nucleic acid testing which offers the potential for more accurate screening of rapidly emerging viruses, bacteria and parasites in blood.
- *Standards for manufacturing processes*--FDA's increased scientific understanding of dietary supplements will enable development of Good Manufacturing Practice (GMP) regulations for these products, for which consumers now spend $12 billion annually.

Amplify FDA's Capabilities Through Effective Collaboration With Allies

The complexity of both risk assessment and risk management challenges in the 21st Century have grown by orders of magnitude. It is no longer plausible for FDA, working alone, to effectively address these problems. Academia, health providers, other government agencies, regulated industry and consumers all have a role to play. Simply put, to meet our public health and safety mission, **FDA must work with others who share our values and our goals.** These collaborations are intended to have a larger net benefit to the American public than could be achieved if the organizations worked independently. Throughout this performance plan, illustrations will be given of collaborative efforts in the areas of research, pre-market review, surveillance and education and outreach, that contribute to the success of the Agency's performance goals.

Focus on the Highest Priority Risks

In an ideal world FD A would like to completely eliminate the risk associated with consumption/use of foods, drugs, biologics and medical devices. Given limited resources, this cannot be achieved. Rather, the Agency will focus its attention on the most serious risks first. The Agency has and will continue to increase the efficiency of 'fast track' review processes in order to address the most urgent needs for new medical products first. Surveillance and compliance efforts also will continue to be directed toward identifying and taking action on the most serious threats to U.S. consumers. Several performance goals in Part Two of this plan address high priority risks.

Address Statutory Requirements in Pre-Market Review and Inspection Coverage

FDA has made significant strides toward meeting its statutory requirements to review new products within prescribed time frames--particularly in the PDUFA-funded areas which address drugs and biologics. In other pre-market review areas, and in all of the programs where biennial inspection coverage is required by statute, FDA will attempt to achieve a balance between:

- Making progress toward more comprehensive statutory coverage;
- Addressing high risk priorities, which could divert resources away from simple coverage goals; and
- Investing in new collaborative arrangements which, in the long run, should enhance the Agency's ability to meet its statutes.

1.2.2 Presidential Initiatives Contributing to FDA's Strategic Goals

Also linked to FDA's mission and strategic goals are three Presidential initiatives that represent current national priorities to prevent unnecessary death and disability. FDA plays a key role in each of these efforts. The three programs address tobacco use among youth, food safety; and bioterrorism. Each priority has been described in detail in the budget justification.

Presidential Initiative	Description	FDA Approach
Tobacco Use Among Youth	To reduce the access and appeal of tobacco products to young people, to enlist retailers and others in these efforts, and to develop regulatory procedures for cigarettes and smokeless tobacco products.	Enforcement and evaluation, compliance outreach, and product regulation
Food Safety	To reduce the risk of foodborne illnesses and death related to microbiological contamination of domestic and imported foods.	Surveillance, coordination, inspection, education, research and risk assessment
Bioterrorism	To respond to chemical and biological threats from bioterrorism, FDA's roles include development of new vaccines and drugs, safeguards for the food supply, and research for diagnosis and treatment of disease outbreaks.	Coordination of vaccine development and inventory; strengthen FDA science capacity

1.2 FDA Programs That Will Implement Agency Goals and Strategies

FDA resources are organized into seven "programs" that coincide with the organization of the President's annual budget. These programs constitute the major sections in Part Two of the performance plan

Foods -- Promotes and protects the public health and economic interest by ensuring that the food supply is safe, nutritious, wholesome, and honestly labeled. The program also ensures that cosmetics are safe and properly labeled.

Human Drugs -- Ensures that all drug products used for the prevention, diagnosis, and treatment of disease are safe and effective; and that information on proper use is available to all users.

Biologics -- Ensures the safety, potency, and effectiveness of biological products for the prevention, diagnosis, and treatment of disease. This includes blood and blood products, blood test kits, vaccines, therapeutic agents, and other biological products.

Medical Devices and Radiological Health -- Ensures that medical devices are safe, effective, and properly labeled; and that the public is not exposed to unnecessary radiation from medical, industrial, and consumer products.

Animal Drugs and Feeds -- Ensures that only safe and effective animal drugs, devices, feeds, and food additives are marketed; and that foods from animals that are administered drugs are safe for human consumption.

National Center for Toxicological Research -- Conducts scientific research to develop methods for regulatory applications.

Tobacco -- Works to reduce young people's use of tobacco through education, enforcement, and partnerships with CDC and other Federal and state health agencies.

In Part Two of the Performance Plan, each of FDA's programs has outlined strategies and identified performance goals that are aligned with and operationalize the Agency's overall strategic framework.

1.3 Partnerships and Coordination

FDA's primary challenge in the 21st Century is to minimize product risk to the consumer as the scientific complexity of these products grows exponentially, and as trade, regulation, new health threats, and consumption patterns continue to change. To meet this challenge, FDA must call upon the capabilities of its various stakeholder communities - regulators, health partners, industry, and consumers - to generate effective solutions to these complex public health and safety challenges.

During the past year, FDA has engaged stakeholders in a series of dialogues to determine how to narrow the gap between current Agency performance and public expectations. FDA has listened closely to stakeholder suggestions and has incorporated these into many of the collaborative initiatives outlined in the FY 2001 Performance Plan. Examples of these initiatives are described in the following paragraphs.

Collaborative Institutes:

To **enhance the regulatory science for medical devices,** FDA plans to create a Joint Institute for Medical Devices and Radiation. Aimed at increasing intellectual capital and cooperation, the effort will represent an important step toward pulling together the knowledge from Cooperative Research and Development Agreements and contracts designed to advance CDRH regulatory science.

FDA is also proposing in FY 2001 the development of a National Regulatory Training Institute. This Institute will develop systematic training programs for safety surveillance involving participants from FDA, state and local government agencies, international regulatory authorities and industry.

The Product Quality Research Institute (PQRI) initiative will continue to be emphasized as a method of leveraging external scientific expertise to help support **sound regulatory policymaking.** PQRI is a nonprofit foundation that serves as a vehicle for FDA, industry and universities to collaborate on key issues in pharmaceutical product quality through research and expert group analysis. Participating members such as the American Association of Pharmaceutical Scientists, the Generic Pharmaceutical Industry Association, and the Nonprescription Drug Manufacturers Association work with FDA and other government and private organizations to determine the optimum type of information that should be submitted in drug approval requests.

FDA also continues to reap applied research benefits from its two food partnership institutes - the Joint Institute for Food Safety and Nutrition with the University of Maryland and the National Institute for Food Safety and Technology in conjunction with the University of Illinois.

Risk Management Communication and Education:

FDA is embarking on several initiatives which capitalize on collaboration with partners in order to disseminate risk management information more cost effectively than FDA could accomplish on its own. To illustrate: In a recently conducted Government-Wide Customer Satisfaction Survey, food shoppers indicated a need for more information on the nutritional content of food, particularly to at-risk groups. FDA is consulting with several organizations, including the Department of Agriculture, CDC, NIH and FTC to develop tools for educators and consumers that are designed to teach consumers how to use food labels. FDA is also working with the National Science Teachers Association to develop a supplementary food science curriculum at the middle and high school levels.

Targeted Collaboration on Critical Health Issues:

FDA scientists play key roles with many national, international and interagency organizations involved in establishing **vaccine policy and practice.** Examples are the National Vaccine Advisory Committee, the Committee on Infectious Diseases of the American Academy of Pediatrics; the World Health Organization; and the National Institute of Biological Standardization and Control (in the United Kingdom). FDA works on committees related to AIDS, such as the NIH HIV Vaccine Selection Committee, as well as working groups on Influenza Pandemic Preparedness, the Adult Immunization Plan, and the TB vaccine development plan.

FDA has key responsibilities for safety of the **nation's blood supply.** This includes standards setting and health education. The American Association of Blood Banks, the American Red Cross, state health agencies, NIH and CDC are a few partners in this effort.

In FY 2001 the Agency will continue the development of a regulatory plan related to current and new **tobacco products.** The Agency may organize an interdisciplinary panel with DHHS agencies such as the National Cancer Institute, the National Heart, Lung, and Blood Institute, the Office on Smoking and Health and the National Institute on Drug Abuse to consider and propose appropriate performance standards.

Integrated/Shared Surveillance Networks:

FDA is working in several venues to realize synergies in multi-organizational surveillance systems. One area of emphasis in the FY 2001 plan is the further development of an **integrated sentinel surveillance network** to include hundreds of participating hospitals across the U.S. Through these sentinel systems a select group of highly trained reporting facilities can provide high quality, informative reports that can be representative of user facility device problems in general.

As part of the Food Safety Initiative for FY 2001, FDA will enhance the Federal-state data-sharing capabilities of two surveillance systems, **FoodNet and PulseNet,** both of which are critical to the early detection and containment of foodborne outbreaks and to the detection of emerging antibiotic resistant pathogens.

The **National Antimicrobial Resistance Monitoring System** will also be strengthened in FY 2001. This system, initiated by FDA, CDC and U. S. Department of Agriculture helps detect whether foodborne pathogens are developing resistance to drug treatment. The system will be enhanced by increasing the number and source of bacterial isolates (human and animal) collected and the number of states covered by the system.

FDA will also continue to coordinate with the U.S. Customs Service to strengthen the Operational and Administrative System for Import Support. This is a monitoring system that screens unacceptable products from entry into U.S. commerce. As information on products and country of origin is further developed, FDA can improve their systematic profiling capabilities in order to better target potential risk.

Cooperative International Standard Setting:

FDA will continue to participate in international forums to ensure that U.S. interests are upheld in establishing standards for products under the Agency's regulatory purview. The Agency will continue to collaborate with the International Committee on Harmonization, The International Standards Organization, Codex Alimentarius, and The World Health Organization among others, to achieve this goal.

The Agency will also continue to make progress in further refining provisions of the Mutual Recognition Agreement with the European Union, and in training overseas counterparts so that those provisions can be successfully implemented.

Third Party Review, Inspection, Testing:

FDA will continue to test the concept of utilizing third parties as independent reviewers, inspectors and testers of FDA-regulated products. The goal of these initiatives will be to outsource these functions where: a) there are no compromises to the health or safety guarantees associated with these products; and b) where the use of third parties is more cost-effective than carrying out the task inside FDA.

1.4 Highlights of FY1999 Performance and Key Performance Goals for FY 2000 and 2001

Each of FDA's programs made significant progress toward achieving the goals that were established in the FY 1999 Performance Plan. FY 2000 and 2001 performance goals will build on the progress achieved in the past year. The Table below provides a sample of the Agency's significant achievements in FY 1999 and outlines major prospects for the next two fiscal years. The table also illustrates the versatility of FDA in achieving a strategic balance in pursuit of diverse goals.

Program	FY 1999 Accomplishments	FY 2000 Goals	FY 2001 Goals	Significance
Foods	Exceeded our goals for reviewing food and color additive petitions.	Focus inspection on high risk imports and foreign food safety systems	Inspect all high risk domestic food firms annually	Reinforces agency strategy of managing highest risk in light of increasingly complex trade environment
Human Drugs	Approved 35 new drugs. These new products, plus the 5 new biologics approvals [see below], target diseases costing society $600 billion annually. On track to meet or exceed all PDUFA performance commitments	Launching major scientific collaboration with academia & industry to address key drug product quality issues [Product Quality Research Institute]	Expand medical error reporting & correction aimed at helping to prevent 100,000 adverse events annually.	Balanced strategic approach which includes collaboration to focus science issues, building networks to minimize adverse product

				effects, and rapidly stewarding critically needed drugs to market
Biologics	Approved 5 new biologics, including vaccines approved for Lyme disease, rheumatoid arthritis and blood disorders	Fully meet statutory inspection requirements for biologics and blood industry	Accelerate review times for standard PLA, BLA applications	Will exceed PDUFA review goals for the seventh consecutive year, while meeting statutory inspection requirements
Animal Drugs & Feeds	Reinvented pre-market review process in collaboration with industry to reduce future review times	Maintain strong anti-microbial resistance sampling program as part of food safety initiative	Amplify veterinary science capability through establishment of Staff College	Performance supports strengthening science capability, & working closely with collaborators to assure consumer safety throughout life span of veterinary drug development and use
Medical Devices & Radiological Health	Streamlined the review process to accelerate review times for important new medical devices	Develop medical device surveillance network (MedSun), which extends power of injury reports	Recruit over 200 more hospitals into sentinel system	Performance highlights reflect increasing reliance on collaboration with health professional and industry allies to

		through use of representative facilities		address significant medical device health and safety issues — both prior to and subsequent to market entry
National Center for Toxicological Research	Completed method to detect 13 foodborne pathogens in one sample, resulting in faster hazard detection	Identify early indicators of cancer in highly susceptible populations	Develop methods for rapidly identifying biological warfare agents for faster response to bioterrorist threats	Performance reflects direct scientific support in addressing critical risk management decisions throughout all Agency programs
Tobacco	Exceeded contracting goals by signing contracts with all 50 states & 3 territories to conduct compliance checks	Conduct 200,000 compliance checks	Expand compliance checks to 228,000	Performance goal demonstrates the amplification of FDA effort as a result of working through two important strategic alliances — with states and retailers

Part 2: Program Planning and Assessment

Key to Reading Part II Program Sections

Each FDA program area has been organized using a common sequence as shown below. The graphic on the next page illustrates the convention for the summary charts found within each program section (Summary of Performance Goals).

2.X Program Area Title

2.X.1 Program Description, Context, and Summary of Performance

- **Total Program Resources--**Identifies funding for FY 98-'01
- **Description** — Provides an overview of the Program, its purpose and how strategic goals support that purpose.
- **Program Accomplishments** — Highlights major program performance results for FY 1999. Performance results are explained in greater detail in the goal-by-goal presentation of performance.

2.X.2 Strategic Goals

Each program section contains two strategic goals — the first addressing effective pre-market review of products; and the second focusing on assuring safety of products once they are on the market. These strategic goals align with the agency-wide pre-market and post market strategic goals, explained in Part One of this Plan.

A. **Strategic Goal Explanation**
   - **Approach** — Describes the strategies that will be employed to pursue the strategic goal. Explains how performance goals support the strategies.
   - **Research and Standard Setting Contributions** — Explains how these two functions are critical to achievement of strategic and performance goals.
   - **Leveraging/Communication** — Explains the importance of working effectively with FDA allies in achieving goals.

B. **Summary of Performance Goals (see graphic)**

C. **Goal by Goal Presentation of Performance**
   - **Goal Statement**
   - **Context of Goal** — Explains the importance of the performance goal in contributing to broader strategic goals and to desirable health and/or safety outcomes.
   - **Data Source** — Identifies the information base that is used to establish baselines, develop goal statements and track progress.
   - **Performance** — Reports on FY 1999 performance results, explains reasons for variance between planned and actual achievements.

2.X.3 Verification and Validation

KEY TO READING PERFORMANCE SUMMARY TABLE

Performance Goals	Targets	Actual Performance	Reference
ASSURE SAFETY **Maintain annual inspection coverage for mammography facilities .....** **(15011)**	FY 01 Goal: 8,900 FY 00 Goal: 8,900 FY 99 Goal: None	FY 01 FY 00 FY 99: Dec 99 FY 98: 9,413	P.25
TOTAL FUNDING (000)	FY 01: FY 00:		

Column 1: Performance goal statements are shown in bold.
Column 2: Shows each year's intended, or "targeted," performance for that goal. If there were changes to the goal statement wording, or added or deleted goals, this will also be noted.
Column 3: Shows performance results or the anticipated date for having results for FY99 (ending on 9/30/99) and, in some cases prior fiscal years.
Column 4: Indicates where additional information can be found in the budget document, or other source.
ID Number (shown in red on the above table): Each performance goal has a unique ID number.
Total Funding: The dollars needed annually to reach the target performance under this strategic goal (dollars in thousands).
FY 00/01 Data: Results for FY 00 and 01 performance goals will be available 6 - 12 months after the end of the fiscal year.

2.1 FOODS

2.1.1 Program Description, Context, and Summary of Performance

Total Program Resources:				
	FY 01	**FY 00**	**FY 99**	**FY98**
Total ($000)	328,907	267,449	235,203	206,249

The FDA's Foods Program is responsible for ensuring a safe, nutritious, wholesome, and honestly labeled food supply and safe and properly labeled cosmetics for the American public. FDA regulates all food except meat, poultry, and frozen and dried eggs, which are regulated by the U.S. Department of Agriculture. The Foods Program accomplishes its mission by: setting standards and developing regulations for the food industry; taking timely and appropriate action on new food ingredients and dietary supplements before they go on the market to ensure their safety and effectiveness; conducting research to provide the necessary basis for its regulatory decisions; assuring the quality of foods, food ingredients, dietary supplements and cosmetics that are available on the market; identifying food-related health hazards; taking corrective action to reduce human exposure to these hazards and the possibility of food-related illnesses and injuries; and expanding food safety education and training for consumers and industry.

As we enter the 21st Century, trends in the food industry promise better nutrition, greater economies and wider choices for the U.S. consumer than ever before. To illustrate:

- The biotechnology explosion has opened new frontiers in product development, thus providing us the ability to genetically alter foods to make produce more resistant to disease, add desirable consumption characteristics to the foods, and to prolong shelf life.
- The volume and diversity of imported foods has risen dramatically over the last few decades, and foods once considered exotic are now found throughout the U.S.
- The globalization of the food supply means that foods we consume are being produced by a much larger number of source countries.
- The dietary supplements industry has grown dramatically, as has consumption of dietary supplements.

Each of these developments also presents regulatory challenges for FDA. The Agency's job is to give consumers the confidence to enjoy the benefits of these expanded food choices.

Two strategic goals define the Foods Program's approaches for meeting the challenges of the 21st century:

- Provide consumers quicker access to new food ingredients and dietary supplements, while assuring their safety and effectiveness.
- Reduce the health risks associated with food and cosmetic products by preventing human exposure to hazards, monitoring product quality and correcting problems that are identified.

By striving toward these two goals, FDA will assure the quality of food ingredients, dietary supplements and cosmetic products both before and after they go on the market. Since only a limited category of food products is subject to FDA premarket approval, FDA relies heavily on its postmarket surveillance and compliance activities to assure the safety and quality of the products it regulates.

FY 99 Program Accomplishments

Review of Food and Color Additive Petitions -In 1997, FDA changed its procedures and redefined first actions as a review of all parts of a petition before notifying a petitioner. As a result of these changes, the agency succeeded in meeting and surpassing its by completing 54% of food and color additive petitions within a year of receipt. In addition to expediting the review of petitions, the Agency has been able to provide sponsors more timely feedback and information on the status of petitions. We expect our performance in this user fee dependent area to improve continuously toward full performance in succeeding years.

Integrated National Food Safety System- As part of the Presidential Food Safety Initiative, FDA collaborated with states, the food industry and other Federal food safety agencies to establish an integrated national food safety system. Key accomplishments included the following:

- **Adoption of the Food Code**-Keeping food from becoming contaminated is the intervention that offers the greatest promise for preventing foodborne illness. As of the end of FY 99, the Food Code had been adopted by 15 states. The Food Code is a reference document for regulatory agencies that oversee food safety in restaurants, grocery stores, and institutions such as nursing homes and childcare centers. Adoption by all jurisdictions of the Food Code would result in uniform national food standards and provide the foundation for a more uniform, efficient, and effective, national food safety system.
- **Training for Prevention of Microbial Contamination of Foods**-The Center for Food Safety and Applied Nutrition (CFSAN), working with FDA's Office of Regulatory Affairs (ORA) and partner Federal agencies, has engaged in training the industry and publishing guidance on safe food handling for food producers and consumers. Targeted education programs were developed and provided to segments of the population that are at high risk of food-related illness and injury. FDA conducted these activities in both the national and international arenas by working with states, industry, and foreign governments to ensure a safe food supply.

- **Surveillance of Foodborne Illnesses**-FoodNet is a sentinel network that provides accurate national estimates of the burden and source of specific foodborne diseases in the United States. FoodNet is a critical component of the national integrated food safety system because it provides data to measure the occurrence of foodborne illnesses and to study trends over time in the prevalence and incidence of foodborne illnesses. In FY 99, the geographic coverage of FoodNet was expanded to 32.2 million people, which represents 12% of the American population.

Monitoring the Food Supply-FDA inspects establishments, examines or analyzes food samples, and conducts investigations to determine whether product safety and quality standards are met at each stage of commercial food production and distribution. FDA also uses these inspection activities as opportunities to provide technical assistance to the industry to correct problems and improve safety. In FY 99, FDA inspections of domestic food establishments resulted in a 98% rate of conformance with FDA requirements.

Surveillance of Imported Foods Overseas and at the Border -FDA completed 82 foreign inspections in FY 99 of food plants (78) and farms (4) that produce food products at high risk of microbial contamination. Of these inspections, 26 Establishment Inspection Reports (EIRs) have been reviewed; 8 establishments were placed on Detention Without Physical Examination (DWPE) because of unsanitary conditions; and 4 establishments were issued warning letters. Fourteen establishments were in compliance with FDA regulations. FDA conducted assessments of the food safety systems in Nicaragua, Costa Rica, El Salvador, Guatemala and Honduras to evaluate food regulatory systems in these countries.

The Agency's approach to achieving the strategic goals identified above, as well as key performance goals that will advance the Program in these directions, are outlined in the next sections.

2.1.2 Strategic Goals

Strategic Goal 1:

Provide consumers quicker access to new food ingredients and dietary supplements, while assuring their safety and effectiveness.

A. Strategic Goal Explanation

Approach

The Foods premarket review program focuses on food and color additive petitions, dietary supplements and substances that are generally recognized as safe (GRAS). Under the FD&C Act, FDA must review and approve food and color additive petitions before food manufacturers and distributors can market them. To initiate this review, sponsors are required to submit a petition that includes appropriate test data to demonstrate the safety

of the intended use of the substance. Under the Dietary Supplement Health Education Act (DSHEA), industry is required to notify the Agency of any "new ingredient" for a dietary supplement. DSHEA requires that companies make certain submissions to FDA when health claims are made for dietary supplements and that companies provide a scientific basis for the safety of new dietary ingredients. The Agency must respond to the sponsor's notification with a decision within 75 days. The Agency also has notification programs for substances that GRAS.

The Food Program's key challenge in the premarket area is to expedite review of new food products without jeopardizing public safety. To provide the U.S. public quicker access to new food ingredients and dietary supplements, FDA will:

- Work closely with petitioners, before and after they file premarket approval applications, to avoid or quickly resolve problems
- Simplify and expedite the food and color additive petition review process
- Make timely decisions on new food and color additive petitions (Performance Goal 1-11001)
- Implement review fee programs for food and color additive petition review
- Respond to dietary supplement notifications within 75 days (Performance Goal 2-11025)
- Give priority to those additives that are intended to decrease the incidence of foodborne illness
- Exempt certain substances that are GRAS from the premarket review process and thus make food products containing these substances available on the market more quickly (Performance Goal 3-11003)
- Improve management systems
- Use multi-disciplinary review teams to rapidly resolve new and ongoing safety issues related to petition reviews
- Recruit and hire reviewer-scientists (including professionals with the special skills to evaluate dietary supplements such as medical doctor, consumer safety officers, chemists, botanists, herbalists and toxicologists)
- Use contract personnel for some petition review

Meeting FDA's statutory goals depends on the implementation of review fee programs. These review fee programs, which have the support of industry, would provide a stable source of resources that will permit the Agency to significantly enhance the efficiency of the review processes of food and color additives. The fees would be used to review applications more quickly and meet established review time frames; to provide the consultation required to help petitioners significantly improve the quality of their submission; and to establish the premarket notification program for food contact substances as outlined in FDAMA.

Research and Standard-Setting Contributions to Premarket Review

Several statutes require FDA to ensure that food ingredients, dietary supplements and infant formulas are safe and that health claims appearing on food product labels are based on sound science. A strong connection exists between research and review decisions. Since many new products use new food technologies, it is critical that FDA reviewers have state-of-the-art scientific knowledge when they evaluate the safety and effectiveness of new food technologies and render review decisions. FDA's Foods Program will use several strategies to strengthen its science base. First, the Agency will provide scientific training to reviewers. Second, the Agency will attract highly skilled medical researchers and health professionals to the FDA. Third, multidisciplinary teams will be used to resolve safety issues related to review decisions.

A strong FDA science base will help FDA to develop regulations and guidance for the safety of special nutritionals to implement the 1994 DSHEA. It will also be used to address potential dietary supplement safety issues such as deaths and injuries associated with use of ephedrine alkaloids, and to establish industry guidelines for complying with good manufacturing practices (GMPs). It is critical that FDA develops sound scientific data and expertise to support standards and guidance for dietary supplements. The Agency also needs to undertake research to close the existing gap in scientific knowledge on dietary supplements. This research will involve analytical techniques and sampling methodologies for ingredients, contaminants, pre-clinical and clinical testing, and models for assessing human risk.

Leveraging/Communication

FDA's ability to provide timely and expeditious review of new food ingredients and dietary supplements depends on enhanced communication, collaboration, and cooperation with the food industry, academia, consumers, professional organizations, and health care organizations. Several approaches to leveraging FDA's review efforts have been noted in previous sections. First, one process improvement initiative involves extensive consultation with prospective petitioners before they file, and working closely with petitioners after they have filed, to quickly resolve problems encountered during review. Investing time early in the petition development process will provide valuable feedback to prospective petitioners and save FDA and the petitioner time during the review process. Second, the FDA's use of contract personnel for some petition reviews will permit FDA reviewers to focus their efforts on the more complex applications. Multidisciplinary review teams will continue to help rapidly resolve new and ongoing safety issues related to petition reviews.

Reinvention

The Agency is reinventing its Food Premarket Review program in two important ways. First, FDA is establishing a notification program for food contact substances under the new section 409(h) of the FD&C Act which was added by the Food and Drug Administration Modernization Act (FDAMA). This premarket notification process will become the primary method by which FDA regulates food additives that are food contact substances. This notification process will be used to authorize the marketing of a food contact substance except when the FDA determines that the submission of a food additive petition is needed to provide adequate assurance of safety. The notification process is intended to expedite the marketing of safe food contact substances. Second, during FY 98, FDA implemented a proposed notification procedure for independent GRAS determinations. The Agency solicited and received comments on the proposed notification procedure and is finalizing the regulation for its implementation. Once the regulation is finalized, this procedure will largely replace the resource-intensive GRAS affirmation petition process with a less resource-intensive process.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Complete first action on 50% of food and color additive petitions within 360 days of receipt. (11001)	FY 01: 50% FY 00: 40% FY 99: 30%	FY 01: FY 00: 12/00 FY 99: 54%	Increase
2. Reduce the percentage of overdue food and color additive petitions to 30% of petitions under review. (11002)	FY 01: NA FY 00: NA FY 99: 30%	FY 01: NA FY 00: NA FY 99: 42% FY 98: 38%	
3. Respond to 90% of notifications for dietary supplements containing "new ingredients" within 75 days. (11025)	FY 01: 90% (new) FY 00: NA FY 99: NA	FY 01: FY 00:NA FY 99: 3/00 FY 98: 100%	
4. Complete processing of 80% of GRAS notifications within the time frame established by the final rule. (11003)	FY 01: 80% FY 00: Finalize GRAS Rule ; 80% FY 99: Finalize the rulemaking creating a	FY 01: FY 00: FY 99: made substantial progress toward finalizing GRAS rule.	

	premarket notification process for independent GRAS determinations.		
TOTAL FUNDING: ($000)	FY 01: 39,694 FY 00: 27,693		
Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-by-Goal Presentation of Performance

1. Complete first action on 50% of food and color additive petitions within 360 days of receipt. (11001)

- **Context of Goal:** In mid-FY 97, FDA changed its procedures and a first action was redefined as a review of all parts of a petition, followed by issuance of a "not approvable" letter, or publication of a response in the Federal Register, if appropriate. The procedure change was made to expedite the review process as well as provide sponsors with more timely, strategic feedback and information about the overall status of a petition. Prior to FY 97, a food and color additive petition was reviewed and if a deficiency in any single area was found, the petitioner was notified and asked for information, and review of the remainder of the petition was suspended. Previously, this notice was defined as a first action.

  In this goal, "time to first action" is not the same as meeting the statutory time frame (i.e., 90 days, extendable to 180 days). It is widely recognized that meeting the current statutory time frame is an unrealistic goal for all food and color additive petitions, especially the more complex ones. The impracticability of the current time frame was acknowledged in the report from the June 1995 House hearing, and a recommendation to change the time frame to '360 days of receipt' was included in the Agency's testimony before the House Committee on Government Reform and Oversight in 1996. The target is a projection of FDA performance given additional resources, including those already provided, and those requested for FY 01; and anticipated workload. Using the PDUFA as a model, user fee performance goals will be developed commensurate with the user fee collections authorized for a given fiscal year.

Since the 1995 and 1996 hearings, the FDAMA established the notification process for food contact substances. The premarket notification program began to operate on January 18, 2000. Several factors will influence future performance on the goal of completing first action on 50% of food and color additive petitions within 360 days. The most important of these factors is the implementation of the new premarket notification process. Although in the past FDA has been able to predict our annual workload for this goal, with the advent of the premarket notification system, it is extremely difficult to predict what the future workload will be. Second, in FY 01, the year after implementation of the notification program, we expect that many of the simpler food additive petitions that can be completed within 360 days will be filed under the notification program and thus decrease the workload for this goal. However, since the remaining petitions are likely to be more complex and take more time to review, the Agency performance on this goal may decline initially. Third, the premarket notification program may also increase the backlog of overdue petitions (see Performance Goal 2-11002). Once the notification and the petition review processes are well established, FDA expects performance on this goal to increase substantially toward full performance in succeeding years.

- **Data Sources:** CFSAN's electronic workflow system
- **Performance:** In FY 99, FDA met and surpassed this goal of 30% by completing "first action" on 54% of food color and additive petitions within 360 days of receipt. The denominator for this measure includes not only the more complex food and color additive petitions, but also petitions of the type that in FY 00 and beyond will be filed under the new premarket notification programs. These less complex petitions contributed substantially to the FY 99 performance level of 54%. In the next few years, we expect that performance on this goal will decline below the actual performance for FY 99 as product sponsors avail themselves of the more rapid review times offered by the premarket notification program. Achievement of this goal also depends on the authorization and collection of review fees in FY 01. This increase in resources is necessary for the Agency to continuously improve performance in the review of food and color additive petitions. These additional resources will be used to hire and train highly qualified personnel to review safety data. In addition, FDA will complete testing and initiate the operation of a document tracking system that will track progress toward the goal and will provide detailed information on the status of petitions and FDA tasks to be completed.

2. Reduce the percentage of overdue food and color additive petitions to 30% of petitions under review. (11002)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. FDA is committed to reviewing food and color additive petitions within 360 days of receipt. The Agency will not be able to meet full performance level on food and color additive petition review until the overdue petitions have been reduced to a level that

permits FDA to devote sufficient resources to reviewing currently incoming petitions within the 360-day timeframe. In this goal, FDA defines "overdue petitions" as petitions under review by FDA for more than 360 days. The denominator for this measure consists of all food and color additive petitions under review. In FY 98, 38% of the petitions under active review were overdue. In FY 99, FDA planned to reduce the percentage of overdue petitions under active review to 30%.

Several factors will influence future performance on this goal. The most important of these factors is the implementation of the new premarket notification process. In the past FDA has been able to predict our annual workload for the goal of completing first actions within 360 days (Performance Goal 1-11001). With the advent of the premarket notification system, it is extremely difficult to predict what the future workload will be. Several product sponsors have already asked the Agency to convert petitions in our current food additive petition inventory into notifications. Since we do not know how many current or overdue petitions in the inventory will be converted or how many new petitions will be submitted in the future, we can not accurately predict our workload for petition reviews. It is also difficult to predict the workload for premarket notifications because under the premarket notification system, each manufacturer or distributor of a food contact substance must submit a notification, whereas approval of a food additive petition allowed any one to manufacture or distribute the additive. The unpredictability of the workload for new petitions and, in turn, for overdue petitions prevents us from setting meaningful targets for FY 00 and FY 01. Second, in FY 01, the year after implementation of the notification program, we expect that many of the simpler food additive petitions that can be completed within 360 days will be filed under the notification program and thus decrease the workload for this goal. However, since the remaining petitions are likely to be more complex and take more time to review, the Agency performance on this goal may decline initially. Third, the premarket notification program may also increase the backlog of overdue petitions (see Performance Goal 2-11002). Once the notification and the petition review processes are well established, FDA expects performance on this goal to increase substantially toward full performance in succeeding years.

In the future, FDA will develop performance baselines for eliminating the backlog of food and color additive petitions and for the notification program. In addition, as discussed in the performance section below, a more appropriate performance metric for assessing FDA's progress toward eliminating the backlog of food and color additive petitions will be developed.

- **Data Sources:** CFSAN's electronic workflow system
- **Performance:** In FY 98, 38% of the petitions under active review were overdue. In FY 99, 42% of the petitions under review were overdue. FDA's Foods Program received an unprecedented increase in the number of food and color additive petitions in FY 99. The Agency postulates that streamlining efforts and timely review of petitions have led industry to submit more petitions than ever before.

This increase in FDA's workload led the Agency to focus its efforts on timely response to newly submitted petitions and prevented the Agency from reducing the backlog as quickly and significantly as planned. The success in meeting the goal of completing a first action on food and color active petitions within 360 days (Performance Goal 1-11001) also artificially inflates the performance measure for this goal even if the absolute number of overdue petitions does not change. This is because the denominator for the FY 99 goal includes both current and overdue petitions. As performance improved on Goal 1, the overdue petitions became a larger proportion of all the petitions under review.

In the future, FDA will develop a more appropriate measure to track its progress toward eliminating the backlog. The Agency will also develop performance baselines for eliminating the backlog of food and color additive petitions.

3. Respond to 90% of notifications for dietary supplements containing "new ingredients" within 75 days. (11025)

- **Context of Goal:** FDA must respond within 75 days to the petitioner with a decision on any new ingredient that will be part of a dietary supplement. The Agency anticipates that notifications for dietary supplements containing "new ingredients" will become more complex and that the volume of such notifications submitted to the FDA will increase. For this reason, the Agency's goal target of 90% for FY 01 is the same as for FY 00. Since the Agency does not know precisely what the workload will be in any given year, the 90% target is considered full performance.
- **Data Sources:** CFSAN's Correspondence Tracking System and manual tracking
- **Performance:** In FY 98, FDA received and responded to 18 (100%) notifications for dietary supplements containing "new ingredients". Data on FY 99 performance will be available in March 2000.

4. Complete processing of 80% of GRAS notifications within the time frame established by the final rule. (11003)

- **Context of Goal:** GRAS notification is a new program and the final rule creating a premarket notification process for independent GRAS determinations is planned for publication in FY 00. Through the GRAS notification process, the FDA seeks to exempt certain substances that are generally recognized as safe from the premarket review process and make food products containing these substances available on the market more quickly. Under the proposed notification procedure, FDA intends to evaluate whether the submitted notice provides sufficient basis for a GRAS determination and whether information in the notice or otherwise available to FDA raises issues that lead the Agency to questions whether use of the substance is GRAS. The proposed notification procedure would allow FDA to direct its resources to questions about GRAS status that are a priority with respect to public health protection. FDA performance will be measured based on the timeframe established by the final rule. Completion of this goal represents

movement from a time and resource intensive review of GRAS affirmation petitions to a streamlined and expeditious review process. The rule replaces the existing process used by sponsors to notify FDA of their independent GRAS determinations.

- **Data Sources:** CFSAN's electronic workflow system; Internal Office of Pre-Market Approval database.
- **Performance:** In FY 99, FDA made substantial progress toward this goal, however due to resource restraints and competing priorities the rule will not be finalized until early 2000. The Agency is accepting new GRAS notifications under the proposed rule.

Strategic Goal 2:

Reduce the health risks associated with food and cosmetic products by preventing human exposure to hazards, monitoring product quality and correcting problems that are identified.

A. Strategic Goal Explanation

Approach

This strategic goal emphasizes three areas of effort-Preventative Control Systems, Compliance Monitoring, and Adverse Event Reporting (AER)-that FDA uses to assure the safety of food and cosmetic products from the point of production through consumption or use by consumers.

Preventative Control Systems

Given the increasing complexity of food safety issues, the most effective strategy for reducing foodborne illness and mortality is to prevent the pathogenic contamination of food through the implementation of food safety standards at all points along the food production chain both in the United States and in foreign countries. FDA's prevention strategies for achieving its objective of reducing health risks associated with food and cosmetic products emphasize:

- Working with states and the food industry to develop and implement food production and preventive control systems that are appropriate to specific product hazard combinations and to establish regulatory processes and systems to more effectively and efficiently monitor the food supply
- Getting more states to adopt the model Food Code, which provides standards and guidance on food safety, sanitation, and fair dealing that may be uniformly adopted by the retail food industry
- Working with foreign countries exporting food and cosmetic products to the U.S. to ensure the implementation of comparable safety standards
- Conducting consumer education and industry education aimed at disease prevention

Compliance Monitoring

Compliance monitoring is a critical component of food safety assurance during and after production and through the commercial distribution stage. FDA has the statutory authority to inspect establishments, examine or analyze samples, and conduct investigations to determine whether product safety and quality standards are met at each stage of commercial food and cosmetic production and distribution. The Agency accomplishes its safety assurance for domestic foods and cosmetics through compliance programs that guide surveillance and enforcement activities.

The greatest challenge the Foods Program faces is how to cope with the growth of the regulated industry and the growth and changes in health risks at a time when resources are decreasing. To improve the coverage for the entire food supply, FDA will:

- Target products with the highest risk of violating food safety and sanitation standards
- Increase the number of domestic establishment inspections,
- Significantly reduce the interval between inspections in domestic food establishments, with an emphasis on dietary supplement establishments and expand import coverage for foods
- Leverage its resources by working with USDA, CDC, other federal agencies and states to establish an integrated food safety system for the nation, including outbreak response coordination and investigation; information sharing and data collection; minimum uniform standards; and laboratory operation and coordination
- Increase the coverage of imports and ensure the existence of an effective international food safety net through three substrategies:
    1. Applying preventive measures at the source of production and thereby reducing the probability that products that violate United States standards will be exported to the United States.
    2. Making rapid and reliable decisions at the border about whether products should be allowed to enter the United States by conducting additional foreign inspections/ evaluations and expanding the reviews of electronic filers.
    3. Targeting products that violate United States standards at the border and preventing their entry, especially those products with a higher risk for violations and those products by firms with historical violations.

The first import substrategy merits further explanation. It is accomplished through several substrategies. First, FDA negotiates bilateral and multinational agreements on specified products and in forums that result in development of acceptable international product standards (for example, the United Nations Food and Agricultural Organization's Codex Alimentarius). These standards can be extended to a large percentage of imports through agreements in which source countries confirm product conformance to these standards. Second, FDA provides educational and technical assistance to foreign governments. Third, the agency evaluates food safety systems in foreign nations. Finally, FDA enters

into international agreements that permit the Agency to establish safety and sanitation standards that food products must meet before they are exported to the United States.

Adverse Event Reporting

Once food and cosmetic products are commercially available to consumers, it is also important to monitor and evaluate adverse events associated with the consumer use of these products. The development of more effective surveillance techniques for detecting, preventing, and controlling potential hazards associated with food and cosmetic products is a top priority for the Agency. The Agency needs better ways of identifying problems with dietary supplements. In view of the rapidly increasing use of, and safety hazards associated with some dietary supplements (e.g., ephedra) and other special nutritional products, improving databases/ surveillance systems for these food products is also a top priority for FDA.

With resources requested in FY 00, FDA will continue to work diligently to enhance the Agency's capacity for collecting, monitoring and evaluating adverse events by:

- Improving the infrastructure with hardware/ software upgrades
- Increasing epidemiological staff
- Creating a series of links with existing database and surveillance systems external to the Agency

Research and Standard-Setting Contributions to Surveillance/Compliance

Research

A strong science-base is vital for effective achievement of the Foods Program's product assurance goals. The Agency's research activities for its food and cosmetics program are directed toward understanding the nature and severity of hazards to the consumer and the means to control these hazards. The Foods Program will strengthen its science base through the following strategies:

- Providing scientific training to field investigators and reviewers
- Attracting highly skilled medical researchers and health professionals to the FDA
- Expanding existing collaborations with industry and academia to build upon other research activities
- Expanding research efforts to fill critical gaps in the Agency food science base

The National Center for Food Safety and Technology (Moffett Center) and the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) are key components of FDA's efforts to achieve established food safety objectives, especially those under the FSI and Produce and Imports Food Safety Initiative (PIFSI). These partnerships with academia and industry allow for more efficient use of research resources and enhance the quality of food safety and nutrition research and public health policy. The additional resources requested for FY 01 will permit FDA to expand risk assessment efforts in JIFSAN and

the Moffett Center to fill critical gaps in its ability to assess exposure to foodborne hazards. This expanded risk assessment research effort will enhance FDA's ability to more rapidly and accurately characterize the nature and size of the risk to human health associated with foodborne hazards, as well as the effects of intervention. More rapid and accurate risk assessment techniques are critical to Agency efforts to provide consumers with greater protection against potential hazards posed by foodborne pathogens and other contaminants.

To fill critical gaps in the FDA food science base, the Agency will develop an intensive research program on dietary supplements that will result in the development of sound scientific data and understanding from which standards and guidance on the safety of these products will be established. The research program will include development of analytical methods for active ingredients and contaminants, pre-clinical tests, clinical trials, epidemiological and other specialized studies, and development of models for assessing human risks. This research program will be a collaborative effort with a major university with an established research program on dietary supplements.

Microbiological research and the development of risk assessment techniques provide the scientific basis for the integrated food safety system. Inspection and surveillance activities in particular require the development of science-based tools through research. Most contamination is no longer detectable by simple visual review, but rather is microbial in nature and requires sophisticated state-of-the-art technologies to detect and control. These activities are critical in providing information about pathogens, how they enter and interact with the human body, and the best methods for attacking them.

Research to improve analytical methods and sampling techniques, two essential tools in postmarket surveillance and other monitoring and compliance activities, will be funded with additional resources in FY 01. Areas of particular emphasis in the research program will be:

- Biotechnology
- Dietary supplements
- Bioterrorism agents

Research is also needed to develop data and scientific understanding from which standards, guidance, and regulations will be revised or established to ensure the safety of foods and cosmetics. The research program will include development of detection methodologies, studies of sources and modifiers of allergic response(s), elucidation of the toxicology of photosensitizers, and market research.

Standard Setting

Regulations are the principal means by which law and policy are translated into standards for compliance. Innovations in technology, manufacturing processes and new products change is constant in the industries the Agency regulates. The Agency endeavors to stay abreast of the changes to develop new regulations and amend or revoke old regulations,

when necessary to protect consumers against potentially hazardous products. In FY 01, activities on standard development will focus on special nutritionals, especially dietary supplements. The following are examples of public health issues to be addressed with additional resources in FY 01.

- The FDA will face a more pronounced "tug-of-war" between consumer demand for protection from hazards and consumer desire for earlier and free access to regulated products such as dietary supplements to improve their health. There is a need for a single, well-defined overall strategy for dietary supplements and special nutritionals that demand objective, measurable standards of safety.
- The dietary supplements industry sells products on which millions of Americans rely. Consumers spend approximately $12 billion a year on dietary supplements according to the 1998 "Nutrition Business Journal" annual report. These products are now readily available in supermarkets, retail stores and the Internet, making them easily accessible to children and adolescents, as well as to adults. A Good Manufacturing Practice (GMP) regulation for dietary supplements will be a useful tool for both the industry and the Agency in preventing significant or unreasonable harm to the consumer. CFSAN will publish a final rule on GMP regulations assisting industry in producing dietary supplements that are not adulterated and that comply with the safety provisions of the FD&C Act.
- Develop regulations and guidance for the safety of special nutritionals to implement the 1994 Dietary Supplement Health and Education Act (DSHEA). Address potential dietary supplement safety issues such as deaths and injuries associated with use of ephedrine alkaloids, and establish industry guidelines for complying with good manufacturing practices (GMPs).
- An effective and efficient system of controls to enhance food safety must be developed for the food industry and for commodities with known histories of illness outbreaks including fresh cut produce, sprouts, and eggs. HACCP regulations are being developed in various sectors of the food industry to reduce food safety risks and increase regulatory efficiency.

Leveraging/Communication

FDA's ability to fulfill its mission to assure the safety of food and cosmetic products depends upon enhanced communication, collaboration, and cooperation with the food industry, states, academia, consumers, professional organizations, domestic and international health care organizations, foreign governments, and international standard setting organizations. To accomplish this, FDA does the following:

- Provides assistance to a variety of agencies and organizations in both the public and private sectors to promote a safe food supply and safe and properly labeled cosmetics.
- Fosters cooperation with trade and professional associations, and others on the implementation of preventative control systems in the food and cosmetic industries through outreach efforts.

- Participates in planning and conducting seminars and workshops, which include the international foods and cosmetics community.
- Engages stakeholders in the decision-making process on program priorities, as required by FDAMA.

In FY 01, the Agency will focus on enhancing information exchange with industry, academia, and trade associations. The following are examples of the public health benefits of the Agency's outreach and communication initiatives.

- Greater stakeholder understanding of food and cosmetic safety issues and risks associated with foods and cosmetics beyond the current emphasis of microbial pathogens.
- Increased technical assistance to state and local governmental jurisdictions will encourage and facilitate compliance with FDA regulatory requirements.
- As the competent U.S. authority for regulating the safety of all foods, except meat and poultry, FDA must either issue export certificates for U.S. food products that are exported, or oversee issuance by other federal and state agencies or third parties.
- Disseminate information via fact sheets and industry assistance materials; respond to increased inquiries via telephone or e-mail; translate videos explaining our basic science-based control programs; conduct consumer studies to develop effective education strategies and approaches; develop partnerships to conduct education campaigns; and target education messages to those especially vulnerable populations.
- Expand research efforts in dietary supplements, applied nutrition, food labeling, and cosmetics through collaborative programs and partnerships to further develop the program for training of professional staff; to increase technical assistance to state and local government jurisdictions; and to encourage and facilitate compliance with FDA regulatory requirements.
- FDA, as the lead federal public health agency involved in food safety, promotes uniform implementation of national food regulatory policy among several thousand federal, state, and local agencies and tribes that have primary responsibility for the regulation of retail food establishments. Experience has shown that industry conformance with acceptable procedures and practices is more likely when regulatory officials speak with one voice about what is required to protect public health, why it is important, and which alternatives for compliance may be acceptable. The model Food Code provides guidance on food safety, sanitation, and fair dealing that may be uniformly adopted by the retail food industry. This document is a result of the efforts and contributions of many individuals, agencies, and organizations. With additional resources, the Agency will increase efforts to get more states to adopt the Food Code. FDA will also expand its work with other federal agencies and states to implement a national education program that ensures greater safety in retail food preparation practices using concepts set forth in the Food Code.
- Partnership agreements with states and equivalence agreements with foreign countries are necessary to help FDA promptly assure that seafood products

available to consumers are produced under effective HACCP-based systems. FDA has developed a national seafood HACCP inspection database to record industry compliance. The Agency will implement the HACCP regulation for the fresh juice industry. In FY 01, the Agency will begin implementing appropriate preventative systems for the egg industry.

To improve the coverage for the entire food supply, FDA will work with USDA, CDC, other federal agencies and states to establish an integrated food safety system for the nation. These federal and state partners collaborated extensively during 1998 and continue to collaborate in 1999 on issues related to the development of an integrated food safety system, including roles and responsibilities, outbreak response coordination and investigation, information sharing and data collection, minimum uniform standards and laboratory operation and coordination. In FY 01, FDA will continue to work with federal and state agencies to increase efforts toward making an integrated food safety system a reality. Effective coordination between all the collaborating food safety agencies involved in ensuring the safety of foods offers the best opportunity to significantly improve protection for consumers and achieve substantial reductions in the annual number of food-borne illnesses.

Other FDA leveraging activities include:

- Signing an agreement with the University of Maryland to form the Joint Institute for Food Safety and Applied Nutrition, is paving the way for both organizations to pool specialized knowledge, equipment and facilities.
- Working with CDC and state health departments to resolve food safety concerns and economic fraud cases.
- Working with international organizations, such as Codex Alimentarius Commission-an international food standard setting organization of the Food and Agricultural Organization and World Health Organization - and foreign governments, to help establish internationally recognized safety standards, rules and regulations for imported foods
- Working with states and the food industry to develop and implement food production and preventive control systems (e.g., HACCP) and establish regulatory processes and systems to more efficiently and effectively monitor the food supply.

The Agency will continue existing collaborations with industry and academia to build upon research activities. The Moffett Center and JIFSAN are key components of FDA's efforts to achieve established food safety objectives, especially those under the FSI and PIFSI. These partnerships with academia and industry allow for more efficient use of research resources and enhance the quality of food safety and nutrition research and public health policy. The additional resources requested for FY 01 will permit FDA to expand risk assessment efforts in JIFSAN and the Moffett Center to fill critical gaps in its ability to assess exposure to foodborne hazards. This expanded risk assessment research effort will enhance FDA's ability to more rapidly and accurately characterize the nature and size of the risk to human health associated with foodborne hazards, as well as the effects of intervention. More rapid and accurate risk assessment techniques are critical to

Agency efforts to provide consumers greater protection against potential hazards posed by foodborne pathogens and other contaminants.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
5. Achieve adoption of the Food Code by at least 25 states in the USA. (11010)	FY 01: 25 FY 00: 18 FY 99: 13	FY 01: FY 00: FY 99: 15 FY 98: 10 FY 97: 3	
6. Increase to at least 70% the proportion of adults who report changing their decision to buy or use a food product because they read the food label. (11007)	FY 01: 55% FY 00: NA FY 99: Increase to at least 77% the proportion of people aged 18 and over who use food labels to make nutritious food selections.	FY 01: FY 00: NA FY 99: Collaborated with several Federal agencies to develop educational material for educators and consumers on how to use food labels.	
7. Use educational campaigns and activities to reduce the prevalence of reported risky food preparation and consumption behavior. (11016)	FY 01: NA FY 00: NA FY 99: Use educational campaigns and activities to reduce the prevalence of reported risky food consumption and behavior.	FY 01:NA FY 00:NA FY 99: Conducted 30 training courses for state and local staff who regulate the retail food industry. Collaborated with other agencies in school-based education for children and consumer education for vulnerable populations.	

8. Increase the percentage of domestic produce produced consistent with voluntary GAPs/GMP broadscope guidance to reduce microbial contamination. (11005)	FY 01: NA FY 00: NA FY 99: Increase the percentage of domestic produce produced consistent with voluntary good agricultural practices (GAPs)/ GMPs) broadscope guidance to reduce microbial contamination.	FY 01: NA FY 00: NA FY 99: Published guidance document met with industry; developed survey to determine compliance.	
9. 50% of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning HACCP systems. (11004)	FY 01: NA FY 00: NA FY 99: 50%	FY 01: NA FY 00: NA FY 99: 3/00	NPR Related
10. Increase the percentage of high-risk domestic food establishment inspected once every year. (11020)	FY 01: 90 -100% once every year FY 00: 90 -100% Once every one to two years FY 99: NA	FY 01: FY 00: FY 99: NA FY 98: Through a combination of FDA and state contract inspections, cover 25% to 33% of the 6,250 high-risk establishments.	NPR Related
11. Assure that FDA inspections of domestic food establishments result in a high rate of conformance (at least 90%) with FDA requirements. (11011)	FY 01: 90-100% FY 00: 90-100% FY 99: 90-100%	FY 01: FY 00: FY 99: 98% FY 98: 98% FY 97: 98%	
12 Increase foreign inspections (from 40 to	FY 01: NA FY 00: NA	FY 01:NA FY 00:NA	

75-100), provide education, outreach and evaluate food production systems in foreign countries. (11021.01)	FY 99:75-100	FY 99:82	
13. Increase the number of import exams of high-risk food products. (11021.02)	FY 01: 66,700 FY 00: 60,600 FY 99: NA	FY 01: FY 00: FY 99: NA	Increase
14. Increase the number of audits and assessments of foreign food safety systems, with an emphasis on high volume exporters to the U.S. (11028)	FY 01: 10 FY 00: NA FY 99: NA	FY 01: FY 00: NA FY 99: 4 FY 98: 2	
15. Work with CDC to develop baseline surveillance data on foodborne illnesses. (11008)	FY 01: NA FY 00: NA FY 99: Work with CDC to develop baseline surveillance data on foodborne illnesses**.**	FY 01: NA FY 00: NA FY 99. Geographic coverage of FoodNet expanded to 32.2 million people or 12% of the American population.	
16. Expand monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 11,000 samples. (11027)	FY 01: 11,000 FY 00: NA FY 99: NA	FY 01: FY 00: NA FY 99: NA FY 98: 7,650 total pesticide and chemical contaminant samples: 3,600 domestic and 4,050 imports.	Increase
17. Increase the frequency of releases of information in the Special Nutritional Adverse Event	FY 01: NA FY 00: NA FY 99: Increase the frequency of releases of	FY 01: NA FY 00: NA FY 99: released one summary of adverse events	

Monitoring system (SN/AEMS) from 2 to 4 per year. (11009)	information in the SN/AEMS from 2 to 4 per year.	information from the Special Nutritionals Adverse Events Monitoring System to the public.	
18. Implement a multi-year research plan to develop and improve methods for detection, control and prevention of microbial contamination on fresh.(11012)	FY 01: NA FY 00: NA FY 99: Implement a multi-year research plan to develop and improve methods for detection, control and prevention of microbial contamination on fresh produce.	FY 01: NA FY 00: NA FY 99: In August 1999, FDA finalized and distributed the Three-Year Plan for Research.	
19. Develop modeling techniques for assessing human exposure to a variety of foodborne pathogens. (11013)	FY 01: NA FY 00: NA FY 99: Develop modeling techniques for assessing human exposure to a variety of foodborne pathogens.	FY 01: NA FY 00: NA FY 99: completed and sent the draft risk assessments for *Listeria monocytogenes* and *Vibrio parahaemolyticus* to the Risk Assessment Consortium.	
20. Work with industry and academia to develop new techniques for eliminating pathogens on sprouts and in citrus juice and apple cider. (11014)	FY 01: NA FY 00: NA FY 99: Work with industry and academia to develop new techniques for eliminating pathogens on sprouts and in	FY 01: NA FY 00: NA FY 99: Generated data on the presence of *S. aureus* on three types of domestic sprouted seeds. Began testing imported	

	citrus juice and apple cider.	sprouted seeds from the Import Compliance Program.	
21. Conduct studies on factors that cause foodborne pathogens to develop multiple antibiotic resistance and resistance to traditional food preservation. (11015)	FY 01: NA FY 00: NA FY 99:Conduct studies on factors that cause foodborne pathogens to develop multiple antibiotic resistance and resistance to traditional food preservation.	FY 01:NA FY 00:NA FY 99: Determined the frequency and nature of mutators among clinically and agriculturally relevant isolates of *Salmonella.*	
22. Develop the HACCP final rule for fruit and vegetable juices. (11006)	FY 01: NA FY 00: NA FY 99: Develop the Hazard Analysis Critical Control Point (HACCP) final rule for fruit and vegetable juices.	FY 01: NA FY 00: NA FY 99: Published the proposed rule for Juice HACCP.	
23. Increase the safety of imported foods through participation in international standard setting organizations. (11017)	FY 01: NA. FY 00: NA FY 99: Increase the safety of imported foods through participation in international standard setting organizations.	FY 01: NA FY 00: NA FY 99: Participated in 14 meetings of the Codex Alimentarius, 3 meetings of the World Trade Organization Committee on Phytosanitary Measures.	
TOTAL FUNDING: ($000)	FY 01: 289,213 FY 00: 248,527		
Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01.			

NPR: Goal supports an FDA National Partnership for Reinventing Government Goal

C. Goal-by-Goal Presentation of Performance

5. Achieve adoption of the Food Code by at least 25 states in the USA. (11010)

- **Context of Goal:** The Food Code is a reference document for regulatory agencies responsible for overseeing food safety in retail outlets, such as restaurants and grocery stores, and institutions, such as nursing homes and child care centers. It is neither federal law nor federal regulation, but may be adopted voluntarily and used by agencies at all levels of government that have responsibility for managing food safety risks at retail.

  To achieve the public health goal of reducing foodborne illness to the fullest extent possible, steps must be taken at each point in the farm-to-table chain where hazards can occur. Adoption by all jurisdictions of the Food Code would result in uniform national standards and provide the foundation for a more uniform, efficient, and effective, national food safety system. FDA endorses the Food Code because the Code provides public health and regulatory agencies with practical science-based advice and manageable, enforceable provisions for mitigating risk factors known to contribute to foodborne disease.

  In June 1998, the Secretary of Health and Human Services, Donna Shalala, and the Secretary of Agriculture, Dan Glickman, wrote to U.S. Governors asking them to support adoption of the Food Code by agencies in their states that have responsibility for regulating retail establishments that sell or serve food should use the Food Code as a model to help develop or update their own food safety rules and provide consistency among jurisdictions.

- **Data Sources:** Field Data Systems
- **Performance:** The Food Code was revised and a notice of its availability was published in the Federal Register on February 22, 1999 (64 FR 8576). In FY 99, agencies in 15 States have adopted the Food Code. State agencies achieving adoption of the Food Code are: Minnesota, Rhode Island, New Hampshire, Missouri, North Dakota, South Dakota, Nebraska, Mississippi, Texas, Florida, Kansas, Florida, Utah, Arizona and Iowa.

6. Increase to at least 70% the proportion of adults who report changing their decision to buy or use a food product because they read the food label. (11007)

- **Context of Goal:** Food labels provide consumers information about the composition and nutritional content of foods that they need to make healthy food choices. To help consumers get the most from food labels, FDA and USDA are continuing their multi-year food labeling education campaign. The campaign involves participation by consumer, trade and health groups, as well as by other government agencies. Its purpose is to increase consumers' knowledge and

effective use of the food label and assist them in making accurate and sound dietary choices in accordance with the Dietary Guidelines for Americans.

- The Health and Diet Surveys that are conducted every five years are the most effective means of measuring the effectiveness of educational interventions in promoting the use of food labels. In FY 90, the Health and Diet Survey (pre-NLEA) found that 30% of adults used the food labels to make a decision on the purchase or use of food products. Data from the 1995 survey disclosed that 48% of people age 18 and older reported changing their decision to buy or use a food product because they read the food label. The FY 99 goal focused on measuring the number of people that currently just look at the label but do not make a decision on the purchase or use of food products. In FY 01 the indicator and target for the goal change. The denominator for the FY 01 goal consists of adults who read food labels. Among those adult, FDA wants to measure the percentage who report changing their decision to buy or use a food product because they read the food label. The next national Health and Diet Survey, scheduled for 2001, will provide data on the percentage of adults who use the food label to make decisions on buying food products. Out of those people, our goal in FY 01 is for 55% of them to read labels and make a decision on the purchase or use of food products based on the label.
- **Data Sources:** FDA National Health and Diet Surveys.
- **Performance:** In FY 99, no survey was conducted to measure this goal. However, FDA collaborated with several Federal agencies to develop education tools for educators and consumers that are designed to teach consumers how to use of food labels. Collaborating agencies included the Interagency Coordinating Committee on School Health, the Interagency Task Group on 'Child Health; USDA's Dietary Guidelines Working Group, the Human Nutrition Coordinating Committee; and CDC, SAMHSA, ODPHP, NIH, FTC, FNS CNPP, and USDA. FDA also engaged in non-governmental liaison activities that contributed to increasing the number of consumers who use the food label to make purchasing decisions. These activities included: networking with the Dietary Guidelines Alliance; working with Shape Up American on a Web program; participation in the Partnership for Health Weight Management; completion of phase I of focus group research in four areas of the country, and shared findings with the 'Girl Power and You!' Coalition.

7. Use educational campaigns and activities to reduce the prevalence of reported risky food consumption behavior, reduce the prevalence of reported risky food preparation/ handling practices, and document the occurrence of food service behaviors, actions, and conditions that fall in to the CDC-identified risk factor categories classified as "contributing factors to foodborne illness outbreaks." (11016)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. The Agency's Food Safety Education efforts are aimed at designing and implementing innovative methods to more effectively deliver food safety messages to retail food operations (especially

institutional service operations such as hospitals, nursing homes and day care centers where a large percentage of food-related infections occur), and directly to vulnerable subpopulations.

- **Data Sources:**Consumer Surveys and Reports
- **Performance:**In FY 98, the Agency offered 30 training courses for state and local retail food regulatory staff. Additionally, the Agency initiated collaborative programs for school-based education and consumer education tailored for vulnerable subpopulations.

8. Increase the percentage of domestic produce produced consistent with GAPs/GMP broadscope guidance to reduce contamination.(11005)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. American consumers enjoy one of the safest food supplies in the world. However, over the past several years the number of reported foodborne illness outbreaks associated with both domestic and imported fresh fruits and vegetables has increased compared to other foods. In October 1998, FDA published a guidance document for industry called *Guide to Minimize Microbial Food Safety Hazards for Fresh Fruit and Vegetables*. In FY 99, FDA also conducted grassroots meetings GAPs and GMPs with domestic fresh and foreign fresh produce growers, producers, processors, and manufacturers. The Guide is intended to assist the U.S. and foreign produce industry in enhancing the safety of domestic and imported produce by addressing common areas of concern in growing, harvesting, sorting, packing, and distributing fresh produce. The Guide identifies the broad microbial hazards associated with each area of concern, the scientific basis for that concern, and good agricultural and management practices for reducing the risk of microbial contamination in fresh produce.

  FDA wants to assess the effectiveness of this guidance in promoting the adoption of agricultural and manufacturing practices that are intended to minimize the risk of microbial contamination of fresh produce. A key objective is to establish baseline data on the adherence by domestic producers to GAPs and GMPs. FDA is collecting, reviewing, and evaluating data collected from surveys and other sources to establish a baseline of agricultural practices to assess the risk of contamination in the U.S. food supply and to focus efforts toward prevention, including the development of guidance and prevention systems, and removal of contaminated product from the marketplace. Based on survey findings, FDA will develop and implement a training curriculum in collaboration with USDA/CREES and in consultation with industry on GAPs and GMPs for domestic fresh produce growers, packers and shippers. This training will ensure that best practices in industry are being used to minimize food safety hazards associated with fresh produce and to encourage industry to adopt the use of safe practices. Plans are also underway to adapt the domestic survey to the international arena. In FY 00, USDA will conduct the National Agricultural Statistics Survey (NASS), which will provide the baseline data regarding current

agricultural practices and a means to measure change in these practices as guidance and other efforts to improve the safety of fresh fruits and vegetables are developed and implemented. In FY 00 a pilot survey will be conducted in Costa Rica.

- **Data Sources:** National Agricultural Statistical Survey (NASS) to be conducted in FY 00
- **Performance:** In October 1998, FDA published a guidance document for industry called *Guide to Minimize Microbial Food Safety Hazards for Fresh Fruit and Vegetables*. This guide is commonly referred to as the GAPs/GMPs. In FY 99, FDA also conducted grassroots meetings on GAPs and GMPs with domestic fresh and foreign fresh produce growers, producers, processors, and manufacturers. In FY 99, FDA also worked with USDA to (1) develop survey questions for the NASS that could be used in surveys for produce operations and (2) complete a pretest of the survey instrument among growers and packers in California and New York. The revised NASS survey will integrate data collection activities for chemical use an for food safety activities. Data collection for the national survey is expected to begin in 2000, and data will be available in 2001. In addition, survey questions are being designed so they can be used in surveys or produce operations in foreign countries.

9. 50% of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning HACCP systems. (11004)

- **Context of Goal:**This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. An automated computer data collection system was established to receive and record inspection findings sent from remote locations by fax machines. To ensure uniformity in determining compliance with the seafood HACCP regulation, only inspection results from HACCP trained and certified inspectors using the standardized inspection forms are accepted. Findings are given a quality control review before entry into the National Seafood HACCP Compliance Database.
- **Data Sources:** FDA's Field Data System; National Seafood HACCP Compliance Database
- **Performance:** In the first round of inspections of approximately 4,100 domestic seafood processors, approximately 1,200 firms achieved full compliance with the regulation. In FY 99, although fewer than 50% of these processors met all the criteria for operating a functioning HACCP system, only 4% of the firms inspected warranted regulatory action due to problems that raise significant public health concerns. FDA's implementation of HACCP in the domestic seafood industry has resulted in increased awareness, compliance and application of food safety principles by the industry. In addition, HACCP implementation enabled FDA to ascertain that the vast majority of the domestic seafood industry uses HACCP principles in a way that minimizes serious public health threats. In evaluating the public health outcome of HACCP implementation in this industry, we feel that the Agency has met the intent of using HACCP as a strategy for to

prevent microbial contamination of seafood produced in the United States. As a consequence, beginning in FY 00, this goal was combined with the performance goal for that relates to conformance rates resulting from the inspection of domestic food establishments (Performance Goal 11).

10. Increase the percentage of high-risk domestic food establishment inspections to once every year. (11020)

- **Context of Goal:** The existing Field Data Systems currently do not differentiate between low-, medium-, and high-risk domestic food establishments. The Agency has established a definition for high risk establishments that includes those involved in the manufacture of low acid canned food (LACF) products, infant formula products, heat and serve products, ready to eat products and other products that do not require heating to a temperature sufficient to kill bacteria prior to consumption. Based on this definition, the Agency estimates that there are approximately 6,250 such establishments in its establishment inventory. It is also estimated that these establishments are currently inspected on an average of once every three to four years or more. In FY 01, the number of high-risk establishment inspections conducted annually will be increased to include coverage of the entire inventory (approximately 6,250 establishments). FDA, in conjunction with the States, will focus on those establishments that produce foods most susceptible to contamination of foodborne pathogens. The percentage range provided for the inspection frequency allows for unanticipated redirection of resources for emergencies or related incidents, such as foodborne illness outbreaks.
- **Data Sources:** Field Data Systems
- **Performance:** This goal is a new commitment in FY 00.

11. Assure that FDA inspections of domestic food establishments (including domestic seafood establishments), in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements. (11011)

- **Context of Goal:** Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector. Before FY 00, the Agency had measured conformance of the domestic seafood industry and conformance of all other domestic food establishments separately. In FY 99, in evaluating the public health outcome of HACCP implementation in this industry, the Agency concluded that it had met its intent of using HACCP as a strategy for to prevent microbial contamination of seafood produced in the United States. As a consequence, beginning in FY 00, the performance goal relating to conformance of the domestic seafood industry with

HACCP (Performance Goal 9) was combined with the performance goal for that relates to conformance rates resulting from the inspection of domestic food establishments (Performance Goal 11)

- **Data Sources:** Field Data Systems; National Seafood HACCP Compliance Database
- **Performance:** In FY 97, 98 and 99, FDA inspections of domestic food establishments (excluding the domestic seafood industry) resulted in a 98% rate of conformance with FDA requirements.

12. During FY 99, enhance the safety of imported products through surveillance of imported food products at the border, increase foreign inspections (from 40 to 75-100), provide education, outreach and evaluate food production systems in foreign countries. (11021.01)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. FDA data show that the number of imported food entries has doubled over the past 7 years and that, based on recent trends, imports are expected to increase by an additional 30% by 2002. The reality of the "global marketplace" means that substantive changes in philosophy and approach are now required to ensure the safety of the U.S. food supply. The agency recognizes that reliance on a limited number of border inspections and foreign establishment inspections as the primary means of ensuring food safety is no longer effective or sufficiently resource efficient to enable the FDA to ensure that imported foods are safe. The Agency has developed a strategy that includes conducting inspections of selected high-risk foreign food establishments to determine their compliance with applicable FDA regulations and inspection of firms that consistently have compliance violations. Inspections provide FDA an opportunity to assess controls that prevent or minimize hazards. FDA uses the results of inspections to promote the use of more effective controls, and thereby prevent outbreaks, reduce or eliminate hazard controls, and reduce the burden of end products sampling. Due to FDA's lack of authority in inspecting foreign food establishments, the Agency is working with foreign countries and foreign establishments in order to seek the necessary permission to inspect / evaluate these firms. These inspections will lead to safer imports and expedited processing of foreign food products.
- **Data Sources:** Field Data Systems
- **Performance:** FDA completed 82 foreign inspections in FY 99 of food plants (78) and farms (4) that produce food products at high risk of microbial contamination. Off these inspections, 26 Establishment Inspection Reports (EIRs) have been reviewed; 8 establishments were placed on Detention without Physical Examination (DWPE) because of unsanitary conditions; and 4 establishments were issued warning letters. Fourteen establishments were in compliance with FDA regulations.

13. Increase the number of import exams of high-risk food products. (11021.02)

- **Context of Goal:** Traditionally, FDA has been viewed as a domestic public health agency, charged primarily with protecting the health and economic interests of American consumers. This traditional, domestically oriented regulatory approach, complemented by selective enforcement programs for imports, was quite effective until the emergence over the last twenty years of the "global marketplace", where foods available to U.S. consumers may originate in any of more than one hundred countries. Imported foods now constitute more than 10% of the U.S. food supply, and for some commodities, such as many fresh fruits and vegetables, 40% or more are imported. The volume of imports is increasing at a rate that far exceeds the level of resources that FDA can devote to inspections, even with recent resource increases received under the Food Safety Initiative. FDA data show that the number of imported food entries has doubled over the past 7 years and that, based on recent trends, imports are expected to increase by an additional 30% by FY 02. FDA is using three main strategies to target its efforts and to better utilize existing resources earmarked for ensuring the safety of imported foods. These strategies include reducing the probability that violative products will be exported to the United States; making rapid and reliable decisions on product entry at the U.S. borders; and targeting violative products at the border and preventing their entry.

  This goal supports the third strategy of targeting suspect products at the border. Import examinations include sample analyses, detentions without physical exams, and import field exams. A small percentage of import entries are directly assessed, through field examinations, and less than 1 percent of imports, through laboratory analyses. The need to directly examine a small percentage of imports is based on empirical evidence that selected product categories from certain source countries or shippers have shown significant violation rates. In addition, surveillance examination of imported products is necessary to identify new problem firms or emerging health concerns. Certain violative firms and products with poor histories of compliance are subject to detention without physical examination at the border until the importer can prove the product complies with FDA standards. FDA uses the Operational and Administrative System for Import Support (OASIS), in coordination with the U.S. Customs Service, to provide data on what products are being imported and at what U.S. port they arrive. It also provides information on compliance actions related to imports. FDA will continue to refine and standardize its risk-based criteria for screening imports as more comprehensive information concerning the product and country of origin are entered into the automated review system.

- **Data Sources:** Field Data Systems
- **Performance:** This goal is a new commitment for FY 00.

14. Increase the number of audits and assessments of foreign food safety systems, with an emphasis on high volume exporters to the U.S. to ensure a level of food safety protection comparable to domestically produced foods. (11028)

- **Context of Goal:** Traditionally, FDA has been viewed as a domestic public health agency, charged primarily with protecting the health and economic interests of American consumers. This traditional, domestically oriented regulatory approach, complemented by selective enforcement programs for imports, was quite effective until the emergence over the last twenty years of the "global marketplace", where foods available to U.S. consumers may originate in any of more than one hundred countries. Imported foods now constitute more than 10% of the U.S. food supply, and for some commodities, such as many fresh fruits and vegetables, 40% or more are imported. The volume of imports is increasing at a rate that far exceeds the level of resources that FDA can devote to inspections, even with recent resource increases received under the Food Safety Initiative. FDA data show that the number of imported food entries has doubled over the past 7 years and that, based on recent trends, imports are expected to increase by an additional 30% by FY 02. FDA is using three main strategies to target its efforts and to better utilize existing resources earmarked for ensuring the safety of imported foods. These strategies include reducing the probability that violative products will be exported to the United States; making rapid and reliable decisions on product entry at the U.S. borders; and targeting violative products at the border and preventing their entry.

  This goal supports the first strategy of reducing the probability that violative products will be exported to the U.S. FDA conducts a thorough assessment of foreign food safety systems to maintain an assurance that a country's exports comply with the standards established by the FD&C Act. The assessment of foreign food safety systems includes food production, storage, transportation and delivery. This is important for determining the equivalence of foreign country standards, for assuring that foreign nations have the regulatory sitemaps in place to meet those standards and for developing international mutual recognition agreements. In addition, the results of these assessments are useful in determining training, education, and infrastructure development needs. Foreign countries must request an audit or assessment of their food safety system from FDA. FDA prompts these requests by contacting foreign officials. The Agency is concentrating on nations with a high volume of exports to the U.S., particularly seafood and produce exporters. Once a food safety system is audited, the Agency plans to re-evaluate the system annually. In FY 98, FDA completed food safety system assessments in two countries: Honduras and Trinidad & Tobago. In FY 99, FDA conducted audits/assessments of foreign food safety systems in four countries: Costa Rica, Nicaragua, Guatemala and El Salvador.

- **Data Sources:** Field Data Systems
- **Performance:** This is a new commitment in FY 01.

15. Work with CDC to develop baseline surveillance data on foodborne illnesses required to evaluate the effectiveness of, set better priorities for, and determine appropriate outcomes for the Food Safety Initiative. (11008)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. This goal relates to FDA's role as a leader in developing an "integrated food safety system." As stated in the National Food Safety Report to the President in 1997, "...prevention of all diseases might not be possible, stopping outbreaks of foodborne illness before they affect large numbers of people is a major goal." Reducing foodborne outbreaks can only be achieved by coordinating efforts of the state and federal agencies involved in food safety assurance. FDA is and will continue to be actively involved in numerous activities to accomplish this goal. This is one of the many process goals necessary to develop the "integrated food safety system." FoodNet, a sentinel network that is producing more stable and accurate national estimates of the burden and source of specific foodborne diseases in the United States through active surveillance and additional studies, has been expanded to eight Emerging Infection Program (EIP) sites. These eight sites provide sufficient geographical coverage and population coverage to allow the frequency and severity of foodborne disease, the proportion of common foodborne diseases that results from eating specific foods and the epidemiology of new and emerging bacterial, parasitic, and viral foodborne pathogens to be determined. FoodNet will also document the effectiveness of new food safety initiatives in decreasing the rate of foodborne diseases in the United States each year.

  PulseNet, an early warning system for outbreaks of foodborne diseases, has been established. PulseNet is a national network of public health laboratories that performs DNA "fingerprinting" on bacteria that may be foodborne. The network identifies and labels each "fingerprint" pattern and permits rapid comparison of these patterns through an electronic database at the Centers for Disease Control and Prevention to identify related strains.

  PulseNet will play a vital role in surveillance for and investigation of foodborne illness outbreaks that were previously difficult to detect. Finding similar patterns through PulseNet, scientists can determine whether an outbreak is occurring, even if the affected persons are geographically far apart. Outbreaks and their causes can be identified in a matter of hours rather than days.

- **Data Sources:** The FoodNet Surveillance System and PulseNet System
- **Performance:** In FY 99, the Agency published "Food-Related Illness and Death in the United States" Emerging Infectious Diseases (in September 1999). This was the first set of estimates for the United States based on active surveillance. The number of illnesses was estimated at 76 million and the deaths at 5,000. In FY 99, FDA also completed three major goals towards developing an integrated food safety system: (1) creation of a coordinating body to focus on a vision and next steps; (2) establishment of work groups to draft proposed plans and projects; and (3) solicitation of input from stakeholders (consumers; federal state, and local officials; industry; and academia.). In addition, the geographic area covered by FoodNet was expanded to include approximately 32.2 million persons or 12% of the American population. Based on data collected at the eight FoodNet sites

existing in 1999, FDA and CDC concluded the following: the rate of *Campylobacter, Salmonella* and *Cryptosporidium* infection has declined; the rate of salmonella enteriditis (SE) infections declined in all states except Oregon; and Cyclosporiasis declined substantially. In addition, a sustained increase in *Vibrio* rates was observed, and the rate of *E. coli 01:57* infections increased slightly.

16. Expand monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 11,000 samples. (11027)

- **Context of Goal:** Three federal government agencies share responsibility for the regulation of pesticides. The Environmental Protection Agency (EPA) registers and approves the use of pesticides and sets tolerances (the maximum amount of residue that is permitted in or on a food) if use of that particular pesticide may result in residues in or on food. The USDA's Food Safety and Inspection Service (FSIS) is responsible for enforcing tolerances in meat, poultry, and certain egg products. FDA is charged with enforcing tolerances in imported foods and in domestically produced foods shipped in interstate commerce. FDA also collects acquires data on particular commodity/pesticide combinations and carries out its market basket survey, called the Total Diet Study. In conducting the Total Diet Survey, FDA personnel purchase foods from supermarkets or grocery stores four times a year, once from each of four geographic regions of the country. The foods are prepared table-ready and then analyzed for pesticide residue and chemical contaminants. The levels of pesticides found are used in conjunction with USDA food consumption data to estimate the dietary intake of the pesticide residues.

  FDA samples individual lots of domestically produced and imported foods and analyzes them for pesticide residues to enforce the tolerances set by EPA. Domestic samples are collected as close as possible to the point of production in the distribution system; Import samples are collected at the point of entry into U.S. commerce. FDA's pesticide program focuses its efforts on raw agricultural products which are analyzed as the unwashed, whole (unpeeled), raw commodity. Processed foods are also included. If illegal residues (those that are above EPA tolerances) are found in domestic samples, FDA can invoke various sanctions, such as a seizure or injunction. For imports, shipments may be stopped at the port of entry when illegal residues are found. "Detention without physical examination" may be invoked for imports based on the finding of one violative shipment if there is reason to believe that the same situation will exist in future lots during the same shipping season for a specific shipper, grower, geographic areas, or country.

  Personnel in FDA Field offices interact with their counterparts in many states to increase FDA's effectiveness in pesticide residue monitoring. In many cases, Memoranda of Understanding or more formal Partnership Agreements have been established between FDA and various state agencies. These agreements provide for more efficient monitoring by broadening coverage and eliminating duplication

of effort, thereby maximizing Federal and state resources allocated for pesticide activities.

In planning the types and numbers of samples to collect, FDA considers several factors. These factors include: recently generated state and FDA residue data, regional intelligence on pesticide use, dietary importance of the food, information on the amount of domestic food that enters interstate commerce and of imported food, chemical characteristics and toxicity of the pesticide, and production volume/pesticide usage patterns. In FY 98, the Agency analyzed a total of 7,650 pesticide and contaminant samples. These samples included 3,600 domestic and 4,050 imports. FDA expects to analyze approximately 7,800 samples in FY 99. The actual number of samples analyzed in FY 99 will not be available until March 2000. In FY 01, FDA expects to analyze 11,000 samples. Recent reductions in non-FSI programs may limit the Agency's capacity to reach this level. FDA must maintain resource levels devoted to the sampling and analyses of pesticide and other chemical contaminant levels in foods.

- **Data Sources:** FDA's Pesticide Residue Monitoring Program and Chemical Contaminant Analyses.
- **Performance:** This is a new commitment in FY 01.

17. Improve public access to timely information on adverse events related to dietary supplement products, infant formulas, and medical foods by increasing the frequency of releases of information in the SN/AEMS from 2 to 4 per year. (11009)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. The FD&C Act requires FDA to monitor and report adverse events associated with food and cosmetics. Adverse event monitoring is particularly important for assuring the safety of dietary supplements because they are not subject to premarket review or approval by FDA. Recent experience with serious adverse events, including death associated with the use of dietary supplements like ephedra, digitalis-containing plantain, and other products, underscores this need. An enhanced system for monitoring and evaluating adverse events associated with the use of dietary supplements would provide a faster more efficient way to evaluate adverse event reports., thus shortening the time FDA needs to take any responsible action, saving lives, and improving public safety. In the past, each component of the Foods program maintained its own adverse event reporting system. The four reporting systems comprising the Foods program's adverse event reporting systems are not linked and lack the technological capacity to provide the data on information. The Foods program has the multi-year goal of developing a single integrated adverse event reporting system that can be used to examine trends in adverse events, identify safety problems early, and respond more quickly to Freedom of Information Act requests regarding adverse events.
- **Data Sources:**.

- **Performance:** In October 1998, one summary of adverse events information from the Special Nutritionals Adverse Events Monitoring System was released to the public. Thereafter, an Internet WEB page was created and is now being used to provide public access to information on adverse events.

18. Implement a multi-year research plan to develop and improve methods for detection, control and prevention of microbial contamination on fresh produce and evaluate the effectiveness of technologies for eliminating this contamination. (11012)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. An essential component of a comprehensive strategy to enhance food safety is the development of an arsenal of rapid and sensitive test methods for detecting pathogens. Real-time detection methods developed will be useful for verification of critical control points to minimize microbial contamination from the 'farm to table'.
- **Data Sources:** Periodic management and peer reviews
- **Performance:** In August 1999, FDA finalized and distributed the Three-Year Plan for Research in Support of the National Food Safety Initiative and Produce and Imported Foods Safety Initiative - 1999-2000 Update.

19. Develop modeling techniques for assessing human exposure to a variety of foodborne pathogens and for describing low dose infectivity rates for infectious and toxicoinfectious microorganisms. (11013)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. An important element in controlling foodborne illness is to improve risk assessment methods for foodborne pathogens that would help regulators better characterize the nature and magnitude of risk to humans and make decisions on how best to allocate resources to control those hazards. In FY 99, FDA's risk assessment was conducted to determine how frequently *Listeria monocytogenes* occurs and in what amounts they occur in certain foods, particularly ready-to-eat foods, and what populations were susceptible to illness as a result of their exposure, the severity of illness, and how much of the pathogen a person had to consume before becoming ill. A similar risk assessment was undertaken for *Vibrio parahaemolyticus*. The risk assessment for and *Vibrio parahaemolyticus* in raw molluscan shellfish will provide the scientific framework for developing food safety guidance and policies to reduce the risk of diseases from this seafood borne pathogen. The risk assessment for *Listeria monocytogenes* will provide the scientific information needed to develop policies to create effective programs designed to minimize the public impact of this pathogen.
- **Data Sources:** Periodic management and peer reviews
- **Performance:** In FY 99, FDA completed the draft risk assessments for *Listeria monocytogenes* and *Vibrio parahaemolyticus* and sent them to the Risk Assessment Consortium.

20. Work with industry and academia to develop new techniques for eliminating pathogens on sprouts and in citrus juice and apple cider. (11014)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. The processing of commercial produce is a rapidly expanding industry that offers convenient products with fresh-like qualities. Preservation and extension of shelf life for produce is frequently achieved through refrigeration, bactericidal rinses, modified atmosphere packaging and other technologies. To assure the safety of minimally processed produce, FDA is accumulating information on the effect of environmental and food formulation factors on the growth and survival of pathogenic bacteria that may be present. For example, the resident microflora on produce, which can vary by product, can alter the growth rates of pathogens on produce. In addition, the growth of pathogenic bacteria during germination of sprouted seeds may greatly increase the risk of foodborne illness. The results of these research efforts will serve as a basis for developing guidelines for produce handling and intervention technologies for minimizing bacterial contamination. As part of the FSI research program, the Agency has developed effective collaborations with industry and academia to achieve specific research goals and objectives.
- **Data Sources:** Periodic management and peer reviews
- **Performance:** In FY 99, FDA generated data on the presence of *S. aureus* on three types of domestic sprouted seeds, including alfalfa, mung beans and mustard. The Agency also began testing imported sprouted seeds from the Import Compliance Program. Finally, the Agency awarded several research grants to major universities to develop critical data on pathogens.

21. Conduct studies on factors that cause foodborne pathogens to develop multiple antibiotic resistance and resistance to traditional food preservation techniques and factors that prevent the development of such resistance. (11015)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. The primary purpose of the three-year research plan for FSI is to ensure that research conducted is directly related to the agency's mission and that research addresses specific regulatory needs. One of the activities that will be conducted through FSI research is to study the factors that cause foodborne pathogens to develop resistance to current techniques designed to reduce the chance of microbial contamination. Bacteria have great ability to adapt rapidly. Although the role that antibiotics play in the emergence of antibiotic resistance has been studied extensively, much less is known about the role that genetic diversity in a bacterial population plays in the development of antibiotic resistance. The findings of this research will facilitate the development of rapid method to detect and identify antibiotic resistant pathogens in our food supply and will improve our understanding of how antibiotic resistance develops. In addition, by identifying bacterial subpopulations that are more apt to resist antibiotics and antimicrobials, appropriate containment procedures can be implemented before the bacteria are widely disseminated.

- **Data Sources:** Periodic management and peer reviews
- **Performance:** CFSAN's Three-Year Plan for Research in Support of the National Food Safety Initiative and Produce and Imported Food Safety Initiative, 1999-2001 (issued August 1999), includes 'Understanding Antibiotic Drug Resistance' and 'Understanding Resistance to Traditional Preservation Technologies' as two of the broad research areas covered by the plan. In FY 99, FDA tested surrogate organisms for acid adaptability and increased thermal tolerance as part of the research studies on resistance to traditional food preservation techniques and factors that prevent the development of such resistance. The Agency determined the frequency and nature of mutators among clinically and agriculturally relevant isolates of *Salmonella*. FDA also examined if genes located near mutators are more susceptible to genetic exchange events, and determined if they are involved in stress responses in *e. coli 0157:H7*.

FDA developed a new protein based mass spectral technique to investigate properties of bacteria, such as antibiotic resistance and acid or heat resistance, that allow quick decision-making on whether to allow a food product to be sold. The Agency also conducted research on safe sprout and apple cider production, and on antimicrobial technology to reduce contamination of unpasteurized juices. Research is ongoing. Preliminary results and key finding are expected to be available in 2000.

Research is being conducted to evaluate the effects of phytochemicals, environmental conditions, modified atmospheres, microflora composition and other factors on the growth and survival of *Listeria monocytogenes, e. coli 0157:H7,* and *Salmonella spp., Bacillus cereus,* as well as appropriate surrogate microorganisms, on assorted fruits and vegetables.

Research is being conducted to understand the molecular genesis and emergence of antimicrobial resistance among bacterial pathogens focusing on the role of mutators, specifically those deficient in methyl-directed mismatch repair, on establishing antimicrobial resistance by genetic change (mutation) and exchange (recombination).

22. Develop the HACCP final rule for fruit and vegetable juices. (11006)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. An effective and efficient system of controls to enhance food safety must be developed for the food industry and for commodities with known histories of illness outbreaks, including fresh cut produce, sprouts, and eggs. HACCP regulations are being developed in various sectors of the food industry to reduce food safety risks and increase regulatory efficiency.
- **Data Sources:** *Federal Register*
- **Performance:** In FY 99, FDA published the proposed rule authorizing the use of HACCP systems in the juice industry. The Agency also reviewed comments that were submitted by the public.

23. Increase the safety of imported foods through participation in international standard setting organizations and the regulations of the free trade agreement of the Americas to ensure that international food safety standards are science-based and properly used. (11017)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY01. Differing national food safety standards and other requirements can impede international commerce and allow substandard products to move in international trade. FDA works with international standard setting organizations and participates in trade negotiations to improve food safety and quality worldwide. FDA will develop, with public input, an affirmative agenda for CFSAN's international program activities, including participation in Codex activities, equivalence determinations and international compliance issues.
- **Data Sources:** Draft CFSAN Affirmative Agenda
- **Performance:** FDA participated in 14 meetings of Codex Alimentarius general subject and commodity committees. Key issues considered by one or more of these committees included: international standards and guidelines for: microbiological risk assessment; principles of risk analysis; the role of science in setting Codex standards; labeling of foods containing allergens; guidelines for vitamin/mineral supplements; general standards for food additives; guidelines for food import control systems; establishing food safety and composition standards for processed fruits/vegetables, milk, and milk products, and fishery products. Agency staff also participated in three meetings of the World Trade Organization Committee on Sanitary and Phytosanitary Measures. And in three meetings of the Free Trade Area of the Americas. In addition, FDA participated in the United Nations Food and Agricultural Organization Conference on International Food Trade Beyond 2000. The goal of this conference was to establish overall standards setting directions for Codex for the next decade. FDA assumed a leadership role for the United States in working to enhance the food safety program of the United Nations World Health Organization.

2.1.3 Verification and Validation

Public health data systems currently are not adequate to provide accurate and comprehensive baseline data needed to draw direct relationships between FDA's regulatory activities and changes in the number and types of foodborne illnesses that occur annually in this country. Because of the need to have better data on food related illnesses, FDA and USDA began working with CDC in 1995 to improve food safety surveillance. FoodNet, an active surveillance program, was created through this joint effort. Currently there are eight FoodNet sites.

These sites, which operate in areas that are representative of the geographic and demographic population distributions in this country, provide much better data on the number of foodborne illnesses and trends in terms of the types of contaminants that are causing these illnesses. This type of information can be critical to efforts by food safety

agencies to redirect their regulatory and research resources to those food safety problems that pose the greatest threat to the health of consumers. Moreover, in 2002 when the data will be sufficient in volume and quality to establish baselines against which to measure changes in foodborne illnesses, FDA will be in a better position to establish broad scope outcome goals that are essential to effective performance planning.

Food Safety regulation development and research activities are planned and tracked through internal management systems. Progress on the development of regulations is tracked mainly through CFSAN's document tracking system and the *Federal Register* document tracking system. These systems permit the Agency to track the processing of regulations from the time they are filed to the point at which action is complete-usually the publication of a final regulation in the *Federal Register*.

CFSAN uses a number of internal data systems to track premarket review progress. These include the Management Assignment Tracking System (MATS) to track progress of petition reviews, Correspondence Tracking System (CTS) to track progress on biotechnology consultations, reviews of GRAS notifications, nutrient content claims, and health claims petitions/notifications. Outcome-oriented performance information can be extracted from MATS only by a labor-intensive manual process. CFSAN's internal data systems are limited to tracking time to a completed review and do not have the capability to track distinct phases of the review process. In FY 98, the Office of Premarket Approval's (OPA) internal database was modified to permit more detailed tracking of CFSAN's action on biotechnology consultations. In FY 99, CFSAN implemented an electronic workflow system that will replace MATS and CTS and permit real-time monitoring of review progress. The electronic workflow system is expected to be in full use in FY 01. The new system will track automatically actions related to the processing of food and color additive petitions, GRAS petitions and biotechnology consultations.

FDA uses a variety of data systems to develop and verify performance goals for its food safety activities. Among these are several field data systems. The most important of the field data systems are the Program Oriented Data System (PODS) and the Operational Administrative System for Imports (OASIS). PODS tracks field activities conducted by FDA's field force and the firms over which FDA has legal responsibility. Information provided by this system includes data on the number of inspections, wharf examinations, sample collections and analyses as well as the time spent on each. OASIS, which is coordinated with the U.S. Customs Service, provides data on what products are being imported as well as where they are arriving. It also provides information on compliance actions related to imports. In FY 01, the Field Accomplishments Tracking System (FACTS) will be the primary mechanism for tracking compliance activities for the domestic food industry. The National Seafood HACCP Compliance Database System maintains information on seafood HACCP inspections conducted by FDA and states in partnership with FDA. Standardized forms (Cardiff forms) assure comparability of HACCP compliance data whether the inspections are conducted by FDA or states. Another field data collection instrument is the field survey. Field surveys are special assignments that are developed and implemented specifically to collect information

needed to more thoroughly evaluate the nature and extent of particular postmarket food safety problems.

Data are also gathered through a number of other surveys designed for specific purposes. These include the Health and Diet Survey that provides information required to evaluate the impact of the Agency's food labeling activities. These surveys include questions that are designed to query consumers on how they use food labeling information to make decisions to use or purchase food products. Another survey is the NASS survey currently being developed jointly by FDA and USDA to evaluate the impact of GAPs and GMPs for improving the safety of fresh fruits and vegetables. The survey questions will be designed to provide data on practices employed in the production and processing of fresh fruits and vegetables. The results of the NASS surveys will be used to establish baselines for industry practices as well as evaluate the impact of voluntary GAPs and GMPs on improving production and processing practices for fresh produce.

Comprehensive data on illness caused by food and cosmetic products is critical to efforts to protect the health of consumers. Some of the illness data are provided by databases that contain information on adverse events, reported by consumers and industry on food and cosmetic products. In FY 00, the Agency will improve the quality of data on adverse events through the development and implementation of an integrated adverse event reporting system.

Proposed research projects are subjected to management reviews prior to implementation and periodic management reviews after the projects have been initiated. The primary planning and management system for food safety research is the Center Program Resources (CPR) plan system that provides quarterly resource use reports and semi-annual reports on accomplishments versus planned milestones. In addition, research projects are subjected to periodic external peer reviews. Peer reviews by recognized scientific experts in various disciplines related to food safety provide objective feedback that helps FDA evaluate the progress, quality and relevance of its research activities. In addition, risk assessment models are verified periodically using statistical models that assess their ability to make rapid and accurate estimates of risks associated with a particular food safety hazard.

2.2 HUMAN DRUGS

2.2.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	329,797	308,882	278,299	262,648

The Human Drugs Program assures that all drug products for the prevention, diagnosis, and treatment of disease are safe, effective and properly labeled. This is accomplished through: prompt and efficient review of clinical research; taking appropriate and timely action on new drugs and their generic equivalents; assuring quality of drugs on the market; and minimizing adverse events associated with use of prescription and over-the-counter (OTC) medications. To meet these goals, FDA frequently consults with experts in science, medicine and public health and also coordinates with consumers, product users and industry.

The challenge of assuring drug quality, safety and effectiveness is an ongoing one. While continual growth in the technological complexity of new products promises great health benefits for a growing number of U.S. consumers, FDA must be vigilant in safeguarding their interests. This challenge frames the Agency's strategic goals:

- Reduce human suffering and enhance public health by providing quicker access to important, lifesaving drugs and assuring availability of safe and effective drugs.
- Prevent unnecessary injury and death to the American public caused by adverse drug reactions, injuries, medication errors and product problems.

Through the successful pursuit of these goals, FDA is providing health protection and promotion for the American public, from the inception of new drug concepts, through research, product development, manufacturing, marketing and consumption. The Agency's approach to achieving the strategic goals outlined above, as well as key performance goals that will move the Program in these directions, are outlined in the next sections.

FY 99 Program Accomplishments

The Human Drugs Program had numerous noteworthy accomplishments during FY 1999. Among these were the following:

FDA Modernization Act--The Agency asked for over 220 studies to be conducted in the pediatric population and has granted pediatric exclusivity to seven products. FDA published a final rule for OTC sunscreen drug products containing the active ingredients that can be used in these products as well as labeling and testing requirements. It provides for uniform, streamlined labeling for all OTC products intended for use as sunscreens to assist consumers in making decisions on sun protection. FDA approved two products under Fast Track for the treatment of HIV. FDA published a draft Memorandum of Understanding between the states and FDA regarding the distribution of compounded drug products. FDA reviewed the current system of labeling products for use in pregnant women and developed a more comprehensive and clinically meaningful approach.

New Drugs - FDA achieved remarkable success by far exceeding the progressively more stringent performance goals agreed to for each successive fiscal year under PDUFA. Approved under accelerated approval was Ziagen (in 5.8 months) for the treatment of

HIV-1 infection in adults and children. FDA approved 11 new drug products and/or new indications for OTC marketing in FY 99.

Antibiotic Resistance - FDA developed an Antibiotic Resistance Coordinating Committee to address the growing problem of antibiotic resistance and its effects on drug development and regulation. Antibiotic resistance refers to the ability of infectious organisms to adapt to new environments. Bacteria may change their cellular structure to be able to survive the attacks of an antibiotic drug. Once bacteria become resistant to a drug, the drug is no longer effective in treating the infection. Some types of resistance also can be passed on to other bacteria so that a growing number of infections can no longer be treated with antibiotic drugs. Because it can affect so many people, resistance is a growing global concern and poses a major public health threat.

Bioterrorism - The Agency continued to develop regulatory policy options for stockpiling and using drug products that may be needed to respond effectively in the event of the deployment of biological weapons.

Generic Drug Review - FDA approved 198 abbreviated new drug applications. Of these, 40 represent the first time a generic drug was available for the brand name product. A first time approval was Ranitidine tablets (generic for Zantac).

Adverse Event Reporting System (AERS) - In FY 99, approximately 261,000 individual safety reports (ISRs) were received for entry into the AERS. FDA evaluates these spontaneous reporting data to identify any serious, rare, or unexpected adverse events.

Establishment Inspections - 773 domestic establishment evaluations were conducted for Good Manufacturing Practices (GMPs) compliance in support of New Drug Applications (NDAs).

Research - FDA continued to strengthen its science base by working with academia and industry to develop an efficient mechanism to conduct pharmaceutical research.

Outreach - FDA gave seminars on new drug therapies and labeling, made information available via the Internet, and established programs to make promising investigational drugs and therapies available to patients with serious and life-threatening diseases.

Electronic Submissions - FDA published guidance for the receipt and archive of full electronic NDAs. The Electronic Document Room was also expanded to manage the receipt and handling of full electronic NDAs.

2.2.2 Strategic Goals

Strategic Goal 1:

Reduce human suffering and enhance public health by providing quicker access to important, lifesaving drugs, and assuring availability of safe and effective drugs.

A. Strategic Goal Explanation

Approach

Approaches to achieving this goal include continuing efforts to meet or exceed mandated review times for new and generic drug application submissions. This will be accomplished through continued collaboration and cooperation with industry, academia, professional societies and health care organizations. FDA will also continue to compile detailed standards for evaluating drugs so that consistent and high-quality reviews are being performed - premarketing reviews continue to be subject to 100 percent quality control. This plan contains a goal pertaining to evaluating and tracking pediatric clinical trials FDA is requesting under FDA Modernization Act of 1997 (FDAMA) or requiring under the new Pediatric Rule. Section 111 of FDAMA grants drug sponsors additional market exclusivity for performing and submitting pediatric studies during drug development. These additional data will provide doctors with more complete information on how drugs affect children and make it more likely that children will receive improved treatment. Efforts towards achieving a totally electronic submissions environment will continue. In 1998 the equivalent of nearly 10 million paper pages in electronic format were received. Beginning in 1999, drug companies could submit an entire NDA electronically.

Research and Standard-Setting Contributions

FDA must maintain the scientific and technical expertise needed to keep pace with current advances in science and technology. FDA scientists must operate from a strong internal research platform to successfully work with the larger scientific community. Strong research is necessary to provide information on emerging technologies that will result in new products requiring review. Examples of where the Agency must keep abreast of current scientific developments are new uses for botanicals and new areas of risk such as antimicrobial resistance. To accomplish this, FDA will create scientific exchange programs with academic institutions and continue research collaborations such as the Product Quality Research Initiative (PQRI). Collaborations such as these are a method of leveraging external scientific expertise with that of the Agency.

FDA must be proactive in assuring that current and sound science underlies regulatory requirements, while at the same time allowing flexibility to industry to use innovative approaches in product development. FDA will continue to develop and finalize guidances that define its thinking about best practice approaches to address product development and monitoring standards, and provide recommendations to pharmaceutical sponsors and FDA reviewers about how to assure safety, efficacy, quality, and appropriate labeling.

Leveraging/Communication

FDA's ability to provide expeditious drug review is dependent upon enhanced collaboration and cooperation with industry, academia, professional societies and health care organizations. Agency scientists must maintain close communication with product sponsors throughout the product research and development phase. The ability to address problems early in the process prevents larger, costly difficulties and delays from occurring later in the review. This is, in essence, realizing major health benefit gains for a relatively small up-front investment. Additionally, opening access to outside expertise is an excellent way to leverage the Agency's limited science resources and apply the expanded knowledge when it is relevant in the review process.

Reinvention

The Agency is reinventing a critical area of its premarket review process as it relates to drug products affecting children under provisions of FDAMA and its new pediatric rule. FDA also continues to improve the efficiency of the premarket review process through its automation initiative. By the end of FY 00, the Agency will be able to process 75% of all review documents by implementing an electronic document management system throughout new drug review divisions. This should increase to 90% by the end of FY 01. FDA will also be able to receive about one quarter of all abbreviated new drug applications (ANDAs) electronically by the end of FY 01.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Review and act on 90% of standard original NDA submissions within 12 months of receipt (70% within 10 months); and 90% of priority original NDA submissions within 6 months. (12001)	Standard NDAs within 12 months: FY 01: 90% FY 00: 90% FY 99: 90% Standard NDAs within 10 months: FY 01: 70% FY 00: 50% FY 99: 30% Priority NDAs within 6 months: FY 01: 90% FY 00: 90% FY 99: 90%	FY 01: FY 00: FY 99: 90% (expected) Final data available 1/01 FY 01: FY 00: FY 99: 30% (expected) Final data available 1/01 FY 01: FY 00: FY 99: 90% (expected) Final	

		data available 7/00	
2. Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule. (12026)	FY 01: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule. FY 00: NA FY 99: NA	FY 01: FY 00: NA FY 99: NA	Increase
3. Review and act upon fileable original generic drug applications within 6 months after submission date. (12003)	FY 01: 50% FY 00: 45% FY 99: 60%	FY 01: FY 00: FY 99: Expect to review and act upon approximately 40% of applications received within 6 months.	
4. Review and act on 90% of resubmitted NDA applications within 6 months of receipt. (12002)	FY 01: NA FY 00: NA FY 99: 90%	FY 01: NA FY 00: NA FY 99: FDA expects to exceed this goal, but final on-time performance information will not be available until 5/00.	
5. Review and act on 90% of standard efficacy supplements within 12 months (30% within 10 months of receipt) and priority efficacy supplements filed within 6 months of receipt. (12004)	FY 01: NA FY 00: NA FY 99: 90% within 12 mos 30% within 10 mos priority within 6 mos	FY 01: NA FY 00: NA FY 99: FDA expects to exceed this goal, but final on-time performance information will not be available until 10/00.	

6. Review and act upon 90% of manufacturing supplements within 6 months and act on 30% of manufacturing supplements requiring prior approval within 4 months. (12005)	FY 01: NA FY 00: NA FY 99: 90% within 6 mos 30% within 4 mos	FY 01: NA FY 00: NA FY 99: FDA expects to exceed this goal, but final on-time performance information will not be available until 4/00.	
7. Continue to automate NDA and ANDA submission and archiving process. (12008)	FY 01: NA FY 00: NA FY 99: Electronic submission and archive capacity for NDAs and ANDAs.	FY 01: NA FY 00: NA FY 99: Approx. 40% of NDAs received include electronic submissions. Published guidance documents and held workshops for industry.	
TOTAL FUNDING: ($000)	FY 01: 234,156 FY 00: 244,017		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-by-Goal Presentation of Performance

1. Review and act on 90% of standard original NDA submissions within 12 months of receipt (70% within 10 months); and 90% of priority original NDA submissions within 6 months. (12001)

- **Context of Goal:** A major objective of the human drugs program is to reduce the time required for FDA's review of all drugs, with emphasis on the review of new drugs that are intended to treat serious or life-threatening diseases, such as AIDS, AIDS-related diseases, and cancer; and those products that demonstrate the potential to address unmet medical needs.
- **Data Source:** Center-wide Oracle Management Information System (COMIS); New Drug Evaluation/Management Information System (NDE/MIS)
- **Performance:** Children and adults with HIV-1 infection, people with cancer, meningitis and antibiotic-resistant infections all benefited from timely reviews of significant new drugs approved in FY 99.

For all open cohorts during FY 99, CDER took 185 actions on NDAs, 77 of which were approvals. The median approval time was 11.9 months, a 1% decrease in median approval time compared with FY 98. Final on-time performance information for the FY 99 submission cohort is not yet available but FDA expects to exceed its targets.

Fiscal Year 1998 Cohort as of 9/30/99

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Priority New Drug Application	30	90% in 6 months	30	100%
Standard New Drug Application	83	90% in 12 months	83	100%

2. Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule; conduct research initiatives and activities to define the quality of the clinical studies, usefulness of data generated from these trials, changes in drug product labeling and resultant public health benefits for children. (12026)

- **Context of Goal:** FDAMA enables FDA to Issue Written Requests (1) for pediatric studies prior to approval of an NDA if FDA has determined that information related to the use of the drug in the pediatric population may produce health benefits and (2) to holders of approved applications for pediatric studies if it has determined that information related to the use of the drug in the pediatric population may produce health benefits. FDAMA also requires FDA to develop, prioritize, and publish a list of approved drugs for which additional pediatric information may produce health benefits in the pediatric populations and update it annually.

  FDA issued a regulation (effective April 1, 1999) requiring pediatric studies of certain new and marketed drug and biological products. Most drugs and biologics have not been adequately tested in the pediatric subpopulation. As a result, product labeling frequently fails to provide directions for safe and effective use in pediatric patients. This rule partially addresses the lack of pediatric use information by requiring that manufacturers of certain products provide sufficient

data and information to support directions for pediatric use for the claimed indications.

- **Data source:** Pediatric Exclusivity Database and the Pediatric Page database. (Database enhancements required to meet goal.)
- **Performance:** This goal is a new commitment for FY 01; therefore there is no report on a specific FY 99 target. FDA took several actions to implement portions of FDAMA that make it more likely that children will receive improved treatment. The Agency issued guidance to assist drug companies planning to conduct pharmacokinetic studies in pediatric populations so that drug products can be labeled for pediatric use. FDA reviewed over 150 proposed Pediatric Study Requests, issued over 100 Written Requests asking for over 220 studies to be conducted in the pediatric population and has granted exclusivity to 7 products. The FDA pediatric Advisory Subcommittee met to discuss important neuropharmacological and controversial ethical issues that have arisen. The Agency formed a Working Group to begin examining products granted exclusivity, data generated from pediatric clinical trials and any resultant changes in product labeling. FDA developed an interactive pediatric web page to provide detailed information to the public regarding FDA's pediatric initiatives.

3. Review and act upon 60% of fileable original generic drug applications within 6 months after submission date. (12003)

- **Context of Goal:** An important part of FDA's mission is to assure that safe and effective generic drugs are available to the American people. FDA has approved several thousand generic drugs that have been used successfully by millions of patients. The use of these products has resulted in substantial savings to consumers and the Federal government (Medicare and Medicaid).
- **Data source:** COMIS; NDE/MIS
- **Performance:** FDA does not expect to meet its FY 99 target. Beginning in January 1997, FDA implemented a procedure to reduce approval times by allowing reviewers to utilize a "facsimile" amendment. Facsimile amendments are requests from reviewers to applicants for clarification/resolution of minor deficiencies (e.g., resubmission of illegible pages or typographical errors). These requests do not close the review of ANDAs and the subsequent amendments/responses are the reviewers' highest priority. This procedure results in review times exceeding 6 months, but shortens overall approval times (a figure FDA believes to be more important than the 6-month goal).

  The inability of FDA to meet the 6-month goal is also a function of the existing backlog of chemistry and microbiology reviews. To address the chemistry backlog, FDA restructured its chemistry review process by adding one additional team (and team leader) to each review division. Additional project managers were hired and assigned to the new chemistry teams. Also, all chemistry vacancies are in the process of being filled. To address the microbiology backlog, FDA assigned a project manager to the microbiology team to monitor the work progress and

assign priorities. FDA also named a microbiology team leader and hired two additional reviewers and are in the process of hiring a third. FDA believes that these initiatives will reduce the chemistry and microbiology backlog allowing reviewers to get to the applications sooner and lessen the effect of the facsimile amendments on the 6-month review goal. With the new changes and procedures in place, FDA expects performance to be 40% by the end of FY 99, 45% by completion of FY 00 and 50% by the end of FY 01.

During FY 99, FDA approved 198 ANDAs. Of these, 40 represent the first time a generic drug was available for the brand name product. FDA also issued 68 tentative approvals in FY 99 compared to 19 in FY 98. The table below demonstrates how the reduction in the number of review cycles, combined with other initiatives, have reduced approval times.

MEDIAN APPROVAL TIME
Abbreviated Applications

FISCAL YEAR	MONTHS
1997	19.6
1998	18.7
1999	17.3

4. Review and act on 90% of complete NDA applications resubmitted following receipt of a non-approval letter, within 6 months after resubmission date. (12002)

- **Context of Goal:** Resubmissions are responses provided by a pharmaceutical company to questions or deficiencies raised by FDA in an approvable or not approvable letter on an original application.
- **Data Sources:** COMIS; NDE/MIS.
- **Performance:** Final on-time performance information for the FY 99 submission cohort is not yet available but FDA expects to exceed this goal. For the FY 99 submission cohort, 60 resubmissions were submitted for review. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

Fiscal Year 1998 Cohort as of 9/30/99

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Class 1 Resubmission	22	30% in 2 months	18	82%
		90% in 6 months	22	100%
Class 2 Resubmission	31	90% in 6 months	31	100%

5. Review and act upon 90% of standard efficacy supplements within 12 months (30% within 10 months of receipt) and priority efficacy supplements filed within 6 months of receipt. (12004)

- **Context of Goal:** Efficacy supplements are requests from drug companies to add a new use or a new group of patients to be treated with an already approved drug. They often represent important new treatment options.
- **Data sources:** COMIS; NDE/MIS.
- **Performance:** Adults with HIV infection, people with cancer, diabetes, arthritis and other conditions all benefited from timely reviews of efficacy supplements approved in FY 99. Additional information on these new medication options follows:
    - Norvir, for use in combination with other antiretroviral agents, for the treatment of HIV-infection.
    - Doxil, for the treatment of metastatic carcinoma of the ovary.

Final on-time performance information for the FY 99 submission cohort is not yet available but FDA expects to exceed this goal. For the FY 99 submission cohort, 140 efficacy supplements were filed. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

Fiscal Year 1998 Cohort as of 9/30/99 Submission Type Number of Submissions Filed with CDER Goal (months) Number of Reviews "On Time" Percent of Reviews "On Time" Priority Efficacy Supplement 9 90% in 6 months 7 78% Standard Efficacy Supplement 120 90% in 12 months 119 99%

6. Review and act upon 90% of manufacturing supplements within 6 months and act on 30 percent of manufacturing supplements requiring prior approval within four months. (12005)

- **Context of Goal:** Manufacturers must notify the Agency in advance of certain manufacturing changes in the form of "manufacturing supplements" to new or generic drug applications. Review of these applications in a timely manner is necessary to assure that any manufacturing changes do not adversely effect strength, identity, quality, purity or potency of the drug product.
- **Data sources:** COMIS; NDE/MIS.
- **Performance:** Final on-time performance information for the FY 99 submission cohort is not yet available but FDA expects to exceed this goal. For the FY 99 submission cohort, 1,468 manufacturing supplements were filed. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

Fiscal Year 1998 Cohort as of 9/30/99

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Manufacturing Supplement	1,463	90% in 6 months	1,442	99%

7. Continue to achieve capability and capacity for electronic submission and archiving of information required to submit NDAs and ANDAs. (12008)

- **Context of Goal:** In 1998, electronic submissions offset the equivalent of nearly 10 million paper pages. Beginning in 1999, drug companies were able to submit an entire NDA electronically in lieu of paper.
- **Data Sources:** Electronic Document Room records.
- **Performance:** FDA published two guidance documents on the receipt and archive of full electronic NDAs. The Electronic Document Room was expanded to manage the receipt and handling of full electronic NDAs, additional workshops were conducted to assist industry in preparing their electronic submissions, and classes were held for FDA reviewers to train them on how to use the electronic documents. Approximately 40% of original NDAs received in FDA now include guidance-compliant electronic submissions. During the period January 1999 through September 1999, FDA received 36 NDAs that included some electronic components and 9 full electronic NDAs. FDA published guidance provides assistance to applicants submitting ANDA data in electronic format. During fiscal year 1999, FDA received 46 electronic submissions for bioequivalence and 69 for chemistry, manufacturing, and controls. FDA expanded its electronic document management system and, as of December 1999, approximately 47,000 review documents have been filed using the system. This system gives reviewers the

capability to electronically capture, sign, and archive their regulatory review products.

This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

Strategic Goal 2:

Prevent unnecessary injury and death to the American public caused by adverse drug reactions, injuries, medication errors and product problems.

A. Strategic Goal Explanation

Approach

FDA uses a number of postmarketing risk assessment approaches to ensure the continued safe use of drug products. The Agency's current adverse event database for drugs and therapeutic biological products, the AERS, contains approximately 2 million reports. In FY 98, more than 230,000 reports of suspected adverse events were received by the AERS. FDA evaluates spontaneous reporting data from the AERS to identify any serious, rare, or unexpected adverse events or an increased incidence of events. Based on its evaluation, FDA may decide to disseminate risk information, such as Dear Healthcare Professional letters, and may initiate regulatory action. Through a program called MedWatch, the FDA Medical Products Reporting Program, healthcare professionals and consumers are encouraged to report serious adverse events and product problems to FDA, the manufacturer, or both. FDA's Drug Quality Reporting System (DQRS) receives reports of deviations from Good Manufacturing Practices that occur during the manufacturing, shipping, or storage of prescription or OTC drug products. FDA receives medication error reports on marketed human drugs and maintains a central database within the DQRS and the AERS for all reports involving a medication error or potential medication error. The Agency puts substantial effort into reviewing medication error case reports to identify serious or potentially serious outcomes that might be avoided by modifying the labeling or packaging.

Research and Standard-Setting Contributions

FDA experiences continuous pressure for speedier approval of new products that hold the promise of new cures or symptom relief. The availability and increased use of medications also raises concern about the nearly inevitable circumstance that, after a drug is placed into general practice, harmful side effects will emerge that were not observed during pre-market investigations. Some side effects may be predictable but many are not. FDA has instituted a comprehensive postmarketing review system for identifying, evaluating, dealing with and possibly preventing adverse drug reactions. Additional research is needed on problem identification and reporting, and better methods of educating medical professionals and consumers on recognizing and reporting medical product problems should be implemented.

Information to support the science and technical positions of a guidance must be located or developed, and then analyzed carefully to allow an optimal set of recommendations to industry sponsors and Agency review staff. To extend Agency resources and incorporate the expertise of stakeholders into developing the information needed to establish policy, FDA supports collaborative efforts with extramural constituencies. Two recent examples include the PQRI and the Collaboration for Drug Development Improvement (CDDI). The PQRI focuses on product quality and the CDDI focuses on safety and efficacy. Both initiatives include stakeholders from the pharmaceutical industry and academia.

A safe medical product is one that has reasonable risks, given the magnitude of the benefit expected and the alternatives available. Research, and as a part of that, the development of standards and guidances has a major impact on the benefits of taking the drug as opposed to the level of risk.

Leveraging/Communication

FDA draws on outside resources to strengthen its ability to assure the quality and safety of approved drugs. Research collaboration is an excellent method of leveraging external scientific expertise with that of the Agency. A prime example is the PQRI, a nonprofit foundation that serves as a vehicle for FDA, industry and academia to collaborate on key issues in pharmaceutical product quality through research and expert group analysis. (See performance goal 5.)

Many examples of leveraging exist in the Agency's compliance activities. FDA works with regulatory scientists in state and local organizations as well as national and international experts. Industry has widely participated in FDA-sponsored workshops to explain safety issues. One example is FDA's informal partnership to share test methods and procedures for drugs with regulatory scientists in the United Kingdom, Germany, Australia, Canada and the Netherlands. Combining samples has allowed the FDA to assemble a database of pharmaceutical ingredients, which serves as a reference in stopping the use of counterfeit drug ingredients. FDA has also worked with industry in technical workshops on laboratory testing of drugs.

The Agency looks upon consumers as partners in safe drug use. Communication is a critical element in managing risk associated with approved medical products. FDA has measured the usefulness of drug label information to the consumer and redesigned the label for OTC drugs, with prescription labels to follow. In partnership with national consumer organizations, FDA is disseminating educational information to consumers and health professionals about choosing the right medications, taking medications correctly and reporting adverse reactions (See performance goal 8). More drug information targeted to consumers is being made available on the Agency's website. "Take Time to Care" is an outreach program directed to women about the safe use of medications. In cooperation with over 80 national organizations, including the National Association of Chain Drug Stores, FDA expects to reach 6.5 million women and positively affect their use of medications.

Reinvention

FDA has increasingly used Agency-industry workshops to address safety issues in specific product areas, partnerships with state regulatory agencies, and research-oriented groups to expand the knowledge base. FDA field offices are encouraged to develop pilot programs in a continual effort to increase safety for consumers in the most effective, efficient manner and successful pilot programs have been adopted by the Agency.

Reinvention-oriented pilot programs have also been used in the surveillance area across the Agency. Development of sentinel sites has been a pilot program in the Medical Device Program, and offers a benefit to consumers and health professionals to be expanded to cover the Human Drugs Program.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
8. Improve adverse drug event reporting system. (12007)	FY 01: Separate data entry and retrieval functions throughout new drug review divisions. Pilot test advanced analytical techniques. Develop and implement special report module. FY 00: Implement software to make the AERS more compatible with International Conference on Harmonization requirements. Develop next generation of the AERS to enhance functionality. FY 99: Implement AERS for the electronic receipt and review of voluntary and mandatory ADE	FY 01: FY 00: FY 99: implementation of selected periodic industry reports expected by end of FY 99.	

	reports.		
9. Initiate all research programs approved by the PQRI Steering Committee (12016)	FY 01: 50% FY 00: 25% FY 99: NA	FY01: FY00: FY 99: NA	Increase
10. Inspect 28% of registered human drug manufacturers, repackers, relabelers and medical gas repackers. (12020)	FY 01: 28% FY 00: 22% FY 99: 22%	FY01: FY00: FY 99: 26% FY 98: 24% FY 97: 26%	
11. Assure that FDA inspections of domestic drug manufacturing and repacking establishments result in a high rate of conformance (at least 90%) with FDA requirements. (12006)	FY 01: at least 90% FY 00: at least 90% FY 99: at least 90%	FY 01: FY 00: FY 99: 95% FY 98: 96% FY 97: 95%	
12. Give consumers and health professionals more easily understandable OTC drug information. (12027)	FY 01: Give consumers and health professionals more easily understandable OTC drug information**.** FY 00: Make new drug approval information increasingly available via the Internet. Develop partnerships	FY 01: FY 00:	Increase NPR Related

	with national organizations to disseminate educational information to consumers. FY 99: NA	FY 99: NA	
13. FDA will evaluate drug information provided to 75% of individuals receiving new prescriptions. (12009)	FY 01: NA FY 00: NA FY 99: FDA will evaluate drug information provided to 75% of individuals receiving new prescriptions**.**	FY 01: NA FY 00: NA FY 99: 1998 National Telephone Survey completed. Risk/Benefit Communication study of gender differences in risk communication completed.	NPR Related
14. FDA will continue to improve the legibility and clarity of OTC drug labels. (12010)	FY 01: NA FY 00: NA FY 99: FDA will continue to improve the legibility and clarity of OTC drug labels.	FY 01: NA FY 00: NA FY 99: Final regulation was issued in 3/99 to require new, easy-to-understand labeling on OTC drugs	NPR Related
TOTAL FUNDING: ($000)	FY01: 95,641 FY00: 64,865		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-by-Goal Presentation of Performance

8. Expedite processing and evaluation of adverse drug events through implementation of AERS which allows for electronic periodic data entry and acquisition of fully coded information from drug companies. (12007)

- **Context of Goal:** FDA's current adverse event database for drugs and therapeutic biological products, the AERS, contains approximately 2 million individual safety reports (ISRs). FDA evaluates spontaneous reporting data from the AERS to identify any serious, rare, or unexpected adverse events or an increased incidence of events. When a signal of a potential adverse reaction is detected, safety evaluators consult with product reviewers, medical officers, and epidemiologists

to review available data and consider further options. FDA may decide to disseminate risk information, such as Dear Healthcare Professional letters, and may initiate regulatory action.

- **Data source:** AERS
- **Performance:** The AERS has been operational for nearly two years. In FY 99, approximately 261,000 ISRs were received for entry into the AERS. In November 1998, FDA published an *Advanced Notice of Proposed Rulemaking for Electronic Reporting of Postmarketing Adverse Drug Reactions* that would require manufacturers of marketed human drugs to submit ISRs to the agency electronically. The proposed rule would help harmonize reporting of postmarketing safety information worldwide and expedite detection of safety problems for marketed drugs, thus enhancing FDA's ability to protect and promote public health. A pilot program for electronic submission of ISRs was conducted involving manufacturers with approved products. In addition, FDA developed and piloted an AERS data retrieval system to provide reviewers with quick access to the AERS data and reduce their reliance on hard copy reports.

9. Initiate all research programs approved by the PQRI Steering Committee in FY 00 and complete 50% of the projects initiated in FY 99 under the auspices of the PQRI, a collaboration among FDA, industry and academia established to provide a scientific basis for policy and guidance development in CDER on issues of drug product quality and performance. (12016)

- **Context of Goal:** The PQRI represents a unique collaboration that brings together scientists to identify and/or develop best practices for manufacture of quality pharmaceuticals products. The information generated by the PQRI will provide CDER, for example, additional means for identifying "low" and "high risk" product development and manufacturing practices, enhancing its efficiency in responding to new and complex drug delivery systems and rapidly changing manufacturing technologies, and developing science-based policies in the areas of biopharmaceutics, chemistry, manufacturing, and controls. This research initiative will support regulatory policy and guidances for the types of product quality information that should be submitted to the Agency in drug approval requests.
- **Data source:** Office of Testing and Research Research Plan; "A proposal - PQRI;" Memorandum of Agreement between FDA and the American Association of Pharmaceutical Scientists; and "Proposed Operating Principles for the PQRI."
- **Performance:** This goal is a new commitment for FY 00; therefore there is no report on a specific FY 99 target. No projects were initiated in FY 99. Eleven projects are awaiting approval of the PQRI Steering Committee for initiation in FY 00.

10. Inspect 28% of registered human drug manufacturers, repackers, relabelers and medical gas repackers. (12020)

- **Context of Goal:** This goal measures performance for the statutory inventory of drug establishments for which inspections are required biennially. The total drug

inventory is 19,749, of which 33 percent, or 6,509, are statutory. Inspections to accomplish this goal may be done by FDA directly, or through state contracts or partnership agreements. Achievement of this goal relies on the willingness and ability of the states to contract with FDA to inspect a large portion of the medical gas repacker industry. To implement these contracts, FDA's experience predicts that a significant investment in training and time is necessary to ensure quality and uniformity of inspections.

- **Data source:** Program-Oriented Data System, Official Establishment Inventory
- **Performance:** FY99: 26%. The data used to determine performance is a fiscal year data estimate derived from 2-year coverage data. Two-year coverage is computed by dividing the number of establishments inspected in the last 2 years by the total number of registered establishments. The fiscal year baseline estimate is half this number.

11. Assure the FDA inspections of domestic drug manufacturing and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements. (12006)

- **Context of Goal:** Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved the rates will better represent the overall status of the industry sector.
- **Data source:** FDA Field Data Systems
- **Performance:** FY 99: 95%; FY 98: 96%; FY 97: 95%. Conformance rates for FY 97, FY 98 and FY 99 have been adjusted to reflect the observed average correction rate for each year.

12. Make available to consumers and health professionals more easily-understandable information on choosing and taking prescription and OTC drugs to prevent and reduce their misuse, take more of an activist role in how consumers use these drugs, and improve drug risk management, analysis, and communication procedures. (12027)

- **Context of Goal:** There is increasing public recognition that marketed drugs can lead to harm as well as benefit. Drug-related injuries and deaths can be reduced by creating a more educated public through expanded outreach activities and collaborative efforts with academia, professional societies and health organizations.
- **Data sources:** Approval Letter for new and generic drugs and the Labeling Text or Final Printed Label (FPL) for new drugs; Consumer Drug Information Sheets for New Molecular Entities (NMEs); Availability of FDA's reviews of new and

generic drugs via the internet; Prescribing Information Sheet for NMEs. Report to the FDA Commissioner - Managing the Risks from Medical Product Uses, An Assessment of FDA's Approval and a Look to the 21st Century.

- **Performance:** This goal is a continuation of FY 99 and FY 00 Agency activities regarding providing more easily-understandable and -accessible drug information to interested individuals and organizations. It incorporates the FY 00 goals 12012 and 12025. There is no commitment to a specific FY 99 target and therefore no FY 99 report.

  Partnerships between FDA and several non-profit agencies resulted in publication of four brochures on the appropriate and safe use of medicines. Public and advisory committee meetings were held to inform consumers and health care professionals about the Agency's work on making the pregnancy section of labeling more useful. FDA used the Internet to publish information on new and innovative drugs approved since January 1998. FDA's CDER website had 250,446 visitors.

13. FDA will: (a) evaluate the availability, quality and usefulness of prescription drug information provided to 75% of individuals receiving new prescriptions; and (b) complete two studies that will aid in development of comprehensive drug information. (12009)

- **Context of Goal:** According to legislative mandate, by the year 2000, 75% of all consumers receiving new drug prescriptions will also receive useful information about their medicine; in the year 2006, 95% would receive such useful information with their new prescriptions. In accordance with this mandate, FDA sponsored a process that resulted in a collaborative group of private-sector organizations drafting an Action Plan to achieve these mandated goals.
- **Data Sources:** Keystone Center
- **Performance:** The Agency is developing a proposed rule for prescription drug labeling and various labeling guidances. The goal is to make prescription drug labeling easier to access, read and use. Public and advisory committee meetings were held to inform consumers and health care professionals about the Agency's work on making the pregnancy section of labeling more useful. The 1998 National Telephone Survey was completed. The results for written information indicate that in 1998, 70% of Americans received written information about their prescription medications that is longer than a brief sticker label, compared with 67% in 1996, 54% in 1994 and 24% in 1992. A Risk/Benefit Communication study of gender differences in risk communication was completed; publication is anticipated in early 2000. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

14. FDA will continue to improve the legibility and clarity of OTC drug labels, and improve the consumer's ability to read and understand important warnings and usage directions. (12010)

- **Context of Goal:** Each year, Americans purchase five billion OTC drug products for a wide variety of ailments, ranging from headaches to arthritis to sore throats. Although OTC drugs are generally very safe, their misuse causes hospitalizations each year. Studies estimate that half of these hospitalizations could be prevented by better consumer education and information.
- **Data Sources:** OTC Labeling Provisions; results of labeling studies.
- **Performance:** FDA issued a final rule establishing a standardized format and standardized content requirements for the labeling of OTC drug products. This final rule is intended to assist consumers in reading and understanding OTC drug product labeling and in using these products safely and effectively. It requires all OTC drug products to carry the new, easy-to-read format and the revised content requirements within prescribed implementation periods. FDA developed a public education campaign to help consumers understand how the new labels can be used to learn more about OTC medications. This educational campaign includes print and radio public service announcements, consumer brochures, point-of-purchase posters and other exhibit materials. FDA worked in partnership with national health and professional organizations such as the Nonprescription Drug Manufacturers Association to disseminate this information across a wide range of education networks. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00 or FY 01.

2.2.3 Verification and Validation

A preliminary assessment for data completeness, accuracy, and consistency and related quality control practices was done for each performance goal. The purpose of the assessment was to determine if the data was of a sufficient quality to document performance, whether the data was appropriate for the performance measure and if it was considered sound and convincing. Assessments will be use to determine the need to conduct further program evaluations.

2.3 BIOLOGICS

2.3.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	153,479	132,703	124,365	123,012

The mission of the Biologics program is to ensure the safety, purity, potency, and effectiveness of biological products (primarily vaccines, blood products, and therapeutics) for the prevention, diagnosis, and treatment of disease. The products that the Biologics Program regulates are on the leading edge of technology. Rapid scientific

advances in biochemistry, molecular biology, cell biology, immunology, genetics, and information technology are transforming drug discovery and development, paving the way for unprecedented progress in developing new medicines to conquer disease.

The number of Investigational New Drug Applications (INDs) and Investigational Device Exemptions (IDEs) received by the Biologics Program has increased almost 40% from FY 96 to FY 99. INDs and IDEs are an indication of future workload. Sponsors submit INDs/IDEs prior to beginning clinical trials to determine the safety and efficacy of the product in humans.

While scientific advances of new biological products promise great health benefits for U. S. consumers, FDA must ensure that these products are safe. FDA is also responsible for ensuring the safety of the nation's blood supply by minimizing the risk of infectious disease transmission and other hazards, while maintaining an adequate supply of whole blood and blood products. These challenges are represented by the Program's two strategic goals for the 21st century:

- **Ensure the expeditious availability of safe and effective human drugs, including biologics, for the prevention, diagnosis, and treatment of disease.**
- **Reduce the risk of biologics products on the market through assuring product quality and correcting problems associated with their production and use.**

FDA has the responsibility for ensuring that vaccines and related products (such as botulinum toxin, skin test reagents for tuberculosis, and allergenic products) are safe and effective and adequately labeled. Vaccines against diseases such as Hepatitis B, polio, *Haemophilus influenzae* type b, mumps, measles, rubella, diphtheria, tetanus, pertussis, and chicken pox are recommended for all U.S. children, and vaccines against influenza and pneumococcal infections are recommended for all adults more than 65 years of age. Periodic tetanus and diphtheria booster vaccinations are recommended for all adults. The use of influenza vaccine among adults has, in recent years, increased markedly (to a current use of about 80 million doses/year). Additional vaccines are recommended for special groups (for example, Hepatitis A) or for travelers to particular areas of the world (e.g., *Salmonella typhi* or Japanese encephalitis virus vaccines). Many additional vaccines are in various stages of investigation (e.g., HIV or Herpes simplex virus vaccines) and their INDs are being reviewed.

FY 99 Program Accomplishments

CBER is continually challenged by the need to regulate new products of increasing technological complexity while still making strides in improving the efficiency and speed of the review process.

In FY 99, CBER completed the following major approval actions: 8 PLA/BLAs (including the approval of 1 vaccine and 7 therapeutics), 10 PMA/510(k)s, and 1 NDA. Major supplement approval actions comprised: 9 PLA/BLA supplements and 2 PMA

supplements. The total approval actions included: 91 PLA/BLA/ELAs; 1,275 PLA/BLA/ELA supplements; 2 PMA and 7 PMA supplements; and 48 510(k)s. The following were among the major FY 1999 approvals.

On November 2, 1998, Etanercept, trade name, Enbrel, was approved. Enbrel brings about a reduction in signs and symptoms of moderate-to-severe active rheumatoid arthritis (RA) in patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDS). Of the approximately two million Americans with RA, as many as a third to a half are estimated to have moderate-to-severe RA. Enbrel is a product of Immunex Corporation of Seattle, Washington.

Enbrel is a new genetically-engineered protein called etanercept. It can also be used in combination with methotrexate if patients do not benefit enough from use of methotrexate alone.

On December 21, 1998, Lyme Disease Vaccine (Recombinant OspA) was approved. The vaccine, LYMErix is for active immunization against Lyme disease in individuals aged 15-to-70 years of age. LYMErix is a product of SmithKline Beecham Biologicals of Belgium.

LYMErix is the first vaccine to aid in the prevention of Lyme disease, which is transmitted to people through the bites of ticks infected with the bacterium *Borrelia burgdorferi*. Approximately 13,000 confirmed cases of Lyme disease were reported to the CDC in 1997. LYMErix is marketed by SmithKline Beecham Pharmaceuticals of Philadelphia, PA.

CBER approved a new indication for a plasma-derived product called Antihemophilic Factor/von Willebrand Factor Complex (Human), marketed as Humate-P, on April 1, 1999. The product is now approved to treat severe or hard-to-treat cases of von Willebrand's disease (vWD), a bleeding disorder. It was previously approved for adult patients with hemophilia A. vWD affects approximately 1% of the U.S. population.

2.3.2 Strategic Goals

Strategic Goal 1:

Ensure the expeditious availability of safe and effective human drugs, including biologics, for the prevention, diagnosis, and treatment of disease.

A. Strategic Goal Explanation

Approach

The FDA is responsible for reviewing and approving biologics covered under the Prescription Drug User Fee Act (PDUFA). These products are primarily vaccines and therapeutics. FDA also has responsibility for reviewing and approving biologic products

not covered by PDUFA. The non-PDUFA biological products are primarily blood and blood products, biotechnology-derived hematologics, allergenic products, and devices associated with their manufacture.

To provide the U.S. public with quicker access to new biologics, FDA consults closely with product sponsors early in product development, and makes prompt decisions on important new biological product applications. FDA will continue to make timely decisions in reviewing PDUFA product license applications (PLAs), Biologic License Applications (BLAs), and New Drug Applications (NDAs) and their supplements (performance goals 13001-13004). FDA will also continue to make timely decisions in reviewing non-PDUFA biologics, primarily blood and plasma products (performance goal 13005).

PDUFA Products: The Food and Drug Administration Modernization Act of 1997 (FDAMA), Public Law 105-115, amended the Prescription Drug User Fee Act (PDUFA) of 1992, and extended PDUFA through September 30, 2002. The PDUFA authorized revenues from fees paid by the pharmaceutical industry to expedite review by the FDA of human drug applications, including biologics. These revenues were directed by section 101(4) of this Act toward accomplishment of goals identified in the letters of November 12, 1997 from the Secretary of Health and Human Services to the Chairman of the Energy and Commerce Committee of the House of Representatives, and the Chairman of the Labor and Human Resources Committee of the Senate.

Fees that FDA collected from drug and biologic firms are used to reduce the evaluation time for certain human drug, including biologics, applications without compromising review quality. FDA primarily spent these PDUFA funds to acquire personnel to review applications and update the information technology (IT) infrastructure supporting the review process. PDUFA II will provide FDA with the resources necessary to sustain the larger application review staff. It will also provide FDA with additional funds to acquire the resources needed to achieve the more stringent performance goals.

The PDUFA time frames and performance goals are the result of in-depth negotiations between the drug industry and FDA. Industry and FDA determined that both the time frames and the percentage goals are realistic, achievable with the additional user fee resources, and desirable. The PDUFA time frames for drug applications differ in some cases from the Food, Drug and Cosmetic Act (FD&C) statutory requirements. Biologics applications are covered by the Public Health Service Act, which does not have any statutory time frames. Industry is pleased with the certainty of a timely action and response from the FDA review process and the net result of a higher percentage of applications being approved faster. Patients benefit by having more therapies available more quickly. Performance goals for PDUFA applications are based on the PDUFA time frames. Some of the more stringent PDUFA II goals are phased in over several years.

Non-PDUFA Products: The Biologics Program also reviews and approves license applications for products not covered by PDUFA. The mission of the Blood Program is to

ensure that blood, blood products, biotechnology-derived hematologics, and devices associated with their manufacture and use, are safe, effective, and adequately labeled.

The blood supply is critical to the nation's health care system, and the United States has the safest blood supply in the world. Each year approximately 14 million blood units are drawn from volunteer donors for use in more than 3.5 million Americans. FDA vigorously continues to strengthen its efforts to protect the nation's blood supply, and to minimize any risk to patients acquiring the human immunodeficiency virus (HIV), hepatitis, Creutzfeldt-Jakob disease (CJD), and other blood-borne diseases.

Factors which affect the Agency's ability to achieve the performance goals are: the quality and complexity of applications, the number of applications received, and commitments which take researchers/reviewers away from their assigned review work, such as regulation/guidance writing.

Research and Standard-Setting Contributions

To provide effective regulatory review of biological products, the Center conducts active mission-related research programs. The research expands the Agency's knowledge of fundamental biological processes and provides a strong scientific base for regulatory review. The functions of CBER's research are:

- Facilitate the approval of safe and effective products;
- Support decisions to withdraw products that are found to be unsafe;
- Anticipate public health needs and support informed decision-making in the prevention of and response to public health crises;
- Encourage industry-wide adoption of new technologies;
- Facilitate development of industry-wide standards and methods;
- Contribute to improvement of existing products and the development of new products; and,
- Aid in the recruitment and retention of excellent scientists.

CBER researchers are fully integrated into the application review process. They participate in the following regulatory procedures: review of INDs, and license applications; development of policy and guidance documents; meetings with sponsors and advisory committees; pre-license and biennial inspections; and evaluation of adverse drug reactions and risk assessment.

CBER's research supports the application review process. Various types of research are performed by CBER scientists. Research is conducted on specific products including but not limited to mechanism of action, potential toxicity, and surrogate measures of efficacy. Research is also performed on specific policy issues related to product class, disease area and therapeutic modality. Research associated with the development of methods and standards is also conducted.

The standardization and testing of vaccines for lot release is also one of FDA's responsibilities, and this activity continues to be a major effort. Each year CBER is responsible for the development of the reassortant influenza viruses that are used by the manufacturers for vaccine production. FDA is also responsible for the development of the sera that is used for the assignment of vaccine potency. CBER tests many vaccines for potency and safety in its laboratories.

The Agency also conducts research of blood and blood products pertinent to FDA's regulatory mission. FDA will continue to develop regulations to screen and test donors for infectious diseases. The ability of FDA to protect the nation's blood supply is enhanced through scientific efforts to understand HIV, hepatitis, CJD, and other blood-borne diseases. The ability of CBER scientific reviewers to ensure the safety and efficacy of blood screening tests and other new technology is increased through applied regulatory research.

Leveraging/Communication

CBER's vision statement (CBER Vision: 2004) includes the following statement: "CBER demonstrates international leadership in regulation through development of innovative regulatory strategies and standards, a managed regulatory process, coordinated research, and use of partnerships." The efficient use of resources through leveraging is a CBER strategic goal. CBER will examine the feasibility of using external resources to perform some application review functions. CBER collaborates with other Department of Health and Human Services (DHHS) agencies (the Centers for Disease Control and Prevention [CDC], the National Institutes of Health [NIH], and the National Vaccine Program Office [NVPO]), the Department of Defense, and the Department of Veterans Affairs on issues relating to biological products. CBER actively participates in several staff fellow programs under the National Research Council (NRC), the NIH, and the Oak Ridge Institute for Science and Education (ORISE). Through these programs, CBER enhances the educational programs offered by academic institutions, strengthens its scientific and technical resource base, transfers its knowledge and technology to the academic community, and supports a growing national commitment to scientific education. Cooperative Research and Development Agreements (CRADAs), under the Federal Technology Transfer Act of 1986, are utilized by CBER.

FDA scientists continue to play an active role in many national and international groups and organizations involved in setting vaccine policy and utilization, including: the Interagency Group of the NVPO; the National Vaccine Advisory Committee; the Advisory Commission on Childhood Vaccines; the Advisory Committee on Immunization Practices; the Committee on Infectious Diseases of the American Academy of Pediatrics; the World Health Organization; the Children's Vaccine Initiative; and national vaccines control agencies such as the National Institute of Biological Standardization and Control (in the UK). For vaccine-related issues, FDA continues to work closely with the NIH (especially National Institute of Allergy and Infectious Diseases [NIAID]), and the CDC. The Office of Vaccines Research and Review

continues to play an active role on committees related to AIDS, such as the NIH HIV Vaccine Selection Committee.

CBER personnel have played key roles in CISET, the PHS Interagency Working Group on Influenza Pandemic Preparedness, the Adult Immunization Plan, and the TB vaccine development plan.

Reinvention

The Biologic's Program implemented a *Managed Review Process* to ensure that the PDUFA performance goals are achieved. This process establishes timeframes for specific review events so that managers can obtain current status of application review and to ensure that goals are met. The current process covers licensing submissions and is initiated by a request from industry for a pre-pivotal trial meeting. The process ends with the licensure of the biological product. The process has been so successful that management has extended the Managed Review Process to include non-PDUFA applications. The full implementation of the Managed Review Process will make the application review process more efficient and speed the review of applications.

FDA will also extend its current blood oversight, and regulation revitalization and reinvention project. The major areas to be addressed include: development of the BLA as it applies to blood establishments; development of Agency-wide goals and direction; coordination of Agency-wide resources to protect the blood supply; and the revitalization and rewrite of blood regulations. The Blood Action Plan was initiated in July 1997, to increase the effectiveness of scientific and regulatory actions, and to ensure greater coordination among PHS agencies. The Action Plan addresses highly focused areas of concern such as emergency operations; response to emerging diseases; monitoring the blood supply; and updating blood regulations. Implementation of the Blood Action Plan has greatly improved the regulatory oversight and safety of the nation's blood supply.

FDA also continues to improve efficiency of its review process by its automation initiative. The Agency is in the process of transitioning from a largely paper-based regulatory submission and review environment to an electronic environment. This process is designed to meet the PDUFA IT goal that "the agency shall develop and update its information infrastructure to allow by FY 02, the paperless receipt and processing of INDs and human drug applications."

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Review and act on 90% of standard original NDA/PLA/BLA submissions within 12	Standard Applications within 12 months:	Standard Applications within 12 months: FY 01:	

months of receipt (70% within 10 months); and review and act on 90% of priority original NDA/PLA/BLA submissions within 6 months of receipt. (13001)	FY 01: 90% FY 00: 90% FY 99: 90% Standard Applications within 10 months: FY 01: 70% FY 00: 50% FY 99: 30% Priority Applications within 6 months: FY 01: 90% FY 00: 90% FY 99: 90%	FY 00: FY 99: 11/00 FY 98: 100% FY 97: 100% FY 96: 100% Standard Applications within 10 months: FY 01: FY 00: FY 99: 09/00 FY 98: NA FY 97: NA Priority Applications within 6 months: FY 01: FY 00: FY 99: 05/00 FY 98: 100% FY 97: 100%	
2. Review and act on 90% of standard efficacy supplements within 12 months of receipt (70% within 10 months); and review and act on 90% of priority efficacy supplements within 6 months of receipt. (13002)	Standard Applications within 12 months: FY 01: 90% FY 00: 90% FY 99: 90% Standard Applications within 10 months: FY 01: 70% FY 00: 50% FY 99: 30% Priority Applications within 6 months: FY 01: 90%	Standard Applications within 12 months: FY 01: FY 00: FY 99: 11/00 FY 98: 100% FY 97: 100% FY 96: 88% Standard Applications within 10 months: FY 01: FY 00: FY 99: 09/00 FY 98: NA FY 97: 44% Priority Applications within 6 months: FY 01: FY 00: FY 99: 05/00	

	FY 00: 90% FY 99: 90%	FY 98: 100% FY 97: 100%	
3. Review and act on 90% of manufacturing supplements within 6 months of receipt, and review and act on 70% within 4 months of receipt. (13003)	Within 6 months: FY 01: 90% FY 00: 90% FY 99: 90% Within 4 months: FY 01: 70% FY 00: 50% FY 99: 30%	Within 6 months: FY 01: FY 00: FY 99: 05/00 FY 98: 99% FY 97: 98% FY 96: 99% Within 4 months: FY 01: FY 00: FY 99: 03/00 FY 98: NA FY 97: 26%	
4. Review and act on 90% of Class 1 resubmitted original applications within 2 months; and review and act on 90% of Class 2 resubmitted original applications within 6 months of receipt. (13004)	Class 1 resubmissions within 2 months: FY 01: 90% FY 00: 70 % FY 99: 50% Class 1 resubmissions within 4 months: FY 01: NA FY 00: 90% FY 99: 90% Class 2 resubmissions within 6 months: FY 01: 90% FY 00: 90% FY 99: 90%	Class 1 resubmissions within 6 months: FY 98: 100% Class 1 resubmissions within 2 months: FY 01: FY 00: FY 99: 100% FY 98: 100% Class 1 resubmissions within 4 months: FY 01: FY 00: FY 99: 100% FY 98: NA Class 2 resubmissions within 6 months: FY 01: FY 00: FY 99: 05/00 FY 98: 100%	
5. Review and act on 85% of complete blood	Complete Submissions:	Complete Submissions:	

bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA Major supplements within 12 months after submission date. (13005)	FY 01: 85% FY 00: 85% FY 99: 60% Major Supplements FY 01: 90% FY 00: 90% FY 99: 90%	FY 01: FY 00: FY 99: 11/00 FY 98: 85% FY 97: 83% FY 96: 95% Major Supplements FY 01: FY 00: FY 99: 11/00 FY 98: 97% FY 97: 98%	
TOTAL FUNDING ($000)	FY 01: $117,677 FY 00: $103,201		
1. Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-By-Goal Presentation of Performance

Note about Baseline Data: In several years of the program, performance (Baseline Data) exceeds the projected performance goals. The projected performance goals are as the Secretary committed to in her letters to Congress. "NA" means the goal is not applicable in that fiscal year.

1. Review and act on 90% of standard original NDA, PLA, and BLA submissions within 12 months of receipt (70% within 10 months); and review and act on 90% of priority original NDA/PLA/BLA submissions within 6 months of receipt. (13001)

- **Context of Goal:** The Prescription Drug User Fee Act authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. Standard original PLAs or BLAs, are license applications for biological products, not intended as therapies for serious or life-threatening diseases. A priority PLA/BLA is a license application for a therapy to treat serious or life-threatening diseases.
- **Data Sources:** CBER's Biologics Regulatory Management System
- **Performance:** CBER has met or exceeded these performance goals since 1994. These applications are tracked by year of receipt, which is the cohort year. The cohort-year review performance is not available until the prescribed review time, i.e., 12 months after receipt, is expired. The FY 99 data for standard applications within 12 months will be available after November 2000. The FY 99 data for standard applications within 10 months will be available after September 2000.

The FY 99 data for priority applications within 6 months will be available after May 1, 2000.

2. Review and act on 90% of standard efficacy supplements within 12 months of receipt (70% within 10 months); and review and act on 90% of priority efficacy supplements within 6 months of receipt. (13002)

- **Context of Goal:** The PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A supplement is a change to an approved licensed product. An efficacy supplement provides information to FDA to modify the "approved effectiveness" in the labeling of a product such as a new indication, and normally includes clinical data.
- **Data Sources:** CBER's Biologics Regulatory Management System
- **Performance:** CBER has met or exceeded these performance goals since 1994. These applications are tracked by year of receipt, which is the cohort year. The cohort-year review performance is not available until the prescribed review time, i.e., 12 months after receipt, is expired. The FY 99 data for standard applications within 12 months will be available after November 1, 2000. The FY 99 data for standard applications within 10 months will be available after September 1, 2000. The FY 99 data for priority applications within 6 months will be available after May 1, 2000.

3. Review and act on 90% of manufacturing supplements within 6 months of receipt, and review act on 70% within 4 months of receipt. (13003)

- **Context of Goal:** The PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A supplement is a change to an approved licensed product. A manufacturing supplement provides FDA information relating to a proposed expiration date change, formulation revision, manufacturing process change, packaging change, or controls change.
- **Data Sources:** CBER's Biologics Regulatory Management System
- **Performance:** CBER has met or exceeded these performance goals since 1994. These applications are tracked by year of receipt, which is the cohort year. The cohort-year review performance is not available until the prescribed review time, i.e., 6 months after receipt, is expired. The FY 99 data for review of manufacturing supplements within 6 months will be available after May 1, 2000. The FY 99 data for review of manufacturing supplements within 4 months will be available after March 1, 2000.

4. Review and act on 90% of Class 1 resubmitted original applications within 2 months; and review and act on 90% of Class 2 resubmitted original applications within 6 months of receipt. (13004)

- **Context of Goal:** PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A resubmitted original application is a complete response to an action letter addressing all identified application deficiencies. Class 1 resubmitted applications are applications resubmitted after a complete response letter that include one or more of the following items: final printed labeling; draft labeling; safety updates; stability updates; commitments to perform Phase IV (postmarketing) studies; assay validation data; final release testing; a minor re-analysis of data; other minor clarifying information; or other specific information requested by the Agency. Class 2 resubmissions include any other items.
- **Data Sources:** CBER's Biologics Regulatory Management System
- **Performance:** These applications are tracked by year of receipt, which is the cohort year. FDA's performance in FY 99 for review of class 1 resubmissions within 2 months was 100%. FDA's performance in FY 99 for review of class 1 resubmissions within 4 months was 100%.

5. Review and act on 85% of complete blood bank and source PLA/BLA submissions, and 90% of PLA/BLA Major supplements within 12 months after submission date. (13005)

- **Context of Goal:** Blood bank and source plasma applications are not covered by PDUFA. The non-PDUFA review resources in CBER are not protected from cuts as the PDUFA resources are by the PDUFA legislation. CBER's non-PDUFA review resources have been cut in recent years to meet unfunded pay raises, increased current service costs, and other budget actions.
- **Data Sources:** CBER's Biologics Regulatory Management System
- **Performance:** These applications are tracked by year of receipt, which is the cohort year. The cohort-year review performance is not available until the prescribed review time, i.e., 12 months after receipt, is expired. The FY 99 data for complete submissions and for major supplements will be available after November 1, 2000.

Strategic Goal 2:

Reduce the risk of biologics products <u>on the market</u> through assuring product quality and correcting problems associated with their production and use.

<u>A. Strategic Goal Explanation</u>

Approach

FDA is required by law to conduct biennial inspections of all licensed establishments to determine compliance with Current Good Manufacturing Practice (CGMP) regulations and to ensure compliance with applicable product and establishment standards and license commitments. In addition, FDA inspects all manufacturing facilities, which are

unlicensed and/or under contract to a licensed establishment. FDA conducts biomedical research inspections to review pivotal clinical trial data, and in inspections of new tissue-cellular based products.

By accomplishing the performance goals 13007 and 13012, the Biologics Program will ensure that biologics establishments are in compliance with regulations and that the products produced in those establishments are safe and pure. The Biologics Program also ensures that high-risk plasma fractionator establishments are in compliance (performance goal 13008).

Factors which affect the FDA's ability to achieve the performance goals are unanticipated crises such as product tampering, which require immediate investigative and enforcement actions and take inspectors investigators away from their planned assignments.

The availability of qualified scientific personnel to review, evaluate and investigate postmarket adverse events affects the Agency's ability to make sound and timely decisions concerning recalls and withdrawals.

Research and Standard-Setting Contributions

The Center statistically evaluates clinical and pre-clinical studies of human products and vaccines, and epidemiologically evaluates post-marketing studies and adverse biologics events.

CBER researchers are fully integrated into the compliance process. They participate in pre-license and biennial inspections and the evaluation of adverse drug reactions and risk assessment. CBER research supports regulatory decisions to recall or withdraw products from the market.

Leveraging/Communication

FDA continues its efforts to leverage the Agency's enforcement capability internationally by working toward mutual recognition agreements (MRAs) with the European Community and other nations so imports entering the United States meet the same high quality and safety standards of U.S. produced products.

FDA will continue to collaborate closely with other government and non-government regulatory organizations such as the National Institute of Health, Centers for Disease Control and Prevention, state health agencies, the American Red Cross, and the American Association of Blood Banks to assure that all policies are mutually consistent in guarding the safety of the nation's blood supply.

Reinvention

In addition to enhancing quality assurance procedures in blood banks, FDA will be defining new strategies for blood bank inspections based on control processes for critical

production points. The Agency will also provide training programs for inspectors to implement the new approaches; conduct workshops to clarify Agency expectations for industry; and evaluate the need for changes in the error and accident reporting requirements. Biologics is working towards the goal of an integrated Agency-wide Adverse Event Reporting Initiative.

FDA will continue to improve donor-eligibility criteria and deferral programs. It will also continue studies to assess the effectiveness of donor interview and education programs, and coordinate a national effort to address concerns regarding donor-deferral registries.

CBER's Managed Review Process is a system implemented to meet PDUFA performance goals. CBER's success with its Managed Review Process impressed upon CBER's senior managers the need to expand the principles of this process to CBER's entire regulatory process. Senior management incorporated the goal of "a managed and integrated regulatory process which is continuous from discovery through post marketing", into their strategic vision for the year 2004.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
6. Assure that FDA inspections of domestic biologics manufacturing, repacking and blood banks establishments result in a high rate of conformance (at least 90%) with FDA requirements (13007)	FY 01: at least 90% FY 00: at least 90% FY 99: at least 90%	FY 99: 98% FY 98: 98% FY 97: 98%	
7. Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80%. (13008)	Currently 26 foreign and Domestic Plasma Fractionator establishments FY 01: 80% FY 00: 80% FY 99: 80%	FY 01: FY 00: FY 99: 62%, 16 out of 26 in compliance FY 98: 54%, 13 out of 24 in compliance	

		FY 97: 41%, 9 out of 22 in compliance FY 96: 75%, 9 out of 12 establishments inspected were in compliance	
8. Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing establishments. (13012)	FY 01: 50% FY 00: 50% FY 99: 43%	FY 99: 64% FY 98: 46% FY 97: 46% of establishments inspected	
TOTAL FUNDING ($000)	**FY 01: $35,802** FY 00: $29,502		
1. Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-By-Goal Presentation of Performance

6. Assure that FDA inspections of domestic biologics manufacturing, repacking and blood banks establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high conformance rate with FDA requirements (at least 90%) (13007)

- **Context of Goal:** Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data on deficiency corrections. This is due to FDA's selection of high-risk firms. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.
- **Data Sources:** FDA Field Information System (FIS)
- **Performance:** Performance for this goal in FY 99 was 98%. Conformance rates for FY 97, 98, and 99 have been adjusted to reflect the observed average correction rate for each year.

7. Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80%. (13008)

- **Context of Goal:** There are 26 foreign and domestic plasma fractionator establishments. It was discovered that very few of these establishments were in compliance with CGMP regulations. In an effort to bring the majority of the plasma fractionator establishments into compliance with CGMPs, the Agency transferred the responsibility for plasma fractionator inspections to the Field. Additionally, the Agency developed program guidance and conducted training for FDA inspectors to bring the establishments into compliance.
- **Data Sources:** Field Information System (FIS)
- **Performance:** Currently, there are 26 foreign and domestic plasma fractionator establishments. The FY 99 goal was to increase compliance to 80%. In FY 99, 62%, or 16 out of 26 were in compliance. Due to the small number of plasma fractionator establishments, the non-compliance of a few establishments with GMPs skews the percentage adversely.

8. Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing establishments.(13012)

- **Context of Goal:** This includes inspections done by FDA directly, or through state contracts or partnership agreements. The law requires FDA to conduct inspections of certain manufacturing facilities once every two years. There are currently 2,790 establishments in the Biologics Program inventory covered under this statute. There are 2,898 additional establishments in the Biologics Program inventory not covered under this statute.
- **Data Sources:** Program-Oriented Data System, Official Establishment Inventory.
- **Performance:** Annual coverage performance in FY 99 was 64%.

2.3.3 Verification and Validation

The Biologics Program uses various databases to mange its diverse programs and to assess performance. The principal CBER database is the Biologics Regulatory Management System (BRMS). The BRMS is CBER's VAX-based, Oracle database that is used to track all PLA, BLA, and supplement submissions; provide information to facilitate the review process (product, application status, milestone tracking, facility, review committee, industry contacts, and other information); and produce a wide variety of management reports. The BRMS records application review information on each license application and supplement received and filed by the Center. The BRMS records information about PDUFA and non-PDUFA license applications. The milestone tracking module is used to track and report on CBER's PDUFA goals. Data entry is done in each of the offices' application review divisions. The Regulatory Information Management Staff (RIMS) monitors and is responsible for maintaining data quality and integrity in BRMS.

The Biologics Investigational New Drug (IND) Management System (BIMS) is CBER's VAX-based, Oracle database that is used to track all Investigational New Drug Applications (IND), Investigational Device Exemption (IDE), and Master Files (MF)

submissions (over 12,000 in 1998); provide product, application status, and other information to facilitate the review process; and produce a wide variety of management reports. The system also stores summaries of telephone conversations and meetings related to the submissions, as well as actually generating some of the correspondence to sponsors. Most data entry is done by the Document Control Center (DCC) or the Consumer Safety Officers in each office's application review division. There are numerous mechanisms established for quality control in DCC, the application review offices, the Regulatory Information Management Staff, and several built into BIMS itself.

The Blood Logging and Tracking System (BLT) is under development by the Office of Blood Research and Review (OBRR) to record and track the various applications reviewed by that Office. The OBRR receives and reviews a wide variety of application types. PLAs, ELAs (Establishment License Applications) and BLAs are tracked by the BRMS, discussed above. INDs are tracked by the BIMS, also discussed above. The Office utilizes the BLT to record and track data concerning device premarket applications (PMAs) and PMA supplements, 510(k)s, and Abbreviated New Drug Application (ANDAs) and ANDA supplements. The Office also has an NDA tracking system.

The data retrieved from these systems are reviewed and validated by the RIMS and the application review offices. If errors are detected, they are corrected.

Federal regulations (21 CFR, Part 600.14) require reporting of errors and accidents in the manufacture of biological products that affect the safety, purity, or potency of the product. The error and accident reporting process enables the Agency to evaluate and monitor establishments, to provide field staff and establishments with trend analyses of the reported error and accident types, and to respond appropriately to reported errors and accidents to protect the pubic health. The regulation applies only to licensed manufacturers.

In May 1995, the DHHS Office of the Inspector General issued a report recommending that the reporting requirements be expanded to include unlicensed blood banks and transfusion services. A proposed rule was issued on September 23, 1997 that expands the reporting requirements to all biological product manufacturers regulated by FDA.

In the past five years, the Agency has received an average of 12,000 error and accident reports annually. FDA estimates that over 116,000 error and accident reports would be received under the proposed regulation. FDA does not have a computer system to permit the electronic submission of error and accident reports. If the Agency is to comply with the intended goals of the error and accident reporting regulation, it will need a system that would allow it to receive electronic submission of reports; and to review, process, and analyze more than 100,000 reports annually.

The Biologics Program relies in the Office of Regulatory Affairs' Field Accomplishments and Tracking System (FACTS) to register and record biologics manufacturing establishment inspection and compliance data. FACTS versions 1 and 2 together will replace the several dozen applications that comprise the current Field Information System

(FIS). The software development contractor delivered FACTS version 1 to the FDA on September 30, 1997. Version 1 functionality includes all sample collections; all sample tracking, accountability, and dispositions; sample analysis of pesticides, additives, colors, elements, mycotoxins and radionuclides; firms inventory, maintenance and registration; work assignments and work management; and other features.

Meanwhile, the design and development of FACTS version 2 is underway. Major features of version 2 include replacing the remaining FIS functions: remainder of lab analyses; inspections; rest of investigations including records and tracking; compliance functions; other core items including personnel management (MUS); and miscellaneous operations including recalls and audit checks.

2.4 ANIMAL DRUGS AND FEEDS

2.4.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	62,761	48,713	43,256	41,354

The mission of the Animal Drugs and Feeds Program is to protect the health and safety of all animals that serve either as companions or food sources for mankind; and to assure that food from animals is safe for human consumption. To support this mission, the Center for Veterinary Medicine (CVM) focuses on two strategic goals:

1. **Increase the availability and diversity of safe and effective animal drugs and feeds.**
2. **Reduce the risks associated with marketed animal drugs and feeds.**

These strategic goals reflect CVM's involvement in the animal drug development process from the point at which the drugs are first developed to after they are on the market. This coverage of the entire drug development process enables CVM to address problems or safety issues before they become a threat to Public Health. CVM accomplishes these goals working with partners in industry, academia, consumers, and other government agencies.

CVM's approach to achieving these strategic goals, and some of the key performance goals that support these strategic goals are explained in the following sections.

FY 99 Program Accomplishments

The Animal Drugs and Feeds Program has worked with our partners in Industry to redesign the New Animal Drug Approval Process to make it more efficient. This collaboration has served as a model for the development and passage of the FDA Modernization Act (FDAMA). Phased Review makes drug review faster by providing more timely feedback and "early detection" of application deficiencies. Electronic submission of Drug Shipment Notices cut the approval time to one third of the original time. CVM continues to increase the number of isolates in the National Antimicrobial Resistance Monitoring System (NARMS) database and achieves a very high conformance rate to FDA regulations of all domestic animal drug and feed manufacturing establishments and repackers.

2.4.2 Strategic Goals

Strategic Goal 1:

Increase the availability and diversity of safe and effective animal drugs and feeds.

A. Strategic Goal Explanation

Approach

Veterinarians and the agricultural community need animal drugs to ensure a safe food supply. As disease-causing agents mutate and become resistant to current drugs, new drugs are needed. The availability of safe and effective drugs allows food animal producers to maintain healthy animals with assurance that products will be safe, wholesome, and free of drug residue when they reach the consumer.

CVM strives to increase the availability and diversity of animal drugs and feeds by being involved through out the new animal drug approval process.

Working with industry early in the drug approval process in pre-submission conferences (Performance Goal 1), workshops, teleconferences, and the availability of CVM guidances through the internet help increase industry efficiency, thereby reducing overall developmental costs. Phased review provides more timely feedback and "early detection" of application deficiencies.

The Agency is committed to improving the review time on new animal drug applications (NADAs) as well (Performance Goal 2). Reinventing the approval process (Performance Goal 3) and improved information systems such as electronic submission of applications (Performance Goal 4) and enhancements to the Submission Tracking and Review System (STARS) will allow FDA to more efficiently perform review activities.

To ensure that FDA has the necessary science base to make regulatory decisions, a staff college is being developed (Performance Goal 5) and risk assessments are being conducted (Performance Goal 6).

These performance goals help the Agency take the specific steps needed to achieve this strategic goal. When the "reinvented review process" is running efficiently and effectively, it is capable of producing outcomes that matter to the US Taxpayer: reduced mortality and morbidity rates due to safer animal products, shortening the cost and time associated with animal drug development, and improved quality of life for selected segments of the human population because of healthy companion animals that have greater longevity.

Research and Standard Setting

Research and standard setting contribute to increasing the availability and diversity of animal drugs and feeds by promoting development of drugs for minor species and allocating scarce resources more efficiently by conducting risk assessments.

Animal drug studies are conducted to prove that the drug is safe and effective in the target animal. But because the rate for recouping drug research related to minor species (sheep, rabbits, fish) is low compared to major species (cows, pigs, poultry), most companies are reluctant to fund minor species research. The term "grouping" refers to combining animals with similar physiology in one group for research purposes, e.g., types of fowl and poultry together. The grouping of animal species will encourage minor species drug development, especially in the area of aquaculture.

The impact of improving risk assessments will be to quantify the public health risks associated with using antimicrobial products in food producing animals. Risk assessment provides a strong foundation upon which efficient allocation of scarce food safety resources can be made. Furthermore, risk assessment often plays a central role in the development of any science-based system of preventive controls. Based on current resource estimates and complexity of the proposed risk analysis, CVM will initiate 2 risk analyses in FY 00 which will be completed in FY 01.

Leveraging and Communication

The Animal Drugs and Feeds Program informs and assists product sponsors throughout the approval process starting with the pre-submission conference. The focus is to inform and assist firms in complying with the new legislation and streamline the product review process through phased review. Instead of waiting until all stages of product development are completed before contacting FDA, phased review helps industry stay on course through the drug development process by communicating requirements (or standards or criteria) for approval at each stage of development.

Staff College programs have been developed in FDA as a means of developing intellectual capital. The addition of a CVM Staff College will allow CVM to increase and maintain the scientific expertise in the Center, especially as it relates to animal science and veterinary medicine issues. The Staff College will use dollars to outsource the planning and implementation of training programs tailored to the needs of in-house scientists.

Collaboration with other agencies such as the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA) is accomplished through interagency agreements. FDA also funds extramural research via contract and cooperative agreements and through collaboration with the University of Maryland known as the Joint Institute for Food Safety and Applied Nutrition (JIFSAN).

Reinvention

In order to increase the availability and diversity of safe and effective products, CVM is reinventing the new animal drug review process in two major ways. First, the Animal Drugs and Feeds Program is implementing the Animal Drug Availability Act[1] of 1996 (ADAA), the FDA Modernization Act (FDAMA)[2] and our reinventing government (REGO) initiative. This involves developing guidance documents which will more accurately reflect the current veterinary medicated feed and drug approval/monitoring processes. These standards reflect changes in the approval processes that have resulted from enactment of the ADAA and CVM's efforts to reinvent its new animal drug approval processes. Availability of guidance documents facilitates the accurate and complete preparation of drug applications.

Secondly, CVM is also helping to reduce drug development and review time by initiating the final and most complex phase of electronic submission, receipt of protocols. Although CVM currently receives some protocol data electronically, there are no standards approved for electronic filing and receipt of a hard copy is still required. The development of these standards will meet the requirements of the government's Paperwork Reduction Act allowing the electronic file to be the official file. Better automated information systems, including those supporting electronic submission of applications by sponsors, are being developed to facilitate and expedite the review process. CVM successfully completed a pilot project to permit one type of electronic submission for review and plans to expand the submission program to include other regulatory reporting requirements.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference [1]
1. Increase the level of pre-submission conferences with industry sponsors to 80%. (14007)	FY 01: 80% FY 00: 75% FY 99: NA	FY 01: FY 00: FY 99: NA	Increase
2. Review and act on 70% of NADAs/ Abbreviated New Animal Drug	FY 01: 70% FY 00: 65%	FY 01: FY 00:	Increase

Applications (ANADAs) within 180 days of receipt. (14017)	FY 99: NA	FY 99: N/A	
3. Revise and develop 14 guidances. (14001)	FY 01: 3 manufacturing, 10 new drug approval process and 1 Veterinary International Conference on Harmonization (VICH) guidances FY 00: Update 12 guidelines (original target was 7 documents which was 10 % of animal drug review guidances). FY 99: Update 1 guideline (1% of animal drug review guidances).	FY 01: FY 00: FY 99: 8 guidelines: including 3 FDAMA and 5 VICH.	Increase
4. Initiate final phase of electronic submission, receipt of protocols. (14002)	FY 01: Initiate the development of a method for receiving protocol submission electronically FY 00: 4 phases - Notices of Slaughter; Notices of Animal Final Disposition; Meeting Agendas; USDA Slaughter Reports FY 99: complete 1 phase - Notices of	FY 01: FY 00: FY 99: 1 phase (NCIE) completed	Increase

	Claimed Investigational Exemptions (NCIE)		
5. Initiate development of Staff College. (14018)	FY 01: Initiate the development of a Staff College FY 00: NA FY 99: NA	FY 01: FY 00: FY 99: NA	Increase
6. Develop an antibiotic risk assessment model using fluoroquinolone, Chickens and Campylobacter. (14003)	FY 01 Goal: Perform 2 risk assessments. FY 00 Goal: Generalize the model by performing risk assessments related to other antibiotics and other animal/bacterial species. FY 99 Goal: Increase Risk Assessments by 10% FY 99: (Baseline-FY 01) Develop an antibiotic risk assessment model using fluoroquinolone as the antibiotic, Chickens as the animal species and Campylobacter as the bacterial isolate	FY 01: FY 00: FY 99: 1 Risk Assessment completed	Increase
TOTAL FUNDING: ($ 000)	FY 01: $23,571 FY 00: $19,485		
1. Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01.			

NPR: Goal supports an FDA National Partnership for Reinventing Government Goal

C. Goal-by-Goal Presentation of Performance

1. Increase the level of pre-submission conferences with industry sponsors to 80%. (14007)

- **Context of Goal:**The Animal Drugs and Feeds Program informs and assists product sponsors throughout the approval process starting with the pre-submission conference. The focus is to inform and assist firms in complying with the new legislation and streamline the product review process through phased review. Instead of waiting until all stages of product development are completed before contacting FDA, phased review helps industry stay on course through the drug development process by communicating requirements (or standards or criteria) for approval at each stage of development.
- **Data Sources:** Submission Tracking and Review System (STARS)
- **Performance:** Presubmission conference tracking was established in FY 99. Based on current data, 75% is a reasonable target for FY 00.

2. Review and act on 70% of NADAs/ANADAs within 180 days of receipt. (14017)

- **Context of Goal:** The animal drugs and feeds program does not have sufficient resources to review and act on all new animal drug application actions received within the statutory time frame of 180 days. Recent resource increases in the drug review area will allow the Center for Veterinary Medicine to recruit and hire review scientists. The increased manpower will increase our compliance rate from 65% in FY-00 to 70% in FY-01.
- **Data Sources:**Submission Tracking and Review System (STARS)
- **Performance:** In FY 99, CVM updated its tracking system to be consistent with procedures under ADAA. Current data indicates a compliance rate of 65% is reasonable for FY 00.

3. Revise and develop 14 guidances for the regulated veterinary industry. (14001)

- **Context of Goal:** Reform legislation and reinvention initiatives, such as the Results Act (RA) and FDAMA, require input from our customers and stakeholders. Input from customer surveys, stakeholder meetings, and other interactions with regulated industry helped FDA target resources toward developing guidance documents which will more accurately reflect the current veterinary medicated feed and drug approval/monitoring processes. These standards reflect changes in the approval processes resulting from enactment of the ADAA and CVM's efforts to reinvent its new animal drug approval processes. Availability of guidance documents facilitates the accurate and complete preparation of drug applications. Development of new guidance documents and updating existing documents to reflect recent changes in legislation were initiated in FY 1999 and will be continued in FY 00. FDA has identified an estimated 14

guidances to be developed or revised according to projected availability of resources and analyses of the complexity of the material.

- **Data Sources:** CVM's priority project tracking system.
- **Performance:** By the end of FY 98, there were 77 guidance documents related to the Animal Drugs and Feeds Program. The original FY 99 target was to perform an initial review of the 77 guidance documents and to initiate revisions or develop new guidance documents as appropriate. In FY 99, we intended to revise or develop "at least" one document (1% of the existing documents). Our goal was exceeded. The staff wrote 8 guidance documents: 3 FDAMA and 5 Veterinary International Conference on Harmonization (VICH). One of the FDAMA guidances is related to dispute resolution and another to supplemental applications.

Reinvention Success Stories:

Reinvention in CVM has succeeded in part because it has been a collaborative process between FDA and our regulated industry. In order to implement the Veterinary Feed Directive (VFD), statutory changes were required. The collaborative process was used to develop the necessary legislation. The VFD project led to a collaborative effort to address additional drug approval processes. The result was the passage of the Animal Drug Availability Act (ADAA). This collaborative process was used as a model for the development and passage of FDAMA. CVM continues to interact with industry to clarify reinvention regulations and develop guidance documents that address industry concerns.

4. Reduce drug development and review time by initiating a process for receiving protocol submissions electronically. (14002)

- **Context of Goal:** The Results Act and FDAMA require input from our stakeholders. Feedback from our stakeholders indicated that better automated information systems, including those supporting electronic submission of applications by sponsors, would facilitate and expedite the review process. In 1998, CVM initiated a pilot project to permit industry to electronically submit one type of notice for review. Plans were developed to expand the submission program to include other regulatory reporting requirements.
- **Data Sources:** CVM's priority project tracking system.
- **Performance:** In 1997 FDA initiated the development of the infrastructure and procedures to allow for electronic submissions. In 1998, FDA worked with industry to successful complete a pilot to permit electronic submissions of Notices of Claimed Investigational Exemptions (NCIE-also known as drug shipment notices). In 1999, the Animal Drugs and Feeds Program completed the implementation of the electronic submission process for all NCIE submissions. An evaluation of the process shows improvement in application processing time. Processing time was reduced to 1/3 the time required for paper processing. Additional phases of electronic submission are being initiated in FY 00. Our intention is to move toward the paperless office as rapidly as possible. Some

changes in regulations will be required before we can implement electronic process for all types and phases of submission.

Electronic Submission Success Stories:

Feedback from our regulated industry indicates that the electronic submission process used in the pre-market approval process was such a success that CVM is going to use the same process for transmitting material to FDA in the postmarket assurance process. We have shared information on our success at veterinary international harmonization meetings and have proposed using our process as the model for international electronic submissions.

5. Leverage our intellectual capital by initiating the development of a Staff College in the CVM to increase and maintain the scientific expertise in the Center. (14018)

- **Context of Goal:** Staff College programs have been developed in FDA as a means of developing intellectual capital. The addition of a CVM Staff College will allow CVM to increase and maintain the scientific expertise in the Center, especially as it relates to animal science and veterinary medicine issues. The Staff College will use dollars to outsource the planning and implementation of training programs tailored to the needs of in-house scientists.
- **Data Sources:** CVM's priority project tracking system.
- **Performance:** FY 00: Develop a strategy to establish a Staff College in CVM; FY 99: Identify need to enhance and maintain scientific expertise

6. Develop an antibiotic risk assessment model using FLQ as the antibiotic, Chickens as the animal species and Campylobacter as the bacterial isolate.(14003)

- **Context of Goal:** The impact of improving risk assessments will be to provide tools that will allow CVM to evaluate the public health risks associated with using antimicrobial products in food producing animals. Risk assessment provides a strong foundation upon which efficient allocation of scarce food safety resources can be made. Furthermore, risk assessment often plays a central role in the development of any science-based system of preventive controls. Based on current resource estimates and complexity of the proposed risk analysis, CVM will initiate 2 risk analyses in FY 00 which will be completed in FY 01.
- **Data Sources:**The NARMS database mentioned later in this report, surveillance systems of other government organizations, such as those of CDC and USDA, and published literature.
- **Performance:** The Center has used the principles of risk assessment to determine that the microbial safety of all antibiotics used in food animals must be assessed prior to approval. The guidance explaining this risk assessment was published November 1998. A risk assessment that evaluated the risk to human health from resistant food borne pathogens associated with the use of antimicrobials in food producing animals was completed in December 1999. The draft risk assessment report was made available on the CVM homepage and was discussed at a

workshop held December 9-10, 1999, and attended by over 200 interested participants from industry, public health, consumer groups, other governments and other US government agencies, and the press. The risk assessment models the risk of having a resistant *Campylobacter* infection attributable to the use of fluoroquinolones in chickens and being treated with a fluoroquinolone. At the workshop the report was applauded for its thoroughness, logical flow, and novelty. A docket was opened to allow people who could not attend the workshop to comment on the risk assessment as well. CVM plans to continue to have a process that is open for public input as it determines what standards to apply to risk assessment results in establishing monitoring thresholds for antimicrobial resistance associated with the use of antimicrobials in food animals.

CVM will be developing a second risk assessment model to assess the transfer of resistance determinants to human pathogens from enterococci originating in animals. Unlike the *Campylobacter* risk assessment where the transfer of resistance is direct through the consumption of products contaminated with resistant *Campylobacter*, this second assessment will model the indirect transfer of resistance. The Center published a request for proposals to develop the model and awarded a contract in September 1999.

Strategic Goal 2:

Reduce the risks associated with marketed animal products.

Approach

Once animal drugs are on the market, CVM continues to be involved in managing public health risks by improving/enhancing our compliance strategy and the development of partnership relationships with industry and the states.

Surveillance of marketed products and the business industry is accomplished through review of drug experience reports and compliance programs implemented by the FDA field offices through inspections (Performance Goal 7, 8 & 9), sample collections and analysis, investigations, and other activities. Regulatory actions are taken as needed to control violative goods and firms.

The immediate outcome of our surveillance systems is the identification of potential human and/or animal health hazards. An intermediate outcome is the development of procedures and strategies to prevent, minimize, or contain problems such as informing the veterinary community of adverse reactions due to drug interactions that were not apparent in clinical trials or withdrawal of marketed drugs as necessary to protect human and animal health. The ultimate outcome is assurance that marketed animal drugs and food additives provide for safe food products derived from animals and ensure quality health care of animals.

Another major post market concern of CVM is the President's Food Safety Initiative. The U.S. population needs an effective early-warning system (Performance Goal 10) that can detect food illness outbreaks early and allow implementation of intervention strategies to prevent their spread. NARMS was developed in conjunction with USDA and CDC, and has greatly improved our ability to detect emerging resistance among foodborne pathogens. This helps ensure the continued effectiveness of both human and veterinary drugs and aids in increasing the availability and distribution of effective drugs. This system also advances understanding of foodborne illness and further prevention efforts.

Research and Standards Setting

Food safety research is critical to developing the means to more rapidly and accurately identify and characterize foodborne risks. This will provide the tools for regulatory enforcement and the development of effective interventions to be used, as appropriate, to prevent hazards at each step from production to consumption.

In order to continue to ensure a safe food supply, USDA must be able to monitor livestock and poultry for illegal drug residues and contaminants at the time of slaughter. FDA is responsible for conducting follow-up investigations. In order to determine the source of the contamination/adulteration, FDA needs to evaluate emerging techniques, develop new techniques, and adapt techniques in order to detect residues/contaminants in animal derived food, animal physiological samples and animal feeds. For example, we will expand the development of modeling techniques for assessing human exposure to a variety of foodborne pathogens and develop animal models for assessing infectivity.

Leveraging and Communication

In order to assure that foods from animals are safe for human consumption, FDA works with other government agencies, state and local governments, and the private sector to take action to prevent or minimize potential public health hazards through development of early warning systems, investigations, risk assessment, scientific research, educational initiatives and regulatory action.

CVM partners with other federal and state agencies, our stakeholders, and regulated industry to develop and sponsor workshops, symposia, and publications with a focus on prevention in order to assure the public that accurate information is disseminated and that marketed animal drugs and feeds are safe and effective.

CVM is making a strong effort to educate its partners in industry by publishing and disseminating guidance, training initiatives in targeted high-risk compliance areas, and in working more closely with industry to resolve problems.

FDA is also involved in international harmonization activities that will remove trade barriers while ensuring the American public that imported products meet FDA's standards related to safety and efficacy. Part of the harmonization effort includes the development of Mutual Recognition Agreements (MRAs) that will address international equivalency

issues. FDA must be able to assure the public that the processes used in other countries are as good as the processes in this country and the resulting products are safe for the intended use. Harmonization activities have been initiated with the European Union and Japan. The assessment of member state regulatory systems is an essential step in the harmonization process.

FDA is dedicated to expanding NARMS by initiating the collection of bacterial isolates from other countries. We decided to begin the expansion by collecting isolates from a neighboring country. Mexico was chosen because it borders on the US, it supports our initiative to partner with Latin American countries, and it is cost effective. The purpose is to identify bacterial trends in Mexico and take action to prevent a foodborne outbreak in the US. In FY 99, we laid the groundwork to establish the international relationship that will ensure the projects success.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
7. Improve biennial inspection coverage by inspecting 46% of registered animal drug and feed establishments. (14009)	FY 01: 46% FY 00: 27% FY 99: 27%	FY 01: FY 00: FY 99: 25%	Increase
8. Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers result in at least 90% conformance. (14004)	FY 01: at least 90% FY 00: at least 90% FY 99: at least 90%	FY 01: FY 00: FY 99: 99% FY 98: 98% FY 97: 97%	
9. Ensure compliance with good manufacturing practices including the newly implemented BSE regulation through a variety of methods.	FY 01: NA FY 00: NA FY 99: Ensure compliance with good manufacturing practices including	FY 01: FY 00: FY 99: 7200 inspections to date. Computer based training module for	

(14006)	the newly implemented BSE regulation through a variety of methods.	BSE inspections developed.	
10. Increase to 7200 the overall isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS). (14005)	CY 01: Total: 7200 - Salmonella Isolates CY 00: Total: 6000 - Salmonella Isolates: 2000 (human), 4000 (veterinary) CY 99: Total: 6000 - Salmonella Isolates: 2000 (human), 4000 (veterinary)	CY 01: CY 00: CY 99: 4/00 CY 98: Total: 4900 - Salmonella Isolates: 1400 (human), 3500 (veterinary) CY 97: Total: 3678 - Salmonella Isolates: 1287 (human), 2391 (veterinary) CY 96: Total: 3193 - Salmonella Isolates: 1272 (human), 1921 (veterinary)	Increase
TOTAL FUNDING: ($ 000)	***FY 01: $39,190*** ***FY 00: $29,228***		

[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01.
NPR: Goal supports an FDA National Partnership for Reinventing Government Goal

C. Goal by Goal Presentation of Performance

7. Improve biennial inspection coverage by inspecting 46% of registered animal drug and feed establishments. (14009)

- **Context of Goal:** FDA exercises considerable discretion regarding the frequency and comprehensiveness of inspections. FDA has a statutory obligation to inspect all regulated animal drug and feed establishments once every 2 years. There continues to be an increased emphasis on postmarket monitoring as a result of public demand for increased drug availability. Routine inspections have lower priority than inspection of firms producing high profile products. This has an impact on the pre-approval process which requires a "recent" inspection prior to approval of a new animal drug.

  This includes inspections done by FDA directly, or through state contracts or partnership agreements on manufacturers, repackers and relabelers (drugs), and manufacturers and growers requiring a Medicated Feed Mill License. Biennial inspection means we are to inspect 50% of registered establishments every year. As of September 1999, there were 1,418 registered establishments.

- **Data Sources:** Program Oriented Data System, Official Establishment Inventory
- **Performance:** FY 98: 34%, FY 97: 31%

  In 1999, 25% of registered animal drug and feed establishments were inspected, falling just short of our target of 27%. The inspection percentages are estimates, based on complexities of inspections, number of firms in inventory, time each inspection takes, and violative and reinspection rates.

8. Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high level of conformance (at least 90%) with FDA requirements. (14004)

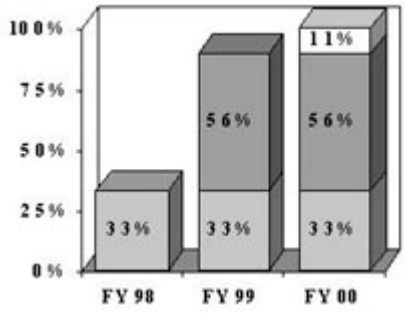
- **Context of Goal:** Routine postmarket surveillance activities and surveys are conducted to assure that sponsors are in compliance with regulations designated to ensure data integrity and good manufacturing practices.
- **Data Sources:** FDA Field Data Systems.
- **Performance:**The FY 99 conformance rate is 99%. FY 98: 98% FY 97: 97%. The conformance rates are based on a statistical modeling from actual inspection and serious deficiency (Official Action Indicated) data. The rates are representative of the firms inspected in the given year. As the statistical model and industry coverage is improved, the rates will better represent the conformance status of the overall industry. The FY 99 conformance rate does not include BSE medicated feed inspection data.

9. Protect public health (human) and animal health by ensuring compliance with good manufacturing practices including the newly implemented BSE (Mad Cow Disease) regulation through education, regulatory inspections and industry/Federal/state partnerships. (14006)

- **Context of Goal:** CVM sought to protect the public through the development of regulations and a comprehensive strategy to educate the industry. Surveillance activities were initiated to ensure compliance with the Bovine Spongiform Encephalopathy (BSE) regulations. In 1998, a program was initiated to decrease the feeding of prohibited materials to ruminants. The program began with a satellite conference and a two year plan to conduct educational inspections aimed at improving the labeling and record-keeping requirements, inspecting foreign processors and domestic importers of bovine materials, and implementing laboratory tests for compliance with the BSE regulation.
- **Data Sources:** FDA Field Data Systems
- **Performance:** Progress: We have completed over 7,200 inspections to determine compliance with 21 CFR 589.2000. The non-compliance rate continues to be approximately 25%. The educational aspects of the inspections are resulting in understanding of the requirements by the firm/individual and the majority of the firms are taking corrective actions to bring the company into compliance. Follow-up inspections are now being scheduled to assure that firms have implemented corrective actions.

  The June 1999 Update Workshop was conducted in Dallas, Texas, with over 170 participants. The workshop was very interactive and focused on problem solving, continuing education of the affected parties, and targeted enforcement action for repeated violators. In addition, CVM continues to provide speakers for state and industry training. CVM is working with ORA to develop interactive Computer Based Training for BSE Feed Regulation inspections. This training initiative includes representatives from CVM, ORA headquarters, FDA field, and the states. We anticipate completion early in FY 2000. Some distribution, start-up, and training in the use of the module will be required.

Percent BSE Inspections Completed by Year



BSE Success Stories:

In March 1996, the British government announced its concern that exposure to BSE-infected beef might cause human disease. This concern grew because of a possible link between BSE (often called "mad cow" disease) and 22 cases of a newly identified variant of Creutzfeldt-Jakob Disease in humans. The potential

impact on animal and human health and the high public health cost of a BSE epidemic in the U.S. led to the passage of BSE regulations. The enforcement of the BSE rule is a high priority for the Agency. FDA has worked with the regulated industry to ensure that the industry understands and complies with the regulations.

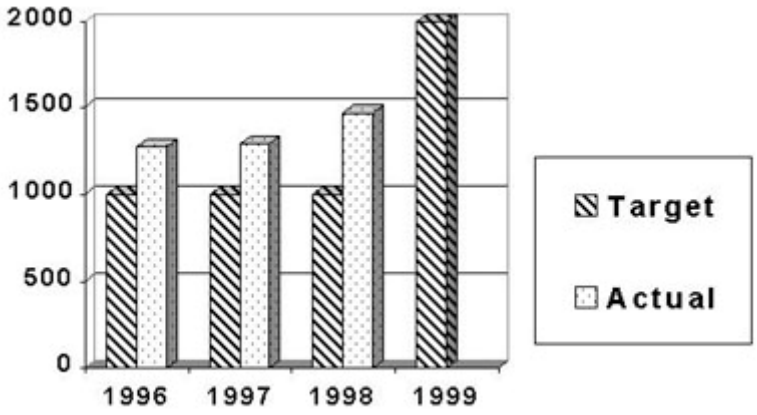
A major objective in preventing BSE in the U.S. is to inspect and educate all renderers, feed manufacturers, and a percentage of ruminant feeders. A significant number (89%) of these inspections have been completed and some states and FDA Districts are beginning to conduct follow-up inspections at those firms that were not in compliance. In FY 00, we will complete the planned initial inspections and continue to devote resources to determine whether corrections have been made.

10. Increase the overall isolate testing rate for Salmonella in NARMS to 7200 for human and animal isolates. (14005)

- **Context of Goal:** A major part of the surveillance aspect of the CVM's Food Safety Initiative (FSI) is NARMS which was initiated in 1996 in collaboration with FDA, CDC, and USDA . It allows the detection of emerging resistance among foodborne pathogens and the detection of potential health hazards through systematic collection, analysis and interpretation of antimicrobial susceptibility surveillance data. In addition, the program serves as a basis for educational efforts and prudent drug use campaigns in humans and in veterinary medicine. It helps ensure the continued effectiveness of both human and veterinary drugs.
- **Data Sources:**FDA-CDC-USDA National Antimicrobial Resistance Monitoring System
- **Performance:** We continue to meet our NARMS goals. Our CY 98 human target was 1000 salmonella isolates and we added data from 1466 isolates to the database. The veterinary target was 3000 and data from 3318 isolates was added to the database. Calendar Year 99 data appear to be on target (CY 99 target: - 2000 human and 4000 animal isolates). Early estimates indicate that we should receive approximately 1600 human salmonella isolates and 5000 animal salmonella isolates during this period.

  Date of Completion: The final results for CY 99 will be available about April 2000. The isolates will be collected through December 31, 1999, then sent for serotyping, susceptibility testing, and quality control testing. Reports will be generated and analyzed.

Salmonella Isolates in NARMS



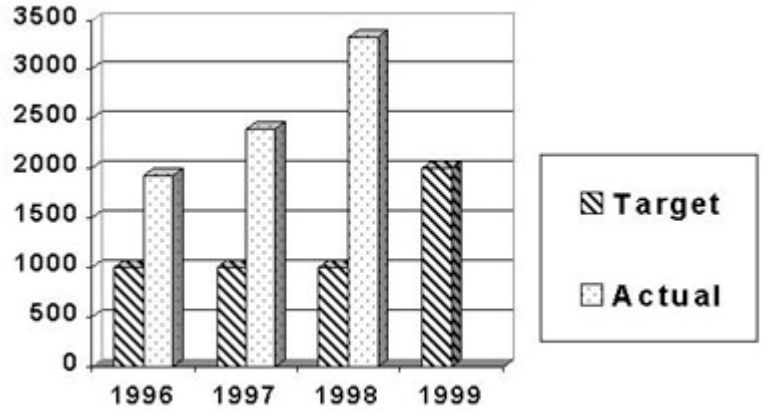
NARMS Success Stories:

NARMS was established in January 1996 as a collaborative effort among the FDA, USDA, and CDC. Funding was used to expand the scope of the monitoring system and conduct follow-on research and investigations. The system now tests *Salmonella, Campylobacter* and *E. coli* isolates collected from animal sources, and *Salmonella Campylobacter*, *Enterococcus, Shigella*and *E. coli* isolates from human clinical samples. In addition, new sites and sources of isolates have been added.

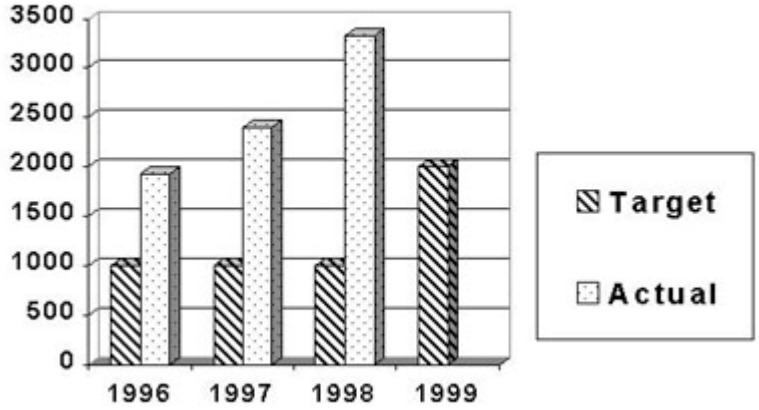
Epidemiological research was initiated in 1998 and expanded in 1999. This research aims to characterize and reduce the incidence of food borne disease associated with emerging and drug-resistant pathogens. Information from this research was used in 1999 to educate farmers about proper drug use and other husbandry practices that would help prevent future outbreaks and spread of the multi-resistant organism, *Salmonella typhimurium DT104*, among animals and to man. Collaborative studies with USDA will significantly improve FDA's ability to monitor the safety of competitive exclusion products and new antimicrobial approvals.

NARMS data has been presented at National and International meetings. Medical microbiologists from hospitals in Mexico and Guatemala are interested in initiating an antimicrobial resistance-monitoring program. This collaboration between the U.S. NARMS officials and the Mexican antimicrobial surveillance group represents the beginning of the first international human and animal monitoring system for foodborne antimicrobial drug susceptibility surveillance in the Americas.

Human Isolates Tested by Year



Veterinary Isolates Tested By Year



2.4.3 Verification and Validation

An integral part of the FDA continual improvement initiative has been an upgrade of our data processing and information systems. This includes automation of manual systems and integration of existing systems which reduces duplication and chances of data keying errors. Our information and data collection systems contain automatic data checks such as comparisons against lists of "valid" responses for a given data field. By programming "business rules" into our systems, the chance for "human" error is reduced. For example, due dates for applications are appropriately assigned and review time is accurately tracked. Data access is restricted to ensure that only appropriate personnel can enter data, review data, or audit the data. (Checks are in place to ensure that the person who enters the data does not audit the data, etc.)

As part of our commitment to seek input from our stakeholders, we are working with industry to be sure that our preapproval performance measures are appropriate for our

stated goals. As we gain experience, we are making changes to ensure that appropriate data are reported. For example, we originally reported progress related to guidance documents as percent revised. We improved the measure by changing it to reflect the actual number of revised guidances updated/developed.

In the postmarket area we are working with, and using data from, other governmental agencies such as CDC and USDA. To ensure that our data needs are addressed by our federal partners, we have established memorandums of understanding and memorandums of need with other agencies. In order to accomplish our Food Safety Initiative goal (Performance Goal 10 - NARMS) we developed databases in-house and entered into Interagency Agreements for the development of other databases. We are therefore dependent to some extent on the data validation processes of our sister agencies.

Some of our program work is dependent upon other agencies' planning processes. This is especially true in our illegal residues in meat and poultry program which targets the follow-up of violative tissue residues received from USDA. USDA prepares an annual residue sampling plan with input from FDA. Under the new Hazard Analysis Critical Control Point plan, the requirements that slaughter plants sample has changed substantially. USDA's Food Safety Inspection Service takes some samples, but only if an animal is suspect. Because the USDA residue plan has changed, it is extremely hard to judge how many residue reports will be sent to FDA for follow-up investigation.

We have also ensured Year 2000 compliance of our data systems including data applications. The Animal Drugs and Feeds program, in conjunction with the Agency, developed a plan to create an inventory of data applications, analyze their degree of Year 2000 compliance, and thus develop a plan to ensure compliance with Year 2000 requirements. The Animal Drugs and Feeds Program developed the Business Continuity Contingency plan for both of our critical data systems, STARS and DERS. We have upgraded our network, tested our servers and desk top units, and replaced the twenty units that were not Year 2000 compliant.

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[1] ADAA substantially alters the way FDA regulates and approves animal drugs and medicated feeds by granting the authority to exercise considerable flexibility in regulatory decision-making. During the implementation phase which includes promulgation of regulations through notice and comment rulemaking, FDA is continuing the dialogue with stakeholders that began prior to the passage of the ADAA.

[2] FDAMA initiatives in the Animal Drugs and Feeds Program premarket area requires the Center to accomplish the following: 1) develop guidance regarding the content and review of applications and supplemental applications for approved products; 2) participate in the development of reports and publications required to meet all statutory review requirements by July 1, 1999; eliminating backlogs of applications under review by January 1, 2000; 3) participate in the development of an information system to track the status of applications described in the act; and 4) participate in the development of training and education programs for employees.

2.5 MEDICAL DEVICES AND RADIOLOGICAL HEALTH

2.5.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	192,457	168,747	159,008	155,705

FDA's Medical Devices and Radiological Health Program is responsible for ensuring the safety and effectiveness of medical devices and eliminating unnecessary human exposure to manmade radiation from medical, occupational, and consumer products. There are thousands of types of medical devices, from heart pacemakers to contact lenses. Radiation-emitting products regulated by FDA include microwave ovens, video display terminals, and medical ultrasound, and x-ray machines.

The FDA Modernization Act of 1997 (FDAMA) requires FDA to conduct more timely and interactive application reviews, improve the quality and timeliness of postmarket surveillance data, expand participation in international harmonization activities, and improve information and education for industry and health professionals. In order to implement these mandates, FDA will identify and concentrate resources on high-risk, high-impact products or work areas, those where its direct intervention helps consumers and health care professionals the most. FDA will build its device science base to maintain and update the organizational capability to make timely regulatory decisions.

Growth in the size of the medical device industry and in the complexity of new medical devices will continue to challenge FDA to stay up to date with breakthrough medical devices and to maintain high quality timely reviews, required interactions with industry, and current review guidance. Research and development expenditures by the industry increased 91% from 1990 to 1996 with an increase of approximately one billion dollars projected from 1997 to the year 2000. Quantum leaps in device miniaturization, microprocessor software control, artificial intelligence decision support, remote operation, and drug/biologics tissue combinations are already revolutionizing medical care.

The pace of technology innovation in this country and around the world requires the Center's cadre of scientists to keep up with the latest technology and scientific advances, in both the development of medical technology and scientific methodologies. Only by doing so can personnel provide high quality, timely and science based regulatory actions on the safety and effectiveness of new medical products and the causes of inferior performance including public health impact. FDA intends to emphasize the need to maintain high quality scientific decision making. This is especially critical for emerging

technologies like computer-related technology: molecular medicine; home-care and self-care devices; minimally invasive technology; combination device-drug combination products; and pioneering organ replacement and patient assist devices.

These challenges are represented by two key strategic goals for the 21st Century:

- **Provide quicker access to important, life-saving and health-enhancing medical devices, while assuring their safety and effectiveness.**
- **Reduce the risk of medical devices and radiation-emitting products on the market by assuring product quality and correcting problems associated with their production and use.**

The Agency's approach to achieving these strategic goals, as well as key performance goals that will move the Program in these directions, are outlined in the strategic goal sections.

FY 99 Program Accomplishments

FDA has worked diligently over the past two years on implementing the FDA Modernization Act (FDAMA) and reengineering initiatives that reaffirmed the device program's traditional regulatory functions and strengthened its scientific and analytical capacity for 21st century regulatory decision making. A strong science base is linked to every decision the agency makes from providing greater patient access to new device technologies to assessing hazards and reducing medical errors. Activities conducted include: the timely implementation of the FDAMA device program.

The Medical Device and Radiological Health Premarket Program is responsible for review of device marketing applications: premarket approval applications (PMAs), premarket notification 510(k)s, and investigational device exemptions (IDEs). In FY 99, CDRH received 9,792 submissions There were no overdue submissions for the third consecutive year. FDA maintained high quality, timely reviews despite increasingly complex device technology. Approximately 800 device applications now in house depend on new or advanced technology. FDA completed a collaborative effort with FDA stakeholders to identify tools and principles to be used in considering the "least burdensome" means that will allow appropriate premarket development and review of a product without unnecessary delays and expense to manufacturers.

FDA exceeded its FY 99 domestic inspection coverage goal of 26 percent with a performance of 30 percent. However, this is still below the statutory requirement of 50 percent, the result of an increasing number of firms to inspect and declining field inspection resources. FDAMA shifts premarket clearance for many low and medium risk devices to postmarket quality systems conformance. Firms may declare conformity to standards or quality systems requirements as part of streamlining premarket clearance. However, FDA will be unable to monitor quality systems conformance at current resource levels. Implementation of FDAMA requirements, ongoing reengineering, and FDA's commitment to a strong science base have resulted in an examination of how FDA

conduct inspections. FDA is working with the medical device industry to reengineer the process used for Quality System inspections. The new technique significantly reduces the inspection time and increases the effectiveness of the inspections.

The quality of mammography services in the United States continues to improve. FY 99, FDA mammography activities included conducting approximately 9,500 facility inspections and issuing 5,499 three-year facility certificates. Additionally, FDA performed 170 audit inspections under the Inspector Quality Assurance Program and hosted a MQSA Satellite Teleconference in February 1999 that provided an interactive platform for over 2,000 viewers to get answers to questions about regulatory requirements.

2.5.2 Strategic Goals

Strategic Goal 1:

Provide quicker access to important, life-saving and health-enhancing medical devices, while assuring their safety and effectiveness.

A. Strategic Goal Explanation

Approach

Medical Devices intended for marketing in the United States are subject to rigorous premarket review by the FDA. Prior to marketing a device, manufacturers must seek FDA safety and effectiveness approval of their products. FDA is responsible for assigning marketed medical devices to a regulatory category. Medical devices vary widely in their complexity and their degree of risk or benefits. They do not all need the same degree of regulation. Thus, FDA places all medical devices into one of three regulatory classes based on the level of control necessary to assure safety and effectiveness of the device. These classes are:

Class I -General Controls
Class II - General Controls and Special Controls
Class III - General Controls, Special Controls and Premarket Approval

Class I devices are subject to the least regulatory control. They present minimal potential for harm to the user and are often simpler in design than Class II or Class III devices. Examples of Class I devices include elastic bandages, examination gloves, and handheld surgical instruments.

Class II devices are those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods are available to provide such assurances. Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.

Class III is the most stringent regulatory category for devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.

FDA reviews: 1) Premarket Notifications (510(k)s -- products substantially equivalent to products on the market; 2) Investigational Device Exemptions (IDEs) -- devices used in clinical investigations on human subjects; and 3) Premarket Approval Applications (PMAs) -- devices that support or sustain human life, which present a reasonable risk of illness or injury. To accomplish this premarket responsibility, FDA is charged with review of submissions within the time frames specified in the law. FDA strives to support a stable and predictable review process, and meet statutory FDAMA requirements for reduced review times for PMAs and 510(k)s and increased interactions with sponsors. FDA is also striving to reduce review time for PMA supplemental applications. Performance Goals 1 through 4 set targets for PMAs, PMA supplements, and 510(k)s.

Research and Standard-Setting Contributions to Premarket Review

FDA's goal is to provide science-based device product safety assurance to the public. Resources are being utilized to increase participation of science expertise in the review and approval of high-risk medical devices during premarket review. In addition, efforts are underway to develop and promote consensus performance standards as guides of safer and more effective medical products and to enhance the quality of regulatory decision making.

FDA would identify in guidance documents those standards that may address aspects of a substantial equivalence determination, such as specified testing. Manufacturers would certify that their devices met the standards, and submit that certification to the Agency in lieu of the underlying data. Manufacturers would retain the option of taking alternative approaches and submitting the underlying data to FDA. In most cases a given standard would address only some aspects of a substantial equivalence determination for a particular device, but there may be instances where a standard or combination of standards would address all aspects of a 510(k) decision. Performance Goal 7 sets targets for standards.

With this increase, FDA will be able to remain current in all scientifically relevant areas, keep abreast of emerging technologies, and translate the knowledge into standards that will expedite getting safe, beneficial medical device products to the public. Areas of possible research include:

<u>Supporting Standards Development</u>

- Develop comprehensive methods and performance requirements for critical device standards to optimize the amount of information manufacturers have to provide in premarket submissions.

<u>Products and Health Safeguards for Critical Patient Groups</u>

- Facilitate the use of products for use by diabetics.
- Develop and test new technologies for the detection and management of changes in mechanical competence of bone.

Reducing Costs of Clinical and Pre-Clinical Trials

- Develop and validate statistical and quantitative methods for reducing costs of clinical studies without compromising scientific validity.

Possible new research projects include:

- Reuse of devices;
- Medical image acquisition and display systems;
- New sensor technologies planned for integration into medical devices;
- Artificial implanted organs and devices that can complement and extend the capabilities of organs whose functions can be partially salvaged.
- Medical devices that are less invasive than open surgery.

Leveraging/Communication

FDA will be able to improve its ability to receive and distribute device-related scientific information into, around, and out of the organization in an efficient manner. Current plans include:

- Developing a scientific exchange program to share information, cross-train staff, and improve communication and support among Agency programs. This approach leverages the resources currently available with academic institutions, the States, and field and headquarters offices to provide developmental opportunities for selected scientific staff.
- Developing a FDAMA communications strategy to improve the dialogue between FDA and its stakeholders. This strategy will allow FDA to provide timely and unbiased information to the public, including approval requirement information to industry.
- Encouraging dissemination of information and scientific exchange through the use of standardized computer systems, integrated technologies, and enhanced web sites on the internet/intranet. These improvements will allow for greater information sharing between FDA and its stakeholders and among the FDA centers.

FDA is moving towards regulatory requirements that are consistent from nation to nation, which benefits both FDA and industry. Toward that end, FDA is recognizing an increasing number of international standards as a way to satisfy part of our 510(k) requirements. FDA has signed a Mutual Recognition Agreement with the European Union and has assumed chairmanship of the Global International Harmonization Task Force.

Reinvention

FDA has been reinventing many medical device premarket processes to use resources more effectively and efficiently. Many of these efforts were already under way before FDAMA. FDAMA accelerated many of these efforts and added others. Reinvention efforts include:

Early Meetings with Manufacturers -- Early meetings benefit both FDA and the manufacturer. FDAMA specifies early collaboration, and FDA is taking this even further. Performance Goals 5 and 6 set targets for early meetings with manufacturers.

Modular Review -- This involves breaking PMAs down into bite-size chunks, which customizes the submission and gives the manufacturer timely feedback.

Streamlined Review -- FDA is pilot testing streamlined review for well-understood PMA products.

Product Development Protocols (PDPs) -- Used in lieu of PMAs, PDPs are advance agreements that clearly identify requirements up front, benefiting both FDA and the firm.

Changing the 510(k) Paradigm -- FDA is making the process more efficient by exempting well-understood, low-risk products; making it easier to notify FDA about changes; encouraging use of FDA recognized consensus standards; and using third party reviews. This saves FDA resources and allows more time for high-impact devices.

Other Improvements in the Review Process- FDA is improving manufacturer access to advisory panels.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed to 90%	PMAs & HDEs FY 01: 90% FY 00: 85% FY 99: 65%	 FY 01: FY 00: FY 99: 67% as of 12/31/99. Final data by 5/2000 FY 98: 79%	 Increase NPR Related

in FY 01. (15001)		FY 97: 65% FY 96: 51%	
2. Review and complete 90% of PMA supplement final actions within 180 days. (15009)	FY 01: 90% FY 00: 85% FY 99: NA	FY 01: FY 00: FY 99: 89% as of 12/31/99. Final data by 5/2000. FY 98: 100% FY 97: 65%	Increase
3. Review and complete 95% of 510(k) (Premarket Notification) first actions within 90 days in FY 01. (15002)	FY 01: NA FY 00: NA FY 99: 510(k): 90% within 90 days; 3rd party 510(k): 75% within 30 days.	FY 99: 99.7% as of 12/31/99. Final data by 2/2000 FY 98: 99.5% FY 97: 98% FY 96: 94%	
4. Review and complete 75% of 510(k) (Premarket Notification) final actions within 90 days in FY 01. (15021)	FY 01: 75% FY 00: 65% FY 99: NA	FY 01: FY 00: FY 99: 73% as of 12/31/99. Final data by 2/2000 FY 98: 69% FY 97: 70% FY 96: 61%	Increase

5. Complete 100% of Investigational Device Exemption (IDE) "Agreement" meetings within 30 days. (15015)	FY 01: 100% FY 00: 80% FY 99: NA	FY 01: FY 00: FY 99 : 23% FY 98: 33%	Increase
6. Complete 95% of PMA "Determination" meetings within 30 days.	FY 01: 95% FY 00: 95% FY 99: NA	FY 01: FY 00: FY 99 : 100% FY 98: 25%	Increase
7. Participate in the development of 20 to 25 application review standards (15003).	FY 01: 20 to 25 standards FY 00: Review 50 standards for continued applicability and review 50 standards for recognition. FY 99: Recognize over 415 standards for use in application review and update the list of recognized standards.	FY 99: 450 standards recognized. FY 98: 370 standards recognized. FY 97: 2 standards recognized.	Increase
TOTAL FUNDING: **($000)**	FY 01: 79,202 FY 00: 64,699		

[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01.
NPR: Goal supports an FDA National Partnership for Reinventing Government Goal

C. Goal-By-Goal Presentation of Performance

1. Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and HDE first actions (within 75 days) completed to 90% in FY 01. (15001)

- **Context of Goal:** PMAs involve potentially high-risk devices that have the highest likelihood of significantly improving the treatment of patients. It is essential that FDA complete the review process for these products quickly and thoroughly. The statutory requirement is to review PMAs within 180 days. An HDE is submitted for a humanitarian use device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the U.S per year. FDAMA established a requirement that FDA review HDEs within 75 days. An HDE is similar in both form and content to a PMA, but is exempt from the effectiveness requirements of a PMA.
- **Data Sources:** Center for Devices and Radiological Health (CDRH) Premarket Tracking System and Receipt Cohorts
- **Performance:** The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to better baseline data and a funding change. So far the FY 99 goal is on schedule with a 67% performance as of 12/31/99. Final data will not be available until May 2000. The performance strategy is to redirect resources from low risk to high risk devices. Also, reinvention efforts like early meetings with manufacturers, modular review, streamlined reviews, and product development protocols have resulted in faster reviews. Faster reviews will give patients quicker access to the important new medical devices they need.

  HDEs provide an easier approval path for devices used to treat rare conditions or diseases. In FY 99, FDA approved six HDEs, including two septal occlusion devices for closing holes between the left and right sides of the heart, a sacral nerve stimulator to aid in urination and bowel evacuation in spinal cord injured patients, and a pulmonary valve for children under age 4 with absent or diseased valves.

2. Review and complete 90% of Premarket Approval Application (PMA) supplement final actions within 180 days. (15009)

- **Context of Goal:** PMA supplements involve potentially high-risk devices that have the highest likelihood of significantly improving the treatment of patients. Supplemental applications are generally submitted for changes in already approved products such as the addition of a new indication. It is essential that FDA complete the review process for these products quickly and thoroughly. This was a new goal for FY 00.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

3. Review and complete 95% of 510(k) (Premarket Notification) first actions within 90 days in FY 01.(15002)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. This goal for first actions on 510(k)s within 90 days addresses the statutory requirement to review a 510(k) within 90 days. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to better baseline data.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** So far the FY 99 goal is on schedule with a 99.7% performance as of 12/31/99. Final data will not be available until February 2000. FDA has been completing nearly 100% of first actions on time. This performance has resulted from FDA changing the way 510(k)s are reviewed. FDA is exempting more low risk products from the 510(k) requirement, is using more consensus standards in its reviews, and is using more third party reviews. As a result, these devices are available more quickly to patients and resources savings are available for high-impact devices.

  FDA is working to improve how critical resources are used. Two efforts that illustrate FDA premarket management improvements are:

  Third Party Reviews, which are consistent with FDAMA's intent to encourage access and use of outside scientific and technical expertise, provides an alternative to FDA review. To date, FDA has recognized 13 third party bodies and made 154 types (mostly Class IIs) of devices eligible for third party review. In FY 99, FDA received only 32 510(k)s with a third party review, but more than 1,200 were eligible.

  Abbreviated and Special 510(k) Submissionsprovide manufacturers with reengineered submission procedures established by CDRH's *New 510(k) Paradigm*. These submissions are simpler to process than traditional 510(k)s, allowing more rapid market clearance. In FY 99, the agency received 396 Special 510(k) applications and 85 Abbreviated 510(k) submissions.

  The agency plans to encourage more firms to use these options.

4. Review and complete 75% of 510(k) (Premarket Notification) final actions within 90 days in FY 01. (15021)

- **Context of Goal:** This final actions goal for 510(k)s responds to stakeholder interest, especially among Congress and the device industry, in having the review completed within 90 days with no further action required. A final action could be the first and only action required prior to marketing or it could be an additional action to complete the review after a first action resulted in the need for additional information from the firm.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

5. Complete 100% of Investigational Device Exemption (IDE) "Agreement" meetings within 30 days. (15015)

- **Context of Goal:** This performance goal deals with FDAMA requirements for increased interactions with sponsors and covers IDE Agreement Meetings. A sponsor prior to submitting an IDE application to discuss specific investigational plans for a Class III or implantable device may request an IDE Agreement Meeting. These meetings will help to expedite the review process and make medical devices available more quickly. FDA will continue to meet statutory review times and increase interactions with the medical device industry. IDEs and PMAs represent pre-market approval actions that deal with devices that are complex and represent new technologies. It is intended that opening a pre-market discussion with the manufacturer will greatly improve the quality of IDE and PMA submissions and result in a reduction of the review time required. This was a new goal for FY 00.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

6. Complete 95% of Pre-market Approval Application (PMA) "Determination" meetings within 30 days.

- **Context of Goal:** This performance goal deals with FDAMA requirements for increased interactions with sponsors and covers PMA Determination Meetings. A PMA Determination Meeting may be requested by a prospective PMA applicant to determine the type of scientific evidence necessary for PMA approval. FDA will continue to work to meet statutory review times and increase interactions with the medical device industry. FDA anticipates that the use of pre-market approval meetings will reduce the pre-market review times and result in moving new products to the market faster. This was a new goal for FY 00.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

7. Participate in the development of 20 to 25 standards to be used in application review. (15003)

- **Context of Goal:** Science, technology and standards activities are directed to improve science support related to the device review process. FDAMA requires FDA to recognize and use standards in the application review process. FDA plans to expand its participation in international harmonization of standards. Additionally, FDA plans to increase the use of consensus standards developed by such national and international organizations as the American Society for Testing and Materials and the International Standards Organizations to improve premarket approval times. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to better baseline data.
- **Data Sources:** Standard status document reports

- **Performance:**FDA recognized 450 standards in FY 99. FDA works closely with standards organizations like the American National Standards Institute (ANSI) and the International Standards Organizations (ISO) to improve its use of consensus standards. FDA is also promoting the use of consensus performance standards as guides in the design of safer and more effective medical products and to enhance the quality of regulatory decision making. Use of standards also helps to expedite reviews of 510(k)s.

Strategic Goal 2:

Reduce the risk of medical devices and radiation-emitting products <u>on the market</u> by assuring product quality and correcting problems associated with their production and use.

<u>A. Strategic Goal Explanation</u>

Approach

Medical device risk reduction activities cover four major areas: (1) Inspections; (2) Mammography; (3) Radiation Control: (4) Adverse Event Reporting. FDA exercises considerable discretion regarding the frequency and comprehensiveness of inspections. For approximately 4,100 device establishments (excluding mammography facilities), the law requires FDA to conduct inspections at least once every two years. There are approximately 10,000 mammography facilities, which must be inspected at least once each year. The performance goals deal with establishments subject to a statutory coverage requirement.

Inspections

FDA enforces numerous regulations to protect the public from unsafe or ineffective medical devices or radiological products. FDA also informs and verifies that medical device firms are knowledgeable and utilize Good Manufacturing Practices (GMP). Inspections of devices fall into three categories: 1) Routine Surveillance Inspections-to determine compliance with FDA's GMP Act; 2) Targeted Inspections-for approval to market high risk devices; inspections triggered by adverse reaction incidents; or product recalls; 3) Compliance Inspections-to collect evidence for pending enforcement actions. Performance Goals 8, 9, and 10 deal with inspections.

Medical devices have become more medically and technologically complex and the device industry is growing domestically and internationally. This growth and a reduction in device and radiological health inspection resources have resulted in lower inspection coverage rates. FDA's inadequate device inspection coverage impairs product safety assurance and impairs FDA's ability to carry out the following responsibilities:

- FDAMA shifts premarket clearance for many low and medium risk devices to postmarket quality systems conformance. Firms may declare conformity to

standards or quality systems requirements as part of streamlining premarket clearance. However, FDA will be unable to monitor quality systems conformance at current resource levels.

- Foreign inspection coverage is very low and the mutual recognition agreement implementation with the EU will require extensive training of EU assessment bodies by FDA. FDA cannot maintain foreign inspections or successfully implement the MRA with current resources. In the long term, when the MRA is successfully implemented, it will reduce the number of foreign firms that FDA will need to inspect.
- Emerging device product safety assurance issues will require increased attention. These include enforcing new standards for patient leads and cables, home health care, medical software, latex products and allergic reactions, interventional fluoroscopy, digital imaging, electronic article surveillance, new laser technology, and electronic magnetic interference.

Mammography

Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer deaths among American women. Experts estimate that during the 1990's as many as 1.8 million women will be diagnosed with breast cancer, and 500,000 will die from it. The probability of survival increases significantly, however, when the disease is detected in its early stages. Currently, the most effective technique for early detection of breast cancer is screening mammography, an x-ray procedure that can detect small breast tumors and abnormalities up to two years before they can be detected by touch. The Mammography Quality Standards Act (MQSA) was signed into law on October 27, 1992, to address the health need for safe and reliable mammography. Performance Goal 12 sets the quality target for mammography facilities.

The MQSA requires that FDA conduct annual inspections of mammography facilities. FDA estimates that there are approximately 10,000 mammography facilities that are covered by MQSA. In some cases inspections are not completed if facilities are not certified, if there is an ongoing effort to correct problems identified during an inspection, or if facilities go out of business. The target of 8,900 inspections is based on past experience with these factors. Federal and state personnel will continue to conduct annual inspections, as well as provide training for new inspectors. The fees collected will pay for the costs of the inspections.

Radiation Safety

Manufacturers of radiation-emitting products such as x-ray machines, lasers, microwave heating equipment, television and ultrasonic therapy equipment are required to submit initial reports, annual reports, and model change reports to FDA. In conjunction with its regulatory efforts, FDA carries on specialized programs to reduce patient exposure during diagnostic x-ray procedures by encouraging improved practice among health professionals and by developing new x-ray techniques. FDA makes continual checks to assure that the potential of radiation can be realized at a minimum risk of harm. As new

radiation-producing electronic products are developed, FDA evaluates them to ensure they are safe. Performance Goal 11 deals with radiation safety.

Adverse Event Reporting

A key element in any comprehensive program to regulate medical devices is postmarket reporting a system through which FDA receives reports of serious adverse events. Such reporting forms the basis for corrective actions by the Agency, which include warnings to users and product recalls. This is especially true as FDA moves towards less direct involvement in the premarket review of lower-risk devices. Performance Goals 13 and 14 deal with a MedSun System for collecting data on adverse events and summary reporting to enhance protection of the public health.

Research and Standard-Setting Contributions

FDA needs to update regulatory science to keep up with increasingly complex, high-tech medical device products. FDA will also be able to conduct forensic research in the field to support criminal investigations of medical devices. Areas of possible research include:

- Develop and evaluate techniques to reduce unnecessary exposures to radiation from electronic products and disease-causing organisms.
- Develop methods for monitoring and controlling microbial resistant biofilms on medical devices.

As technology progresses, the scope of radiation-emitting products increases much faster than the knowledge of bioeffects. Adverse event reports, recalls, and noncompliance rates are monitored for adjustments in priorities. Personnel of multiple disciplines and specialized training, along with specialized test equipment, are utilized to assess bioeffects and safety, to enforce performance standards, to develop proposals for new standards, both regulatory and consensus, and to present recommendations to an advisory committee prior to publication of Federal Register notices. Interpretive policies are developed to permit greater flexibility in meeting requirements that are not critical to radiation safety.

Leveraging/Communication

Achievement of FDA's domestic inspection coverage goal relies on the willingness and ability of the states to contract with FDA to inspect a portion of the medical device industry. To implement these contracts, FDA's experience predicts that a significant investment in training and time is necessary to ensure quality and uniformity of inspections.

FDA will maintain inspection coverage of a growing number of Class II and Class III foreign device firms by working more closely with foreign regulatory bodies and conducting inspections most needed to develop joint inspection standards thus improving the safety of future U.S. device imports. This includes joint inspections of high-risk

device manufacturers with European Union Conformance Assessment Bodies. Foreign workload is expected to increase by approximately 20 to 25%. Due to the workload increase, additional resources are necessary to maintain the present coverage rate for all firms. No class I manufacturers will be inspected

In the area of Bioresearch Monitoring, recent feedback from Institutional Review Boards (IRBs) has shown that many need a better understanding of the differences between drug and medical device clinical trials. To respond to this need, FDA has increased outreach to IRBs. We've encouraged them to access our web page, and we've increased our participation in IRB seminars and workshops.

Reinvention

FDA is pursuing a number of reinvention efforts in the postmarket area. These include:

Summary Reports -- We're saving FDA and industry resources by eliminating individual adverse event reports where such events are well known and clearly defined. We're now using summaries for 12 device types, and we're ready to expand the list.

Design Controls -- Our Quality System regulation will strengthen design controls for devices. We just completed a transition and education period, showing that most firms are using design controls, but some need improvement.

Changes in the Inspection Process -- FDA is pilot-testing several new approaches: a new system for warning letters that will consider a firm's written response to the inspection report and make special provision for 510(k) and labeling violations; new guidance on when to inspect for changes in PMA'd devices; a new model to prioritize inspections based on risk; a new approach, the Quality System Inspection Technique (QSIT) system, to evaluate quality systems; and the "HACCP" concept to focus on specific safety parameters.

The purpose of the QSIT reengineering effort is to develop an inspection program covering the quality systems regulation, which results in more focused and efficient inspections. The effort should help FDA investigators focus in on key manufacturing and quality areas at the manufacturer during inspections, in order to determine their state of compliance with the Quality Systems Regulation. FDA believes that this effort will lead to increased compliance with the Quality Systems Regulation, and thus improved medical device product quality. Improved medical device product quality could result in fewer problems with medical devices. In addition, fewer enforcement actions may be needed for Quality Systems Regulation violations, and better public health should result. Since several aspects of this program have been derived from the Global Harmonization Task Force's document entitled Guidelines for Regulatory auditing of Quality Systems of Medical Device Manufacturers, a third benefit is harmonization.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
8. Improve inspection coverage for Class II and Class III domestic medical device manufacturers to 28%. (15005.01)	FY 01: 28% FY 00: 24% FY 99: 26%	FY 01: FY 00: FY 99: 30% FY 98: 33% FY 97: 40% FY 96: 30%	Increase
9. Assure FDA inspections of domestic medical device manufacturing establishments result in at least 90% conformance. (15018)	FY 01: 90% FY 00: 90% FY 99: 90%	FY 01: FY 00: FY 99: 95% FY 98: 95% FY 97: 96%	
10. Maintain inspection coverage for Class II and Class III foreign medical device manufacturers. (15005.02)	FY 01: 10% FY 00: 9% FY 99: NA	FY 01: FY 00: FY 99: 10% FY 98: 14% FY 97: 23% FY 96: 30%	Increase
11. Initiate regulatory actions and recalls for 95% of high-risk, non-compliant or defective electronic products within 30 days. (15008)	FY 01: NA FY 00: NA FY 99: 95%	FY 01: FY 00: FY 99: 95% FY 98: 95%	

		FY 97: 95% FY 96: 95%	
12. At least 97% of mammography facilities meet inspection standards, with less than 3% with Level 1 problems. (15007)	FY 01: 97% FY 00: 97% FY 99: 97%	FY 01: FY 00: FY 99: 97% FY 98: 97% FY 97: 97% FY 96: 95%	
13. Recruit over 200 more hospitals into a MedSun System. (15012)	FY 01: Recruit over 200 more hospitals into a MedSun System. FY 00: Develop MedSun Surveillance System based on approximately 75 to 90 user facilities. Report results to Congress. FY 99: NA	FY 01: FY 00: FY 99: Pilot completed FY 98: Recruited 24 pilot facilities.	Increase
14. Increase the number of low-risk postmarket reports processed in summary form from 20,000 in FY 98 to over 25,000 in FY 99. (15004)	FY 01: NA FY 00: NA FY 99: Over 25,000 summary reports.	FY 99: 38,000 (est.) FY 98: 33,149 FY 97: 21,880	
15. Commit over 75% of inspection	FY 01: NA	FY 01: NA	

resources to high-risk devices (15016)	FY 00: NA FY 99: 75%	FY 00: NA FY 99: 50% FY 98: 50% (est.)	
TOTAL FUNDING: **($000)**	FY 01: 113,255 FY 00: 104,048		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-By-Goal Presentation of Performance

8. Improve inspection coverage for Class II and Class III domestic medical device manufacturers to 28%. (15005.01)

- **Context of Goal:** This goal includes inspections done by FDA directly, or through state contracts or partnership agreements on Class II and III domestic medical device manufacturers. Achievement of this goal relies on the willingness and ability of the states to contract with FDA to inspect a portion of the medical device industry. To implement these contracts, FDA's experience predicts that a significant investment in training and time is necessary to ensure quality and uniformity of inspections. The full benefit of additional contract inspections will not be realized until FY 2002 since part of FY 2001 will be devoted to contract set up. Also, domestic workload is expected to increase by almost 20% from FY 1999 to FY 2001. Due to the workload increase, additional resources will be needed to both maintain and increase the coverage rate. No class I manufacturers will be inspected. The FY 99 goal was added in the FY 00 Performance Plan as a result of its inclusion in the FDA Plan for Statutory Compliance, published in November 1998. Class II and III manufacturers are required by statute to be inspected at least once every two years. FDA is working toward meeting this statutory requirement of a 50% annual coverage rate.
- **Data Sources:** CDRH Field Data Systems
- **Performance:** The FY 99 goal of 26% was met with a performance of 30% in spite of reduced field resources and an increased workload. However, inspection coverage has declined each year since FY 97 and is expected to continue to decline in FY 00 because of an increasing number of firms and reduced field inspection resources. Implementation of FDAMA requirements, ongoing reengineering, and FDA's commitment to a strong science base have resulted in an examination of how FDA conducts inspections. FDA plans changes which will improve the statutory inspection coverage rate beginning in FY 01.

FDA has worked with the medical device industry to reengineer the process used for Quality System inspections. The new technique will significantly reduce the inspection

time and increase the effectiveness of the inspections. This will be an essential tool as the device program faces declining resources and a growing industry. FDA implemented the Warning Letter Pilot Test. The pilot allows firms 15 days to respond to and/or correct problems identified during an inspection. FDA does not issue warning letters if the problems are adequately corrected. FDA believes that this is beneficial in getting firms to correct problems quickly. FDA plans to make inspections more useful to manufacturers and consumers.

Summary of Performance	FY 1999 Actual	FY 2000 Goal	FY 2001 Goal
Improve Class II & III Inspection Coverage	30%	24%	28%

9. Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements. (15018)

- **Context of Goal:** Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected, and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector. This goal excludes mammography inspections, which are covered by goal # 12. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to reduced funding.
- **Data sources:** CDRH Field Data Systems
- **Performance:** FDA exceeded the FY 99 goal of 90% with a performance of 95%. Conformance rates for FY 97, FY 98, and FY 99 have been adjusted to reflect the observed average correction rate for each year.

10. Maintain inspection coverage for Class II and Class III foreign medical device manufacturers. (15005.02)

Context of Goal: This goal includes joint inspections of high-risk device manufacturers with European Union Conformance Assessment Bodies. Foreign workload is expected to increase by approximately 20 to 25%. One of the major initiatives introduced to assist in reducing the inspection workload associated with medical device review is the U.S./European Union (EU) Mutual Recognition Agreement (MRA). In FY 99, FDA continued to implement the MRA with the EU which will help facilitate transatlantic

trade and reduce costs for compliance with regulatory requirements. Activities are currently taking place to prepare third parties in the EU to perform work in the EU for FDA and to prepare third parties in the US to perform work in the US for the EU. FDA plans to proceed with MRA activities pending the availability of funds. FDA posted a web site in 1999 dedicated to MRA activities, including the implementation plan, eligible device lists, MRA meeting minutes, and the list of nominated U.S. and EU Conformity Assessment Bodies (CABs) that are participating in confidence building activities. The site is: http://www.fda.gov/cdrh/mra/index.html

No class I manufacturers will be inspected. This was a new goal for FY 00.

- **Data Sources:** CDRH Field Data Systems
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

Summary of Performance	FY 1999 Actual	FY 2000 Goal	FY 2001 Goal
Improve Foreign Class II & III Inspection Coverage	10%	9%	10%

11. Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95% of identified high risk, non-compliant or defective products within 30 days of discovery. (15008)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. Under the Radiation Control for Health and Safety Act (RCHSA), FDA conducts an electronic radiation control program to assess the biological effects resulting from all types of radiation exposure, evaluates radiation emissions from electronic products, conducts research to minimize exposure, and sets and enforces radiation performance standards. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to minor editorial changes.
- **Data Sources:** CDRH Tracking Data, FDA and state laboratory guides, recall files and Inspection reports.
- **Performance:** FDA met the FY 99 goal of 95% for the 4th consecutive year. Because of this consistent performance, this goal is being dropped from the performance plan.

12. Ensure that at least 97% of mammography facilities meet inspection standards, with less than 3% of facilities with Level 1 (serious) inspection problems. (15007)

- **Context of Goal:** This goal will ensure that mammography facilities remain in compliance with established quality standards and to improve the quality of

mammography in the United States. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to minor editorial changes.

- **Data Sources:** Mammography Program Reporting and Information System (MPRIS)
- **Performance:** The FY 99 goal of ensuring that mammography facilities meet inspection standards was achieved with a 97% rate. This was the third consecutive year of achieving this high standard. Inspection data continue to show facilities' compliance with the national standards and in the quality of x-ray images. Improving the quality of images should lead to more accurate interpretation by physicians and, therefore, to improved early detection of breast cancer. FDA worked cooperatively with the states to achieve this goal. Under MQSA, trained inspectors with FDA, with State agencies under contract to the FDA, and with States that are certifying agencies, performed annual MQSA inspections. State inspectors did approximately 94% of inspections. Inspectors performed science-based inspections to determine the radiation dose, to assess image quality, and to empirically evaluate the quality of the facility's film processing. MQSA requires FDA to collect fees from facilities to cover the cost of their annual facility inspections. FDA also employed an extensive outreach program to inform mammography facilities and the public about MQSA requirements. These included a quarterly newsletter for facilities, an internet website, collaboration with NIH to provide a list of MQSA-certified facilities, a consumer brochure, meetings with consumer groups, and interactive teleconferencing for facilities.

13. Recruit over 200 more hospitals into a MedSun System that uses improved data format and collection methods to enhance the validity and reliability of data provided, thus affording a higher level of public health protection. (15012)

- **Context of Goal:** FDAMA authorizes FDA to discontinue universal user facility reporting and implement a MeDSuN surveillance system composed of a network of user facilities that constitute a representative profile of user reports. The user surveillance system currently under development is based on the premise that a select group of highly trained reporting facilities can provide high quality, informative reports that can be representative of user facility device problems in general. The Medical Device Surveillance Network (MeDSuN) is FDA's response to FDAMA's provision that universal user reporting can be replaced with a system that is limited to a subset of user facilities that constitutes a representative profile of user reports. FDA has successfully completed a pilot. FDA will evaluate the pilot and report to Congress and plans to proceed if funds are available.
- **Data Sources:** CDRH Adverse Events Reports
- **Performance:** This goal is a new commitment in FY 00 and FY 01.

14. Increase the number of low-risk postmarket reports received and processed in summary form. The total number of summary reports will be increased from 20,000 in FY 98 to over 25,000 in FY 99. (15004)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. FDA is responsible for monitoring the market for injuries related to medical devices. The major efforts in the postmarket area are focused on the improvement of our ability to detect and analyze medical device problems by focusing on high-risk devices and expanding scientific efforts. Summary reporting of lower risk reports streamlines reporting requirements and allows priority to be placed on high-risk reports. FDA received over 63,000 postmarket reports plus 20,000 summary reports in FY 98. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised due to reduced funding.
- **Data Source:** CDRH Adverse Events Reports
- **Performance:** The FY 99 goal was accomplished by using innovative surveillance methods and improving quality and analysis needed for Safety Alerts and other actions. In FY 99, FDA took steps to further reduce the reporting burden by enhancing the current system with the new Alternative Summary Reporting (ASR) system that will allow summary data elements to be submitted in line-item format. Approximately 38,000 summary reports were received in FY 99. Forty-five manufacturers are now participating in the summary reporting program and 52 individual product classification codes are included in the program.

In 1996, a medical device reporting (MDR) network was established in the Los Angeles District as a cooperative venture with the medical device community, regulatory consultants, and the Orange County Regulatory Affairs Association to exchange information on FDA requirements. FDA was invited to participate. The group received the Vice President's Hammer Award in 1999.

15. Improve quality conformance of high-risk products like cardiovascular devices by committing over 75% of inspection resources to high-risk devices. (15016)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. Goal was discontinued in FY 01 and dropped in FY 00 due to a change of emphasis among goals. The original FY 99 goal, as shown in the FY 99 Congressional Justification, was revised to measure specific resource investment.
- **Data sources:** CDRH Field Data Systems
- **Performance:** The FY 99 goal of 75% was not met. Approximately 50 % of resources were committed to high risk devices due to competing priorities within the Agency. This goal will not be continued because it is a basic activity goal that does not focus on results or outcomes.

2.5.3 Verification and Validation

Premarket --To help ensure Agency consistency in tracking and reporting premarket activities, the Medical Device Program utilizes the Premarket Tracking System, which contains various types of data taken directly from the premarket submissions. FDA

employs certain conventions for monitoring and reporting performance; among these are groupings of premarket submissions into decision and receipt cohorts. Decision cohorts are groupings of submissions upon which a decision was made within a specified time frame, while receipt cohorts are groupings of submissions that were received within a specified time frame. The premarket performance goals are based on receipt cohorts. Final data for receipt cohorts are usually not available at the end of the submission year. Because the review of an application received on the last day of the submission year, e.g. a PMA with 180 day time frame, may not be completed for at least 6 months or longer, final data for the submission or goal year may not be available for up to a year after the end of the goal year.

Mammography -- The Mammography Program Reporting and Information System (MPRIS) is a set of applications used to support all aspects of the FDA implementation of the Mammography Quality Standards Act of 1992. This includes the collection, processing and maintenance of data on mammography facility accreditation, certification, FDA inspections and compliance actions. MPRIS is envisioned as a centralized repository of information that supports FDA's mission to improve the quality of mammography and improves the overall quality, reliability, integrity, and accessibility of facility certification, inspection, and compliance data by eliminating multiple versions of the data while expanding and automating data edits, validation, and security of a single integrated database.

Adverse event reporting -- FDA's adverse event reporting systems are dependent upon the MedWatch program. MedWatch, the FDA Medical Products Reporting Program, is an initiative designed both to educate all health professionals about the critical importance of being aware of, monitoring for, and reporting adverse events and problems to FDA and/or the manufacturer and; to ensure that new safety information is rapidly communicated to the medical community thereby improving patient care.

The purpose of the MedWatch program is to enhance the effectiveness of postmarketing surveillance of medical products as they are used in clinical practice and to rapidly identify significant health hazards associated with these products.

The program has four goals:

1. To increase awareness of drug and device-induced disease
2. To clarify what should (and should not) be reported to the agency.
3. To make it easier to report by operating a single system for health professionals to report adverse events and product problems to the agency.
4. To provide regular feedback to the health care community about safety issues involving medical products

The MEDWATCH program is supported by over 140 organizations, representing health professionals and industry, that have signed on as MedWatch Partners to help achieve these goals.

CDRH Field Data Systems - Data systems include the Program Oriented Data System (PODS) and the Field Accomplishments Tracking System (FACTS). PODS tracks field activities conducted by FDA's field force and the firms over which FDA has legal responsibility. PODS provides most of the information on inspections and other field activities. Field personnel have the major responsibility for assuring the quality of PODS data. CDRH also has its own systems to supplement these Agency systems.

Other Data Sources -- These include miscellaneous reports, guides, and files as cited in the data sources for several of the goals.

2.6 NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

2.6.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	37,868	34,186	32,109	32,189

The National Center for Toxicological Research (NCTR) conducts FDA mission-critical, peer-reviewed research that is targeted to develop a more scientifically sound basis for regulatory decisions and reduce risks associated with FDA-regulated products to protect, promote, and enhance America's public health. Specific aims of NCTR's research are:

- To develop new strategies, methods, and systems to predict toxicity and anticipate new product technology in order to support FDA's commitment to bring this technology to the market rapidly.
- To understand mechanisms of toxicity and design better risk assessment/detection techniques and methods for use in pre-market review and product health surveillance.

The NCTR provides the Agency with a high-quality, cost-effective, health science research program, which provides new scientific knowledge through the application and leveraging of research findings from the National Institutes of Health (NIH) and academia to enhance the FDA's regulatory practices. NCTR also leverages Agency scientific research resources through partnerships with other federal agencies, national and international organizations, and industry to best meet Agency needs.

As a critical resource for enhancing the science base of the FDA, the center director and scientists foster scientific forums with NCTR's stakeholders, namely the product centers and the Office of Regulatory Affairs (ORA). These recurring discussions allow NCTR the opportunity to present and validate its planned/ongoing research, as it relates to the

Agency's priorities, as well as to solicit the anticipated research needs of the product centers and the ORA. NCTR's strategic research goals support the FDA's mission to bring safe and efficacious products to the market rapidly and to reduce the risks of products on the market. NCTR's strategic goals are as follows:

1. Develop new strategies and methods to test/predict toxicity and assess/detect risk for FDA regulated products (new and those already on the market).
2. Develop computer-based systems (knowledge bases) that predict human toxicity to enhance the efficiency and effectiveness of pre-market product reviews.
3. Conduct research to understand mechanisms of toxicity, assess new product technology, and provide methods for use in FDA standards development and product risk surveillance.

FY 99 Program Accomplishments

Some NCTR accomplishments that highlight the Center's multidisciplinary capabilities and high quality research are: 1) Geneticists and toxicologists developed better and new biological assays to predict human risk. 2) Preliminary studies in genetics show that women possessing a specific gene mutation in the folate metabolism pathway are more likely to have children with Down's syndrome. 3) Molecular epidemiologists worked with academia and industry to develop and validate a microchip product designed to identify individuals at risk to cancer and/or adverse drug interactions. 4) Toxicologists in partnership with industry, other government agencies and FDA Centers, have developed a computer technology to model the interaction of naturally occurring estrogen with its receptor; this technology can quickly identify chemicals or drugs with estrogenic activity that may cause unwanted effects including reactions with other drugs and therapies. 5) Through an interagency agreement with the NIH, National Institute of Environ-mental Health Sciences (NIEHS), studies to establish safe levels of the corn contaminant, fumonisin B1, in the diet were completed, and a phototoxicity center to evaluate toxic interactions between drugs or cosmetics and exposure to sunlight was constructed. 6) Within the Presidential Food Safety Initiative (FSI), NCTR scientists developed techniques to simultaneously detect multiple species of food borne pathogens, and developed a consumer product, licensed to industry under the trademark, Fresh Tag TM, to detect seafood decomposition, ensuring a safer food supply. 7) Finally, to support the Presidential Initiative on Antiterrorism, NCTR researchers have reported a novel method to rapidly identify pathogenic characteristics associated with naturally-occurring and bioengineered microorganisms that could be used in a terrorist attack; the technique works equally well with mixtures of organisms.

2.6.2 Strategic Goals

Strategic Goal 1:

Develop new strategies and methods to test/predict toxicity and assess/detect risk for FDA regulated products (new and on the market).

Strategic Goal Explanation

Approach

One of the Agency's and the NCTR's highest priorities is to increase the ability of FDA reviewers to evaluate and predict rapidly and accurately the adverse effects of FDA regulated human products. This capability is critical to the Agency's ability to carry out its mission to analyze the safety and efficacy of FDA-regulated products during the premarket application review process. The human response to a toxic agent is a complex process. To adequately predict the adverse effects of human exposure to a toxic agent, a group of tests must be developed, validated, and applied. NCTR uses a multidisciplinary approach to predict human toxicity and to evaluate human risk using appropriate animal and non-animal models.

Toxicologic research, often long-term and animal intensive, studies chemical toxicity in animal and cell cultures to predict risk to humans. The science of toxicology is moving away from its dependence on whole animal test systems that use large numbers of animals and seek relatively few endpoints because costly, time intensive animal systems do not mimic human systems exactly. This forces scientists to develop and use alternate systems and tests to better understand chemical toxicity and strengthen the extrapolation from animal models to humans. Increasing evidence of adverse drug/chemical reactions in humans points to a need to identify and protect susceptible subpopulations of people at higher risk from exposure to drugs, contaminated foods, or other regulated products because the American public has greater access to these products. In addition, the emphasis of toxicologic research has shifted from descriptive studies, that explain what happens, to studies that are designed to gain a better understanding of the biological mechanisms that cause the underlying effects of a toxic agent. NCTR uses transgenic rodents (such as those carrying easily assayed reporter genes) and human cell lines to predict human toxicity (Performance Goal 1). NCTR researchers continue to develop laboratory methods that closely mimic human genetic response and predict human genetic damage due to drug interactions. Other NCTR programs through partnerships and collaborative projects with other federal agencies, use human data they have collected to understand the mechanisms of carcinogenesis, particularly as they are related to individual susceptibility (Performance Goal 2).

Human studies are conducted by our scientists in collaboration with peers at the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER); other agencies (for example, the Environmental Protection Agency (EPA), the National Institute for Environmental Health Sciences (NIEHS), the National Toxicology Program (NTP); and universities, and medical centers around the world. International collaborative studies exploring human biomarkers will help to identify and potentially screen subpopulations at higher risk for developing certain types of cancer. This will improve the FDA's ability to determine and ultimately manage risk both in the United States and in collaboration with regulators and scientists throughout the world.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Introduce the knowledge of new genetic systems into the application review process. (16001)	FY 01: Provide peer reviewed articles on new genetic and transgenic systems and knowledge to product reviewers. FY 00: New biological assay to measure genetic change and validate two existing models that predict human genetic damage. FY 99: Develop better biological assays to measure genetic changes and predict human genetic damage.	FY 01: FY 00: FY 99: The Big Blue Rat and NCTR $Tk^{+/-}$ *in vivo* bioassays were developed and two cell lines were used to predict human genetic damage. FY 98: Utilized model animal and cell culture transgenic systems to evaluate risk to the human genome. FY 97: Conducted genetic screening and evaluated additional toxic results (e.g., cell death and mutagenesis) in relationship to DNA biomarkers of damage.	Increase
2. Develop with other organizations gene chip and gene array technology. (16002)	FY 01: Develop, "risk chip" technology to screen large numbers of people for biomarkers simultaneously.	FY 01: FY 00:	Increase

	FY 00: Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly susceptible subpopulations. FY 99: Complete biochemical and epidemiology studies to define the basis of susceptibility of humans to the toxicity of regulated products.	FY 99: Biochemical studies on pancreatic and colorectal cancer were completed and epidemiology studies on cancer are in the enrollment phase. FY 98: Conducted case control molecular epidemiology studies to assess breast and prostate cancer in African-American women/men. FY 97: Initiated studies to evaluate the use of molecular biomarkers in clinical studies and to identify subpopulations at increased risk.	
TOTAL FUNDING: ($000)	FY 01: 17,798 FY 00: 16,068		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal by Goal Presentation of Performance

1. Introduce the knowledge of new genetic systems, specifically transgenic systems and data, into the application review process. (16001)

- **Context of Goal:** Currently, industry has been submitting drug applications with data from transgenic systems. It is critical that NCTR scientists in collaboration with Agency reviewers understand and accurately interpret data derived from these systems in safety assessment. NCTR is developing, evaluating and

comparing in vivo and in vitro transgenic tools for this purpose. Reviewer request for data or information on transgenic systems will be the measure of applicability to the review process.

- **Data Sources:** NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings, manuscripts prepared for publication in peer-reviewed journals.
- **Performance:** A panel of transgenic cell lines has been developed and characterized; assayed phenolpthalein and diphenylhydrazine for CDER to assess mutation induction in the human genome.

2. Develop, in partnership with industry, academia, and government, gene chip and gene array technology to provide high volume screening of biomarkers for susceptible subpopulations identified in molecular epidemiology. (16002)

- **Context of Goal:** The importance of risk chip technology is that it allows researchers to screen large numbers of people simultaneously for different types of biomarkers. This will allow the identification of individuals at risk for adverse drug reactions and will facilitate FDA review of individual susceptibility using profiles of agents with known toxicities and allow selection of a diverse group for clinical trials. For instance, the technology will allow scientists to identify people at high risk for various cancers. Development of these techniques is being done in collaboration with private industry.
- **Data Sources:** NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings, manuscripts prepared for publication in peer-reviewed journals.
- **Performance:** Collaborative Research and Development Agreement established to automate the assessment of polymorphism's using gene chip technology.

Strategic Goal 2:

Develop computer-based systems (knowledge base) that predict human toxicity to enhance the efficiency and effectiveness of premarket product reviews.

Strategic Goal Explanation

Approach

An Agency-wide need, as identified by the NCTR Stakeholders, is the application of unique computer-based predictive systems to aid in assessing human toxicity to optimize non-clinical and clinical predictability. The FDA reviewers face an ever-increasing quantity and complexity of data in new drug and product applications. Clearly, tools that provide reviewers quick access to relevant scientific information and a capability for predicting toxicity can expedite review decisions. The NCTR, in partnership with other FDA centers, government agencies and industries, is developing a computer-based

predictive system that can predict the toxicological activity of a compound by using biological indicators of damage, chemical structures via molecular modeling, and advanced mathematical and computational tools.

Performance Goal 3 within this strategic goal is designed to build on the prototype knowledge base system established to assess estrogenic compounds. Data developed at the NCTR on the toxicity of estrogen and anti-estrogen compounds, coupled with data obtained through scientific collaborations (government, industry, and academia) and published in the literature is incorporated into a learning set for predictive computations. The NCTR adapted statistical techniques and applied computational techniques to construct this model system. This knowledge will now be applied to other receptor binding systems such as androgens, anti-thyroid compounds, and chemicals effecting the neuroendocrine system. This technology will save FDA and other agencies both time and money in evaluating over 85,000 chemicals which require testing under legislative mandate. Natural and synthetic estrogens are found in a broad range of FDA regulated compounds such as food packaging, drugs, devices, etc. Predictive modeling can assist FDA and other regulatory agencies to assess the need for regulation based on predicted toxicity and risk.

The Agency needs to maintain a strong scientific computing capability to devise better tools to facilitate product approval. NCTR uses Center and on-site contractor resources (FTEs and dollars) from analytical chemistry, computational science, neurotoxicology, genetic and reproductive toxicology, and molecular epidemiology to achieve this performance goal. The novelty of this approach is the combination of several disciplines focused on a common goal. NCTR has also partnered with the Chemical Manufacturers Association (CMA) to develop the capabilities needed.

B. Summary of Performance Goals

Performance Goals	**Targets**	**Actual Performance**	Reference[1]
3. Develop computer based model to predict the health impact of increased exposure to estrogens and anti-estrogen compounds. (16003)	FY 01: Validate a predictive model for androgens. FY 00: Validate predictive model for estrogenic or estrogenic-like compounds. FY 99: Demonstrate a model toxicity knowledge base to support and expedite	FY 01: FY 00: FY 99: Thirty chemicals for CFSAN and six chemicals for CDER have been used to confirm the predictive value of the computer	Increase

	product review.	modeling system. Partnering continues with other agencies (EPA, etc.) and industry (CMA). FY 98: Computer-based predictive system used to develop model for rodent and human estrogen receptor binding. FY 97: Prototype presented at FDA Science Forum.	
TOTAL FUNDING: ($000)	FY 01: 4,544 FY 00: 4,102		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal by Goal Presentation of Performance

3. Develop a computer based model to predict the impact of increased exposure to estrogens and anti-estrogen compounds on public health.(16003)

- **Context of Goal:** Recent recognition that drugs, food additives, food packaging (all regulated by FDA) and environmental chemicals (regulated by EPA) may have estrogenic activity has affected mechanisms that regulate human systems. This has raised the level of concern regarding adverse effects on human development and reproduction and contributions to high incidences of cancer and/or toxicity. NCTR scientists will identify and predict, using the Endocrine Disrupter Knowledge Base (EDKB), whether the elevation of exposure to the American public to naturally occurring and synthetic estrogens and anti-estrogens can adversely impact public health.
- **Data Sources:** Use of the EDKB computer-based predictive system by the FDA reviewers and other government regulators; NCTR Project Management System; peer-review through the FDA/NCTR Science Advisory Board, presentations at national and international.
- **Performance:** Predictions have been made on the estrogenic properties of specified compounds for CDER and Center for Food Safety and Applied Nutrition (CFSAN). Collaborating with EPA, NCTR is evaluating 52,000

compounds for estrogenic properties, 8,000 of these are regulated by FDA. The baseline was established in FY 99 and computer-based predictive systems used to evaluate toxins became available in FY 99.

Strategic Goal 3:

Conduct research to understand mechanisms of toxicity, assess new product technology, and provide methods for use in FDA standards development and product risk surveillance.

Strategic Goal Explanation

Approach

Most regulatory research begins as a precise exploration of a specific agent, a concept, or the use of a particular method. Once techniques are developed, these novel approaches can be applied to answer compelling questions of human health and safety. This goal includes three performance goals that address the Agency strategy for developing science-based product and process standards.

Research supported through an interagency agreement with the NIEHS/NTP permits the NCTR to enhance rodent bioassay studies to include those based on mechanisms of toxic action to improve bioassay interpretation and potentially speed up product review and ultimately reduce the costs of pre-clinical trials (Performance Goal 4). Currently, the NCTR is conducting special studies on three compounds of special concern to the FDA: chloral hydrate, malachite green, and urethane in the presence of alcohol. Recently, phototoxicology facilities have been completed to evaluate the harmful effect of skin exfoliants, such as alpha hydroxy acid. Additionally, NCTR is conducting long-term multi-generation studies of compounds that disrupt normal endocrine function. These studies provide data on how estrogens and anti-estrogens may affect the developing fetus.

The Agency needs state-of-the-art quantitative identification of toxic agents to strengthen its risk assessment of products on the market. In collaboration with the FDA's CFSAN, Center for Veterinary Medicine (CVM) and as part of the Food Safety Initiative (Performance Goal 5), the NCTR is developing methods to identify markers of foodborne pathogens and to assess whether these microorganisms are undergoing change, thus becoming more virulent. To address the question of human risk from foodborne pathogens, NCTR scientists are working to build biologically based dose-response models of microbial infection to assess survival, growth, and infectious components of microbial risk. Research within this goal capitalizes on partnerships with other FDA centers and with other agencies such as the United States Department of Agriculture (USDA). Working with CFSAN and CVM, NCTR has committed resources to investigate the safety of genetically modified foods.

The Presidential Initiative to combat terrorist activities is a combined activity of the Department of Justice, Federal Emergency Management Agency, Department of Health

and Human Services, Department of Defense (DOD), Veterans Administration, and state and local health departments. A focus of this activity is to enhance research and development to provide new capabilities to identify and to respond to potential chemical and biological threats of terrorism. NCTR is developing novel techniques to identify newly arising bacteriological and chemical contaminants in the food supply (Performance Goal 6). These techniques can crossover to provide methods of assessment for potential biochemical terrorist capabilities. To accomplish these goals, the NCTR needs continued review and input from other FDA centers, and outside experts to encourage and promote FDA-relevant research. NTP studies require the NCTR to maintain an accredited animal facility that includes a quality assurance staff, pathology capabilities, computerized record keeping, and high-quality animal husbandry and diet preparation support. The scientific expertise to support these goals range from analytical chemists to microbiology, biochemistry, molecular biology, neurotoxicology and biometry.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
4. Study FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity. (16004)	FY 01: Study two or more FDA-regulated compounds. FY 00: Conduct studies that relate how a compound causes damage to the damage itself to strengthen scientific basis for regulation of compounds. FY 99: Develop faster, more accurate tests based on mechanisms of toxic actions. FY 99: (Baseline FY 01) Continue two-year chronic bioassays on urethane in ethanol and malachite	FY 01: FY 00: FY 99: The experimental portion of the two year chronic study on urethane in ethanol has been completed and malachite green animal studies continue. Preliminary studies to assess risk of alpha and beta hydroxy acids in skin formulations continue using hairless mice. Portions of the studies on genistein,	Increase

	green. Begin studies to assess risk of alpha hydroxy acids and endocrine disrupters.	an endocrine disrupter, are completed. The chronic two- year component is ongoing. FY 98: Report to regulate fumonisin B1 exposure in foods and long term chloral hydrate usage. FY 97: Comprehensive mechanistic studies on FDA-nominated potential carcin-ogens include: complete dosing regimen for two year chronic bioassay on chloral hydrate and fumonisin B1; range finding studies on genistein, methoxychlor, and nonylphenol were completed and data is being analyzed for toxic effects; phototoxicity assessment of alpha hydroxy acids was nominated for study.	
5. Develop methods and build biological dose-response models to replicate bacterial survival in the stomach. (16007)	FY 01: Provide model to replicate bacterial survival in stomach. Initiate collaborative studies on genetically	FY 01: FY 00:	Increase

	modified foods. FY 00 : Develop methods of predicting, more quickly and accurately, the risk associated with foodborne pathogens as *Salmonella spp., Shigella spp., and Campylobacter spp*. FY 99: Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants.	FY 99: A project to simultaneously detect 13 species of foodborne pathogens in a single food sample was completed and is undergoing validation. CVM has been alerted to the danger associated with using antibiotic resistant bacteria for competitive exclusion product in the poultry industry.	
6. Catalogue biomarkers for biological warfare agents using new imaging techniques. (16012)	FY 01: Publish and disseminate list of biomarkers to FDA product reviewers and other interested scientists. FY 00: Begin developing solid-phase colorietric bacterial detection system. Acquire non-invasive imaging capability. FY 99: Develop method to identify biomarker proteins; translate method to colorimetric field kit.	FY 01: FY 00: FY 99: A novel method has been reported and is being used nationally and internationally (CDC, DOD, etc.) to rapidly identify pathogenic characteristics associated with naturally occurring microorganisms that could be used for bioterrorism.	Increase

TOTAL FUNDING: ($000)	FY 01: 15,526 FY 00: 14,016	
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal		

C. Goal by Goal Presentation of Performance

4. Conduct studies on FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity to the biological outcome. These studies enhance the relevance of the data for prediction of human toxicity; expand the number of FDA compounds studied by two per year. (16004)

- **Context of Goal:** This goal examines endocrine disrupting compounds such as nonylphenol, a component of plastic food wrap, so that the Agency can determine what adverse effects result from extensive use of plastics in packaging food materials. Resource limitations (e.g. staff, laboratory space and equipment) along with other NCTR Agency Center projects and priorities permit NCTR to initiate studies on only high priority, FDA nominated compounds. These compounds are chosen by an FDA committee for study under NIEHS/NTP Interagency Agreement. The compounds are submitted by the centers for discussion and evaluation and the representatives vote for the ones that need to be assessed via the NTP mechanism. These are taken to the NTP and if selected for funding, NCTR develops the protocols in conjunction with the nominating center and submits to NTP for review and approval. Protocols involve a comprehensive look at the chemical in question (both bioassay and mechanistic studies tailored to the regulatory questions of risk/benefit assessment.)
- **Data Sources:** Evidence that mechanistic data are used in the regulatory process, NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board.
- **Performance:** Bioassay for malachite green has been initiated to assess the toxicity of the use of this as an aquaculture antibiotic for use in aiding FDA in setting risk guidance for this chemical. The target level for FY 99 was goal 16005 in the FY 99 Performance Plan.

5. Develop methods and build biological dose-response models to replicate bacterial survival in the stomach to quickly and accurately predict risks associated with antimicrobial resistance and foodborne pathogens/contaminants. (16007)

- **Context of Goal:** Certain pathogens are rapidly becoming resistant to drugs due to their common use. This effort addresses this problem as part of the Presidential Food Safety Initiative to assure the American public is eating safe food.
- **Data Sources:** NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international

scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.
- **Performance:** A rapid screening method to detect the presence of 12 foodborne pathogens including *Salmonella spp.*, *Listeria monocytogenes* and *Campylobacter jejuni* has been developed. The target level for FY 99 was goal 16006 in the FY 99 Performance Plan.

6. Identify biomarkers of toxicity associated with biological warfare agents using innovative new technologies. (16012)

- **Context of Goal:** A major administration initiative is the concern that biological agents may be released on the American public by a hostile force. NCTR is focusing its efforts to develop ways to quickly respond to minimize the impact. Techniques being developed in support of food safety have crossover potential to support this national effort. Identification of biomarkers is important because it will allow rapid identification of and response to potential biological threats of terrorism. These proteins identify specific genes that are potential targets for introduction of pathogenicity. The methodology as well as the biomarkers will be useful for rapid identification of hazards.
- **Data Sources:** NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board; the NTP Scientific Board of Counselors, and the Food Safety Initiative Coordinating Committee; presentations at national and international scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.
- **Performance:** Novel mass spectrometer technique has been developed to detect and identify pathogenic microbes.

2.6.3 Verification and Validation

As a research component of the FDA, the National Center for Toxicological Research provides peer-reviewed research that supports the regulatory function of the Agency. To accomplish this mission, it is incumbent on the Center to solicit feedback from its stakeholders and partners, which include other FDA centers, other government agencies, industry and academia. Scientific program services are provided by the Science Advisory Board (SAB) composed of non-government scientists from industry, academia, and consumer organizations. The SAB is guided by a charter that defines the scope of the review to include quality of the science and the overall applicability to FDA regulatory need. This board is further supplemented with subject matter experts and scientists representing all of the FDA product centers. Programs described under each Performance Goal are evaluated at least once every five years by the SAB.

Research proposals are monitored through partnerships with other scientific organizations. Scientific and monetary collaborations include inter-agency agreements with other government agencies, Cooperative Research and Development Agreements and technology transfer with industry, and grants or informal agreements with academic institutions.

NCTR uses several strategies to ensure the quality of its research and the accuracy of data collected in specific research studies. Study protocols are developed collaboratively by principal investigators and FDA product centers. Findings are recorded by and verified by internal and external peer review. Statistical analyses are performed by the principal investigator and reviewed by members of the Biometry staff. The analytic approach is checked by different members of the scientific staff and the Deputy Director for Research to verify the scientific integrity of the data.

To ensure that the performance data are accurate and timely, the NCTR Planning and/or the Quality Assurance staff uses a project management system to monitor research progress at the project level on a quarterly basis. Specific good laboratory practices are monitored by the Quality Assurance staff for the experiments that fall within these guidelines. NCTR's computer based project management system is capable of tracking planned and actual research expenditures for research projects in all three strategic goals and in the performance goals. Accomplishments and goals are published annually in the NCTR Research Accomplishments and Plans document. Publications reporting research findings are tracked by project, and final reports are archived and distributed to interested parties. Over the past four or five years, NCTR has published yearly 175-250 research documents, manuscripts, book chapters, and abstracts in recognized scientific journals.

NCTR's research findings are also presented at national and international scientific meetings and published in peer-reviewed scientific journals. Many of the scientific meetings are sponsored or co-sponsored by NCTR scientists. The scientists make over 400 presentations and invited speeches a year at local science seminars and at national and international meetings. Many NCTR scientists also serve on international scientific advisory boards.

2.7 TOBACCO

2.7.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 01	FY 00	FY 99	FY98
Total ($000)	39,000	34,000	34,000	34,000

Smoking is the leading preventable cause of death in the United States. Every year, another one million young people become regular smokers and one-third of them will eventually die prematurely as a result of their smoking. The average teenage smoker starts smoking at 141/2 years of age and becomes a daily smoker by the age of 18.

Tobacco products are responsible for more than 430,000 deaths each year, or one in every five deaths. The Centers for Disease Control and Prevention (CDC) report an estimated

47 million adults smoke cigarettes in the United States, even though this behavior will result in death or disability for half of all regular users. Paralleling this enormous health burden is the economic burden of tobacco use: more than $50 billion in medical expenditures and another $50 billion in indirect costs.

The FDA Tobacco Program seeks to promote and protect the health of our nation's youth by reducing the number of young people who begin to use and become addicted to tobacco products each year. FDA's long-term goal is a 50% decline in young people's use of tobacco within seven years of full program implementation. To help reach this goal, FDA is working with other organizations within the Department of Health and Human Services (DHHS) such as the Substance Abuse & Mental Health Services Administration (SAMHSA), CDC, and the National Cancer Institute (NCI).

The challenge of the Tobacco Program is represented by the following strategic goal:

Reduce the easy access to tobacco products and inform and enlist the support of our stakeholders (for example, retailers) and the public to assist in reducing young people's use of and demand for tobacco products.

FDA's role is threefold: enforcement and evaluation, compliance outreach, and product regulation. FDA's overall goals are to reduce the access and appeal of tobacco products to young people; to enlist retailers' and other stakeholders' assistance in these efforts; and to develop regulatory procedures for cigarettes and smokeless tobacco products. FDA's efforts are supported by and coordinated with activities in other agencies within DHHS. For example, SAMHSA uses its authority to withhold substance abuse grants to states that do not achieve required access compliance rates by retailers and also conducts surveys to gather information about tobacco use. CDC's Office of Smoking and Health is primarily involved with public education, research, and surveys. Finally, NCI is also involved in research and education programs. FDA will use data gathered by these agencies to both carry out and evaluate its tobacco program. FDA will also work closely with state governments, especially in its enforcement role. The ultimate goal of these combined and coordinated efforts will be a significant reduction of tobacco use by young people.

On August 23, 1996, FDA issued its final regulation restricting the sale and marketing of nicotine-containing cigarettes and smokeless tobacco products. The rule contained a comprehensive set of provisions that limit young people's access to tobacco products, as well as restrictions on the marketing of these products to minors. The rule was the culmination of an intense multi-year investigation that sought to determine if FDA has jurisdiction over these products, and if so, what form regulation should take.

The cigarette, smokeless tobacco, advertising and retail industries, and others brought suit in the United States District Court for the Middle District of North Carolina (Greensboro Division) to invalidate FDA's assertion of jurisdiction and enjoin its regulations. Argument was heard on February 10, 1997, and the Court issued its decision on April 25, 1997, upholding FDA's jurisdiction and its access and labeling regulations. The Court

held that the statutory provision relied on by FDA does not provide FDA with authority to regulate advertising and promotion of tobacco products. Furthermore, the court delayed implementation of all remaining provisions, pending appeal, except those for age and photo identification that had gone into effect on February 28, 1997.

Both the government and plaintiffs appealed to the United States Court of Appeals for the Fourth Circuit. On August 13, 1998, the Fourth Circuit issued its decision finding the FDA's assertion of jurisdiction and issuance of regulations invalid. On April 26, 1999, the U.S. Supreme Court granted the Petition for a Writ of Certiorari filed by the Solicitor General. The Supreme Court heard oral arguments on December 1, 1999, and a decision is expected by Summer 2000. The granting of the petition continues a stay of the issuance of the Fourth Circuit's mandate while the Supreme Court considers the case. The age and identification provisions of FDA's tobacco rule in effect since February 1997 therefore remain in effect pending the Supreme Court's final decision.

FY 99 Program Accomplishments

In FY 99, the most important responsibility related to implementing the age and identification restrictions was to ensure that the estimated 500,000 to 1.5 million tobacco retailers were aware of and in compliance with the new rules prohibiting sales of cigarettes and smokeless tobacco to minors. FDA engaged in two major activities in support of its rule - enforcement and outreach. Most of the program's resources were dedicated to contracts which leveraged State and local tobacco control experience in conducting investigations to ensure that tobacco products were not sold to minors and for contracts to ensure that those industries directly affected by the rule knew what their new responsibilities were. In FY 99, the Agency achieved significant increases both in enforcing the age and identification requirements and informing stakeholders about the Tobacco Program.

While the Program is still in the early stages of implementation, there is already an indication that FDA's enforcement program has contributed to a decline in the number of youth who reported having easy access to tobacco products. The 1999 "Monitoring the Future" study, conducted at the University of Michigan's Institute for Social Research and supported by research grants from the National Institute of Drug Abuse, one of the National Institutes of Health, reported that, "[w]hile the great majority of young teens feel that they could get cigarettes 'fairly easily' or 'very easily' if they wanted them (72 percent of eighth-graders and 88 percent of 10th-graders), ... accessibility has been falling since 1996, particularly among the eighth-graders. According to the study's principal investigator, "[t]his suggests that the efforts by federal and state governments are starting to have an effect."

2.7.2 Strategic Goal

Strategic Goal:

Reduce the easy access to tobacco products and inform and enlist the support of stakeholders, including retailers and the public, to assist in reducing young people's use of and demand for tobacco products.

A. Strategic Goal Explanation

Approach

A key influence on a retailer's decision to comply with the rule is the extent to which the retailer perceives that he or she is likely to be found in violation and the certainty of punishment for that violation. The Agency's enforcement strategy is designed to ensure that every retailer will be inspected and re-inspected if found to be in violation of the rule. Most of the program's funds will continue to be expended for contracts and in support of investigations to ensure that tobacco products were not sold to minors and to ensure that those industries directly affected by the rule knew what their new responsibilities were.

Under the current enforcement plan, retailers who refuse to sell tobacco to the minor participating in an FDA inspection receive a letter informing them that they are in compliance with the rule. Those who do sell to the minor receive a letter informing them that they have violated the rule, and that another compliance check may occur in the near future. If on the second purchase attempt the retailer sells to the minor, the Agency seeks a $250 civil money penalty. Penalties escalate for subsequent violations of the access restrictions in effect: third violation-$1500; fourth violation- $5000; fifth violation-$10,000. In FY 99, FDA began seeking civil money penalties from retailers who were found to have violated the age and identification restrictions for a third time. Improvements in efficiency and productivity, coupled with an increased number of compliance checks conducted, has resulted in an almost 1,000% increase in the civil money penalty caseload, from 220 cases filed in FY 98 to 2,280 cases filed in FY 99. As a result, the penalties collected from retailers who have violated the rule two or more times have increased from $42,625 in FY 98 to $ 553,400 in FY 99. As of January 12, 2000, FDA has collected $820,000 in penalties from retailers who have violated the rule two or more times.

In FY 01, relying on increased experience, leveraging and efficiency, FDA expects to conduct more inspections and file more cases for civil money penalties than in the previous fiscal year. In addition, by FY01, the Agency expects to seek penalties for fourth and fifth violations. A penalty schedule for violations of other portions of the regulation will be developed when these provisions go into effect.

Assuming other parts of the tobacco regulation are in effect, the Agency will increase the investigators' responsibilities during each check to include checking on the removal of vending machines and self-service displays and illegal advertising. Fewer inspections for compliance with the age and identification provisions would result if the additional provisions of the rule go into effect because longer and more complicated inspections would be required.

A review of the literature and discussions with tobacco control experts indicate that the combination of compliance checks and an active outreach program maximizes retailer compliance with access restrictions. A strong compliance outreach program ensures that those directly affected by the age and photo identification provisions understand what their responsibilities are, why such measures are needed, and the consequences of failing to comply.

In FY 99, the Agency received the marketing industry's highest honor for effective advertising, the EFFIE Award, for its 1998 compliance-based advertising and education campaign. The Agency's multi-faceted program is intended to ensure retailer compliance and boost retailer awareness of the regulation. This program consisted of free retailer materials, advertising, direct mail, exhibits and speeches, and a toll-free hotline. In FY 01, the Agency will develop new creative elements for the campaign, including a TV advertisement. FDA will hold a series of focus group discussions with retailers, sales clerks, young people between 18 and 27, children ages 12 to 18, and the general public to test the advertising campaign before it is launched.

Research and Standard Setting Contributions

By FY 01, the Supreme Court will have determined FDA's jurisdiction over nicotine-containing cigarettes and smokeless tobacco. FDA is regulating cigarettes and smokeless tobacco products under the restricted medical device provisions of the FD&C Act. The FD&C Act requires that all medical devices be classified according to the level of controls necessary to provide reasonable assurance that the product will be safe and effective (see Section 513 of the FD&C Act). Depending upon the classification adopted for tobacco products, it may be appropriate for the Agency to develop performance standards, which could include provisions regarding the construction, components and ingredients, and properties of the device and provisions for the testing of the device. All devices are also subject to the requirement that they conform to quality system regulations pursuant to *21 CFR, Part 820*. The application of the Act's requirements to tobacco is essential to ensure that the health consequences of products or their ingredients, additives or constituents are made less harmful in order to reduce the death and disease caused by tobacco use.

In FY 01, FDA will continue to address the immediate issues posed by new products and nicotine replacement therapies. In addition, the Agency will begin exploring the questions associated with product regulation including questions raised by classification and quality system regulations. In FY 01, the Agency will continue the establishment of a regulatory framework necessary to properly analyze the issues related to current and new products.

Leveraging and Communication

FDA enforces the restrictions currently in effect primarily through the commissioning of state and local regulatory officials, who conduct unannounced purchase attempts using young people under the age of 18. FDA currently uses a multitude of media and

approaches to ensure the greatest reach and utility of its messages. FDA maintains a toll free hot line and an Internet site, which provide retailers and the general public with easy access to brochures; materials and answers to frequently asked questions. As of January, 2000, the hotline has received more than 9,500 calls from retailers and consumers requesting materials, asking questions about the program, or reporting concerns. FDA also has provided retailers with in-store materials. In FY 98 and 99, the Agency mailed retailer kits to stores selling tobacco products. In addition, advertising is placed on radio, in newspapers, and on billboards reminding retailers of their responsibility.

The Agency has begun analyzing methods to monitor industry compliance with the restrictions on advertising even though these provisions are not yet in effect. For example, the tobacco rule prohibits all outdoor advertising within 1,000 feet of schools and playgrounds, as measured from the perimeter of the property. FDA has looked at satellite or computer mapping technology as an aid in determining the appropriate 1,000-foot area around schools and public playgrounds. This technology can then be made available to state and local government agencies as well as to private groups who can report violations to FDA. Similarly, the tobacco rule requires that all advertising appear in black and white text-only format except in publications read primarily by adults, as measured by a percentage and gross number of adult readers. FDA has met with industry officials in an attempt to identify an appropriate methodology for measuring adult and youth readership of publications.

Reinvention

Because the Agency is unable to inspect all known retailers in 2001, it will use some of its FY 01 budget to create targeted demonstration-enforcement areas. Although the vast majority of inspections will be distributed randomly within each state, the targeted demonstration areas will be subject to more intense outreach and enforcement efforts in an attempt to measure the effectiveness of different mixes of interventions and levels of effort on sales of tobacco products to minors. These projects will allow the Agency to plan for more effective use of its enforcement dollars in the future by using the information gathered from these areas to redesign compliance check procedures. In addition, data gathered from these areas will help the Tobacco Program determine how effective it is in reducing illegal sales to youth and in reducing youth smoking rates.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference[1]
1. Increase by 12.5% the number of compliance checks conducted in FY 01 to 225,000 and conduct follow-	FY 01: Increase by 12.5% the number of compliance checks conducted in FY 01 to 225,000 and conduct follow-	FY 01:	Increase

up compliance checks of 100% of retailers found to be in violation of the rule. (17001)	up compliance checks of 100% of retailers found to be in violation of the rule. FY 00: Conduct 200,000 compliance checks and conduct follow-up compliance checks of 100% of retailers found to be in violation of the rule. FY 99 Contract with states to conduct an average of 16,500 unannounced compliance checks each month of retail establishments that sell tobacco products.	FY 00: FY 99: Conducted approximately 9,000 compliance checks per month, totaling 107,200 in FY 99, resulting in a 166% increase over FY 1998.	
2. Conduct multimedia advertising campaign in top media markets to maintain retailer awareness of FDA tobacco rule at 90%. 17003)	FY 01: Target 50 top media markets; distribute new retailer kit to 200,000 retailers; and increase retailer recognition program to 10,000 retailers. Maintain retailer awareness of FDA tobacco rule at 90% or above. FY 00: Conduct a multimedia campaign in 40 top media markets;	FY 01 FY 00: FY 99: Communicated to stakeholders their	Increase

	distribute 150,000 retailer kits; and pilot test a retailer recognition program for 3,000 retailers. Maintain retailer awareness at 90%. FY 99: Conduct meetings and a multimedia campaign; educate retailers .	obligations under the tobacco rule and the consequences for non-compliance. FY 98: • 97% aware of rule. • 84% aware of age requirements . • 31-34% aware of ID check • 16% knew penalties.	
3. Within constraints permitted by court orders, begin to design and implement a regulatory program for cigarettes and smokeless tobacco products. (17005)	FY 01: NA FY 00: NA FY 99: Within constraints permitted by court orders, begin to design and implement a regulatory program for cigarettes and smokeless tobacco products.	FY 99: Began to design and implement a regulatory framework for cigarettes and smokeless tobacco products, within the constraints imposed by court order.	
TOTAL FUNDING: ($000)	**FY 01: $39,000** FY 00: $34,000		
[1] Increase: Indicates achievement of the goal is dependent upon increased resources in FY 01. NPR: Goal supports an FDA National Partnership for Reinventing Government Goal			

C. Goal-By-Goal Presentation of Performance

1. Increase by 12.5% the number of compliance checks conducted in FY 01 to 225,000 and conduct follow-up compliance checks of 100% of retailers found to be in violation of the rule. (17001)

- **Context of Goal:** In FY 01, the Agency intends to expand its enforcement program by inspecting 225,000 retailers each year, as compared to the 200,000

planned with FY 00 money. This will provide for inspection coverage in approximately one fourth of identified retail outlets at least once every year and reinspection of each violative retailer within 3 months after notifying the retailer of the violation or after adjudication of civil money penalty. The Agency also intends to continue its own enforcement program in those states that are unable or unwilling to contract with the Agency. Because the Agency is unable to inspect all known retailers in 2001, it will use some of its FY 01 budget to create targeted demonstration-enforcement areas. These projects will allow the Agency to plan for more effective use of its enforcement dollars in the future by using the information gathered from these areas to redesign compliance check procedures.

- **Data source:** FDA Tobacco database
- **Performance:** The FY 99 goal has not been met. The Agency believes it is important to retain this goal. With increased Federal and state experience, and efficiencies gained through automation, the goal will be attainable. A key influence on a retailer's decision to comply with the rule is the extent to which the retailer perceives that he or she is likely to be found in violation and the certainty of punishment for that violation. The Agency's enforcement strategy is designed to ensure that every retailer will be inspected and re-inspected if found to be in violation of the rule. Taking into account such factors as the newness of FDA's tobacco rule, the political climate in some states and the inexperience of these and other states in conducting tobacco control enforcement, FDA established goals that would gradually increase the number of checks to be conducted each year. Even though the Agency did not reach its goal of completing 198,000 compliance checks in FY 99, this goal remains valid FY 00, given the same level of funding as in FY 00 as in FY 99.

2. Increase distribution of multimedia advertising campaign to 50 top media markets; create, print, test and distribute new retailer kit to 200,000 retailers; and increase retailer recognition program to 10,000 retailers. Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90% and double the percentage of retailers who understand the age and ID provisions and the consequences of not complying with the rule in all markets subject to the intensified media campaign. (17003)

- **Context of Goal:** FDA is conducting a national advertising campaign aimed at raising retailers' awareness of the new regulations and motivating them to comply. The campaign's primary target audience is managers and clerks in stores that sell tobacco and consisted of free retailer materials, advertising, direct mail, exhibits and speeches, and a toll-free hotline. The campaign was first introduced in FY 98 in one media market in one state for a four-week period. A survey was conducted in two markets each in ten states (one treatment and one control) to assess the effect of the media campaign in raising retailer awareness of and compliance with the regulations. A total of 2,000 managers and clerks were surveyed immediately prior to the campaign and another 2,000 were surveyed after the campaign. Data have been collected and analyzed.

The revised FY 00 campaign is scheduled for testing among retailers, clerks and consumers in late FY 99, with results expected by mid-FY 00. The FDA will continue to measure the effectiveness of its outreach efforts in this manner and to compare results over time. The Agency will use these results to redesign the mix of media tools and messages to maximize knowledge of and compliance with the regulations. FDA will also provide retailers with kits that contain explanations of the requirements, and posters and materials, which help explain the rules to customers and assist in defusing customer anger or anxiety.

As part of FY 2000 efforts, FDA will conduct a multimedia campaign in 40 top media markets for a four-week flight to include: create and produce two radio, one TV, three billboard, and three print advertisements; run radio, billboard, and print ads in up to 40 major media markets; distribute 150,000 retailer kits; and distribute 400,000 direct mail pieces to retailers. FDA will visit up to 15,000 retailers to educate them about program; exhibit at 30 retailer or other trade shows and participate in up to 60 one-on-one meetings with retailers. FDA will also pilot test a retailer recognition program for 3,000 retailers.

- **Data Sources:**FDA sponsored surveys of known retailers of cigarettes and smokeless tobacco. A survey was tested in two markets each in ten states in FY 98. The results are analyzed and will be used to develop baseline data. Based on this limited survey of retailers:
    - 97% were aware of the FDA tobacco rule.
    - 84% were aware that the legal age for purchase is 18.
    - 31-34% were aware that they had to check the ID of every customer under the age of 27.
    - 16% knew the specific level of penalties for violations

  A national survey testing the effectiveness of the FY 99 campaign will be conducted.

- **Performance:**FDA achieved this goal through a variety of vehicles to communicate to stakeholders their obligations under the tobacco rule and the consequences for non-compliance. For the first time, FDA exhibited and took orders for free retailer materials at national or regional retailer conferences and at approximately 15 national consumer conferences. FDA also launched a multi-faceted media campaign in 66 media markets for a single four-week period and, for the first time, ran media throughout five states. The Agency also designed and pilot-tested a retailer rewards program in five media markets and received approximately 2,000 hotline calls from consumers and retailers and, for the first time, arranged for calls to be fielded by live operators. Through direct promotion, nearly 400,000 retailers received free retailer materials by the end of September 1999.

  FDA pilot-tested a new program to encourage retailers to follow the regulation and to use the free retailer kit; approximately 2/3 of the retailers agreed to post the

materials in their stores. In FY 99, the Agency received the marketing industry's highest honor for effective advertising, the EFFIE Award, for its 1998 compliance-based advertising and education campaign. The Agency's multi-faceted program is intended to ensure retailer compliance and boost retailer awareness of the regulation. This program consisted of free retailer materials, advertising, direct mail, exhibits and speeches, and a toll-free hotline. In FY 99, the Agency developed new creative elements for the campaign, including a TV advertisement. FDA held a series of focus group discussions with retailers, sales clerks, young people between 18 and 27, children ages 12 to 18, and the general public to test the advertising campaign before it was launched.

FDA funded advertising campaigns in 11 individual media markets and 5 States with which FDA had a contract to conduct compliance checks. In order for advertising to have a lasting effect, experts recommend that the message be disseminated repeatedly over a 12-month period. For this reason, in FY 99, FDA instituted a compliance-based outreach strategy in 5 states that includes continuous, statewide media coverage. Retailers and sales clerks are the primary target audience for this campaign. In addition to reminding retailers and sales clerks not to sell to minors and to check young peoples' photo identification, the campaign also urges customers to cooperate with retailers attempting to meet their responsibilities to help keep young people tobacco-free. FDA conducted two waves of a tracking study in 15 media markets to evaluate the effectiveness of the campaign. The second wave is being conducted during the first quarter of FY 00.

3. Design and to the fullest extent permitted under any court orders addressing such activities, begin to implement a regulatory program for cigarettes and smokeless tobacco products, including: Begin to examine the appropriate scientific and regulatory framework to evaluate products that state or imply that they are less hazardous; Assist other agencies within DHHS in providing the FTC with an analysis of the public health issues associated with the testing and reporting of the tar and nicotine content of the smoke of cigarettes; and Establish an evaluation and review procedure for new products. (17005)

- **Context of Goal:** This is the FY 99 goal. It is included here only for FY 99 reporting. There is no similar goal in FY 00 or FY 01. The program was unable to begin most of its product regulation activities. The U.S. Court of Appeals for the Fourth Circuit found FDA's assertion of jurisdiction to be invalid and that decision was appealed to the U.S. Supreme Court. The age and identification provisions of the tobacco rule remain in effect pending a decision by the Supreme Court.
- **Data Sources:** Internal Agency documents will substantiate progress made. These programs have yet to be established and therefore the baseline is zero.
- **Performance:** The goal has been met. FDA has achieved its goals for beginning to design and implement a regulatory framework for cigarettes and smokeless tobacco products, within the constraints imposed by court order. The Agency has leveraged the tobacco prevention and cessation expertise of other Federal

Agencies, including the National Cancer Institute and the Centers for Disease Control, as the Federal Trade Commission's expertise in consumer risk perception, to begin to study collaboratively the risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine.

FDA has commissioned the Institute of Medicine (IOM), a member of the National Academy of Sciences, to convene a national panel of experts to evaluate the scientific and regulatory issues raised by drug and tobacco products that may claim to reduce exposure to harmful substances in tobacco and to reduce health risks. These products include nicotine replacement therapies and tobacco products modified to reduce specific harmful compounds.

2.7.3 Verification and Validation

FDA is enforcing the restrictions on youth access that are currently in effect by training and commissioning state regulatory officials, who conduct unannounced purchase attempts using young people under the age of 18 to determine if retailers will sell to minors. The results of each attempt are faxed or mailed to FDA by state officials. FDA has established a computerized tobacco database to gather these results, prepare follow-up compliance check forms, send notification of the results to the retailer and ultimately, if necessary, to prepare documents to seek civil money penalties. The database contains an inventory of retailers of cigarettes and smokeless tobacco products as they are identified. The database allows FDA to track the number of compliance checks, the number of violations (total and broken down by type of store, state, etc.), the number of civil money penalty actions, etc. The data will permit FDA to measure the progress of its enforcement program. However, the data is not statistically projectable, because it is not based on a random sampling of retailers.

In addition, a survey was conducted in two markets each in ten states (one treatment and one control) to assess the effect of the media campaign on raising retailer awareness of and compliance with the regulations. A total of 2,000 managers and clerks were surveyed immediately prior to the campaign and another 2,000 were surveyed after the campaign. The data have been collected and are analyzed. FDA intends to continue measuring the effectiveness of its outreach efforts in this manner and to compare results over time. Key findings include:

- Retailers aware of the ad knew better than those not aware the FDA tobacco rule and the cut-off age for checking identification;
- Stores with FDA materials better knew the age required for checking ID, the $250 fine, and were more prone to use the correct cut-off ages for sales and checking ID.
- A small, but significant decline occurred in the number of minors who tried to purchase tobacco products after the ad campaign (from 3.4 times to 2.8 times).
- Adult customers who were asked to present ID often were less irritated when carded (down from 34% to 28%).

- 9 in 10 managers and clerks whose stores displayed FDA materials felt they helped educate clerks and customers about the tobacco rule requirements.
- Twice as many clerks after the campaign (30%) as before (16%) volunteered the correct cut-off age for checking ID.
- A three-fold increase in recall of the $250 fine occurred after the campaign.

The FTC collects and publishes industry-wide data on advertising expenditures by category (e.g., newspapers, outdoor advertising, and specialty items). FDA intends to establish baselines for advertising from FTC data indicating levels of expenditures for each category for the base year, and measuring decreases in spending for each subsequent year. Although this data source cannot measure all of the changes required by the rule (conversion of advertising in publications to black and white text only), it should be able to document whether expenditures for banned advertising (e.g. hats and tee shirts with logos) has ceased and whether declines in expenditures are observed for heavily restricted advertising (e.g., outdoor advertising is banned within 1,000 feet of schools and playgrounds and is otherwise restricted to black and white text only format).Additionally, the Agency will discuss with FTC the possibility of including additional questions in their survey of company advertising expenditures to help FDA more accurately measure compliance with the tobacco rule.

In FY 01, the Agency plans to have an information system in place that will greatly enhance its ability to collect data and measure its performance. In the second half of FY 98, the Agency contracted with Battelle Memorial Institute to study the tobacco program's business processes, outline the program's workflow and conduct a requirements analysis. From this analysis, Battelle proposed a system design to automate the program's processes. In addition, Battelle presented a proposed plan to obtain and maintain a list of retailers selling tobacco in each state that would be more complete, accurate and user friendly than the lists constructed by the Agency during its first full year of operation.

Based on the design, Battelle has launched a multi-year effort to provide reliable retailer lists and an infrastructure designed to maintain the list and make it user friendly for FDA and for all contracting states. Battelle will also implement an information technology system which will automate all the program's various functions, including contracting, outreach, enforcement, compliance checks, litigation, collection of civil money penalties, etc. The new system will increase the efficiency of the program and will improve communications internally as well as with state contractors and with other stakeholders. The various system design components will be implemented incrementally as they are developed beginning in early 1999. The entire system should be operational by 2001.

Even though FDA's tobacco program is not fully in effect, the Agency has the tools in place to measure progress toward intermediate goals. FDA is working closely with CDC's Office on Smoking and Health, SAMHSA and the Data Council of DHHS to devise and conduct surveys to measure success in reducing initiation and use of tobacco by young people. The Agency also is monitoring compliance with the rule, assessing buy rates, determining reach and effect of outreach efforts, and assessing the risks of various

components of tobacco products to determine whether it is possible to reduce the overall health risks associated with tobacco products. One of the first responsibilities of the Tobacco Program following lifting of the court stay or enactment of comprehensive legislation, will be to devise and implement a surveillance mechanism to establish bench mark levels for these goals including but not limited to youth tobacco initiation and use rates and risk levels of current products and ingredients. This surveillance effort will enable the Agency to validly measure progress.

DISPOSITION TABLE

Goal ID	Original FY 2000 Goal Statement*	Disposition	Revised FY 2000 Targets	Explanation
FOODS				
11001	Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the Federal Register, if appropriate) on 40 percent of food and color additive petitions within 360 days of receipt.	Unchanged		
11002	Reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 20 percent of petitions under review.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11003	Complete processing of 80 percent of generally recognized as safe (GRAS) notifications within the time frame established by the final rule.	Revised	FY 00: Finalize GRAS Rule ; 80%	New target incorporates unfinished FY 99 target in addition to the unchanged FY 00 target.
11004	Eighty percent of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning Hazard Analysis and Critical	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication.

	Control Point (HACCP) systems.			Goal will be used for internal management.
11005	Continue to develop and implement voluntary guidance and other efforts to improve the safety of fresh fruits and vegetables, and work with USDA to conduct a 1999-2001 National Agricultural Statistics Survey (NASS) of microbial contamination of fresh produce to collect the data required to evaluate program effectiveness.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11006	Initiate HACCP in the juice industry.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11007	Increase to at least 55 percent the proportion of adults who report changing their decision to buy or use a food product because they read the food label.	Unchanged		
11008	Work with the CDC, USDA, and states to increase food safety surveillance and to	Dropped		Dropped in order to streamline the Performance

	improve responses to foodborne illness outbreaks.			Plan for purposes of clearer external communication. Goal will be used for internal management.
11009	Establish an integrated adverse event reporting system for food and cosmetic products, with emphasis on increasing efforts to design and implement modules needed to record dietary supplement adverse event information.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11010	Achieve adoption of the Food Code by at least 35 percent of the states.	Revised	FY 00: 18 states	Changed target from a percent to the number of states.
11011	Assure that FDA inspections of domestic food establishments (excludes domestic seafood establishments), in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.	Unchanged		

11012	Develop and make available an improved method for the detection of hepatitis A virus, Cyclospora cayetanensis and Escherichia coli O157:H7 on additional fruits and vegetables, and provide knowledge and technologies needed to develop guidance and methods for the control and elimination of pathogens on particular fruits and vegetables such as Escherichia coli O157:H7 and Salmonella spp. from juices, leafy vegetables and sprouted seeds and Cyclospora from soft fruit (e.g., berries).	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11013	Develop modeling techniques to assess human exposure and dose-response to certain foodborne pathogens, the potential risk for those pathogens causing human illness, and the setting of safety performance standards to regulate microbial content of food towards reducing incidence of foodborne disease.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11018	Complete initial processing of 80 percent of biotechnology	Dropped		Dropped in order to streamline the Performance

	consultations within established time frames.			Plan for purposes of clearer external communication. Goal will be used for internal management.
11019	Respond to 95 percent of nutrient content claim and health claim petitions/notifications within the statutory and regulatory time frames.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11020	Increase the frequency of high-risk domestic food establishment inspections to once every one to two years, and annually beginning in FY 2001.	Revised	FY 00: 90 - 100% Once every one to two years	Reduced funding and increased workload.
11021.01	Increase the number of inspections/evaluations of foreign food establishments from 100 to 250.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11022	Develop more rapid and accurate analytical methods for foodborne chemical contaminants (including bacterial	Dropped		Dropped in order to streamline the Performance Plan for

	toxins).			purposes of clearer external communication. Goal will be used for internal management.
11023	Maintain the restored level of activity for cosmetic voluntary reporting to protect consumers against potentially hazardous cosmetic ingredients or products	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
11026	Finalize guidance and regulations necessary to support operations of the premarket notification program for food contact substances established by FDAMA and as set out in Sec. 409(h) of the FD&C Act.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
HUMAN DRUGS				
12001	Review and act on 90% of standard new drug applications (NDAs) filed within 12 months after receipt (30% within 10 months of receipt); and 90% of priority applications within six months.	Revised	Standard NDAs within 12 months: FY 00: 90% Standard NDAs within 10 months: FY 00: 50% Priority NDAs within 6 months: FY 00: 90%	Original FY 00 target was incorrect. The revised target now matches PDUFA goals.

12004	Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and 90 percent of priority efficacy supplements within 6 months.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12006	Assure the FDA inspections of domestic drug manufacturing and repacking establishments in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements by the end of the fiscal year.	Unchanged		
12007	Expedite processing and evaluation of adverse drug events through implementation of the Adverse Events Reporting System (AERS) which allows for electronic periodic data entry and acquisition of fully coded information from drug companies.	Revised	FY 00: Implement software to make the AERS more compatible with International Conference on Harmonization requirements. Develop next generation of the AERS to enhance functionality.	More specific target.
12008	Establish the capability and capacity to receive	Dropped		Dropped in order to

	and archive ANDAs submitted electronically.			streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12011	Provide written responses to industry within 14 days of receipt on 80 percent of formal meeting requests; make meeting minutes available to sponsors within 30 calendar days for 80 percent of meetings; and, ensure that 80 percent of Type A meetings are scheduled within 30 calendar days of receipt of the meeting request, Type B within 60 calendar days of receipt of meeting request, and Type C meetings within 75 calendar days of receipt of meeting request.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12012	Make new drug approval information increasingly available and targeted and promoted to specific user groups, such as consumers, patients, health-care practitioners and industry via the internet, resulting in a	Revised		Goal was combined with 12025 and incorporated into new goal 12027.

	decrease in serious medication errors.			
12014	Complete 75 percent of projects identified in CDER's OTR Research Plan (dated November 24, 1997) designed to lead to appropriate policy for applying modern in vitro and ex vivo technology to assess of drug metabolism and drug interactions.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12015	Develop a list of bulk drug substances that may be used in compounding and publish a rule to be used for pharmacy compounding.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12016	Complete 25 percent of the research projects started in FY 1999 under the auspices of the Product Quality Research Initiative (PQRI), a collaboration among FDA, industry and academia established to provide a scientific basis for policy and guidance development in CDER on issues of drug product quality and performance.	Unchanged		

12017	Complete 75 percent of research projects identified in the OTR Research Plan (dated November 24, 1997) designed to develop rational, scientific-based requirements for drug substances, drug products and excipients to ensure a high standard of drug product quality and product performance for making regulatory decisions.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12018	Reduce the number per application of post-approval changes requiring chemistry supplements.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12019	Process 75 percent of all review documents by implementing an Electronic Document Management System (EDMS) throughout new and generic drug review divisions.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12020	Improve inspection coverage by inspecting 36 percent of registered human drug manufacturers,	Revised	FY 00: 22%	Reduced funding level required lowering target level.

	repackers, relabelers and medical gas repackers.			
12024	Increase the average monthly number of actions (approvals, tentative approvals, not approvals, and facsimile requests) completed on ANDAs by 3.2 percent from the FY 1997 level.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
12025	Develop partnerships with 8 national organizations to disseminate educational information to consumers about choosing the right medications, taking medicines correctly and reporting adverse reactions.	Revised		Goal was combined with 12012 and incorporated into new goal 12027.
BIOLOGICS				
13001	Review and act on 90 percent of standard New Drug Applications (NDA), Product License Application (PLA) and Biologic License Application (BLA) submissions within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority original NDA/PLA/BLA submissions within 6	Unchanged		

	months of receipt.			
13002	Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority efficacy supplements within 6 months of receipt.	Unchanged		
13003	Review and act on 90 percent of manufacturing supplements within 6 months of receipt, and review and act on 50 percent within 4 months of receipt.	Unchanged		
13004	Review and act on 90 percent of Class 1 resubmitted original applications within 4 months of receipt (review 50 percent within 2 months); and review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.	Revised	Class 1 resubmissions within 2 months: FY 00: 70 %& Class 1 resubmissions within 4 months: FY 00: 90% Class 2 resubmissions within 6 months: FY 00: 90%	Additional target was added to conform to PDUFA goals.
13005	Review and act on 85 percent of complete blood bank and source plasma Product License Application (PLA)/Biologic License Application	Unchanged		

	(BLA) submissions and 90 percent of PLA/BLA Major supplements within 12 months after submission date.			
13007	Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high conformance rate with FDA requirements (at least 90 percent).	Unchanged		
13008	Increase the percentage of plasma fractionator establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 80 percent.	Unchanged		
13012	Meet the biennial inspection statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments.	Unchanged		
ANIMAL DRUGS AND FEEDS				
14001	Update 10 percent of the animal drug review guidelines which serve	Revised	FY 00: Update 12 guidelines (original target	More specific target.

	as aids to industry in the animal drug review process.		was 7 guidance documents which was 10 % of animal drug review guidances).	
14002	Reduce drug development and review time through implementation of additional phases of electronic submission in the investigational new animal drug development process.	Revised	FY 00: 4 phases - Notices of Slaughter; Notices of Animal Final Disposition; Meeting Agendas; USDA Slaughter Reports	More specific target.
14003	Increase the scientific basis for prioritizing research and surveillance activities by increasing the number of risk assessments performed regarding antimicrobial products to two per year.	Revised	FY 00 Goal: Generalize the model by performing risk assessments related to other antibiotics and other animal/bacterial species.	More specific target.
14004	Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high level of conformance (at least 90 percent) with FDA requirements.	Unchanged		

14005	Maintain the bacterial isolate testing rate from human and animal origin in the National Antimicrobial Resistance Monitoring System (NARMS) database at 2,000 and 4,000 respectively	Unchanged		
14007	Maintain a 75 percent level for pre-submission conferences with industry sponsors.	Unchanged		
14009	Meet the statutory biennial inspection requirement by inspecting 50 percent of registered animal drug and feed establishments.	Revised	FY 00: 27%	Reduced funding level required lowering target level.
14010	Maintain the number of Adverse Drug Event (ADE) reports reviewed at 7,000 through consumer participation in the pharmocovigilance program for veterinary drugs by publication and distribution of educational material.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
14013	Properly target resources related to education and enforcement initiatives by maintaining the number of follow-up violative tissue residues investigations at 600 in targeted food producing animals.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal

				management.
14014	Expand the geographical scope and capacity of NARMS by the establishment of an international resistance database.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
14015	Improve our ability to monitor for Adverse Events by initiating the development of an integrated agency-wide system.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
14016	Increase bioresearch monitoring inspections completed and results received to 115.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
14017	Review and act on 65 percent of New Animal Drug Applications (NADAs)/Abbreviated New Animal Drug	Unchanged		

	Applications (ANADAs) within 180 days of receipt.			
MEDICAL DEVICES AND RADIOLOGICAL HEALTH				
15001	Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed from 67 percent in FY 1998 to 85 percent in FY 2000 and 95 percent by FY 2002.	Unchanged		
15002	Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
15003	Update list of recognized standards.	Dropped	Review 50 standards for continued applicability and review 50 standards for recognition.	More specific target.
15004	Apply improved analytical methodology to approximately 30,000 manufacturer event reports, an increase of at least 20 percent over	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external

	FY 1999.			communication. Goal will be used for internal management.
15005.01	Improve inspection coverage for Class II and Class III domestic medical device manufacturers from 26 percent in FY 1999 to 39 percent in FY 2000.	Revised	FY 00: 24%	Reduced funding level required lowering target level.
15005.02	Improve inspection coverage for Class II and Class III foreign medical device manufacturers from 12 percent in FY 1999 to 19 percent in FY 2000.	Revised	FY 00: 9%	Reduced funding level required lowering target level.
15007	Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level 1 (serious) inspection problems.	Unchanged		
15008	Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
15009	Review and complete 85 percent of Premarket Approval Application (PMA)	Unchanged		

	supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002.			
15010	Investigate correlation of device failures with aging biomaterials and provide quality assurance for device software.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
15011	Maintain annual inspection coverage for mammography facilities (8,900 inspections of a total of approximately 10,000 facilities) in FY 2000.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
15012	Develop Sentinel Surveillance System for injury reporting based on approximately 75 to 90 representative user facilities.	Revised	FY 00: Develop MedSun Surveillance System for injury reporting based on approximately 75 to 90 representative user facilities. Evaluate pilot and report results to Congress.	Additional targets were added.
15013	Develop baseline data	Dropped		Dropped in

	to estimate problem and risk magnitude for marketed medical devices.			order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
15014	Review and complete 85 percent of complex 510(k) (Premarket Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002.	Dropped		Dropped due to change of policy regarding complex 510(k)s. There is a new final actions goal (15021) for all 510(k)s with a target of 65% for FY 00.
15015	Complete 95 percent of Investigational Device Exemption (IDE) "Agreement" meetings and Premarket Approval Application (PMA) "Determination" meetings within 30 days.	Revised	"Agreement" meetings FY 00: 80% "Determination" meetings FY 00: 95%	Goal was split into two separate goals to allow different target levels for these different meetings.
15016	Improve quality conformance of high-risk products like cardiovascular devices by committing over 90 percent of inspection resources to high risk devices.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.

15018	Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.	Unchanged		
15020	Implement the Mutual Recognition Agreement (MRA) with the European Union (EU).	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH				
16002	Develop a new biological assay to measure genetic change and validate two existing models that predict human genetic damage.	Revised	FY 00: Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly susceptible subpopulations.	Broadening of research efforts to involve private sector.
16003	Conduct molecular epidemiology studies to identify biomarkers of the most frequently	Revised	FY 00: Validate predictive model for estrogenic or	Change of research focus.

	occurring cancers in highly susceptible subpopulations.		estrogenic-like compounds.	
16004	Validate a model computer-based predictive system to support and expedite product review of estrogenic or estrogen-like compounds.	Revised	FY 00: Conduct studies that relate how a compound causes damage to the damage itself, in order to strengthen the scientific basis for regulation of compounds of FDA significance.	Broadening of research efforts to involve other agencies in a common interest.
16005	Conduct studies that relate how a compound causes damage to the damage itself, in order to strengthen the scientific basis for regulation of compounds of FDA significance.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
16007	Develop partnerships with government, industry, and academic scientists to conduct studies that demonstrate cross-species comparability and eliminate assumptions necessary for extrapolating laboratory toxicity data to human disease.	Revised	FY 00 : Develop methods of predicting, more quickly and accurately, the risk associated with foodborne pathogens as *Salmonella spp., Shigella spp., and Campylobacter spp*.	Narrowing of research focus to support FSI.

16008	Develop methods of predicting, more quickly and accurately, the risk associated with foodborne pathogens.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
TOBACCO				
17001	Conduct 400,000 compliance checks and select certain sites to target for intensified enforcement efforts to determine the effectiveness of different levels of effort.	Revised	FY 00: Conduct 200,000 compliance checks and conduct follow-up compliance checks of 100% of retailers found to be in violation of the rule.	Reduced funding level required lowering target level.
17002	Ensure the elimination of certain forms of advertising, especially outdoor advertising within 1000 feet of schools and playgrounds (including transit advertising) and specialty item distribution such as hats and tee shirts with tobacco logos.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
17003	Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90 percent and	Revised	FY 00: Conduct multimedia campaign in 40 top media markets for four-week flight to include: create and	Additional targets were added.

	increase the percentage of retailers who understand the age and ID provisions of the rule to 50 percent.		produce 2 radio, 1 TV, 3 billboard, and 3 print advertisements; run radio, billboard, and print ads in up to 40 major media markets; distribute 150,000 retailer kits; distribute 400,000 direct mail pieces to retailers. Visit up to 15,000 retailers to educate them about program; exhibit at 30 retailer or other trade shows and participate in up to 60 one-on-one meetings with retailers; pilot test retailer recognition program for 3,000 retailers. Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90% and increase the percentage of retailers who understand the	

			age and ID provisions of the rule to 50%.	
17004	Promote availability of free FDA retailer information kits, used to remind customers and young people about the requirements of the FDA tobacco rule, to at least 400,000 retailers of cigarettes and smokeless tobacco products and provide kits to those who request them.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
17005	To the fullest extent permitted under any court order, establish the scientific and regulatory framework to address the challenges posed by new and novel nicotine-containing tobacco products as well as issues raised by current products and replacement therapies.	Dropped	FY 00: NA	Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
17006	Conduct follow-up compliance checks of 100 percent of retailers found to be in violation of the rule.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be

				used for internal management.
IMPORTS				
18002	Establish Agency screening guidelines that emphasize risk-based decisions through program Information.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.
18005	Complete analysis of variations in criteria used by FDA programs to screen import entries. Establish Agency screening guidelines that emphasize risk-based decisions through program information.	Dropped		Dropped in order to streamline the Performance Plan for purposes of clearer external communication. Goal will be used for internal management.

* As shown in FY2000 Congressional Justification

GLOSSARY OF ACRONYMS

510(k): Premarket notification for medical devices substantially equivalent to products already on the market

AADA: Abbreviated Antibiotic Drug Application

ADE: Adverse Drug Event

ADAA: Animal Drug Availability Act of 1996

ADR: Adverse Drug Report

AERS: Adverse Events Reporting System

AHI: Animal Health Institute

AIDS: Acquired Immune Deficiency Syndrome

ANDA: Abbreviated New Drug Application

ANSI: American National Standards Institute

BLA: Biologic License Application

BLT: Blood Logging and Tracking System

BRFS: Behavioral Risk Factors Survey

BRMS: Biologics Regulatory Management System

BSE: Bovine Spongiform Encephalopathy (Mad Cow Disease)

CABS: Conformity Assessment Bodies

CARS: Compliance Achievement Reporting System

CBER: FDA Center for Biologics Evaluation and Research

CDC: Centers for Disease Control and Prevention

CDDI: Collaboration for Drug Development Improvement

CDER: FDA Center for Drug Evaluation and Research

CDRH: FDA Center for Devices and Radiological Health

CFSAN: FDA Center for Food Safety and Applied Nutrition

CGMPs: Current Good Manufacturing Practices

CJD: Creutzfeldt-Jakob disease

CMA: Chemical Manufacturers Association

CMC: Chemistry, Manufacturing, and Controls

COMIS: Center-wide Oracle Management Information System

COMSTAS: Compliance Status Information System

CRADA: Cooperative Research and Development Agreement

CRS: Contamination Response System

CSTE: Council of State and Territorial Epidemiologists

CTS: Correspondence Tracking System

CVM: FDA Center for Veterinary Medicine

CY: Calendar Year (January - December)

DDC: Document Control Center

DHHS: Department of Health and Human Services

DMARDS: Disease Modifying Antirheumatic Drugs

DNA: Deoxyribonucleic acid

DOD: Department of Defense

DoL: Department of Labor

DQRS: Drug Quality Reporting System

DRLS: Drug Registration and Listing System

DSHEA: Dietary Supplement Health and Education Act

DWPE: Dentention Without Physical Examination

EDKB: Endocrine Disrupter Knowledge Base

EDR: Electronic Document Room

EDMS: Electronic Data Management System

EIP: Emerging Infection Program

EIR: Establishment Inspection Report

ELA: Establishment License Application

EPA: Environmental Protection Agency

ERS: Economic Research Service

ETS: Environmental Tobacco Smoke

EU: European Union

FACTS: Field Accomplishment and Compliance Tracking System

FAO: United Nations Food and Agricultural Organization

FAS: USDA Foreign Agriculture Service

FDAMA: Food and Drug Administration Modernization Act of 1997

FD&C Act: Federal Food, Drug and Cosmetic Act

FIS: Field Information System

FLQ: Fluoroquinolone

FORCG: Food Outbreak Coordination Response Group

FPL: Final Printed Label

FPLA: Fair Packaging and Labeling Act

FSI: National Food Safety Initiative

FSIS: Food Safety Inspection Service (USDA)

FTC: Federal Trade Commission

FTE: Full-time equivalents

FY: Fiscal Year (October - September)

GAO: Government Accounting Office

GAPs: Good Agricultural Practices

GATT: General Agreement on Tariffs and Trade

GPRA: Government Performance and Results Act of 1993

GMPs: Good Manufacturing Practices

GRAS: Generally Recognized as Safe food ingredients

GSFA: General Standards for Food Additives

HACCP: Hazard Analysis Critical Control Points (a quality assurance and inspection technique)

HDE: Humanitarian Device Exemption

HIV: Human Immunodeficiency Virus

HUD: Humanitarian Use Device

ICH: International Conference on Harmonization

IDE: Investigational Device Exemption

INAD: Investigational New Animal Drug

INADA: Investigational New Animal Drug Application

IND: Investigational New Drug

IOM: Institute of Medicine

ISO: International Standards Organization

ISRS: Individual Safety Reports

IT: Information technology

JIFSAN: Joint Institute for Food Safety and Applied Nutrition

LACF: Low Acid Canned Foods

LAN: Local Area Network

MATS: Management Assignment Tracking System

MDR: Medical Device Reporting system

MOU: Memorandum of Understanding

MPRIS: Mammography Program Reporting and Information Systems

MQSA: Mammography Quality Standards Act

MRA: Mutual Recognition Agreement

NADA: New Animal Drug Application

NAFTA: North Atlantic Free Trade Agreement

NAFTA TWG: North American Free Trade Agreement Technical Working Group

NARMS: National Antimicrobial Resistance Monitoring System

NASS: National Agricultural Statistics Survey

NCI: National Cancer Institute

NCIE: Notice of Claimed Investigational Exemptions

NCTR: FDA National Center for Toxicological Research

NDA: New Drug Application

NDE/MIS: New Drug Evaluation Management Information System

NIAID: National Institute of Allergy and Infectious Diseases

NIDA: National Institute on Drug Abuse

NIEHS: National Institute for Environmental Health Sciences

NIH: National Institute of Health

NLEA: Nutrition Labeling and Education Act

NME: New Molecular Entity

NPR: National Partnership for Reinventing Government

NRC: National Research Council

NSE: Not substantially equivalent determination

NTP: National Toxicology Program

NVPO: National Vaccine Program Office

OASIS: Operational and Administrative System for Import Support

OBRR: Office of Blood Research and Review

OPA: CFSAN, Office of Premarket Approvals

ORA: FDA Office of Regulatory Affairs

ORISE: Oak Ridge Institute for Science and Education

OSHA: Occupational Safety and Health Administration

OTC: Over-the-counter

OTR: Office of Testing and Research (CDER)

PAS: FDA Public Affairs Specialist

PDPs: Product Development Protocols

PDUFA: Prescription Drug User Fee Act of 1992

PIFSI: Produce and Food Safety Initiative

PLA: Product License Application

PMA: Premarket Approval (Application to market medical device that requires premarket approval)

PODS: Project-Oriented Data System

PQRI: Product Quality Research Initiative

QSIT: Quality System Inspection Technique

RA: Rheumatoid Arthritis

RCHSA: Radiation Control for Health and Safety Act

REGO: Reinventing government initiative

RIMS: Regulatory Information Management Staff

RVIS: Residue Violation Information System

SAB: Science Advisory Board

SAMHSA: Substance Abuse and Mental Health Services Administration

SE: Salmonella Enteriditis

SN/AEMS: Special Nutritionals Adverse Events Monitoring System

STARS: Submission Tracking and Review System

StmDT104: Salmonella typhimurium DT 104

TB: Tuberculosis

TRIMS: Tissue Residue Information System

UK: United Kingdom

UMCP: University of Maryland-College Park

USDA: United States Department of Agriculture

VFD: Veterinary Feed Directive

VICH: Veterinary International Conference on Harmonization

WHO: United Nations World Health Organization

WTO: World Trade Organization