Performance Plan and Summary

FY 2002 Annual Performance Plan and Summary
FY 2001 Revised Final Performance Plan
FY 2000 Annual Performance Report

April 2001

Contents

Introduction

FDA's FY 2002 Performance Plan is organized into two parts.

Part One describes an overview of FDA, its mission and long term goals, strategies for achieving the goals, and how FDA will work with partners to carry out the strategies. The summary highlights thirteen strategies that are the Agency's highest priorities for protecting the health and safety of the American Public in the 21st Century. Each strategy addresses these questions:

1. What are the desired outcomes of this strategy?
2. What are key performance goals that will lead to the outcomes?
3. Why is FDA's contribution important?
4. How will FDA achieve its goals?
5. What are the consequences of not achieving the goals?
6. How is the Agency doing currently?

Part Two of the Plan is organized by FDA's major programs. Each program section includes the complete inventory of FY 1999, FY 2000, FY 2001 and FY 2002 performance goals and the strategies necessary to achieve these goals. The latest status on actual performance is also provided. The figure below identifies how the strategies in Part One link to FDA's Programs discussed in Part Two.

Strategies Linkage with FDA Program						
Strategies	**Food**	**Human Drugs**	**Biologics**	**Animal Drugs**	**Medical Devices**	**NCTR**
Rapid Access to New Medical Technologies		X	X		X	X
Safe Food Supply	X			X		X
Safe Blood and Tissues			X			X
Safe Medical Products		X	X	X	X	
Reduce Adverse Events		X	X		X	
Protecting Volunteers in Clinical Research		X	X		X	
Cutting Edge Risk Assessment		X	X		X	X
Improved Mammography					X	
Managing Antibiotic Resistant Bacteria		X	X	X		X
BSE	X		X	X		
Imports and International Activities	X	X	X	X	X	

Biotechnology	X	X	X	X	X	X
Dietary Supplements	X	X			X	X

Crosswalk of FDA Strategies that Support HHS Strategic Goals						
FDA Strategies	**1. Reduce the major threats to the health and productivity of all Americans.**	**2. Improve the economic & social well-being of individuals, families, & communities in the United States.**	**3. Improve access to health services & ensure the integrity of the nation's health entitlement & safety net programs.**	**4. Improve the quality of health care and human services.**	**5. Improve the nation's public health systems.**	**6. Strengthen the nation's health sciences research enterprise & enhance its productivity.**
Quick and Safe Access to New Medical Technologies					X	X
A Safe Food Supply	X				X	
Safe Blood and Tissues Products					X	
Safe Medical Products					X	
Reduce Adverse Events Related to Medical Products	X				X	
Protecting Volunteers in Clinical Research				X	X	X
Cutting Edge Risk Assessment to Protect Public Health				X	X	X
Early Detection of Breast Cancer Through Improved Mammography					X	
Manage the Threat of Antibiotic Resistance	X				X	
BSE	X				X	
Imports and					X	

International Activities						
Biotechnology					X	X
Dietary Supplements					X	

Part 1: Performance Plan Summary

PRODUCING PUBLIC HEALTH RESULTS THROUGH REGULATORY SCIENCE

1.1 Agency Mission and Strategic Goal

FDA is charged with assuring the safety of a vast array of consumer products. As such, the Agency manages many programs and monitors performance in each of these program areas. (See Appendix to this Plan). Certain functions, however, are critical to the Agency's success in fulfilling its mission. This Plan focuses on these core functions, and establishes goals to protect the Public Health and Safety of the Nation.

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.

- Our responsibilities are far reaching: 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 food-producing animals.
- We monitor a quarter of the Nation's consumer expenditures: 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 the Public of a penny per day per person.
- We judge the safety of an expanding scientific revolution: Public and private entities invest an estimated $50 billion in biomedical research and technology each year on products that the Agency regulates - and FDA is the gateway to ensuring that the fruits of that cutting-edge research and technology are safe when they reach the market.
- We assure the safety of the Nation's manufacturing and processing: FDA is a 9,000 person agency, but it is responsible for monitoring over 100,000 U.S. firms that manufacture or process products.
- We also monitor the safety of imported products: FDA tracks almost 6 million import shipments that enter this country each year, and prevent violative products from reaching the U.S. consumer.

When FDA is able to carry out the full scope of its responsibilities and successfully achieve its goal, the Nation enjoys a wide range of positive public health outcomes.

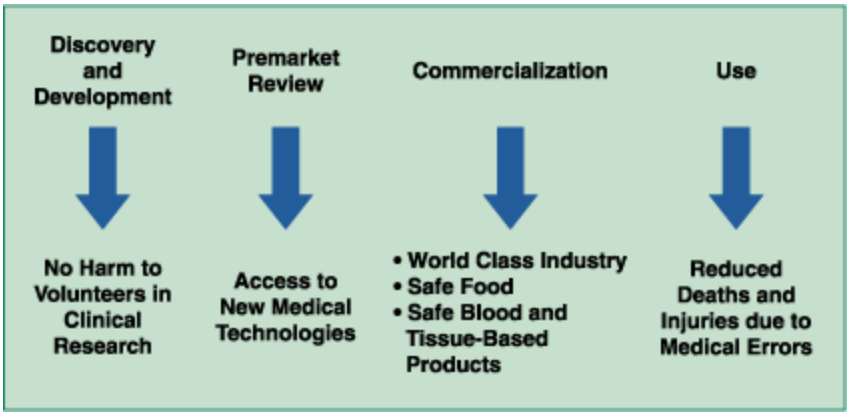
FDA's Performance Plan--A blueprint for achieving public health outcomes

FDA's Performance Plan highlights thirteen desired outcomes that will improve the health and safety status of the American Public. If the Plan is fully implemented, the public can realize such benefits as:

- Rapid and safe access to the latest medical technologies
- A safe food supply
- Safe blood and tissue-based products
- An industry that manufactures and markets products under 'world class' standards
- Reduced deaths and injuries resulting from errors in the prescribing and use of medical products

- Protection of individual volunteers from harm during clinical research studies

These outcomes provide a safety net for the Nation that span the life cycle of FDA's regulated products from initial research through ultimate consumption.



The Performance Plan identifies the specific goals and strategies that will help to achieve these outcomes. The Plan will also compare desired vs. actual performance in each of these areas. Some areas demonstrate great success in achieving our goals. Others reflect substantial gaps between goals that are necessary to protect the Public Health and what the Agency has been able to achieve. In those areas where there is a significant shortfall, we will explain the barriers that must be overcome to achieve 'full performance,' as well as the consequences to the Nation if these goals are not met.

FDA's Successes ...

The overall success of FDA's efforts is reflected in a recent survey by the PEW Research Center in cooperation with Princeton Survey Research. That survey gathered constituents' opinions on government agencies. FDA received an overall favorable rating of over 80%, more than twice the approval rate of the entire government. The pollsters' report noted that

> [t]he FDA is unique among the agencies we studied for how similarly--and highly--its very different customers rate its performance. Regulated industry as well as medical professionals, advocates and the chronically ill all credit the FDA for making a positive contribution to the safety of the Nation's food, drugs and other medical products.

FDA has scored several significant public health gains which reinforce our stakeholders' confidence that we are 'on the job.' Here are some illustrations that demonstrate how the public benefits when FDA achieves its goals:

When FDA Acted:	The Public Gained:
FDA approved NDAs, BLAs in record time.	New medicines and therapies were available to doctors and patients 18 months earlier.
FDA ensured that mammography facilities Mortality rates for breast cancer were operating at the 'gold standard.'	Mortality rates for breast cancer dropped as a result of more accurate diagnoses.
FDA approved significant new therapies for arthritis, diabetes and hepatitis C.	Over 30 million people with these diseases received new, critically needed therapies.
FDA cooperated with other federal agencies to improve a science-based food safety surveillance system.	Foodborne illness and death declined by 20%.

Summary of FY 1999 and FY 2000 Reporting

With this submission, FDA has reported on all 70 of its FY 1999 performance measures. There were 58 FY 1999 goals with some goals having multiple measures. FDA is also reporting on 42 of 60 FY 2000 performance measures (70%). There were 50 FY 2000 goals with some goals having multiple measures. The most common reason for the delay in reporting data for FY 2000 is that there is a time lag for reporting final data for premarket review goals. This is discussed further in the reporting sections for individual goals in Part Two of the Plan.

Selected FY 2000 Performance Highlights by Program

Foods

- FDA set forth its overall dietary supplement strategy. This strategy establishes a clear program goal to accomplish, by the year 2010, having a science-based regulatory program that fully implements the Dietary Supplement Health and Education Act of 1994.
- FDA issued an import alert for bulk or finished dietary supplements and other products that may contain aristolochic acid. Aristolochic acid is a potent carcinogen and nephrotoxin.

Human Drugs

- FDA continues to exceed the rigorous performance goals agreed to for each consecutive year under the PDUFA. FocalSeal-L Surgical Sealant was approved as a surgical sealant for use in lungs to seal air leaks following removal of cancerous lung tumors.
- In 2000, FDA's Generic Drugs Program approved Taxol a drug that is used for the firstline treatment of advanced carcinoma of the ovary and non-small cell lung cancer in patients who are not candidates for potentially curative surgery and/or radiation therapy.

Biologics

- Approved ReFacto, a biological product for the treatment and prevention of hemorrhagic episodes in patients with hemophilia A, a genetically inherited blood clotting disorder.
- Approved Prevnar, the first vaccine to prevent invasive pneumococcal diseases in infants and toddlers - diseases that can cause brain damage and, in rare cases, death.

Animal Drugs and Feeds

- FDA continues to work with its partners in industry to redesign the New Animal Drug Approval (NADA) process, thereby making it more efficient (phased review).
- FDA continues to increase the number of isolates in the National Antimicrobial Resistance Monitoring System (NARMS) database.

Medical Devices and Radiological Health

- There were no overdue submissions for the fourth consecutive year. FDA maintained high quality timely reviews despite increasingly complex device technology.
- The quality of mammography services in the United States continues to improve. In FY 2000 the goal of ensuring that mammography facilities meet inspection standards was achieved with a 97 percent rate, the fourth consecutive year of achieving this high standard.

National Center for Toxicological Research

- Geneticists are developing and validating sensitive and predictive in vitro and in vivo systems to identify, measure and understand how chemicals damage human genes.
- Biologists are studying gene-nutrient interactions involved in carcinogenesis and birth defects.

Tobacco

- On March 21, 2000, the United States Supreme Court, in a 5-4 decision, ruled that FDA lacks jurisdiction under the Federal Food, Drug, and Cosmetic Act to regulate tobacco products. The Court held that, although premature deaths from tobacco use present "one of the most troubling health problems facing our nation today," FDA lacks the authority to issue and enforce its tobacco regulations. Therefore, as of March 21, 2000, FDA commenced an orderly shutdown of the Office of Tobacco Programs.

Performance Challenges for the Future

Despite the achievements outlined above, there are many additional areas in which FDA has not yet had similar success. To illustrate:

- Rigorous and punctual review of new product applications from industry, and post-market inspections, are the backbone of FDA's system of public health protections. But FDA has been unable to completely fulfill its mandated responsibilities and public expectations in these two areas.
- A major gap exists between FDA's current clinical research monitoring capability and the level of monitoring that is necessary to assure that volunteers in these studies are being protected.
- The Agency is unable to assure the U.S. public that it can prevent unsafe imports from entering the country.

The goals outlined in this Performance Plan hold great promise for closing these gaps and realizing significant new gains for the American public. The stories of how these gains might be achieved are described in the pages that follow.

1.2 Strategies and Program Overview

1.2.1 Strategies

Quick and Safe Access to New Medical Technologies

Desired Outcome

To provide quick and safe access to the medical products of new technology and to enhance consumer access to these new products, as well as to less expensive generic drugs'.

Key Performance Goals

Pioneer Drugs and Biologics

Review and act on 90% of standard original NDA/PLA/BLA submissions within 10 months of receipt and 90% of priority original NDA/PLA/BLA submissions within 6 months. (PDUFA goal)

	PDUFA Goal	Performance
FY 1997	90%	100%
FY 1998	90%	100%
FY 1999	90%	100%
FY 2000	90%	*90%
FY 2001	90%	*90%
FY 2002	90%	*90%
* Target		

Generic Drugs and Pioneer Medical Devices

Review and act upon 100% of fileable original generic drug applications within 6 months after submission date.

Complete 100% of Premarket Approval Application (PMA) first actions within 180 days.

	Statutory Goal	Performance	
		Generic Drugs	Medical Devices
FY 1997	100%	N/A	65%
FY 1998	100%	N/A	79%
FY 1999	100%	28%	74%

FY 2000	100%	45%*	85%*
FY 2001	100%	50%*	90%*
FY 2002	100%	55%*	90%*
* Target N/A Not Available			

Why is FDA's contribution important?

FDA's signature activity and a prime service to the American public is the review of safety and effectiveness of drugs, biologics, and medical devices before they are allowed on the market. FDA is the regulatory gateway through which the medical products resulting from an estimated $50 billion annual biomedical research and development investment must pass and be judged.

A major objective of the human drug review process is to reduce the time required for FDA's review of drugs and biologics applications without sacrificing standards of performance and safety. The Agency emphasizes the review of new drugs that are intended to treat serious or life-threatening diseases, such as AIDS.

Similarly, improving the efficiency and quality of the medical product application review process will assure that safe and effective medical products are available to the American people more quickly. In addition to the obvious health benefits, shortening drug development times also results in significant savings to the pharmaceutical industry.

FDA has approved several thousand generic drugs that are used successfully by millions of patients. Substituting generics for brand name drugs has resulted in savings to consumers of $8 to $10 billion annually.

How are we going to do this?

FDA has adopted a number of strategies to improve its product review processes, including:

- The Prescription Drug User Fee Act (PDUFA) authorizes 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.
- Developing standards for new products of emerging technologies, such as novel drugs and biologics, to facilitate product develop- ment, expedite reviews and move products to market faster.
- Strengthening external ties. Expeditious medical product review is dependent upon enhanced collaboration and cooperation with industry, academia, professional societies and health care organizations.

- Implementing a comprehensive quality control system to ensure the Agency's pre-marketing review processes meet its public health responsibilities. FDA is working with stakeholders to implement this in the least burdensome way.
- FDA will continue prioritizing products to increase the efficiency of 'fast track' review processes in order to address the most urgent needs for new medical products first.
- FDA has been working to improve the generic drug review program to reduce review backlogs and achieve the 6-month review goal.

FDA needs to develop knowledge bases that will improve the scientific basis of regulatory guidance and advance science and product development. Formal scientific collaborations and stakeholder interactions are needed as a means to educate and increase the availability of scientific knowledge to consumers, health care providers and academia.

FDA also needs to install and implement current information technology (IT) systems that would ultimately permit the Agency to review drug applications more efficiently (for example, a single Web portal).

Consequences of Not Achieving the Goal

Delays in getting new products to market can postpone critically needed disease prevention and treatment, especially for a growing population of elderly and immune-compromised patients. Failure to achieve the goals for drug and device review will prevent innovative drugs and devices from being made available to patients and doctors in a timely manner. Therapies for treatable conditions would not reach the market in enough time to save lives.

Increased review times impact the amount of time a product is in development which in turn increases the cost of bringing a new product to market. Delays in approving generic drug equivalents result in fewer or no low-cost alternatives and overall higher costs for patients.

How are we doing?

For new drugs and biologics, the story is one of great success. FDA has moved from criticisms of a "drug lag" with other countries a decade ago to the current situation in which new drugs are approved in the U.S. as fast or faster than anywhere in the world, with the same high standards Americans expect. This was accomplished largely by the assurance of sufficient scientific staff funded by industry fees that complement appropriated funds.

Approval times for medical devices are also improving. In FY 2000, although FDA received the highest number of applications in years, the average approval of a new medical device took only 12.0 months, over 25% quicker than in FY 1997. However, in

FY 1999, FDA acted upon only 28% of generic drug applications within the goal of 6 months. Reasons included a significant backlog of applications.

Time to Approval			
	FY 1990	**FY 1995**	**FY 2000**
	Months	Months	Months
Drugs (PDUFA)	23.8	25.7	11.6
Generics	23.0	28.2	18.9
Biologics (PDUFA)	43.8	31.7	16.8
Medical Devices	13.7	25.4	12.0

1.2.1 Strategies

A Safe Food Supply

Desired Outcome

Ensure the safety of the food supply, including both imported foods and foods produced in the U.S., by minimizing contamination of food by pathogens, unlawful animal drug and pesticide residues and environmental contaminants.

Key Performance Goals

Inspect annually all domestic establishments that produce high-risk food products.

Implement an imported food safety program that emphasizes inspection of foreign manufacturers and border surveillance of products.

Monitor pesticide residues and environmental contaminants through analysis of food samples.

Why Is FDA's contribution important?

One of the Federal Government's most important and enduring roles, dating back to the beginning of the 20th century, is the protection of the food supply from such threats as microbial contamination, unlawful animal drug and pesticide residues, and environmental

contaminants, such as dioxin. FDA regulates 80 percent of all food consumed in the U.S. Recent estimates indicate that microbial foodborne disease causes approximately 76 million illnesses, 325,000 hospitalizations and 5,000 deaths each year in the United States. Hospitalization costs alone for these illnesses are estimated at more than $3 billion a year, and costs from lost productivity are much higher. Foodborne illness is preventable, and FDA's food safety activities are crucial to significantly reducing the enormous societal costs related to these illnesses.

FDA is responsible for ensuring the safety of foods produced and distributed by 59,000 domestic food establishments, 1,240 medicated feed mill establishments, and 5.1 million food imports that are expected to cross the U.S. border. Many of these imports come from countries that do not have the regulatory infrastructure to assure the safety of foods they produce.

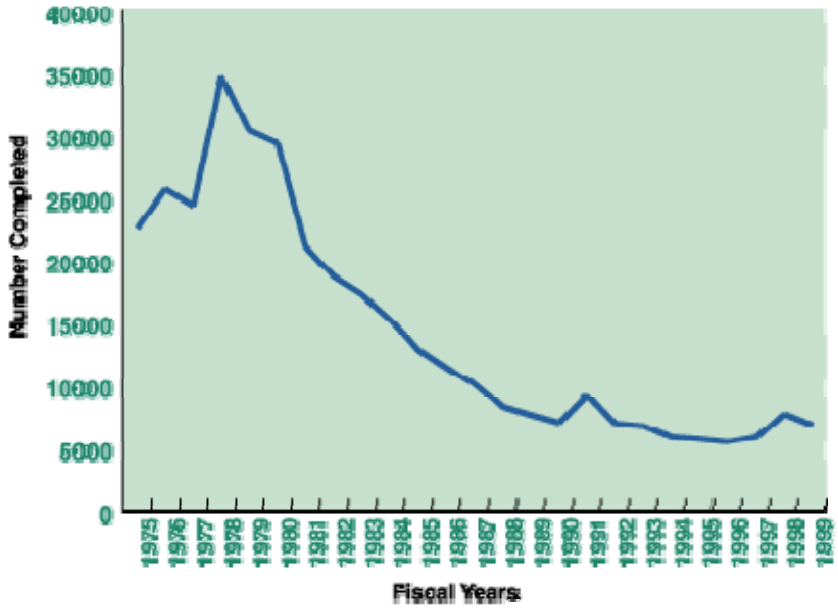
The task of ensuring a safe food supply has become more difficult because the nature of food and foodborne illness has changed significantly. For example, foods are more technologically complex; the number of foodborne pathogens has increased fivefold in the last 50 years; consumers are eating more seafood, fresh produce, imported produce and other foods, and "convenience" ready-to-eat foods; and our vulnerable populations have increased.

FOODS PRODUCED IN THE UNITED STATES

How are we going to do this?

As part of its mandate from Congress to ensure that the food supply is safe and wholesome, FDA is expected to inspect all food manufacturing establishments in the U.S. on a regular basis. The number of inspections conducted by FDA has fallen steadily over the past 25 years (see Figure 1). This decline corresponds to the decline in FDA's investigational work force. Since FDA has always adhered to the principle of addressing the most serious risk first, the Agency has focused its available resources on inspecting establishments that produce high-risk foods as well as those with a history of noncompliance. The U.S. food supply remains among the safest in the world.

Figure 1. Domestic Food Inspection Activity



Beginning in 1997, FDA has sought new funding to restore the Agency's food inspection capabilities. Congress appropriated some increases in funds in FY 1999, FY 2000 and FY 2001. In addition, the Agency has adopted a number of strategies to address its public health mission including:

- Focusing resources on high-risk products, firms that have a history of not complying with food laws, and firms with an unknown compliance history
- Increasing the knowledge of FDA investigators about the new, more complex food technologies
- Conducting training for the industry to promote good agricultural and manufacturing practices
- Emphasizing problem correction in addition to regulatory and enforcement measures
- Leveraging FDA resources through state contracts and partnership agreements with the Department of Agriculture, the Centers for Disease Control and Prevention and other federal agencies
- Conducting training for industry to promote good manufacturing and agricultural practices and educating consumers about safe food preparation and handling practices
- Collecting and analyzing samples for animal drug and pesticide residue and environmental contaminants

Consequences of Not Achieving the Goal

If FDA is unable to inspect food establishments to monitor and promote compliance with U.S. food laws and regulations, the Agency will be unable to promote good manufacturing and agricultural practices, ascertain the conditions under which our food is produced, identify manufacturing problems that threaten public health, or work with industry to correct problems that are identified during inspections. In addition, FDA cannot develop test methods to identify hazards in genetically modified foods, drug residues in food, and antibiotic resistant strains of bacteria in food. Thus, FDA will not be able to detect hazards or to do so in a timely and cost-effective manner. As a consequence, public health will be compromised, and the credibility of the U.S. food safety system will suffer. Most importantly, FDA will not be able to play its role in preventing foodborne illnesses, and associated hospitalizations, deaths and losses in productivity.

The absence of test methods to evaluate foods that are more technologically complex and diverse presents new regulatory challenges. In addition, FDA does not have the explicit statutory authority to require registration of all domestic food processing plants. Without a required, descriptive registration of all food firms, we are unable to assess accurately the number and type of establishments that FDA is responsible for regulating. Without this capability, we cannot accurately plan our activities by focusing on those firms that produce high-risk foods. Registration information may result in an increase in the number of firms that are targeted for annual inspection.

How are we doing?

Through a combination of FDA and state contract inspections, domestic firms that produce high-risk food products have been inspected on an average of once every three to four years. In FY 2000, 91% of the estimated 6,250 firms that produce high-risk food products were inspected. In 1999, about 90% of domestic seafood firms received a HACCP inspection. In FY 2001 and FY 2002, all high-risk establishments will be inspected. Inspection data for FY 2001 accomplishments will be assessed begin the basis for even better targeting of inspection resources.

IMPORTED FOODS

How are we going to do this?

The assurance of food safety is best monitored at and by the country of origin. FDA is using several approaches to better utilize existing resources to address safety of imported foods. These are:

- Conduct inspections of foreign food processors
- Conduct border inspections of food evaluations of the filers who supply the data upon which we make our border decisions

- Collect and analyze samples for pesticide residue and environmental contaminants
- Leverage resources through a joint program with U.S. Customs Service targeting importers who knowingly distribute unsafe foods
- Proceed with efforts to establish dairy and seafood equivalence
- Leverage resources through collaborative exchanges with other countries and extensive food safety outreach and education programs

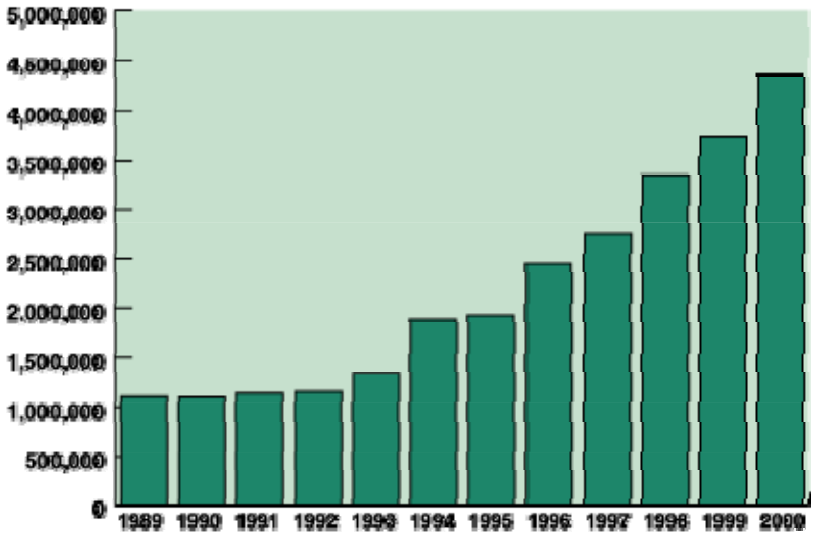
The inspections provide FDA not only with an on-site evaluation of a specific foreign firm, but also with a picture of the foreign industry's ability to produce safe food and of that country's food safety system.

Based on these approaches and the compliance documentation provided by importers and audited by FDA, the Agency can focus its resources on border inspection of the highest risk. Many imported foods come from countries that are characterized as emerging economies with emerging regulatory infrastructures. These countries are least able to assure a food safety system equivalent to ours. FDA will develop methods to detect illegal drug residues in imported aquaculture. By working with other domestic and foreign government agencies, we can accomplish more and devote our resources to the highest-risk products.

Consequences of Not Achieving the Goal

The volume and variety of food products imported into the U.S. has increased significantly in recent years (see Figure 2). The safety of the U.S. food supply depends on countries exporting to the U.S. assuming more responsibility for preventing foods that do not comply with U.S. safety standards from being exported to the U.S. Without these controls, compliance inspections of foreign manufacturers and appropriate surveillance at the border, FDA can not provide the assurances of safety that the American public has come to expect.

Figure 2. FDA Food Import Entries



Increased consumption of imported foods, the variety and nature of those foods and the number and variety of countries from which these foods are imported have greatly increased the workload of ensuring the safety of imported foods. Not only are there significantly more products entering at the border but there are also more foreign firms to inspect and more countries' food safety systems to audit. In addition, as for domestic food products, there are no test methods to evaluate hazards in imported foods that are genetically modified, drug residues in food, and antibiotic resistant strains of bacteria in food are lacking.

Because of the lack of explicit statutory authority, FDA does not have an accurate description of the scope of high-risk foods that we can reasonably expect to be imported into the country. In addition, FDA has limited authority to ensure that food imported to the U.S. is produced under food safety measures that are the same or equivalent to ours. Therefore, it is up to the Agency, using border surveillance, to identify problems and to determine corrective actions.

How are we doing?

Countries that export to the U.S. do not currently provide FDA with assurance that foods coming to this country are safe. FDA has proposed legislation that would require such assurances but Congress has not adopted the proposed legislation. A small percentage of imported food entries are directly assessed through field examinations and less than 1% through laboratory analysis.

In FY 2000, we increased our surveillance of microbial contamination by completing examination of 1,000 imported produce samples and conducting inspections of foreign produce farms in response to findings of pathogen contamination. In FY 2001, we plan to

conduct 250 inspections of foreign food processors. Data on FDA's examination of imported food products and inspections of foreign food establishments will be assessed beginning in November 2001. The results will provide the basis for better targeting our foreign inspection and border surveillance resources. However, at current resource levels, we expect coverage of imported food products will be less than 1% as the volume of imported food products continue to increase.

1.2.1 Strategies

Safe Blood and Tissue Products

Desired Outcome

To ensure the safety of the nation's blood supply and human tissues for transplantation.

Key Performance Goals

Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80%.

Why is FDA's contribution important?

Blood: FDA is responsible for the safety of the United States' blood supply. 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 units are drawn from volunteer donors for use in more than 3.5 million Americans.

The AIDS epidemic in the mid-1980s prompted a critical concern about blood safety, which was exacerbated by the subsequent identification of other blood hazards (such as Hepatitis A, B, and C and transmissible spongiform encephalopathies, including "mad cow" disease).

Tissues: All human tissue and tissue-related products have the potential to transmit communicable disease, and FDA believes every reasonable effort should be made to prevent the transmission of disease, while ensuring the continued availability of safe human tissue products. Of particular concern are HIV, Hepatitis B, and Hepatitis C. Due to reports of unsafe practices in select numbers of tissue banks, FDA issued an interim rule that required certain minimum infectious disease screening and testing standards and provided for the inspection of tissue banks and the destruction of unsafe human tissue.

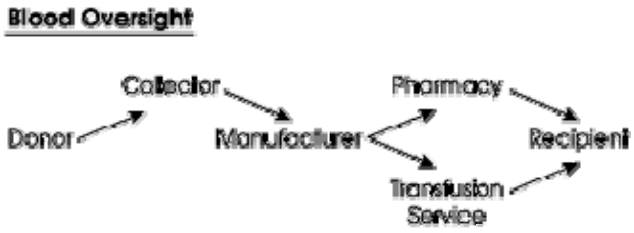
FDA announced Reinventing the Regulation of Human Tissue and A Proposed Approach to the Regulation of Cellular and Tissue-based Products in February 1997. This risk-

based, tiered regulatory framework addressed fragmented policies and regulations for tissues and cellular products and linked the level of regulation to the level of risk involved.

How are we going to do this?

Blood: The blood safety system established by FDA consists of five-layers that begin at the blood collection center and encompasses the manufacturers and distributors of blood products. These are: 1) Donor screening to determine suitable donors; 2) Testing for blood-borne agents such as HIV, hepatitis, and HTLV-I; 3) Requiring blood establishments to keep a current list of deferred donors; 4) Quarantining blood products until the products have been thoroughly tested and the donation records have been verified; and 5) Requiring blood establishments to investigate any breaches of these safeguards and to correct any system deficiencies that are found.

In the United States today, licensed establishments include more than 1,000 donor centers that collect, process and distribute blood and blood products in interstate commerce under federal regulations. FDA investigators across the country conduct inspections of all licensed blood establishments each year. During the inspection, investigators monitor donor screening; blood testing, labeling, storage, and handling; and record keeping and other manufacturing practices.



FDA initiated a Blood Action Plan in July 1997 to increase the effectiveness of its scientific and regulatory actions, and to ensure greater coordination with other federal agencies.

The Blood Action Plan involves several initiatives: updating and reinventing the blood regulations; addressing emerging infectious diseases; ensuring compliance of plasma fractionation establishments; blood donor/recipient notification and lookback; and FDA emergency recalls affecting blood safety response procedures.

Tissues: In consultation with the tissue industry, FDA proposed implementation of a four-tiered approach to tissue regulation:

1. Communicable disease controls. The Agency would set screening and testing requirements and recommendations, but in many cases would not require individuals to

file information with the Agency. All uses of tissues (except removing and re-implanting tissue in the same patient) would be subject to some infectious disease controls.

2. Handling and processing. All uses of tissue products (except removing and reimplanting tissue in the same patient) would be subject to handling and processing controls to prevent contamination.

3. Clinical safety and effectiveness. Tissue products that are manipulated such that their biological characteristics or relevant functions are altered, would be subject to more comprehensive regulatory requirements than other tissue products, including submissions of clinical trial data demonstrating safety and effectiveness.

4. Registration and listing. The Agency would require that all tissue product processing facilities register with the Agency and list their products via a simple electronic system.

Consequences of Not Achieving the Goal

Blood: The blood supply is essential to the nation's health care system. History has shown that emerging infectious diseases such as HIV/AIDS can be transmitted through blood transfusions. Unknown or emerging agents that may not be inactivated or removed during processing pose the greatest threat to the blood supply. If we fail to successfully regulate blood, the public health consequences could be alarming.

Tissues: Failure to fully implement the Tissue Action Plan increases the chances of the transmission of infectious diseases through tissue products.

How are we doing?

Blood: To date, FDA has:

- Implemented procedures for managing emergencies related to blood safety;
- Continued its systematic update of the blood regulations, resulting in increased compliance by the blood industry;
- Simplified the blood application licensing process. There is now one license application required, replacing the two previously required applications;
- Streamlined the inspection of blood and plasma collection establishments by combining them under one authority within FDA;
- Written new regulations and other effective strategies to clarify industry's responsibility to notify product end-users in recall and look- back situations, as well as regulations requiring medical notification of permanently deferred donors; and
- Initiated a three-year pilot monthly surveillance program to monitor and evaluate the adequacy of the blood supply.

FDA has been successful in many areas in the Blood program; however, there is still work to be done. FDA needs to establish a process for identifying and reacting to the

constantly changing new threats to the blood supply, such as Creutzfeldt-Jakob Disease ("mad cow" disease).

FDA still needs to:

- develop guidance documents relating to blood safety;
- prepare proposed and final regulations;
- conduct industry and patient workshops; and
- conduct necessary studies on emerging infectious diseases.

Tissues: FDA published the proposed rule, Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products: Inspection and Enforcement, on January 8, 2001. On January 19, 2001, FDA published the final rule, Human Cells, Tissues, and Cellular and Tissue-Based Products: Establishment Registration and Listing.

FDA still needs to:

- Ensure that tissues are retrieved from suitable donors and that tissues are processed in a manner that ensures they are safe and suitable for their intended uses;
- Publish needed final regulations and guidance documents;
- Continue interaction with DHHS concerning regulation of assisted-reproductive technologies;
- Complete database development and initiate new establishment registration and product listing reporting system; and
- Determine regulatory oversight for new areas such as unrelated allogeneic hematopoietic stem cells (transference of stem cells between two unrelated persons); and cellular and gene therapy.

1.2.1 Strategies

Safe Medical Products

Desired Outcome

To ensure that domestic manufacturers produce safe medical products.

Key Performance Goal

Inspect 50 percent of high-risk domestic medical product manufacturers.

Why is FDA's contribution important?

FDA is responsible for ensuring the safety of medical products produced by all domestic medical product establishments. These comprise a wide array of products that have become medically and technologically more complex. They can pose great risks if not designed and manufactured properly.

Congress and the American People expect FDA to inspect medical product manufacturers on a regular basis, for compliance with high product quality and safety standards.

Although a direct causal and quantitatively defined relationship between inspections and desired public health outcomes cannot be established with certainty, it is reasonable to assume that regular inspections are more likely to reveal problems that require correction. The Agency uses its statutory inspectional authority, to provide this assurance. This was the wisdom and rationale behind the law requiring FDA to conduct inspections at specified maximum time intervals, such as once every two years. The Agency's ability to identify and remove unacceptable medical products from the marketplace is closely related to the level of inspections it is able to conduct.

How are we going to do this?

FDA continues to make the most effective use of limited inspection resources by implementing four key strategies:

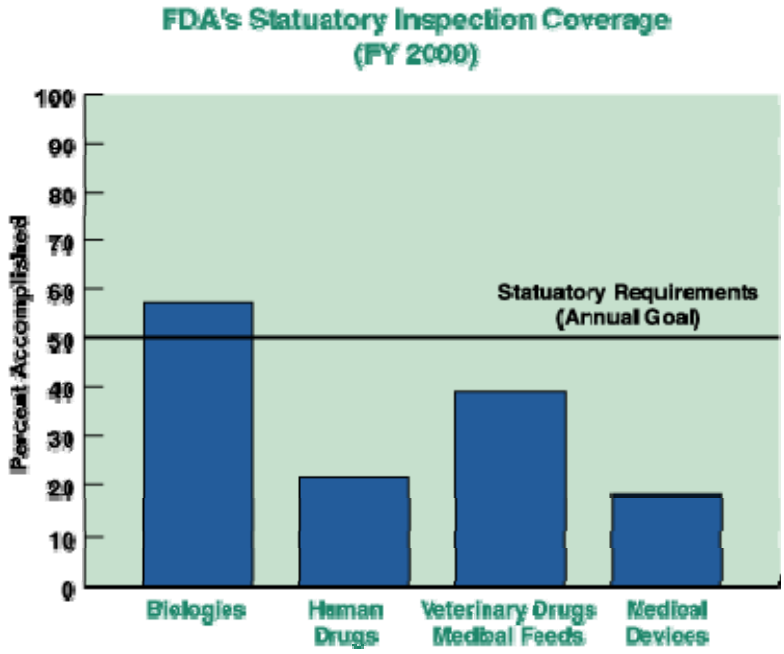
- Leveraging through contracts with the states, other third parties and outreach to small firms;
- Focusing resources on the highest risk firms and medical products - areas which will bring the greatest benefit to health;
- Ensuring that inspectors have the scientific and technological support necessary to make quick and valid judgements about medical device compliance; and
- Reengineering the inspection process by implementing quality system inspections that will significantly reduce inspection time and increase effectiveness.

Based on experience, a significant investment in training and time is necessary to ensure quality uniform inspections.

Consequences of Not Achieving the Goal

Long delays in visiting firms will increase the potential for unsafe medical products to present themselves to the American Public. In FY 2000, FDA was alerted by local hospitals of what proved to be contaminated iodine surgical swabs. The firm that had produced the swabs had not been inspected for seven years resulting in estimates the 200,000 people had been infected. Earlier detection could have prevented and corrected the problem.

FDA's inspection force is attempting to monitor a regulated industry in an environment that has changed rapidly and become significantly more complex over the past several years. Contributing to this change have been much more technologically complex and diverse products both domestically and internationally and increasing use of the internet by industry to develop, produce, distribute and market their products.



How Are We Doing?

The law requires that FDA inspect certain biologics, human and animal drug, and medical device manufacturers at least once every 2 years. In recent years, coverage has fallen short of meeting these statutory requirements. Although at least 50 percent of statutory establishments should be inspected annually, only 22 percent of human drug, 39 percent of animal drug, and 13 percent of medical device statutory establishments were inspected in FY 2000. The Agency did inspect 57 percent of the biologics statutory establishments in FY 2000.

1.2.1 Strategies

Reduce Adverse Events Related to Medical Products

Desired Outcome

Reduce preventable deaths and injuries associated with the use of medical products.

Key Performance Goal

Develop and enhance surveillance of FDA-regulated products to identify harm resulting from use, understand harm through expert analysis, and prevent harm to other patients by taking action.

Why is FDA's contribution important?

Approximately 1.3 million people are accidentally injured by medical therapy in the U.S. annually. Many errors are associated with the misuse of drugs and medical devices regulated by FDA. Costs from these medical errors range from $20 to $75 billion annually. The Institute of Medicine estimates that as many as 98,000 Americans die annually as a result of preventable medical errors.

For its part in attacking this problem, FDA is adopting a systems approach, of which the most significant component is the identification of and response to adverse events that are reported in the U.S. FDA is planning to expand its knowledge of adverse events and medical errors by linking with new sources of data.

How are we going to do this?

Most injuries and deaths associated with medical products result from known side effects. Some side effects are unavoidable but others can be prevented or minimized by careful product choice and use. The greatest need is to identify potential threats and then educate patients and health care professionals to avoid them. FDA will do this by:

1) Implementing a MeDSuN system. MeDSuN is a pilot program designed to educate and encourage hospital personnel to accurately identify and report injuries and deaths associated with medical products. MeDSuN includes a representative network of hospitals. The initial phase of the MeDSuN pilot was a success, with actual adverse event reports from participating hospitals increasing 15-fold for medical devices.

2) Linking with existing data sources. FDA epidemiologists and safety evaluators will link to existing external data sources held by both private and government organizations. For example, emergency rooms, poison control centers, health care systems, and the Centers for Disease Control and Prevention (CDC) all collect important information on adverse reactions.

3) Upgrading AERS. FDA is upgrading its Adverse Event Reporting System (AERS) for drugs to allow electronic submission of adverse event reports. This will bring about harmonization with manufacturers, reduce the amount of paper copies and encourage more reporting by making it easier for drug manufacturers to enter reports. Reports will be entered into the AERS database within days versus weeks with manual entry and it will allow FDA to get quicker information to identify signals and trends.

4) Continuing MedWatch. MedWatch, the FDA Medical Products Reporting Program is designed to educate all health professionals about the critical importance of being aware of, monitoring for, and reporting adverse events and problems related to medical products including problems associated with look-alike/ sound-alike names and product packaging confusions. Over 140 organizations representing health professionals and industry support MedWatch. Individual consumers may also submit reports to MedWatch.

5) Medical Errors Reporting System in Transfusion Medicine (MERS-TM). MERS-TM has been endorsed by the PHS Advisory Committee on Blood Safety and Availability. This system was developed under NIH funding and will serve as the model for the FDA blood error reporting. MERS-TM encourages non-punitive reporting with a well-defined codified method of reporting. It includes a root cause analysis for each error and focuses on methods and systems shortcomings rather than human error.

6) Analysis and Response. The Agency analyzes and responds to reports by taking appropriate action including: providing important product safety information, making labeling changes, requiring a product design change, or even withdrawing a product from the market. Once the Agency's systems are at full capability, FDA will be able to reduce preventable deaths and injuries associated with the use of medical products.

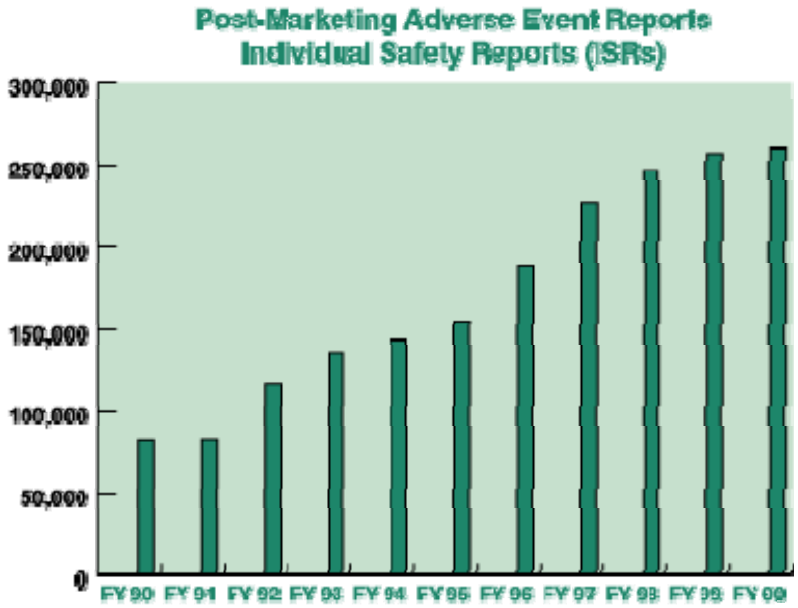
7) Improved Labeling. FDA is spearheading labeling reform and plans to propose new regulations and guides to improve the format and content of labeling to make it more user-friendly.

Consequences of Not Achieving the Goal

Many patient deaths and injuries are associated with the use of FDA-regulated medical products within a complex and time-pressured health care system. The Agency believes that roughly half of these deaths and injuries can be avoided by fully implementing its strategies.

Thousands of lives and billions of dollars can be saved. But if the strategies cannot be implemented, these savings will not be realized.

The following table represents a snapshot of actual adverse events. We believe there is serious under-reporting of adverse events.



When a medical error occurs in a hospital, a risk manager examines the system and takes preventive steps. Often these incidents are not reported or shared with other hospitals, health care professionals, FDA or drug manufacturers. Unless these incidents are reported, we cannot take action to prevent them.

FDA needs a comprehensive safety evaluation system for medical products. This requires strengthening existing systems as well as implementing new ones. The Agency also requires additional expertise in medical epidemiology and statistical analysis to conduct the safety evaluations.

How are we doing?

- FDA plans to publish a proposed rule that would require manufacturers of marketed human drugs to submit Individual Safety Reports to the Agency electronically. The rule would decrease the FDA's costs for data entry of these reports as well as increase the efficiency and timeliness of detection of safety problems.
- The Agency has developed new standards for over-the-counter drug product labeling designed to increase patient knowledge about the medication and decrease errors in use. FDA is using a nationwide media campaign to inform consumers of how to use the new labeling. FDA plans to propose a new format for the drug package insert to communicate risks and warnings more effectively.
- FDA plans to propose a regulation improving the process for submission of adverse event reports by manufacturers, including conformance to international standards. For example, the FDA has adopted the international thesaurus (MedDRA) that provides standardized terminology and coding to allow data to be compared globally. The regulation would require manufacturers to submit precoded reports using MedDRA.

- Through the interagency Patient Safety Task Force, FDA is working with other agencies in the Department to evaluate the feasibility of sharing existing data resources.
- FDA staff participated in national meetings related to improving patient safety, including attention to reducing drug, biologic and medical device errors.
- Published a regulation that requires the reporting of any event associated with biologics, including blood and blood components and source plasma that represents a deviation in manufacturing. o Initiated a new program for the review and risk-analysis of proprietary names for drug products.
- Initiated development of packaging standards to prevent dosing and drug mix-ups.

1.2.1 Strategies

Protecting Volunteers in Clinical Research

Desired Outcome

To better protect the rights and welfare of volunteers who participate in clinical research studies

Key Performance Goals

Protect human research subjects' participation in drug studies and assess the quality of data from these studies by increasing the number of onsite inspections.

Increase the number of inspections of medical device studies with an emphasis on vulnerable populations such as the mentally impaired and children.

Why is FDA's contribution important?

FDA is the only government agency with a regular program of on-site inspections to evaluate the performance of Institutional Review Boards (IRBs), clinical investigators (CIs), sponsors, and others involved in the conduct of research involving human subjects.

Heightened concern for the rights and welfare of volunteers in clinical studies followed the recent death of a research subject in a gene therapy trial, and studies by the HHS Inspector General and others criticizing existing Bioresearch Monitoring (BIMO) oversight programs.

Two other developments underscore the need for a well-funded, effective oversight body. First, the rapidly changing research environment has led to a proliferation of multi-site clinical trials, an increase in clinical trials using vulnerable populations, and the growth of new types of research, particularly related to genetic therapies and new technologies.

Second, FDA's inspection program continues to uncover problems in clinical research practices related to: failure to follow the study protocol, failure to maintain accurate case histories on study subjects, problems with informed consent documents, failure to report adverse events to FDA, and failure to obtain IRB approval for protocol changes.

FDA believes that it can enhance safety of volunteers in clinical studies by significantly increasing the number of inspections, focusing on high-risk situations and responding rapidly to potential problems.

How are we going to do this?

FDA will:

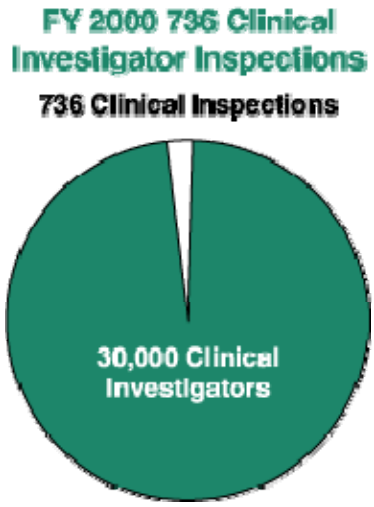
- increase the number of inspections and target high risk clinical trials
- increase training for investigators
- improve the inspection process for Institutional Review Boards (IRB)
- enhance follow-up compliance activities

Consequences of Not Achieving the Goal

Failure to achieve the goals may result in needless deaths and suffering of participants in clinical trials.

How are we doing?

The following chart shows that FDA inspected a small sample of all the clinical trials in FY 2000. While the Agency understands it cannot inspect every clinical investigator, added funds will allow the FDA to focus its inspectional efforts to lower the risks to volunteers in clinical trials.



1.2.1 Strategies

Cutting-Edge Risk Assessment to Protect Public Health

Desired Outcome

Improve the FDA science base to develop and/or modify research standards used for definitive risk/policy decisions.

Key Performance Goals

Integrate new genetic systems and computer-assisted toxicology (bio-informatics) in the application review process.

Integrate gene chip, gene array and proteomic technologies as standards for FDA review/risk management.

Why is FDA's contribution important?

Toxicology research is moving away from using large numbers of animals with relatively few endpoints. These animal test systems are costly, time intensive and do not always mimic the human response. Because of American consumption, increasing evidence of adverse drug/chemical reactions in humans points to a need to identify and protect people at higher risk from exposure to drugs, contaminated foods, or other regulated products. In addition, toxicological research is focused on a better understanding of the biological mechanisms that cause toxic reactions. Currently, industry has been submitting drug applications with data from transgenic systems. In response, FDA scientists and reviewers are developing, evaluating and comparing in vivo and in vitro transgenic systems and computer-assisted toxicology knowledge bases.

Risk chip technology permits researchers to screen large numbers of people simultaneously for different biomarkers. This allows the identification of individuals at risk for adverse drug reactions and facilitates FDA review of individual susceptibility using profiles of agents with known toxicities and allows selection of a diverse group for clinical trials. DNA gene expression microarrays lead to better understanding of inter-species extrapolation and provide biomarkers that predict human outcomes. A less defined but more powerful technology called proteomics is also being developed. These techniques are being developed in collaboration with private industry.

How are we going to do this?

Agency scientists will continue to develop/modify and apply new technologies to evaluate models as useful substitutes to determine human toxicity.

In addition, we will conduct studies using transgenic, imaging, microarray, proteomics and informatics to evaluate toxic responses in individuals and identify biomarkers that predict human outcomes.

Consequences of Not Achieving the Goal

Product/drug development is exploding due to rapid scientific advances and new technologies, such as human genome sequencing. Should FDA continue to fall behind in understanding and incorporating these technologies into its applied research and

regulatory review process/policy systems, the ability of the Agency to guide industry submissions and/or review new applications will be detained along with products being delayed to patients.

In order for FDA's National Center for Toxicological Research to establish a core DNA Microarray Group to facilitate expanded research in this area, it will need:

- Scientists skilled in understanding and using these new technologies and
- Advanced instrumentation and equipment.

How are we doing?

To support goal 1, Agency researchers have developed new bioassays for use in assessing genetic damage. The National Center for Toxicological Research is actively collaborating with other FDA Centers, other agencies and academia to expand this potential. NCTR has also developed and validated a prototype computer-assisted predictive toxicology model for estrogenic compounds. The prototype predictive system has been used successfully by CFSAN and CDER to assess the estrogen-like effect of compounds. This research has been conducted in partnership with other federal agencies (NIEHS & EPA) and with industry.

To achieve goal 2, scientists have completed studies to identify markers of frequently occurring cancers in highly susceptible subpopulations. These data have been used to work with industry to develop a "risk chip" (array technology) to identify and protect large numbers of people who are highly susceptible to having adverse reactions from exposure to certain drugs, and contaminated foods. This "risk chip" has potential to be expanded to identify other biomarkers provided funds are made available.

1.2.1 Strategies

Early Detection of Breast Cancer Through Improved Mammography

Desired Outcome

Improved mammography images should lead to more accurate interpretation by physicians and improve early detection of breast cancer.

Key Performance Goal

Ensure at least 97% of mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems in FY 2002.

Why is FDA's contribution important?

Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer deaths among American women. Experts estimate that one in eight American women will contract breast cancer during their lifetime.

The probability of survival increases significantly 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 2 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.

Achieving this goal will ensure that mammography facilities remain in compliance with established quality standards and improve the quality of mammography in the United States. This would lead to more accurate interpretation by physicians and improve early detection of breast cancer.

A 1% improvement in image quality of community mammography screening programs should reduce 5-year and 20-year mortality by13 and 28 lives, respectively, due to earlier detection and treatment. Economic costs of mammography would not change, but benefits of nearly $4 million annually would be expected by eliminating 2,200 false positive readings.

How are we going to do this?

MQSA requires that FDA conduct annual inspections of the approximately 10,000 mammography facilities covered by MQSA. Inspectors perform science-based inspections of these facilities to determine the radiation dose as well as to review quality control records and personnel qualifications documentation and to empirically evaluate the quality of the facility's film processing. In addition, FDA will work with manufacturers to ensure that advanced technologies like digital mammography are safe, effective and used correctly.

Federal and state personnel will continue to conduct annual inspections, as well as provide training for new inspectors. MQSA ensures that sufficient resources will be available to carry out inspections of all facilities annually, with all inspection fees paid by those facilities being inspected.

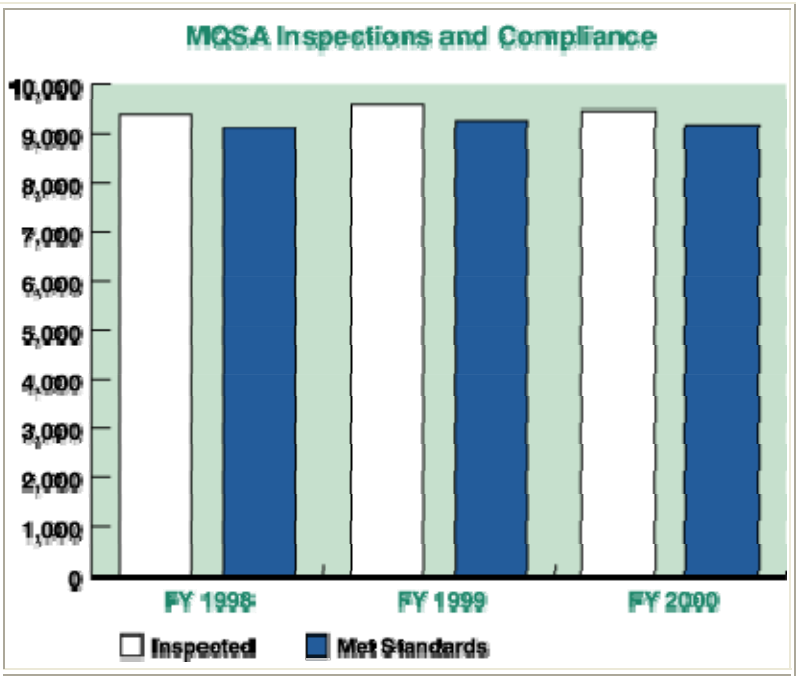
Consequences of Not Achieving the Goal

Mammography facilities not conforming with inspection standards could produce poor quality mammograms which could lead to interpretation difficulties for physicians, resulting in decreased early detection of breast cancer, and more associated fatalities.

In some cases, facilities are not aware of their responsibilities under MQSA. There are ongoing outreach efforts to increase facility awareness of and compliance with MQSA.

How are we doing?

The FY 2000 goal of ensuring that 97% of the Nation's mammography facilities meet inspection standards was achieved for the fourth consecutive year.



Data Sources: Mammography Program Reporting and information System (MPRIS)

1.2.1 Strategies

Manage the Threat of Antibiotic Resistant Bacteria

Desired Outcome

Reduce the occurrence of antibiotic resistant bacteria:

"Resistance to antibiotics and other anti-infective agents constitutes a major threat to public health and ought to be recognized as such more widely than it is at the present time." --Lord Soulsby, U.K. Select Committee on Science & Technology

Key Performance Goal

Maintain the overall testing rate for Salmonella, which is used as an antimicrobial resistance indicator, in the National Antimicrobial Resistance Monitoring System (NARMS) of 7,200/year.

Why is FDA's contribution important?

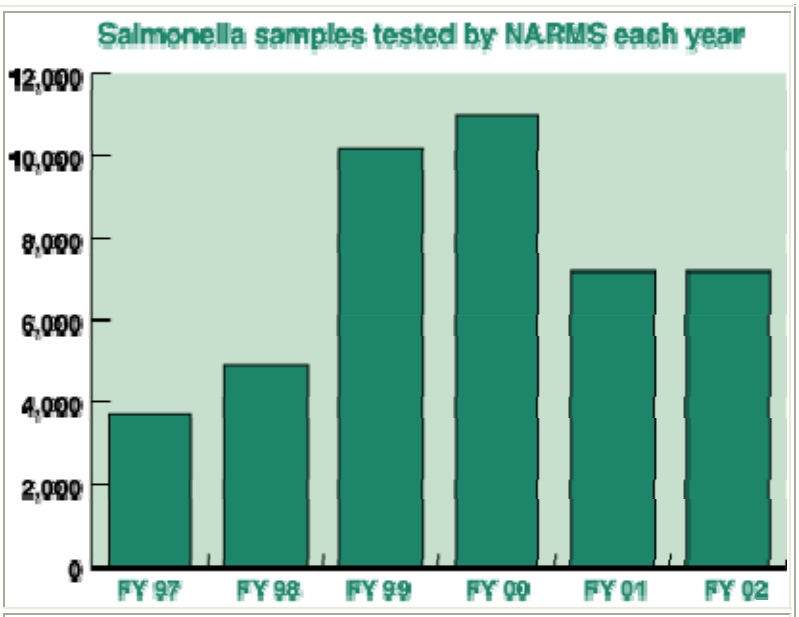
FDA, CDC, and USDA have teamed up as part of a multi-organization effort to control the threat of antibiotic resistance. FDA oversees NARMS. This is a program that tracks bacterial resistance to antibiotics, detects emerging problems, and establishes a baseline to evaluate prevention control measures. This real-time system allows public health officials to monitor the occurrence of antibiotic resistant bacteria, which could aid in preventing outbreaks.

Consequences of Not Achieving the Goal

Antimicrobial resistance decreases treatment options available to physicians which may compromise public health.

The misuse of antibiotics can be found everywhere and is believed to increase antimicrobial resistance. For example, physicians choose the newest and most powerful antibiotics as their first line of treatment when such therapies may not be recommended. Patients often fail to complete a course of antibiotics, and even self-medicate using leftover pills. Veterinarians use antibiotics in food-producing animals to promote growth and such practices are suggested to increase antibiotic resistant bacteria that reach consumers in meat and dairy products.

How are we doing?



Note: Each bar represents the total number of veterinary and human samples added to NARMS each year. Veterinary samples are collected from production animals and submitted by selected diagnostic laboratories. Human samples are collected from state/local health departments.

FY 2000 - FY 2002 are performance targets. The numbers for these years shown in the chart above are wrong. The goals for fiscal years 2001 and 2002 are actually 12,000.

Data Source: FDA-CDC-USDA National Antimicrobial Resistance Monitoring System

"Antibiotic resistance ... is worrying because it is accumulating and accelerating while the world's tools for combating it decrease in power and number."--Joshua Lederberg, Nobel Prize winner.

1.2.1 Strategies

Prevent Outbreak of Bovine Spongiform Encephalopathy (BSE)

Desired Outcome

The continued absence of BSE, commonly known as "Mad Cow Disease," in the U. S.

Key Performance Goal

Assure 100 percent compliance with the BSE Regulation through inspection and compliance actions.

Why is FDA's contribution important?

BSE belongs to a group of progressive degenerative neurological diseases known as transmissible spongiform encephalopathies (TSEs). TSE diseases are always fatal. There are six TSE diseases that affect humans: kuru, classical Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD), Gerstamann-Straussler-Scheniker syndrome, fatal familial insomnia, and sporadic fatal insomnia.

To protect consumers it is essential that a multi-layered safeguard system be implemented and monitored to ensure that BSE regulations are followed. A final rule (Title 21 Part 589.2000 of the Code of Federal Regulations) implemented by FDA in August 1997, prohibits the feeding of mammalian protein to ruminant animals.

The Animal and Plant Health Inspection Service (APHIS), of the United States Department of Agriculture, has also placed restrictions banning the importation of live ruminants and certain ruminant products from thirty-one countries to prevent BSE from entering the United States. Many products regulated by FDA contain these banned substances and it is important to establish a comprehensive monitoring system to identify products that may pose a health risk and ensure they do not enter the US.

The FDA also needs to consider areas not covered by the APHIS ban such as: ruminant protein-containing cosmetic products that are packaged and ready for sale; bovine-derived materials intended for human consumption as either finished dietary supplement products or for use as ingredients in dietary supplements; vaccines; blood and blood products; human drugs; and human food other than meat, such as gelatins.

The United States has the safest blood supply in the world. FDA continues to strengthen its efforts to protect the nation's blood supply and to minimize the risks from BSE. FDA will continue to conduct research of blood and blood products and develop regulations to minimize the risk of infectious disease.

Consequences of Not Achieving the Goal

Active surveillance efforts have yet to identify BSE in the United States. If BSE was to enter the U S, it could pose a serious health risk to humans, and be financially devastating to the United States beef industry. In a recent survey in Germany, more than 50 percent of those polled said they had little or no confidence in the safety of beef products. So far the ensuing crisis in the farm industry has cost British taxpayers more than $6 billion. In

the US the cost of lost revenue to the beef industry alone is estimated to reach over $15 billion.

Monitoring imports for bovine products has proven to be challenging. Often banned animal proteins will be shipped to countries with less stringent BSE regulations, re-labeled, and re - exported, obscuring the true country of origin. It is also difficult for inspectors monitoring imports to verify the presence of high-risk tissues in finished dietary supplements, drugs, vaccines, or cosmetic products.

How are we doing?

The Agency developed an enforcement plan with the goal of 100 percent compliance with the BSE feed regulations through education, inspections, and compliance actions for egregious actions or repeated noncompliance. In 1998 District Offices were assigned to conduct inspections of 100 percent of all renderers and feed mills to determine compliance. To date, FDA has conducted initial inspections of approximately 84 percent of renderers, 85 percent of the licensed feed mills, that produce medicated animal feeds, and 82 percent of the known unlicensed feed mills. Of these inspections conducted 79 percent were conducted by State officials, and FDA is seeking assistance from State feed control officials to conduct additional inspections and identify non-FDA licensed feed mills.

Percentage of Firms Handling Prohibited Material that are Out of Compliance

	Commingling	Labeling	Records
Renderers	14%	4%	3%
FDA Licensed Feed Mills	13%	15%	1%
Non-FDA Licensed Feed Mills	18%	33%	.04%
Other*	12%	18%	3%

* Examples include ruminant feeders, on-farm mixers, haulers, and distributors.

Field offices have been assigned to re-inspect over 800 firms that handle prohibited material that were not in full compliance with the rule. They will also continue to develop and implement an import monitoring program that will capture all products containing high risk products. In January of 2001 FDA issued an import alert to facilitate the detention of high risk products.

FDA has asked all licensed vaccine manufacturers to evaluate all bovine derived material used at any stage in vaccine production. FDA has asked manufacturers to identify the country from which the animals originated, the date the material was obtained, and the date the material was used in the production of vaccines.

The risk of transmission of vCJD in humans by blood or blood products is still considered to be theoretical. Nevertheless, in 1999, as a precautionary measure the FDA

issued recommendations for the deferral of blood donors who resided for 6 months or more in the UK between 1980 and 1996. In January 2001, the FDA's Transmissible Spongiform Encephalopathies Committee recommended that the deferral be expanded to include individuals who resided 10 years or more in the Republic of Ireland, Portugal, or France between 1986 and the present.

FDA continues to chair the Interdepartmental Steering Committee for BSE/TSE Affairs. This group includes representatives of CDC, FDA, NIH, USDA, the United States Trade Representative, the Office of Management and Budget, the Customs Service, the Department of State, the Department of Defense, the State Association of Feed Control Officials, the National Association of State Departments of Agriculture, and the White House Office of Science and Technology Policy. The functions of this committee are to assure ongoing coordination between agencies, to integrate contingency planning for the possibility that a case of BSE or of vCJD might be found in the United States, to identify and address potential vulnerabilities in the United States to BSE and vCJD, and to coordinate development and implementation of risk communication plans by the various agencies.

Finally, FDA has worked closely with the CDC, NIH, and the Office of the Secretary to produce a departmental TSE Action Plan that has recently been submitted to the Secretary for his consideration. This Action Plan outlines further expansion of these initiatives to continue to improve the BSE/TSE safety net.

1.2.1 Strategies

Imports/International Activities

Desired Outcome

Increase the safety of imported products.

Key Performance Goals

Increase the number of foreign inspections.

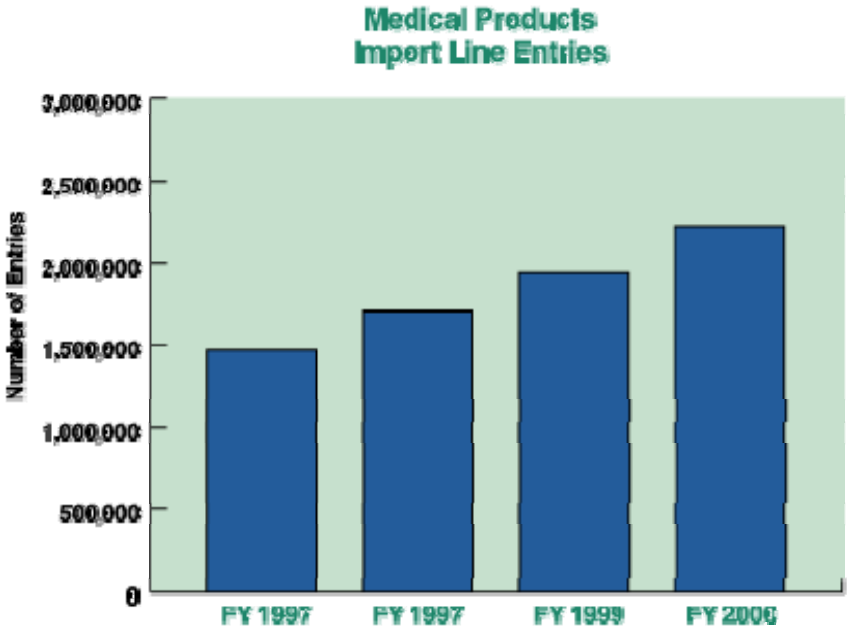
Expand import coverage for all medical products.

Why is FDA's contribution important?

FDA is responsible for ensuring the safety of over 6 million import line entries (imported products) that cross our borders annually. The sources of these entries are diversifying and include more products from countries that are typically categorized as emerging economies, with emerging regulatory infrastructures. FDA conducts sampling and end

point product testing as a means of determining that imported products have been properly produced.

Sampling and testing of imported products cannot be relied on as the only method of confirming that the products were manufactured in conformance with Good Manufacturing Practices (GMPs).



The Agency's foreign inspection program is an important part of attaining confidence that all imported products meet the same standards as domestic goods.

How are we going to do this?

FDA will:

- Expand import coverage at ports of entry for all medical products to keep pace with the increase in imports; o Increase criminal investigation of fraudulent medical product imports;
- Increase sample analyses of imported animal feeds;
- Improve public confidence in the safety of foreign medical products by implementing the European Mutual Recognition Agreement;
- Modernize the OASIS import data processing system so import reviewers will have more rapid and direct access to information necessary for entry decisions;
- Increase the number of foreign inspections;
- Intensify drug inspections in developing countries; and
- Invest in training and time to ensure quality uniform inspections.

FDA continues efforts on the International Trade Data System (ITDS) initiative, intended to create an important electronic link to Customs, by which FDA can more effectively

and efficiently decide which import entries can proceed and those for which we want to take samples or other administrative actions. When fully implemented, ITDS will establish a standard data set and a "single window" clearance mechanism for cargo, conveyance and crew. ITDS will increase public health by improving compliance with regulatory requirements, reduce the cost and burden of processing international trade transactions, and provide access to accurate and timely statistical international trade data and information."

Consequences of Not Achieving the Goal

Inspections and import surveillance are the primary means of assuring the safety of marketed products. Consumers rely on the FDA to prevent dangerous and unreliable products from entering into commerce. Public safety and confidence could be jeopardized by a failure to increase surveillance activities.

Products may enter the U.S. through one of approximately 300 Customs ports located throughout the country. While the FDA continues to undertake initiatives to improve import coverage, there is no substitute for physically examining products.

FDA's inspection force is attempting to monitor a regulated industry in an environment that has changed rapidly and become significantly more complex over the past several years. Contributing to this change have been the growth in international trade leading to a tripling of imports during the past 10 years; much more technologically complex and diverse products both domestically and inter- nationally; and increasing use of the Internet by industry to develop, produce, distribute and market their products.

How are we doing?

Despite a decrease in the overall number of inspections, FDA's foreign inspection program continues to be one of the Agency's top priorities as more FDA regulated products originate from foreign sources. FDA conducted 880 foreign inspections in FY 2000, which represented a 12 percent increase over FY 1999. For FY 2001, approximately 1,100 foreign inspections are planned.

Imports of all FDA regulated products have been increasing over the last several years, however, FDA has only about 150 field investigators and inspectors assigned to import operations to review entry documents, determine product admissibility, collect samples, and conduct investigations. For FY 2000, FDA physically examined less than one percent of all entries offered for import into the United States.

1.2.1 Strategies

Biotechnology

Desired Outcome

Ensure the safety of food and feed, and safety and effectiveness of drug, device, and biological products that are derived from biotechnology.

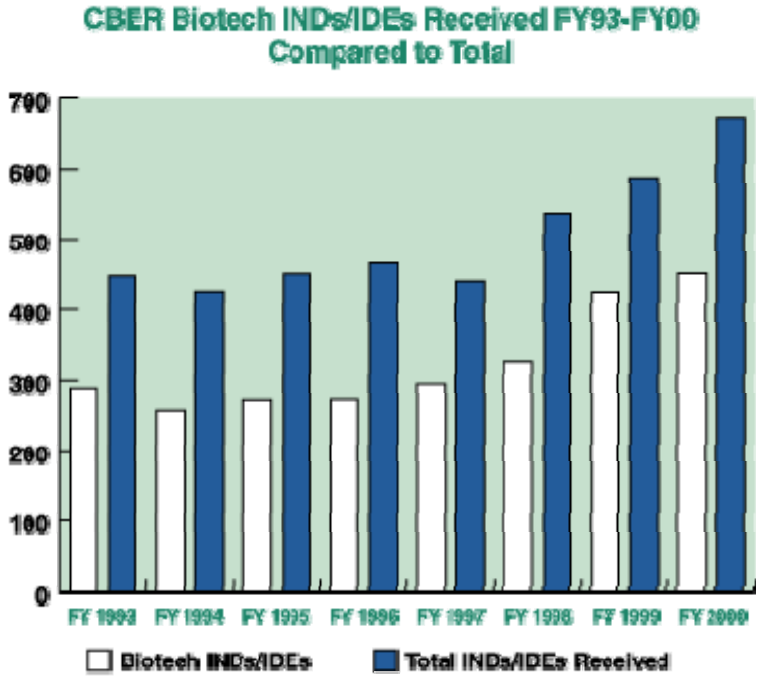
Key Performance Goal

Publish a final rule to require premarket notification for bioengineered foods.

Why is FDA's contribution important?

Biotechnology refers to the techniques that allow scientists to modify DNA, the genetic material of living things. From bioengineered corn, to drugs such as insulin, to gene therapy research, to diagnostic test kits, biotechnology is incorporated into almost all the product areas that FDA regulates.

The following chart shows the increase in biologic biotech IND's/IDE's received by FDA from 1993 - 2000.



While drugs and biologics produced using biotechnology have been widely accepted by the public, that has not been entirely true for foods from bioengineered plants. There are

also safety and ethical concerns regarding the use of cell and gene therapies. Without rigorous FDA oversight, the promises of gene therapy and biotech medicines will not be realized. Safety and effectiveness concerns may not be adequately addressed, and public confidence in bioengineered foods will not be assured.

How are we going to do this?

Foods: Currently, FDA has a voluntary process through which companies marketing bioengineered foods and feeds consult with the Agency on safety and other regulatory issues. However, FDA has recently proposed a regulation that will make this process mandatory. Companies will be required to notify the Agency at least 120 days before marketing a new bioengineered food or feed, and to provide the Agency with sufficient data and other information to establish that the food or feed is as safe as its conventionally-derived counterparts. The proposed rule, if finalized, will ensure that FDA has the appropriate amount of information about bioengineered foods to help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law.

FDA also recently issued draft guidance on the voluntary labeling of foods indicating whether they have or have not been developed through bioengineering. The guidance will aid manufacturers in ensuring that their labeling is truthful and not misleading.

Gene Therapy: From 1989 to 1993, FDA received 48 gene therapy investigational new drug applications (INDs). In contrast, FDA received 265 gene therapy INDs from 1994 through 2000. Additionally, there have been over 800 amendments (changes to the product or new protocols, etc.) to these INDs submitted since FY 97. The Agency has yet to receive the first application to license a gene therapy product.

FDA is continually evaluating its review and oversight processes and has taken numerous steps to ensure better patient protection, such as issuing a Dear Gene Therapy IND Sponsor/Principal Investigator Letter and conducting workshops for gene therapy sponsors, investigators, and monitors to make them aware of reporting requirements. The Agency also has provided additional substantive guidance and standards to facilitate preparation of INDs through educational outreach conferences, meetings, and policy development.

Also, FDA and NIH together are committed to establish a gene therapy database that will support collection of short-and long-term effects of gene-transfer products that can be analyzed for safety trends.

Devices: Industry is researching and developing many types of biotechnology devices, and FDA is responsible for reviewing these devices for safety and efficacy. Some exciting new technologies include:

- Nucleic acid amplification tests -- These tests allow small amounts of nucleic acid (DNA or RNA) from microorganisms or other sources to be amplified and easily

detected. This amplification process allows for very accurate and reliable detection of a wide variety of important pathogens such as TB, chlamydia, and others.

- Biosensors -- New systems are being developed using biosensors and near infrared technologies to allow for glucose measurements using noninvasive techniques. These devices will allow for less painful or painless collection of specimens for glucose measurements and will allow for increased frequency of testing. A major review challenge is properly assessing and labeling products to reflect the trade-off between performance and access to frequent painless procedures afforded by these devices.

Animal Drugs: Genetically engineered animals fall into two product categories: Bio-Pharm, used to produce products such as tissues for harvest and use as medical products, and Ag-Biotech, improving animal health or productivity. FDA has taken the position that these products and the animals producing them are subject to pre-market approval as new animal drugs. FDA expects to prepare guidance on this issue this year. In addition, the Agency is contracting with the National Academy of Sciences/National Research Council to examine risks and risk assessment methods for animal biotechnology products.

Consequences of Not Achieving the Goal

Biotechnology offers many benefits and for these to be realized, FDA must continue to keep pace with the explosive growth of new science. State-of-the-art scientific expertise is essential for FDA to determine the safety and efficacy of these biotechnological products. Without this expertise, public health could be compromised and public confidence in these products will erode.

How are we doing?

Foods: FDA believes no safety problem exists with any genetically engineered food or feed that is currently on the market. However, FDA has proposed requiring companies to provide the Agency with information prior to marketing foods and feeds because it expects that biotechnology methods likely will be used to an increasingly greater extent by plant breeders and that the products of this technology are likely in some cases to present more complex safety and regulatory issues than have been seen to date.

Approvals: FDA has approved about 130 drug and biologic biotechnology products since 1987, and has approved over 500 device biotechnology products in the last 10 years.

Vaccines: FDA conducts research to ensure the safety and efficacy of new technology-based products such as DNA plasmid vaccines. DNA vaccines have successfully prevented infection in a number of animal models, including flu, malaria, TB, herpes, anthrax, and others.

Gene Therapy: FDA has not yet approved any human gene therapy product for sale. However, FDA has received many requests from medical researchers and manufacturers to study gene therapy and to develop gene therapy products. Such research could lead to gene-based treatments for cancer, cystic fibrosis, heart disease, hemophilia, wounds, infectious diseases such as AIDS, and graft-versus-host disease.

1.2.1 Strategies

Dietary Supplements

Desired Outcome

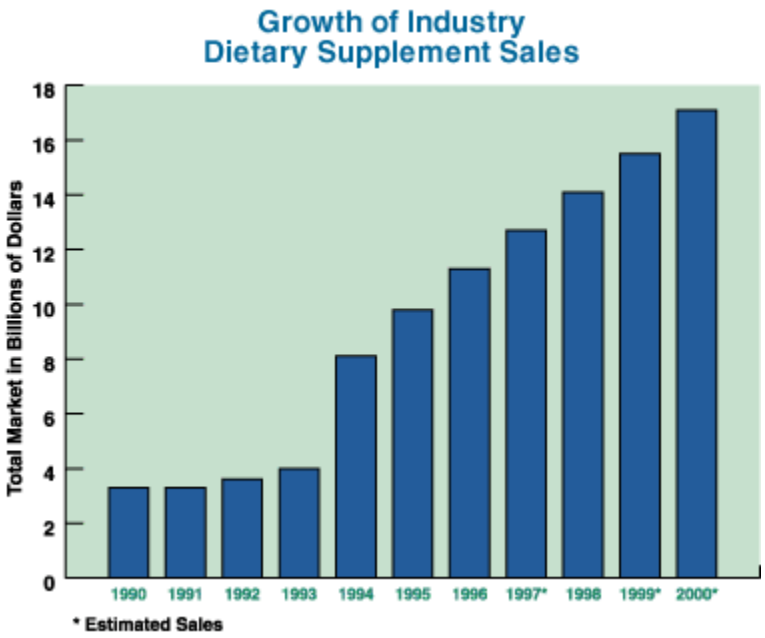
Provide consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products.

Key Performance Goal

Review 95 % of notifications for dietary supplements containing "new ingredients" within 75 days.

Why is FDA's contribution important?

Dietary supplements are estimated to be over a $17 billion a year business, and it's booming as consumers search for a fast fix - an easy way to feel better and stay healthy. The dietary supplement industry is one of the fastest growing industries in the world. Surveys show that over half of the US population now uses some type of dietary supplement and FDA estimates that the industry markets approximately 29,000 of these products which are sold under 75,000 distinct labels.



Just as consumption has grown, access also to dietary supplements has changed. In the past, except for vitamin and mineral products, dietary supplements were available mainly in health food stores and were principally marketed to adults. Now products are available through supermarket, other retail stores, mail order, TV programs, and via the Internet. This makes dietary supplements readily available to children and adolescents, as well as adults. This presents new regulatory challenges.

Dietary supplements include vitamins, minerals, herbs, and amino acids as well as substances such as enzymes, organ tissues, metabolites, extracts or concentrates. Dietary supplements can be found in many forms such as pills, tablets, capsules, liquids, or powders. They must be identified as a dietary supplements on the label.

Federal law requires manufacturers of dietary supplements to ensure that the products they put on the market are safe. Except for new dietary supplements, FDA review of supplement ingredients and products is not required before marketing. Under the 1994 Dietary Supplement Health and Education Act (DSHEA), once a dietary supplement is marketed, FDA has the responsibility for showing that the product is unsafe before it can take action to restrict the product's use.

The growing market for supplements, in a less restrictive regulatory environment, creates the potential for supplements to be prone to quality control problems. For example, FDA has identified several manufacturers who were buying herbs, plants and other ingredients without first adequately testing them to determine whether the product they received was what they ordered, and whether it was free from contaminants. FDA is working to provide a high level of confidence in the safety of dietary supplements.

How are we going to do this?

FDA must take a proactive approach in determining and monitoring the safety of dietary supplements, as opposed to merely reacting to crises. FDA has developed a Dietary Supplement Ten-Year Plan to position itself to respond to these challenges. The strategy can be accelerated or decelerated, depending on resource availability and safety concerns.

The dietary supplement industry is predicted to grow at a rate of 12 to 14 % annually. To keep pace, FDA must focus on the scientific review of new dietary supplement products. FDA must review within 75 days the petitioner notification on any new ingredient that will be part of a dietary supplement. Dietary supplement manufacturers that wish to market a new ingredient that was not marketed in the U.S. before 1994 have two options. The first involves submitting to FDA at least 75 days before the product is expected to go on the market, information that supports their conclusion that a new ingredient can reasonably be expected to be safe. - Another option is to petition FDA to establish conditions under which the new dietary ingredient would reasonably be expected to be safe.

DSHEA gives FDA the authority to establish good manufacturing practices (GMPs) regulations governing the preparation, packing, and holding of dietary supplements under conditions that ensure their safety.

FDA oversees safety, manufacturing, and product information, such as claims in a products labeling, package inserts, and accompanying literature. To protect the public health, FDA must have a strong system to monitor products once they are on the market and in daily use.

Consequences of Not Achieving the Goal

While there are some likely benefits from the use of some of dietary supplement products, without a visible FDA regulatory presence, the potential for exaggerated claims, unpredictable composition, and toxicity are of considerable concern. There is also a real and growing concern about interactions between dietary supplements and over-the-counter and prescription medications.

FDA anticipates that notifications for dietary supplements containing "new ingredients" will become increasingly more complex, and that the volume of such notifications submitted to FDA will increase.

The passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA) greatly expanded the marketing opportunities for dietary supplements. Subsequent to enactment, the marketplace has grown significantly.

To effectively regulate this marketplace FDA needs: (1) to address the large number of safety and quality issues presented by the large increase in the numbers and variety of products in the marketplace; (2) an effective Adverse Event Reporting System to enable

all adverse event reports to be evaluated in a timely fashion; (3) effective inspectional oversight of domestic manufacturers and imported products; and (4) to take effective enforcement action against adulterated and/or misbranded products.

When Congress passed DSHEA, it created a regulatory framework for dietary supplements that previously did not exist. The purpose of the framework was to strike the right balance between providing consumers access to both products and truthful information about the products while retaining authority for FDA to take actions against products that present safety problems or are improperly labeled. We are now being engaged in the difficult task of delineating boundaries between drugs, dietary supplements, and conventional foods. The definition of supplement is broad, but it must not allow the inclusion of ingredients never intended to fit within the universe of dietary supplements. Now, products that contain substances similar to those found in prescription drugs are marketed for children as dietary supplements. Likewise, products with ingredients that simulate illicit street drugs are marketed as dietary supplements to adolescents via the Internet and shops specializing in drug paraphernalia. FDA is working toward a solution that will be consistent with the intent of DSHEA.

How are we doing?

Since FY 1998, FDA has exceeded its dietary supplement premarket performance goal by reviewing 100% of all notifications for dietary supplements containing "new ingredients" within 75 days.

1.2.2 Program Overview

FDA organizes its resources 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. The Tobacco program ended abruptly in FY 2000 when the United States Supreme Court affirmed that FDA lacks jurisdiction to regulate tobacco products.

- **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 standards and improve risk assessment for regulatory applications.
- **Tobacco** -- The Tobacco program worked to reduce young people's use of tobacco through education, enforcement, and partnerships with CDC and other Federal and state health agencies. On August 23, 1996 FDA issued its final regulation on tobacco products. From February 28, 1997 until March 21, 2000, when the Supreme Court ruled, ending the program, FDA enforced the age and photo identification restrictions of the rule. During this time, FDA contracted with all 50 states to conduct nearly 200,000 compliance checks of retailers.

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 two years, 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 2002 Performance Plan. Examples of these initiatives are described in the following paragraphs.

Collaborative Institutes:

FDA is proposing in FY 2002 to establish a manufacturer college that will feature collaborations with industry to improve the medical device review process; and a virtual corporate university in cooperation with academic institutions to augment the Agency's scientific and technological expertise, also associated with medical devices. Both of these new institutional arrangements should enable FDA to realize scientific and regulatory synergies that could not be accomplished by the Agency and its stakeholder working independently.

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 Center for Food Safety and Technology in conjunction with the University of Illinois.

Risk Management Communication and Education:

About half of the patients who fill the nearly 3 billion prescriptions from their doctors each year don't take the medicine as prescribed which can lead to serious health consequences. Under it's Take Time To Care program, FDA has partnered with the National Association of Chain Drugstores and 80 national organizations to distribute millions of copies of the brochure My Medicines to women to educate themselves and their families about using medicines wisely. The brochure delivers four key messages: read the label, avoid problems, ask questions, and keep a record.

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.

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 2002 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.

The **National Antimicrobial Resistance Monitoring System** will also be strengthened in 2002. 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. To illustrate, FDA is recognizing an increasing number of international standards as a way to satisfy part of our 510(k) requirements (medical device approvals).

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.

One example of successful third party inspections is the Mammography program. Over 90% of inspections of mammography facilities are conducted by states under contract to FDA. Another example is the expansion of third party reviews of medical devices. FDA has developed a third party review program and is expanding the number and types of devices that are eligible for third party review.

Part 2: Performance Plan and Report

Introduction

Part Two of the Performance Plan presents FY 2002 performance goals and the final FY 2001 performance goals for each of FDA's programs, the performance report for FY 2000 goals, and an update on performance for some FY 1999 goals.

In this section of the Plan, readers will be able to obtain greater detail to support their understanding of the key Performance goals described in Part One.

Each program section includes the following information:

- Total program funding
- A broad description of program activities
- Strategic goals
- Approaches for achieving goals
- A performance goal summary table; and
- A goal-by-goal explanation including some updated FY 1999 results.
- A verification and validation section which addresses sources and quality of data used in the plan.

The following programs will be covered:

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

- Tobacco -- The Tobacco program worked to reduce young people's use of tobacco through education, enforcement, and partnerships with CDC and other Federal and state health agencies. On August 23, 1996 FDA issued its final regulation on tobacco products. From February 28, 1997 until March 21, 2000, when the Supreme Court ruled, ending the program, FDA enforced the age and photo identification restrictions of the rule. During this time, FDA contracted with all 50 states to conduct nearly 200,000 compliance checks of retailers.

2.1 FOODS

2.1.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 02 Budget Estimate	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**319,505**	**284,641**	**279,704**	**235,168**

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; 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.

On January 3, 2000, CFSAN set forth its overall dietary supplement strategy. This strategy is built on the foundation of law and science. This strategy establishes a clear program goal to accomplish, by the year 2010, having a science-based regulatory program that fully implements the Dietary Supplement Health and Education Act of 1994, thereby providing consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products.

FDA will continue to seek additional resources for initiatives identified in this plan through the established budget process. The success of this strategy will not only depend on adequate funding levels, but also on FDA's new and continued partnerships with other governmental agencies, academia, health professionals, industry, and consumers. FDA will continue its outreach to stakeholders to enhance two-way dialogue, establish stronger working relationships, leverage resources, and communicate dietary supplement information. On July 6, 2000, FDA issued an import alert for bulk or finished dietary supplements and other products that may contain aristolochic acid. Aristolochic acid is a potent carcinogen and nephrotoxin. Products containing aristolochic acid cause renal damage and can cause or contribute to renal failure. Its nephrotoxic potential has been shown in animals and has been demonstrated in humans in both case reports and in at least one human clinical study. Products that contain a large amount of aristolochic acid have been documented to result in the rapid onset of acute toxicity symptoms. Outbreaks of aristolochic acid-associated renal failure have been reported in several countries, including Belgium, France, Spain, Japan, Australia, and the United Kingdom. Recent chemical analysis of currently marketed Chinese herbal medicines and dietary supplements by British and Canadian health authorities identified products that contained aristolochic acid. However, the labels of the products did not indicate that they contained an ingredient known to contain aristolochic acid. This indicates that there is a potential for dietary supplements and some traditional herbal medicines to inadvertently be formulated using aristolochic-acid containing ingredients. FDA is aware that these and similar products are being sold in the United States.

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, bioengineered foods, and dietary supplements, while assuring their safety.**
- **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, bioengineered foods, 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.

2.1.2 Strategic Goals

Strategic Goal 1:
Provide consumers quicker access to new food ingredients, bioengineered foods, and dietary supplements, while assuring their safety.

A. Strategic Goal Explanation

The Foods premarket review program focuses on food and color additive petitions, dietary supplements, substances that are generally recognized as safe (GRAS), and bioengineered foods. Under the FD&C Act, FDA must review the safety of food and color additives before food manufacturers and distributors can market them. To initiate this review, sponsors are required to submit a petition or notification 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 a notification program for substances that are GRAS. Finally, the Agency consults with developers of foods derived from bioengineered plants to ensure that all safety and regulatory questions are resolved prior to marketing, and has proposed a mandatory premarket notification program for these foods.

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)
- Respond to dietary supplement notifications within 75 days (Performance Goal 3-11025) … Give priority to those additives that are intended to decrease the incidence of foodborne illness
- Improve management systems
- Recruit and hire reviewer-scientists (including professionals with the special skills to evaluate dietary supplements and food and color additives, such as medical doctors, consumer safety officers, chemists, botanists, herbalists and toxicologists)

- Conduct specific research to develop science-based policies for effective regulation and effectively communicate any risks associated with bioengineered foods
- Use contract personnel for some petition reviews

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Complete first action on 65% of food and color additive petitions within 360 days of receipt. (11001)	FY 02: 65%	FY 02:	1999 Update
	FY 01: 50%	FY 01:	
	FY 00: 40%	FY 00:10/01	
	FY 99: 30%	FY 99: 77%	
2. Reduce the number of remaining overdue food and color additive petitions. (11002)	FY 02: 50%	FY 02:	
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
	FY 99: 30%	FY 99: 42%	
3. Respond to 95% of notifications for dietary supplements containing "new dietary ingredients" within 75 days. (11025)	FY 02: 95% FY 01: 90% FY 00: 90% FY 99: NA	FY 02: FY 01: FY 00:100% FY 99:100% FY 98:100%	
4. Complete processing of 85% of GRAS notifications within the time frame established by the final rule. (11003)	FY 02: 85%	FY 02:	1999 Update
	FY 01: 80%	FY 01:	
	FY 00: Finalize GRAS Rule late in year or early 01	FY 00: made progress toward finalizing GRAS rule	

	FY 99: Finalize the rulemaking creating a premarket notification process for independent GRAS determinations.	FY 99: rule not completed, no measurement	
5. Complete review of 100% of premarket notifications for food contact substances within 120 days. (11034)	FY 02: 100%	FY 02:	
	FY 01: NA	FY 01: Issued proposed rule	
	FY 00: NA	FY 00: 99%	
6. Publish a final rule to require premarket notification for bioengineered foods.	FY 02: Issue final rule	FY 02:	
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
TOTAL FUNDING: ($000)	FY 02: 44,720		
	FY 01: 39,850		
	FY 00: 39,661		
	FY 99: 25,196		

C. Goal-by-Goal Presentation of Performance

1. Complete first action on 65% 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 02; 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 a notification process for food contact substances. The premarket notification program began to fully operate on January 18, 2000. Several factors will influence future performance on the goal of completing first action on 65% of food and color additive petitions within 360 days. The most important of these factors is the implementation of the new premarket notification process. By FY 01, 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. Similarly, the premarket notification program may also initially increase the fraction of pending petitions that are overdue because many recently submitted petitions for food contact substances will have been converted to notifications. 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 beginning in FY 02.

- **Data Sources:** CFSAN's electronic workflow system
- **Performance:** The data for FY 00 will be available October 2001. In FY 99, FDA exceeded its goal of completing the review of 30% , respectively, of food and color additive petitions within 360 days. Continued progress to full performance on this goal is dependent on the continued provision of adequate resources to the food and color additive review program. With the continued provision of necessary resources, the Agency can continuously improve performance in the review of food and color additive petitions by gradually hiring and training highly qualified personnel. In addition, FDA will complete testing and initiate the operation of a document tracking and workflow system that will track progress toward full performance and provide detailed information on the status of petitions and FDA tasks to be completed.

2. Reduce the number of remaining overdue food and color additive petitions by 50%. (11002)

- **Context of Goal:** This goal has been revised since FY 99. 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. In the past, 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%. This goal was not met in part because of the significant gains in timeliness of review of recently submitted petitions (see goal 1), so that action was completed on many petitions that were not overdue. To continue its progress on reducing the percentage of overdue petitions under active review, in FY 00 the Agency focused on those petitions that are most overdue (four years).

  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. More than 50 product sponsors have already converted 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 targets for FY 00 and FY 01 similar to the one set in FY 99; rather, as noted above, we are focussing on clearing the oldest petitions in the inventory. As the notification program is fully implemented, we expect that many of the simpler food additive petitions that were previously often 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 implementation of the premarket notification program may also increase the initially increase the percentage 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:** As noted above, in FY 00, the Agency focussed on reducing the number of petitions that were overdue by more than four years. These petitions

often present particularly problematic issues for the Agency. In FY 00, we completed action on 11 of 25 such petitions. Also, during FY00, we reduced the total number of food and color additive petitions in the inventory from 147 to 66.

3. Respond to 95% of notifications for dietary supplements containing "new dietary ingredients" within 75 days. (11025)

- **Context of Goal:** Within 75 days, FDA reviews notifications for new dietary ingredients that will be part of dietary supplements. 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 95% target is considered full performance in FY 02.
- **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". In FY 99 FDA received and responded to 100%. In FY 00, FDA received and responded to 24 notifications for new dietary ingredients.

4. Complete processing of 85% 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 01. 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 00, FDA made substantial progress toward the goal of publishing a final rule for this program. However, due to resource restraints and competing priorities the rule was not finalized.

5. Complete review of 100% of premarket notifications for food contact substances within 120 days. (11034)

- **Context of Goal:** As provided in the Food and Drug Administration Modernization Act (FDAMA), the Agency was mandated to establish a premarket notification program for food contact substances as a vehicle to re-inventing the premarket review process for food and color additives. The Congress appropriated resources in FY 2000 to fully fund this Program, and the first notifications became effective in March 2000. The statute provides that a food contact substance notification shall become effective (i.e., the food contact substance may be lawfully marketed) 120 days after receipt unless the agency objects that the use of the food contact substance has not been shown to be safe. Thus, to ensure that unsafe food contact substances do not enter the marketplace, the program goal is to review all notifications within 120 days. Doing this will require that adequate resources continue to be provided for this program.
- **Data Sources:** CFSAN's electronic workflow system; Internal Office of Pre-Market Approval database.
- **Performance:** In FY 00, the Agency completed review of 82 of 83 notifications for food contact substances within 120 days.

6. Publish a final rule to require premarket notification for bioengineered foods.

- **Context of Goal:** Currently, FDA has a voluntary process through which companies marketing bioengineered foods consult with the Agency on safety and other regulatory issues. FDA believes no safety problem exists with any genetically engineered food that is currently on the market. However, as part of a government-wide initiative to strengthen science-based regulation and improve public access to information about bioengineered foods, FDA has proposed a regulation that, if finalized, would require developers of bioengineered foods to notify the agency 120 days prior to marketing a new bioengineered food (66 FR 4706; January 18, 2001). As part of the proposed rule, FDA would make available, through an Internet-based electronic reading room, the information provided by the developer to FDA. FDA also would update its food biotechnology Internet site to make more information available to the public, including FDA's memoranda of evaluation and letters to sponsors of bioengineered foods. FDA took this action because it expects that biotechnology methods are likely to be used to an increasingly greater extent by plant breeders, and because it expects that the products of this technology are likely in some cases to present more complex safety and regulatory issues than has been seen to date.
- **Data Sources:** Federal Register; FDA's Internet site
- **Performance:** FDA already has issued a proposed rule to require premarket notification for bioengineered foods. The proposed rule, if finalized, will ensure that FDA has the appropriate amount of information about bioengineered foods to help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law. The proposed action will permit

the agency to assess on an ongoing basis whether plant-derived bioengineered foods comply with the standards of the Federal Food, Drug, and Cosmetic Act. FDA also has already updated its Internet site to provide more information about bioengineered foods that the agency has evaluated under the current, voluntary process. At the halfway point in the comment period, FDA had received more than 1000 comments on the proposed rule. In order to complete the goal, FDA must analyze the comments and determine whether the complete administrative record of the rulemaking (including the comments) supports the requirement as proposed. If the complete administrative record supports the issuance of a final rule, FDA intends to issue a final rule by the end of FY 2002.

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

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 01, 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

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
7. Achieve adoption of the Food Code by at least one state agency in 28 states in the USA. (11010)	FY 02: 28	FY02:	
	FY 01: 25	FY 01:	
	FY 00: 18	FY 00: 20	
	FY 99: 13	FY 99: 15	
		FY 98: 10	
		FY 97: 3	
8. 50% of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning HACCP systems. (11004)	FY 02: NA	FY 02: NA	1999 Update
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
	FY 99: 50%	FY 99: 56%	
9. Increase the percentage of high-risk domestic food	FY 02: at least 95% once every year	FY 02:	

establishment inspected once every year. (11020)	FY 01: at least 90% once every year	FY 01:	
	FY 00: 90 - 100% Once every one to two years	FY 00: 91%	
	FY 99: NA	FY 99: NA	
10. Assure that FDA inspections of domestic food establishments result in a high rate of conformance (at least 90%) with FDA requirements. (11011)	FY 02: at least 90%	FY 02:	
	FY 01: at least 90%	FY 01:	
	FY 00: 90-100%	FY 00: 97%	
	FY 99: 90-100%	FY 99: 98%	
		FY 98: 98%	
		FY 97: 98%	
11. Increase the number of import exams of food products. (11021.02)	FY 02: 60,000	FY 02:	
	FY 01: 60,000	FY 01:	
	FY 00: 60,600	FY 00: 56,300	
	FY 99: NA	FY 99: NA	
12. 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 02: 10	FY 02:	
	FY 01: 10	FY 01:	
	FY 00: NA	FY 00: NA	
	FY 99: NA	FY 99: 4	
		FY 98: 2	
13. Maintain current level of monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 8,000 samples. (11027)	FY 02: 8,000 +	FY 02:	
	FY 01: 8,000 +	FY 01:	
	FY 00: NA	FY 00: NA	
	FY 99: NA	FY 99: 9,400 total pesticide and chemical contaminant samples: 3,400 domestic and 6,000 imports.	
		FY 98: 8,500 total pesticide and chemical contaminant samples: 3,600 domestic and 4,900 imports.	

TOTAL FUNDING: ($000)	FY 02: 274,785		
	FY 01: 244,791		
	FY 00: 240,044		
	FY 99: 209,972		

C. Goal-by-Goal Presentation of Performance

7. Achieve adoption of the Food Code by at least one state agency in 28 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 adopted the Food Code. State agencies achieving adoption of the Food Code were: Minnesota, Rhode Island, New Hampshire, Missouri, North Dakota, South Dakota, Nebraska, Mississippi, Texas, Florida, Kansas, Florida, Utah, Arizona and Iowa. In FY 00, agencies in 20 states have adopted the Food Code. This exceeds FDA's goal of 18 states adopting the Code.

8. 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:** There were approximately 3600 domestic seafood processors in the first round of inspections. In FY 99, 56% of these processors met all the criteria for operating a functioning HACCP system. A recent GAO report indicated that there were fewer than 50% of these processors that had fully developed HACCP plans. The reason for a lower figure for plans than for complete systems is because a significant percentage of processors did not need plans as part of their HACCP systems. 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 or to prevent microbial contamination of seafood produced in the United States. As a consequence, in FY 00, this goal was combined with the performance goal that relates to conformance rates resulting from the inspection of domestic food establishments (Performance Goal 10).

9. 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 defined high-risk establishments as those producing foods with the greatest risk for microbial contamination and those foods requiring specific components for a safe and nutritious product. Foods following under this definition were infant formula, medical foods, scrombotoxic seafood, molluscan shellfish, low acid canned and acidified foods, ready to eat foods such as processed fresh fruits and vegetables, bakery goods (with filling), soft and soft ripened cheeses, cooked pasta dishes, prepared salads and heat and serve products. Based on this definition, the Agency estimates that there are approximately 7,000 such establishments in its establishment inventory. In FY 01, the number of high-risk establishment inspections conducted annually will be increased to include coverage of the entire inventory. 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. In FY 02, the entire high-risk

establishment inventory is expected to increase and thus the target for FY02 has been changed from 90 -100% to at least 95%, to anticipate the level of increase in the number of high-risk establishment inspections.
- **Data Sources:** Field Data Systems
- **Performance:** In FY 00, the number of high-risk food inspections was approximately 5700.

10. 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 to prevent microbial contamination of seafood produced in the United States. As a consequence, in FY 00, the performance goal relating to conformance of the domestic seafood industry with HACCP (Performance Goal 8) was combined with the performance goal for that relates to conformance rates resulting from the inspection of domestic food establishments (Performance Goal 10)
- **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. FDA inspections of domestic food establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, resulted in a 97% rate of conformance in FY00.

11. Increase the number of import exams of 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:** There were 56,300 import exams of products conducted in FY00.

12. 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.

13. Maintain current level of monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 8,000 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 8,500 pesticide and contaminant samples. These samples included 3,600 domestic and 4,900 imports. In FY 99, the Agency analyzed a total of 9,400 pesticide and contaminant samples. These samples included 3,400 domestic and 6,000 imports. In FY 01, FDA expects to analyze 8,000 plus. 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 was a new commitment in FY 01.

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 FDA or states conduct the inspections. 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 01, the Agency will begin improving the quality and accessibility of data on adverse events through the development and implementation of a new adverse event reporting system for dietary supplements. In FY 02, the Agency will build upon the system nodule for dietary supplements by developing and implementing an integrated adverse reporting system for all food and cosmetic products.

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 FY 00, the Center formed a research management task group responsible for evaluating related processes and systems and developing recommendations for improvement. 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.

In FY 99, the Center began implementation of its Resource Planning, Prioritization, and Allocation Process. The primary purpose of this Process is to provide pertinent data throughout the fiscal year on program activities, including GPRA performance goals, Center program priorities, Congressional directives, statutory responsibilities under FDAMA, and Food Safety Initiative objectives.

2.2 HUMAN DRUGS

2.2.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 02 Budget Estimate	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**347,829**	**317,066**	**311,234**	**278,299**

The Human Drugs Program assures that all drug products used for the prevention, diagnosis, and treatment of disease are safe and effective. Premarket review is accomplished through prompt and efficient review of clinical research and by taking appropriate and timely action to review new drugs and their generic equivalents, over-the-counter (OTC) drugs and labeling, and through quality assurance/quality control. Once drugs have been approved, they may be marketed and distributed for use. At that time, postmarket surveillance assures the quality of drugs on the market and the minimization of adverse events associated with the use of prescription and OTC medications. To meet these goals, FDA frequently consults with experts in science, medicine and public health and 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.**

This performance plan illustrates the Agency's ongoing efforts and continuing progress in achieving it's mission, which will result in maximizing the pharmaceutical industry's ability to provide the safe and effective medications that will continue to improve the public health. Premarket performance goals include those in the areas of: testing investigational new drugs (INDs), evaluating new drug applications (NDAs); reviewing and taking action on efficacy supplements, manufacturing supplements and generic drug application review; reviewing and labeling for OTC drugs; and reviewing requests from industry for manufacturers who conduct pediatric studies. Postmarket surveillance performance goals include: assessing risk to identify adverse events; and expanding scientific capabilities to respond and contribute to major breakthroughs in pharmaceutical research and technology via research, continuing professional development and training, and continued collaborations with stakeholders.

FY 2000 Performance Highlights

Drug Approvals

- **New Drugs**-- FDA continues to exceed the rigorous performance goals agreed to for each consecutive year under the PDUFA. FocalSeal-L Surgical Sealant was approved as a surgical sealant for use in lungs to seal air leaks following removal of cancerous lung tumors. Betaxon was approved for lowering intraocular pressure in patients with chronic open-angle glaucoma or ocular hypertension. Also approved is the drug Kaletra, which is one of a class of AIDS drugs called protease inhibitors for use by adults and by HIV infected infants and children who are older than six months.
- **Generic Drug Review**--In 2000, FDA approved Taxol, a drug that is used for the firstline treatment of advanced carcinoma of the ovary and non-small cell lung cancer in patients who are not candidates for potentially curative surgery and/or radiation therapy. Taxol is indicated in combination with cisplatin.

Postmarket Surveillance--In calendar year 2000, 261,000 individual safety reports (ISRs) were received for entry into the Adverse Event Reporting System (AERS). FDA uses these reports as part of the postmarket surveillance to identify any unexpected, rare or serious events.

Outreach-- FDA is committed to providing the public quicker access to drug information. It has developed several new web sites, such as the Consumer Drug Information web site and the FDA Oncology Tools web site. The Agency has also completed a campaign designed to increase consumer awareness about the problems related to online drug purchases by developing a brochure and newspaper article describing the potential dangers of buying medical products on the Internet. In addition, the Agency has completed the first phase of a new Over-the-Counter Medicine Label Campaign by placing 245 newspaper articles in 45 states reaching more than 17 million people and by reaching an additional 137 million with radio PSA.

Leveraging/Communication--The Agency continues to conduct expeditious drug reviews and provide information by collaborating and cooperating with industry, health care organizations and academia. A web site called ACTIS (www.actis.org) was developed as a resource to provide current information on federally and privately funded clinical trials for AIDS patients. This service is provided collaboratively by the National Institute of Allergy and Infectious Diseases, Food and Drug Administration, National Library of Medicine and the Center for Disease Control.

Reinvention--The Agency is dedicated to developing new standards and guidances that will establish explicit training requirements for staff reviewers such as the Good Review Practice (GRP) guidance. FDA is also in the process of creating a clinical review documentto assess whether an application meets established standards for the clinical portion of a submission.

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 the key performance goals that will move the Program in these directions, are outlined in the next sections.

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

Improving the efficiency and quality of the application review process will assure that safe and effective drugs are available to the American people. Third party outsourcing of application parts, stronger quality assurance and quality control monitoring, more timely inspections, and greater utilization of external expertise such as industry, academia and professional associations will result in significant payoffs. Payoffs to the American people include reduced drug development time, increased and quicker access to new drug products, and an increased number of therapeutic options for health professionals to choose from. Improving product review will also advance the safe and appropriate use of medicines in children. FDA is authorized to grant six months of marketing exclusivity to manufacturers who conduct and file pediatric studies in new or approved drugs. Since 1998 FDA has reviewed over 210 Proposed Pediatric Study Requests (PPSR), issued over 185 Written Requests (WR) asking for over 407 studies to be conducted in the pediatric population and has granted exclusivity to 27 products. Fourteen of the 27 products granted exclusivity now have approved labeling that incorporates information from the pediatric studies. Important information regarding dose and adverse events in pediatric patients has been obtained. Developing a hospital-based

pediatric drug use and adverse event reporting system, hiring additional pediatric reviewers, and increased interaction and leveraging with the scientific and academic communities and researchers will facilitate the advancement of pediatric medicine. Goals 12026 and 12001 will support efforts to achieve this strategic goal.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Review and act on 90% of standard original NDA submissions within 10 months of receipt and 90% of priority original NDA submissions within 6 months. (12001)	Standard NDAs within 10 months: FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30%	FY 02: FY 01: 01/03 FY 00: 01/02 FY 99: 66%	1999 Update
	Standard NDAs within 12 months: FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90%	FY 02: FY 01: 01/03 FY 00: 01/02 FY 99: 100% FY 98: 100%	
	Priority NDAs within 6 months: FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	FY 02: FY 01: 7/02 FY 00 7/01 FY 99: 100% FY 98: 100%	
2. Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule. (12026)	FY 02: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	FY 02:	
	FY 01: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	FY 01: (1st 4 months) **Exclusivity:** - 19 PPSR's reviewed - 28 WR's issued - 14 Amended WRs issued - 4 Exclusivity	

		determinations - 2 Exclusivities granted - 3 Labels changed **Ped Rule:** - PediatricAssessments Deferred = 3	
	FY 00: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	FY 00: **Exclusivity:** - 39 PPSR's reviewed - 62 WR's issued - 59 Amended WR's issued - 19 Exclusivity determinations - 16 Exclusivities granted - 7 Labels changed **Ped Rule:** - Pediatric Assessments Deferred = 76 - Pediatric Assessments Waived = 91	
	FY 99: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	FY 99: **Exclusivity:** - 155 PPSR's reviewed - 95 WR's issued - 15 Amended WR's issued - 9 Exclusivity determinations - 9 Exclusivities granted - 4 Labels changed	
3. Review and act upon fileable original generic drug applications within 6 months after submission date. (12003)	FY 02: 55%	FY 02: Final data avail. 4/03	1999 Update
	FY 01: 50%	FY 01:Final data avail. 4/02	
	FY 00: 45%	FY 00: 42% as of 2/01. Expect final	

		data 4/01	
	FY 99: 60%	FY 99: 28%	
4. Review and act on 90% of resubmitted NDA applications within 6 months of receipt. (12002)	FY 02: NA	FY 02: NA	1999 Update
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
	FY 99: 90%	FY 99: 100%	
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 02: NA	FY 02: NA	1999 Update
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
	FY 99: 90% within 12 mos 30% within 10 mos priority within 6 mos	FY 99: 87% (priority efficacy supplements) 99% (standard efficacy supplements)	
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 02: NA	FY 02: NA	1999 Update
	FY 01: NA	FY 01: NA	
	FY 00: NA	FY 00: NA	
	FY 99: 90% within 6 mos. 30% within 4 mos.	FY 99: 99% within 6 mos. 73% of supplements requiring prior approval within 4 mos.	
7. Protect human research subjects participation in drug studies and assess the quality of data from these studies by conducting approximately 780 onsite inspections and data audits annually. (12032)	FY 02: 780	FY 02: 1/31/03	
	FY 01: NA	FY 01:	
	FY 00: NA	FY 00: 697 inspections completed FY 99: 683 inspections completed	
	FY 99: NA Note: The number of inspections completed each year is dependent on the number of applications received,		

	has averaged approximately 100-120 per year.		
TOTAL FUNDING: ($000)	FY02: 260,872		
	FY01: 254,593		
	FY00: 233,425		
	FY99: 208,724		

C. Goal-by-Goal Presentation of Performance

1. Review and act on 90% of standard original NDA submissions within 10 months of receipt 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. Emphasis is put 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 Sources and Issues:** Center-wide Oracle Management Information System (COMIS); New Drug Evaluation/Management Information System (NDE/MIS): FDA has a quality control process in place to ensure the reliability of the performance data in COMIS. This process provides information on how document room contractors and the Records Management Team quality control this data. See 2.2.3 Verification and Validation Section for a description of this process.
- **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 open cohorts during FY 99, FDA took 185 actions on NDAs, 77 of which were approvals. Final on-time performance information for the FY 2000 submission cohort is not yet available.

Fiscal Year 1999 Cohort as of 12/31/00

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Priority New Drug	31	90% in 6	31	100%

Application		months		
Standard New Drug Application	95	30% in 10 months	63	66%
		90% in 12 months	95	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 Sources and Issues:** Pediatric Exclusivity Database and the Pediatric Page database. (Database enhancements required to meet goal):

  The Pediatric Exclusivity Database tracks all data regarding pediatric exclusivity as mandated by FDAMA. Specifically, this database tracks the number of Written Requests issued and the number of products for which pediatric studies have been submitted and for which exclusivity determinations have been made.

- **Performance:** 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. Since 1998 FDA has reviewed over 210 Proposed Pediatric Study Requests (PPSR), issued over 185 Written Requests (WR) asking for over 407 studies to be conducted in the pediatric population and has granted exclusivity to 27 products. Fourteen of the 27 products granted exclusivity now have approved labeling that incorporates information from the pediatric studies. Important information regarding dose and adverse events in pediatric patients has been obtained.

The fourth Pediatric Advisory Subcommittee is being planned for April 2001 to discuss issues in pediatric drug development. The Report to Congress mandated by FDAMA was prepared during 2000 and sent to Congress on January 9, 2001. FDA developed an interactive pediatric web page to provide detailed information to the public regarding FDA's pediatric initiatives.

In October 2000, the Children's Health Act was signed into law. As required, the Agency has drafted an interim final rule incorporating Subpart D of the DHHS regulations into FDA regulations. The document is currently with OMB for clearance.

FDA completed 2 pilot studies to evaluate inpatient databases to assist in our assessment of needed pediatric trials. Using information garnered from these pilots FDA has defined the criteria necessary for development of a pediatric inpatient database.

3. Review and act upon 55% 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 Sources and Issues:** COMIS; NDE/MIS: FDA has a quality control process in place to ensure the reliability of the performance data in COMIS. This process provides information on how document room contractors and the Records Management Team quality control this data. See 2.2.3 Verification and Validation Section for a description of this process.
- **Performance:** Preliminary data indicate CDER may meet its goal for FY 2000. In the six months from November 1999 to April 2000, CDER's Office of Generic Drugs (OGD) acted on 47 percent of original applications. This is an increase from the 31 percent acted on during the previous six months.

  During FY 2000, OGD approved 232 ANDAs. This is an increase over the 198 approved last fiscal year. Of these, several represent the first time a generic has been approved for a product.

Significant strides were made toward a paperless review environment. With $1.5 million in funding earmarked for satisfying information technology needs, CDER purchased upgraded hardware and software, and contractual support for the review of electronic submissions. CDER received 101 ANDAs containing at least a portion of the data in electronic format (30 percent of all submissions). This is an increase over the 88 ANDAs with some portion in electronic format submitted last fiscal year. The increase reflects the commitment of OGD to support the Agency's efforts to increase overall efficiency of the review process.

FDA did not meet its expected performance goal (to act upon 60% of original generic drug applications within 6 months) in FY 99. In FY 99, FDA acted on 28% of fileable original applications within 6 months. 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 did not stop the review of ANDAs and the subsequent amendments/responses were the reviewers' highest priority. This procedure resulted in review times exceeding 6 months, but shortened overall approval times. For example, although FDA did not act on 60% of the original ANDAs in 6 months, the facsimile amendment procedure allowed for approval of 75% of the ANDAs in about 8 months. In June 2000, a slight modification to the facsimile amendment procedure was made that would stop/start the review clock upon issuance of a fax deficiency/amendment. This modification to the procedure will better enable FDA to act upon its target percentage of ANDAs within 6 months.

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 these changes in place, the initial performance is expected to decrease due to training of new team leaders and reviewers. As the new personnel become more experienced, the review process is expected to run more efficiently and the backlog is expected to decrease (given a constant number of receipts). FDA expects performance to be 45% by the end of FY 00, 50% by completion of FY 01 and 55% by the end of FY 02.

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 and Issues:** COMIS; NDE/MIS: FDA has a quality control process in place to ensure the reliability of the performance data in COMIS. This process provides information on how document room contractors and the Records Management Team quality control this data. See 2.2.3 Verification and Validation Section for a description of this process.
- **Performance:** FDA exceeded this goal in FY99. For the FY 99 submission cohort, 64 resubmissions were submitted for review. This FY 99 goal is included for reporting purposes. For purposes of the Performance Plan, this goal has been dropped for FY 00, FY 01 and FY 02.

Fiscal Year 1999 Cohort as of 5/31/00

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Class 1 Resubmission	17	50% in 2 months	17	100%
		90% in 4 months	17	100%
Class 2 Resubmission	47	90% in 6 months	47	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 and Issues:** COMIS; NDE/MIS: FDA has a quality control process in place to ensure the reliability of the performance data in COMIS. This process provides information on how document room contractors and the Records Management Team quality control this data. See 2.2.3 Verification and Validation Section for a description of this process.
- **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. The Standard Efficacy Supplement portion of this goal was met for FY 99. However, of the 15 priority efficacy supplements 13 were reviewed, resulting in only 87% of the 90% goal was met. For the FY 99 submission cohort, 138 efficacy supplements were filed. This FY 99 goal is included for reporting purposes. For purposes of the Performance Plan, this goal has been dropped for FY 00, FY 01 and FY 02.

Fiscal Year 1999 Cohort as of 8/31/00

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Priority Efficacy Supplements	15	90% in 6 months	13	87%
		30% in10 months	95	77%
Standard Efficacy Supplements	122	90% in 12 months	121	99%

6. Review and act upon 90% of manufacturing supplements within 6 months and act on 30% 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 and Issues:** COMIS; NDE/MIS: FDA has a quality control process in place to ensure the reliability of the performance data in COMIS. This process provides information on how document room contractors and the Records

Management Team quality control this data. See 2.2.3 Verification and Validation Section for a description of this process.

- **Performance:** For the FY 99 submission cohort, 1,459 manufacturing supplements were filed. This FY 99 goal is included for reporting purposes. The goal does not continue into FY 00, FY 01 and FY 02.

Fiscal Year 1999 Cohort as of 8/31/00

Submission Type	Number of Submissions Filed with CDER	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
Manufacturing Supplements	1,459	30% in 4 months	662	73%
		90% in 6 months	1,438	99%

7. Protect human research subjects' participation in drug studies and assess the quality of data from these studies and assess the quality of data from these studies by conducting approximately 780 on-site inspections and data audits annually. (12032)

- **Context of Goal:** This is a new goal for FY 02. FDA approves drug products only after the manufacturers/sponsors have provided adequate and reliable information on which FDA can base its decision. Manufacturers/sponsors generate, collect, and report data from both clinical (human subjects) and non-clinical (animal and other) studies in support of their applications. Under FDA's Bioresearch Monitoring (BIMO) Program, FDA inspects sponsors, contract research organizations, monitors, and institutional review boards to ensure that the rights and welfare of human subjects who participate in research are protected, and to verify that data collected by the regulated industry are accurate and reliable. FDA is the only government agency with an active program of on-site inspections, and the necessary expertise, to evaluate the conduct of these studies. The Prescription Drug User Fee act mandates specific deadlines for review of manufacturers'/sponsors' submissions.
- **Data Source and Issues:** COMIS, Field Accomplishments and Compliance Tracking System (FACTS), and ACCESS Databases will be used to track assignments and reviews, and establish baseline-monitoring information.
- **Performance:** DSI completed 627 BIMO inspections in FY 98, 683 in FY 99, and 697 in FY 2000. The number of inspections completed each year is dependent on the number of applications received.

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

FDA cannot learn everything about the safety of a drug before it is approved. FDA must be vigilant to protect Americans from injuries and deaths caused by unsafe, illegal, fraudulent, substandard or improperly used products. FDA assures safe products are marketed by continued surveillance for adverse events and use problems, increased inspectional coverage of both foreign and domestic producers, increased enforcement efforts to prevent fraudulent activities involved with the sale of approved and unapproved prescription drugs over the Internet, and increased educational programs that address the interests of medical professionals, patients and consumers.

A comprehensive safety system for medical products is a critical priority. FDA's current systems are not intended to, and cannot, uncover the incidence of adverse events, their preventability, or the overall health and economic impact on Americans. A DHHS partnership to promote patient safety and prevent medical errors is being developed, with FDA taking the lead on a national critical event reporting system. This program is designed for broader monitoring and prevention of adverse events involving both new and already marketed products and would substantially reduce preventable injuries and death from the use of FDA-regulated products.

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 adverse event reports from health care professionals (see goal 12007). In calendar year 1999, over 275,000 individual safety reports (ISRs) were received into entry into the AERS of which over 30% represented serious and unexpected events. As of July 20, 2000, 137,000 individual safety reports (ISRs) have been received for entry into the AERS for this calendar year. The first quarter data for calendar year 2000 projects over 300,000 reports for the full year. 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 from pharmacists 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 from pharmacists 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.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
8. Streamline adverse drug event reporting system. (12007)	FY 02: Issue final rules on ADRs and electronic submissions	FY 02:	1999 Update
	FY 01: Issue Proposed Rule on adverse event reporting requirements. Issue Guidance on electronic submission of adverse event reports. Grant waivers to companies wishing to submit adverse event reports electronically. Continue AERS development (post 2.0 functionality). Roll out of AERS datamart to medical officer in new drug review divisions.	FY 01:	
	FY 00: Develop next generation of the AERS to enhance functionality.	FY 00: Development and roll-out of AERS 2.0 was completed. Pilot program to increase participation in electronic expedited reporting is ongoing. Regulation requiring that adverse event reports be precoded using MedRA on target for release for public comment this FY.	

	FY 99: Implement AERS for the electronic receipt and review of voluntary and mandatory ADE reports.	FY 99: The AERS was successfully implemented and has been operational for nearly three years.	
9. CDER will initiate laboratory research on at least three projects identified and related to the mission of PQRI. (12016)	FY 02: Initiate laboratory research on at least 3 projects	FY 02:	
	FY 01: Initiate laboratory research on at least 3 projects	FY01:	
	FY 00: 25% Goal metric changed for FY 01 ,02. See Context Section	FY00: Studies were initiated in all the project areas including presentations at a professional meeting. There were two studies for physical attributes, two studies for BACPAC, and seven studies for in vivo bioequivalence.	
	FY 99: NA	FY 99: NA	
10. Inspect registered human drug manufac-turers, repackers, relabelers and medical gas repackers.1 (12020)	FY 02: 26%	FY 02:	
	FY 01: 26%	FY01:	
	FY 00: 22%	FY00: 22%	
	FY 99: 22%	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	FY 02: at least 90%	FY 02:	
	FY 01: at least 90%	FY 01:	
	FY 00: at least 90%	FY 00: 93%	
	FY 99: at least 90%	FY 99: 95%	
		FY 98: 96%	
		FY 97: 95%	

least 90%) with FDA requirements. (12006)			
12. Give consumers and health profes-sionals more easily understandable OTC drug information. (12027)	FY 02: Give consumers and health professionals more easily understandable OTC drug information.	FY 02:	
	FY 01: Give consumers and health professionals more easily understandable OTC drug information.	FY 01:	
	FY 00: Make new drug approval information increasingly available via the Internet. Develop partnerships with national organizations to disseminate educational information to consumers.	FY 00: OTC label education campaigns were targeted to grassroots consumers and key health professional organizations.	
	FY 99: NA	FY 99: NA	
TOTAL FUNDING: ($000)	FY02: 86,957		
	FY01: 62,473		
	FY00: 77,809		
	FY99: 69,575		
1 Some adjustments in counting inventories and inspectional coverage were necessary due to a few problems resulting from the transition to a new database (FIS to FACTS) in FY 2000.			

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:** The Adverse Event Reporting System (AERS) is an Oracle based computerized information system designed to support the Agency's post-marketing safety surveillance program for all approved drug and therapeutic biologic products. The structure of the database is in compliance with the

international safety reporting guidance (ICH E2B), including content and format for electronic submission of the reports from the manufacturers. Features include on-screen review of reports, searching tools, and various output reports in support of postmarketing drug surveillance and compliance activities. 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 Sources and Issues:** Adverse Events Reporting System
- **Performance:** The AERS has been operational for nearly three years. In calendar year 99 over 275,000 ISRs were received for entry into the AERS of which over 82,000 (30%) represented serious and unexpected events (30%). In calendar year 2000 261,000 individual safety reports (ISRs) were received for entry into AERS. The processing costs for data entry, coding and database management for this number of reports are substantial and a continuing burden for the CDER.

Currently reports are received either on paper as MedWatch forms or electronically. AERS assigns an individual safety report (ISR) identification number for each report. Paper submissions are scanned and stored in retrieval software. All data elements are entered and undergo data entry quality control to ensure completeness and accuracy. All reported adverse event terms are coded into a standardized international terminology, MedDRA (the Medical Dictionary for Regulatory Activities). This process is also subjected to coding quality control. After data entry, the reports are routed directly to assigned clinical reviewers in the postmarketing office. The reports are assessed individually and in aggregate for safety concerns.

The functions and tools developed in AERS provide the ability to easily customize queries; such queries are performed by multiple users on a daily basis for any drug and/or adverse event of interest. Standardized report outputs from AERS provide useful postmarketing information to many users within and outside FDA. These functions, combined with appropriate management and processes developed by the FDA, make AERS an effective tool for pharmacovigilance. There is an ongoing process in place to further improve the performance and functionalities of AERS.

AERS was designed to allow for electronic submission of individual case safety reports. Electronic submissions provide CDER, FDA, and the public with several tangible benefits. Specifically, automating the receipt and processing of safety reports will allow CDER to be more responsive to public health issues, greatly reduce resources associated with data management, and apply better data and better science to the drug regulatory process. However, there are FDA regulatory and infrastructure changes needed for full-scale implementation of electronic submissions. Accordingly, CDER has proposed a step-level implementation that will allow CDER to identify and resolve several process issues while the regulatory and infrastructure changes are implemented. This step-level

implementation includes a pilot program in which manufacturers may submit safety reports electronically. This will be followed by proposed rulemaking to require that manufacturers submit suspected adverse drug reaction reports electronically.

In summary, the AERS database in the FDA assures that postmarketing adverse event reports are completely and accurately data entered, quality controlled and reviewed to monitor product safety and to protect the public health.

9. CDER will initiate laboratory research on at least three projects identified and approved by the PQRI. (12016)

- **Context of Goal:** The Product Quality Research Institute (PQRI) is a first-ever collaboration among CDER, academic, and industry scientists to conduct research in the areas of pharmaceutical chemistry, biopharmaceutics, and science management. The purpose of this research is to establish better testing methods, standards, and controls for assessing product quality and manufacturing and management processes. This knowledge aids the Agency in developing consistent and reasonable requirements for product quality information in regulatory filings. Leveraging scientific expertise in this way contributes to streamlining the drug development and approval processes for industry and the FDA while ensuring the highest level of product quality.
- **Data Sources and Issues:** Office of Testing and Research (OTR) Research Plan; "A proposal - PQRI;" Memorandum of Understanding between FDA and the American Association of Pharmaceutical Scientists; and "Proposed Operating Principles for the PQRI."

  The data sources for this goal are the written research plan, the PQRI proposal, a memorandum of agreement, and proposed operating principles. These documents should be examined to verify: that precise definitions have been established to delineate the universe (or listing) of research programs being evaluated; that the definitions of what constitutes a research plan being "initiated" and what "complete 50%" of the projects initiated in FY 99 have been clearly and unambiguously established; and that the percentage of research projects completed are measurable relative to the defined universe of research projects.

  A detailed assessment of the reliability of these data sources will be conducted in the coming year to determine whether the data are valid and meaningful to judge successful performance of this goal.

- **Performance:** In FY 2000, PQRI initiated seven working groups to address the following regulatory issues: blend uniformity, manufacturing changes, packaging changes, bulk drug post-approval changes, drug substance impurity testing, drug substance particle size analysis, and topical and aerosol forms.

The Blend Uniformity Working Group is expected to make recommendations to FDA by early next year on science-based changes to regulations for blend uniformity testing.

These recommendations will ensure that there is thorough mixing of the drug within the blend and dosage unit. Current regulations advocate the testing of each production batch of a powder-blend drug. However, industry experience suggests that testing every batch is not necessary or meaningful because the current blend sampling technology is flawed and doesn't necessarily provide representative results.

10. Inspect 26% 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. In addition, the Human Drugs program has shifted its emphasis away from inspecting medical gas establishments to establishments in other risk categories. Since medical gas inspections represent a large portion of the statutory inspection workload, the statutory inspection coverage will be adversely affected.
- **Data Sources and Issues:** Program-Oriented Data System, Official Establishment Inventory
- **Performance:** The FY 2000 goal of 22% was met. Due to a few problems resulting from the transition to a new database (FIS to FACTS) in FY 2000, some adjustments in counting the inventory and inspectional coverage were necessary. It is expected that any inconsistencies will be corrected when the FY 2001 performance is reported.

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 Sources and Issues:** 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) Goal will remain the same for FY 02

- **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 and Issues:** 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.

  The program indicated that the following information on the processing procedures for this data is reliable and of sound quality. The information demonstrates that the appropriate quality control practices are in place.

  The project manager copies the approval letter and final labeling text to a secured drive. The Freedom of Information (FOI) component completes necessary redaction and transfers them to another secured drive. FOI then notifies the web team that they are ready to post. Posting is verified by FOI. There are time limits for each of these steps as stipulated in a Center policy.

  Consumer Drug Information Sheets for NMEs are prepared by Center pharmacists using information from the approved label and other sources and then cleared by the appropriate components. The information is then posted on the internet to a site for "Consumer Drug Information".

  It was determined that these data are valid based on the logical assumption that once this information is disseminated, the American public would benefit positively due to reduced drug misuse. A detailed assessment of the quality control process will be conducted in the coming year to ensure that performance data are reliable.

- **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. In March 1999, the Agency issued a new ruling that sets minimal standards and requirements for the format of OTC drug product labeling which should increase patients knowledge about the medication. In addition, the Agency completed the first phase of a new Over-the-Counter Medicine Label Campaign by placing 245 newspaper articles in 45 states reaching more than 17 million people and by reaching an additional 137 million with radio PSA. Throughout the year 2000, more companies began using the new OTC medicine label. Subsequently, the Agency launched phase two of this educational campaign by producing a new color print public service announcement and a completely revised newspaper article.

In FY 2000 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.

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 and report program results, whether the data was appropriate for the performance measure and if it was considered sound and convincing. The Center obtained from its programs a description of the means that are used to verify and validate measured values for each performance goal. CDER has a number of quality control processes in place to ensure that performance data is reliable. Below are descriptions of several data systems used by CDER.

- Adverse Event Reporting System (AERS)

The Adverse Event Reporting System (AERS) is an Oracle based computerized information system designed to support the Agency's post-marketing safety surveillance program for all approved drug and therapeutic biologic products. The structure of the database is in compliance with the international safety reporting guidance (ICH E2B), including content and format for electronic submission of the reports from the manufacturers. Features include on-screen review of reports, searching tools, and various output reports in support of postmarketing drug surveillance and compliance activities. The ultimate goal of AERS is to improve the public health by providing the best available tools for storing and analyzing safety reports.

Currently reports are received either on paper as MedWatch forms or electronically. AERS assigns an individual safety report (ISR) identification number for each report. Paper submissions are scanned and stored in retrieval software. All data elements are entered and undergo data entry quality control to ensure completeness and accuracy. All reported adverse event terms are coded into a standardized international terminology, MedDRA (the Medical Dictionary for Regulatory Activities). This process is also

subjected to coding quality control. After data entry, the reports are routed directly to assigned clinical reviewers in the postmarketing office. The reports are assessed individually and in aggregate for safety concerns.

The functions and tools developed in AERS provide the ability to easily customize queries; such queries are performed by multiple users on a daily basis for any drug and/or adverse event of interest. Standardized report outputs from AERS provide useful postmarketing information to many users within and outside FDA. These functions, combined with appropriate management and processes developed by the FDA, make AERS an effective tool for pharmacovigilance. There is an ongoing process in place to further improve the performance and functionalities of AERS.

AERS was designed to allow for electronic submission of individual case safety reports. Electronic submissions provide CDER, FDA, and the public with several tangible benefits. Specifically, automating the receipt and processing of safety reports will allow CDER to be more responsive to public health issues, greatly reduce resources associated with data management, and apply better data and better science to the drug regulatory process.

However, there are FDA regulatory and infrastructure changes needed for full-scale implementation of electronic submissions. Accordingly, CDER has proposed a step-level implementation that will allow CDER to identify and resolve several process issues while the regulatory and infrastructure changes are implemented. This step-level implementation includes a pilot program in which manufacturers may submit safety reports electronically.This will be followed by proposed rulemaking to require that manufacturers submit suspected adverse drug reaction reports electronically.

In summary, the AERS database in the FDA assures that postmarketing adverse event reports are completely and accurately data entered, quality controlled and reviewed to monitor product safety and to protect the public health

- Pediatric Exclusivity Database and the Pediatric Page database (Database enhancements required to meet goal)

The pediatric databases are complete and accurate and appropriate quality control practices are in place. The data are valid for this goal because they measure the required performance indicators e.g., the number of requested pediatric studies. A detailed assessment of the pediatric Exclusivity Database and the Pediatric Page database quality control process will be conducted in the coming year to ensure that performance data are reliable.

- Center-wide Oracle Management Information System COMIS

The Center-wide ORACLE Management Information System (COMIS) is CDER's enterprise-wide system for supporting premarket and postmarket regulatory activities. It consists of multiple applications, or components, that store and retrieve data in a single

integrated database. COMIS is the core database upon which most mission-critical applications are dependent. The new drug evaluation (NDE) portion of COMIS contains information about investigational new drug applications (INDs), new drug applications (NDAs), supplements, and amendments, and it tracks their status throughout the review process. The type of information tracked in COMIS includes status, type of document, review assignments, status for all assigned reviewers, and other pertinent comments.

CDER has in place a quality control process for ensuring the reliability of the performance data in COMIS. Document room task leaders conduct one hundred percent daily quality control of all incoming data done by their IND and NDA technicians. Senior task leaders then conduct a random quality control check of the entered data in COMIS.

The task leader then validates that all data entered into COMIS are correct and crosschecks the information with the original document. Once the data are saved in COMIS, the document room staff no longer have the capability to change certain document fields. If a data entry change is necessary, the task leader must request the change in writing. Once the change has been made, the document room is notified and the senior task leader/task leader rechecks the data for accuracy.

The Records Management Team (RMT) conducts weekly quality control checks of the various document rooms. These checks include random quality control of division files, loose files, application jackets, outgoing letters, memoranda, and reviews. Each document room is visited monthly and no advanced notice is given.

Overall, the data in COMIS are complete and accurate, and appropriate quality control practices are in place. The limited number of people with authority to input data into COMIS helps to protect the integrity of the data. Once entered into the system, data are immediately accessible to users. In order to ensure that the system is functioning as needed, a committee consisting of staff from RMT and the Office of Information Technology meet once a month to discuss and ensure that the system reflects changes in policy and legislative requirements. The data obtained from COMIS are valid for this goal because they measure the required performance indicators, e.g., the numbers and types of submissions, receipt dates, and review times.

Preliminary discussions have taken place to alleviate system weaknesses and redesign the system in phases over the next few years to improve efficiency. These weaknesses include a manual, paper-driven quality control process, inflexibility of the system to reflect policy and legislation changes in a timely manner, slow or unavailable network connections impeding a user's ability to acquire requested data, and unrecognizable codes requiring tracking to be done manually.

2.3 BIOLOGICS

2.3.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 02 Budget Estimate	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**155,507**	**140,251**	**140,717**	**124,365**

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 or injury. 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 44% from FY 96 to FY 2000. 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 biologics, for the prevention, diagnosis, and treatment of disease or injury.**
- **Reduce the risk of biologics products on the market through assuring product quality and correcting problems associated with their production and use.**

FDA is responsible 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, persons with Hepatitis A) or for travelers to particular areas of the world (for example, *Salmonella typhi* or Japanese encephalitis virus vaccines).

Many additional vaccines are in various stages of investigation (for example, HIV or Herpes simplex virus vaccines), and their INDs are being reviewed.

FY 2000 Performance Highlights

Blood and Blood Products

Approved ReFacto, a biological product for the treatment and prevention of hemorrhagic episodes in patients with hemophilia A. Hemophilia A is a genetically inherited blood clotting disorder caused by a deficiency in specialized proteins instrumental in promoting the normal clotting process. ReFacto is a product of Genetics Institute, Incorporated of Andover, MA.

Vaccines

Approved Prevnar, the first vaccine to prevent invasive pneumococcal diseases in infants and toddlers - diseases that can cause brain damage and, in rare cases, death. The vaccine prevents invasive diseases caused by the organism Streptococcus pneumonia (also known as pneumococcus) including bacteremia (an infection of the bloodstream) and meningitis, an infection of the lining of the brain or spinal cord. Prevnar is a product of Wyeth-Ayerst Laboratories, a Division of American Home Products Corporation in Philadelphia, PA.

Each year public health experts collaborate to determine the strains of virus to be used to manufacture the influenza vaccine that will be administered that fall. The recommendations are based on the data provided from laboratories worldwide as the strains are continuously evolving or mutating. As soon as the strains are recommended, manufacturers begin to grow virus strains in fertile hen's eggs. The parent strains of vaccine, know as "seed strains," used by each manufacturer are tested by CBER to assure they are the same as the recommended strains. CBER pre-approves seed strains, conducts tests for potency, sterility, and endotoxin as well as other tests to assure the safety and efficacy of the vaccine. CBER also performs lot release on each lot of vaccine manufactured prior to distribution of the product. Lot release consists of CBER's review of the manufacturer's test results, including tests on the lots of monovalent virus strains and tests on the final trivalent product. CBER also performs additional testing as appropriate to assure the safety and efficacy of these products.

Therapeutic Products

Approved a new indication for Actimmune that delays the time to disease progression of severe, malignant osteopetrosis in children. Osteopetrosis is a life-threatening, congenital disorder in which an overgrowth of bony structures leads to blindness, deafness and increased susceptibility to infections. In the most serious form of the disease, most patients become blind or anemic by six months of age and die within the first ten years of life, frequently in the first two years. The disease is an orphan indication. Actimmune is a product of InterMune Pharmaceuticals, Incorporated of Palo Alto, California.

2.3.2 Strategic Goals

Strategic Goal 1:

Ensure the expeditious availability of safe and effective biologics, for the prevention, diagnosis, and treatment of disease or injury.

A. Strategic Goal Explanation

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 is also responsible 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 to accomplish 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 hire 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 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 of 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.

B. Summary of Performance Goals l

Performance Goals	Targets	Actual Performance	Reference
1. Review and act on 90% of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90% of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt. (13001)	Standard Applications within 12 months: FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90%	Standard Applications within 12 months: FY 01: FY 00: 11/01 FY 99: 100% FY 98: 100% FY 97: 100%	1999 Update
	Standard Applications within 10 months: FY 02: 90%	Standard Applications within 10 months: FY 02:	

	FY 01: 70% FY 00: 50% FY 99: 30%	FY 01: FY 00: 09/01 FY 99: 80%	
	Priority Applications within 6 months: FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Priority Applications within 6 months: FY 02: FY 01: FY 00: 04/01 FY 99: 100% FY 98: 100% FY 97: 100%	
2. Review and act on 90% of standard PDUFA efficacy supplements within 10 months; and review and act on 90% of priority PDUFA efficacy supplements within 6 months of receipt. (13002)	Standard Applications within 12 months: FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90%	Standard Applications within 12 months: FY 01: FY 00: 11/01 FY 99: 100% FY 98: 100% FY 97: 100%	1999 Update
	Standard Applications within 10 months: FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30%	Standard Applications within 10 months: FY 02: FY 01: FY 00: 09/01 FY 99: 100%	
	Priority Applications within 6 months: FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Priority Applications within 6 months: FY 02: FY 01: FY 00: 04/01 FY 99: 100% FY 98: 100% FY 97: 100%	
3. Review and act on 90% of PDUFA manufacturing supplements within 6 months of receipt, and review and act on	Within 6 months: FY 02: 90% FY 01: 90%	Within 6 months: FY 02: FY 01:	1999 Update

90% of PDUFA manufacturing supplements requiring prior approval within 4 months of receipt. (13003)	FY 00: 90% FY 99: 90%	FY 00: 04/01 FY 99: 100% FY 98: 99% FY 97: 98%	
	Within 4 months: FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30%	Within 4 months: FY 02: FY 01: FY 00: 02/01 FY 99: 93%	
4. Review and act on 90% of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90% of Class 2 resubmitted original PDUFA applications within 6 months of receipt. (13004)	Class 1 resubmissions within 2 months: FY 02: 90% FY 01: 90% FY 00: 70 % FY 99: 50%	Class 1 resubmissions within 2 months: FY 02: FY 01: 12/01 FY 00: 100% FY 99: 100% FY 98: 100%	1999 Update
	Class 1 resubmissions within 4 months: FY 02: NA FY 01: NA FY 00: 90% FY 99: 90%	Class 1 resubmissions within 4 months: FY 00: 02/01 FY 99: 100%	
	Class 2 resubmissions within 6 months: FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Class 2 resubmissions within 6 months: FY 02: FY 01: FY 00: 04/01 FY 99: 100%	
5. Review and act on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA supplements within 12 months after submission date. (13005)	Complete Submissions: FY 02: 90% FY 01: 90% FY 00: 85% FY 99: 60%	Complete Submissions: FY 02: FY 01: FY 00: 11/01 FY 99: 100% FY 98: 85% FY 97: 83%	1999 Update
	Supplements	Supplements	

	FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	FY 02: FY 01: FY 00: 11/01 FY 99: 99% FY 98: 97% FY 97: 98%	
TOTAL FUNDING ($000)	FY 02: 118,959 FY 01: 108,357 FY 00: 111,968 FY 99: 98,032		

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 PDUFA II goals were set forth in letters from the Secretary of Health and Human Services to Congressional Committee Chairmen on November 12, 1997. FDA developed these goals in consultation with the pharmaceutical and biological prescription drug industries. "NA" means the goal is not applicable in that fiscal year.

1. Review and act on 90% of standard original PDUFA NDA, PLA, and BLA submissions within 10 months; and review and act on 90% of priority original PDUFA 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 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 2000 data for standard applications within 12 months will be available after November, 2001. The FY 2000 data for standard applications within 10 months will be available after September, 2001. The FY 2000 data for priority applications within 6 months will be available after April, 2001.

2. Review and act on 90% of standard PDUFA efficacy supplements within 10 months; and review and act on 90% of priority PDUFA 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 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 2000 data for standard applications within 12 months will be available after November, 2001. The FY 2000 data for standard applications within 10 months will be available after September, 2001. The FY 2000 data for priority applications within 6 months will be available after April, 2001.

3. Review and act on 90% of PDUFA manufacturing supplements within 6 months of receipt, and review act on 90% of PDUFA manufacturing supplements requiring prior approval 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 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 FY 2000 data for review of manufacturing supplements within 6 months will be available after April, 2001. The FY 2000 data for review of manufacturing supplements within 4 months will be available after February, 2001.

4. Review and act on 90% of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90% of Class 2 resubmitted original PDUFA 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 Regulatory Management System
- bThese applications are tracked by year of receipt, which is the cohort year. FDA's FY 2000 performance for review of class 1 resubmissions within 2 months was 100%. The FY 2000 data for review of class 1 resubmissions within 4 months will be available after February, 2001. The FY 2000 data for review of class 2 resubmissions within 6 months will be available after April, 2001.

5. Review and act on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90% of PLA/BLA 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 Regulatory Management System
- b 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 2000 data for review of complete submissions and for major supplements will be available after November, 2001.

Strategic Goal 2:

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

A. Strategic Goal Explanation

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.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
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 02: at least 90% FY 01: at least 90% FY 00: at least 90% FY 99: at least 90%	FY 02: FY 01: FY 00: 96% 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 02: 80%	FY 02:	
	FY 01: 80%	FY 01:	
	FY 00: 80%	FY 00: 69%, 18 out of 26 in compliance	
	FY 99: 80%	FY 99: 62%, 16 out of 26 in compliance	
		FY 98: 54%, 13 out of 24 in compliance	
8. Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing	FY 02: 50% FY 01: 50% FY 00: 50% FY 99: 43%	FY 02: FY 01: FY 00: 57% FY 99: 64% FY 98: 46% FY 97: 46%	

establishments. [1] (13012)			
TOTAL FUNDING ($000)	FY 02: 36,548 FY 01: 31,894 FY 00: 28,749 FY 99: 26,333		
[1] Some adjustments in counting inventories and inspectional coverage were necessary due to a few problems resulting from the transition to a new database (FIS to FACTS) in FY 2000.			

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 2000 was 96%. Conformance rates for FY 97 through FY 2000 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. In FY 2000, 69%, or 18 establishments of 26 were in compliance. There has been steady compliance improvement. However, inspections continue to find compliance discrepancies. 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:** In FY 2000, FDA inspected 57% of the establishments in the Official Establishment Inventory, exceeding the goal of 50%. The drop in inspection coverage from 64% in FY 1999 to 57% in FY 2000 is attributed to changes in risk priorities. Some resources were re-allocated to other high-priority areas such as tissues. Due to a few problems resulting from the transition to a new database (FIS to FACTS) in FY 2000, some adjustments in counting the inventory and inspectional coverage were necessary. It is expected that any inconsistencies will be corrected when the FY 2001 performance is reported.

2.3.3 Verification and Validation

The Biologics Program uses various databases to manage its diverse programs and to assess performance. The principal CBER database is the Regulatory Management System (RMS). The RMS is CBER's new VAX-based, Oracle database that is used to track all 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 RMS records application review information on each license application and supplement received and filed by the Center. The RMS 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 RMS.

The Biologics Investigational New Drug 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 1999); 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 RMS, 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 deviations in the manufacture of biological products that affect the safety, purity, or potency of the product. The Biological Product Deviation Reports (BPDRs) (previously called error and accident reports) enable 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 to licensed manufacturers, unlicensed registered blood establishments, and transfusion services which had control over the product when a deviation occurred to report to FDA the biological product deviation if the product has been distributed.

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 biologics product deviation reports annually. FDA estimates that over 116,000 biologic product deviation reports would be received under the proposed regulation. FDA does not have a computer system to permit the electronic submission of biologic product deviation reports. If the Agency is to comply with the intended goals of the biologic product deviation reporting regulation, it will need a system that would allow it to receive electronic submission of reports; and to process, analyze and evaluate 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 02 Congressional Request	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**81,809**	**63,928**	**49,593**	**43,253**

The mission of the Animal Drugs and Feeds Program is to protect the health and safety of all animals that serve as food producing, companion animals or other non-food producing 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:

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

These strategic goals reflect CVM's involvement in the animal drug development process from the point at which the drugs are first developed through the time 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 by 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.

Program Accomplishments

The Animal Drugs and Feeds Program continues to work with its partners in industry to redesign the New Animal Drug Approval (NADA) process, thereby making it more efficient (phased review). This collaboration has served as a model for the development and passage of the FDA Modernization Act (FDAMA).

The program uses several strategies to expedite the animal drug review process. The practice of Phased Review makes drug review faster by providing more timely feedback and "early detection" of application deficiencies. Electronic submission of Drug Shipment Notices cuts the approval time to one third of the original time. On the postmarket side, 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 inspection 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

Veterinarians and the agricultural community need animal drugs to ensure a safe food supply and the health of companion animals. 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 the resulting products will be safe, wholesome, and free of drug residue when they reach the consumer and also ensures that companion animals and animals used to assist individuals with disabilities have a beneficial impact on the quality of life for human beings.

CVM promotes the availability and diversity of animal drugs and feeds by being involved throughout the new animal drug approval process.

CVM reduces overall developmental costs of these products by working with industry sponsors early in the drug approval process. For example, pre-submission conferences (Performance Goal 1), workshops, teleconferences, and guidance documents made available through the internet all help to increase industry efficiency and reduce costs. CVM's practice of "Phased Review" provides industry sponsors with timely feedback on product applications, and may detect application deficiencies early in the process.

The Agency is committed also to improving the review time for new animal drug applications (NADAs) (Performance Goal 2). For example, development of an enhanced information system for electronic submission of applications and data will allow FDA to perform more efficiently its application review activities (Performance Goal 3).

Animal drugs and feeds must also be safe and effective. The bioresearch monitoring program (BIMO) assures that scientific studies and data submitted to FDA comply with our data integrity standards.

To ensure that FDA has the necessary science capability (intellectual capital) necessary to assess data and to make regulatory decisions, a staff college is being developed (Performance Goal 4).

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 will produce outcomes that matter to the U.S. taxpayer: reduce mortality and morbidity rates by assuring safer animal products; reduce the cost and time associated with animal drug development; and, improve quality of life for segments of our population because companion animals are healthy and live longer.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80%. (14007)	FY 02: 80% FY 01: 80% FY 00: 73% FY 99: NA	FY 02: FY 01: FY 00: 75% FY 99: 73%	
2. Review and act on 80% of NADAs/ Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt. (14017)	FY 02: 80% FY 01: 75% FY 00: 73% FY 99: NA	FY 02: FY 01: FY 00: 74% FY 99: 73%	
3. Pilot and validate the procedure for receiving protocol submissions electronically. (14002)	FY 02: Pilot and validate the procedure for receiving protocol submissions electronically.	FY 02:	
	FY 01: Initiate the development of a method for receiving protocol submission electronically	FY 01:	
	FY 00: 4 phases - Notices of Slaughter; Notices of Animal Final	FY 00: Wrote guidance on 4 phases. Developed technology for	

	Disposition; Meeting Agendas; USDA Slaughter Reports	logging/routing of electronic submissions.	
	FY 99: complete 1 phase - Notices of Claimed Investigational Exemptions (NCIE)	FY 99: 1 phase completed (NCIE)	
4. Begin to design and implement a Staff College. (14018)	FY 02: Plan and design the option selected in Phase I.	FY 02:	
	FY 01: Initiate the development of a Staff College (phase I: further needs assessment, feasibility studies, and analysis of alternatives).	FY 01:	
	FY 00: NA	FY 00: NA	
	FY 99: NA	FY 99: NA	
5. Revise and develop 14 guidances. (14001)	FY 02: NA	FY 02:	
	FY 01: 3 manufacturing, 10 new drug approval process and 1 Veterinary International Conference on Harmonization (VICH) guidances	FY 01:	
	FY 00: Update 12 guidelines (original target was 7 documents which was 10 % of animal drug review guidances).	FY 00: Published 19 draft and/or final guidances (including 7 VICH documents).	

	FY 99: Update 1 guideline (1% of animal drug review guidances).	FY 99: 8 guidelines: including 3 FDAMA and 5 VICH.	
6. Develop an antibiotic risk assessment model using fluoroquinolone, chickens and Campylobacter. (14003)	FY 02: NA	FY 02:	
	FY 01 Goal: Perform 2 risk assessments.	FY 01:	
	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 00: Draft FQRA published/comments received. Model broadened to include virginiamycin use in food animals & indirect transfer of Enterococcus faecium.	
	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 99: 1 Risk Assessment completed.	
TOTAL FUNDING: ($ 000)	FY 02: 28,198 FY 01: 27,287 FY 00: 21,117 FY 99: 18,522		

C. Goal-by-Goal Presentation of Performance

1. Maintain the level of requested 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 to 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 throughout 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. The FY 00 goal was met. Based on current data, 80% is a reasonable target for FY 02.

2. Review and act on 80% 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 CVM to recruit and hire review scientists. These increased personnel resources will boost our compliance rate from 75% in FY 01 to 80% in FY 02.
- **Data Sources:** Submission Tracking and Review System (STARS)
- **Performance:** In FY 99, CVM updated its tracking system to be consistent with procedures under ADAA. CVM slightly exceeded the FY 00 goal. Current data indicates a compliance rate of 80% is reasonable for FY 02.

3. Pilot and validate the procedure for receiving protocol submissions electronically. (14002)

- **Context of Goal:** We have initiated processes to obtain input from our stakeholders in order to develop meaningful performance measures to assess progress consistent with our reinvention initiatives. Better-automated information systems, including those supporting electronic submission of applications by sponsors, are being developed to facilitate and expedite the review process. CVM has successfully completed electronic submission processes for use by the animal industry.
- **Data Sources:** CVM's priority project tracking system.
- **Performance:** In 1999, the Animal Drugs and Feeds Program completed implementing the electronic submission process for all Notices of Claimed Investigational Exemptions (NCIE) submissions. An evaluation indicated processing time was reduced to 1/3 the time required for paper processing. Additional phases of electronic submission were initiated in FY 00 and FY 01. 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. The goal for FY 00 was met and additional work was accomplished in support of this goal.

4. Begin to design and implement a Staff College in 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 continuously building the scientific and intellectual capability of its staff. The addition of a CVM Staff College will allow CVM to increase and maintain a level of scientific expertise that is critical in order for us to address evolving animal science and veterinary medicine issues. The Staff College will use funds 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 01: Initiate Phase I-- conduct further needs assessment, feasibility studies, and analysis of alternatives; FY 00: Develop a strategy to establish a Staff College in CVM; FY 99: Identify need to enhance and maintain scientific expertise

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

- **Context of Goal:** (Dropped for FY 2002). 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 that 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:** This goal was dropped for FY 2002 because measuring the number of revised or new guidances reflect activities but not necessarily outcomes. Nevertheless, this is an important responsibility on which FDA and industry worked closely. 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. In FY 00, CVM published 19 draft and/or final guidances (including 7 VICH documents).

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

- **Context of Goal:** (Goal dropped for FY 2002.) Improving risk assessments will 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.
- **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:** This goal was dropped for FY 2002 because of challenges in determining good measurements for achieving it. 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. In April 2000, issued Federal Register notice requesting data and public comment.

Strategic Goal 2:

Reduce the risks associated with marketed animal products.

A. Strategic Goal Explanation

Once animal drugs are on the market, CVM continues managing public health risks through activities such as inspections and antimicrobial resistance monitoring. These CVM strategies for assuring safety compliance and scientific monitoring are made possible through partnerships 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. This involves inspections (Performance Goal 7 and 8), 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. CVM's ultimate outcome is to assure 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 9) that can detect food illness outbreaks early and prevent their spread. NARMS was developed in conjunction with USDA and CDC, and has greatly improved our ability to detect emerging antibiotic resistance among foodborne pathogens. This helps ensure the continued effectiveness of both human and veterinary drugs and aids in increasing the availability of effective drugs for treatment of foodborne disease. This system also advances understanding of foodborne illness and further prevention efforts.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
7. Maintain biennial inspection coverage by inspecting 50% of registered animal drug and feed establishments. (14009)	FY 02: 50% FY 01: 50% FY 00: 27% FY 99: 27%	FY 02: FY 01: FY 00: 39% FY 99: 25%	
8. Assure that FDA inspections of domestic animal drug	FY 02: at least 90% FY 01: at least 90% FY 00: at least 90%	FY 02: FY 01: FY 00: 97%	

and feed manufacturing establishments and repackers result in at least 90% conformance. (14004)	FY 99: at least 90%	FY 99: 99% FY 98: 98% FY 97: 97%	
9. Increase isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000. (14005)	CY 02: Total: 12,000 - Salmonella isolates	CY 02:	1999 Update
	CY 01: Total: 12,000 - Salmonella isolates	CY 01:	
	CY 00: Total: 6,000 - Salmonella isolates: 2,000 (human), 4,000 (veterinary)	CY 00: Total: 11,000 - Salmonella isolates: 2,000 (human), 9,000 (veterinary)	
	CY 99: Total: 6,000 - Salmonella isolates: 2,000 (human), 4,000 (veterinary)	CY 99: Total: 10,216 - Salmonella isolates: 1,706 (human), 8,510 (veterinary)	
		CY 98: Total: 4,900 - Salmonella isolates: 1,400 (human), 3,500 (veterinary)	
		CY 97: Total: 3,678 -Salmonella isolates: 1,287 (human), 2,391 (veterinary)	
		CY 96: Total: 3,193 -Salmonella isolates: 1,272 (human), 1,921 (veterinary)	
10. Assure 100% compliance with the BSE feed regulation through inspections and compliance actions. (14006)	FY 02: 100%	FY 02:	
	FY 01: NA	FY 01:	
	FY 00: NA	FY 00: NA	
	FY 99: Ensure compliance with good manufacturing practices including the	FY 99: 7200 inspections to date. Computer based training module for	

	newly implemented BSE regulation through a variety of methods.	BSE inspections developed.	
TOTAL FUNDING: ($ 000)	FY 02: 52,597 FY 01: 36,641 FY 00: 28,476 FY 99: 24,731		

C. Goal by Goal Presentation of Performance

7. Maintain biennial inspection coverage by inspecting 50% 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 two years. In response to public demand for increased drug availability, FDA continues to emphasize postmarket monitoring. Routine inspections have lower priority than inspection of firms producing high profile products. This has an impact on the pre-approval process that requires a "recent" inspection before 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. In FY 1999, there were 1,418 registered establishments. (FY 2000 estimate is 1,420.) The increases in inspection coverage targets from 27% to 50% in FY 2001 and FY 2002 are mainly attributed to an increase in state contract inspections and anticipated work related to BSE.
- **Data Sources:** Field Accomplishment Compliance Tracking System (FACTS) [formerly known as the Program Oriented Data System (PODS)], Official Establishment Inventory
- **Performance:** FY 00 = 39%, FY 99 = 25%, FY 98 = 34%, FY 97 = 31% In 1999, 25% of registered animal drug and feed establishments were inspected, falling short of our target of 27%. The inspection percentages are estimates, based on the complexity of inspections, the number of firms in inventory, the time needed for each inspection, and the violative and re-inspection rates. In FY 2000, FDA inspected 39% of the establishments in the Official Establishment Inventory, exceeding the goal of 27%. Due to a few problems resulting from the transition to a new database (FIS to FACTS) in FY 2000, some adjustments in counting the inventory and inspectional coverage were necessary. It is expected that any inconsistencies will be corrected when the FY 2001 performance is reported.

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. In FY 00 and FY 01, routine surveillance included monitoring the industry that must comply with the BSE regulations. In FY 98 through FY 00, FDA worked with the industry to bring it into compliance with BSE regulations.
- **Data Sources:** FDA Field Data Systems.
- **Performance:** The FY 2000 conformance rate is 97%. FY 99 = 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.

9. Increase isolate testing rate for Salmonella in National Antimicrobial Resistance Monitoring System to 12,000 for human and animal isolates. (14005)

- **Context of Goal:** NARMS was initiated in 1996 as a major national surveillance effort of CVM's Food Safety Initiative (FSI) in cooperation with FDA, CDC, and USDA. NARMS detects emerging antibiotic resistance among foodborne pathogens and the possible associated health hazards through systematic collection, analysis and interpretation of antimicrobial susceptibility surveillance data. In addition, the program data help to justify educational efforts and prudent drug use campaigns in humans and in veterinary medicine. NARMS is adding to our knowledge of drug susceptibility and is helping ensure the continued effectiveness of human and veterinary drugs.
- **Data Sources:** FDA-CDC-USDA National Antimicrobial Resistance Monitoring System
- **Performance:** In FY 2000 collected 9000 animal and 2000 human isolates. We will increase the goal to 12,000 isolates per year, which we will continue to send for serotyping, susceptibility testing, and quality control testing. Reports will continue to be generated and analyzed.

  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 non typhoid *Salmonella, Campylobacter, Enterococcus* and *E. coli* isolates collected from animal sources, and non typhoid *Salmonella, Campylobacter, Enterococcus, Shigella, salmonella typhi* and *E. coli* isolates from human clinical samples. In addition, new sites and sources of isolates have been added.

NARMS data has been used to initiate field investigations of outbreaks of illness marked by a pathogen which displayed an unusual antimicrobial resistance pattern, assess the human health impact of fluoroquinolone use in poultry, stimulate research in molecular

characteristics of resistance emergence and transfer, improved our knowledge of risk factors associated with the development of an antimicrobial-resistant infection, and has triggered broader research projects of prudent antimicrobial use in animals and the role of the environment in the emergency and spread of antimicrobial resistance.

NARMS was also expanded into the international arena during FY 2000. Conducted a pilot study with medical microbiologists from hospital in three states in Mexico that have significant animal agriculture in close proximity to the hospitals. The pilot study consisted of initial training of the investigators at the USDA Russell Research Center (in Athens, Georgia) in standardized laboratory methodologies for the isolation, identification, and antimicrobial susceptibility testing of foodborne *Salmonella.* Sample collection and isolation of *Salmonella* took place from clinically ill humans in the Mexican hospitals and from healthy children in community daycare centers.

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.

10. Assure 100% compliance with the BSE feed regulation through inspections and compliance actions. (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:** On October 4, 1997 FDA's regulation 21 CFR 589.2000 (Animal Proteins Prohibited From Use in Animal Feed) became fully effective. The purpose of the regulation is to prevent the establishment and amplification of BSE through animal feed. The regulation prohibits the use of certain proteins derived from mammalian tissue in feeding to ruminant animals. The Center has completed various educational components of preparing for the zero tolerance of the use of certain proteins derived from mammalian tissue in feed to ruminant animals.

  The inspections are two-tiered in approach. They are meant to educate the establishment on BSE and to inspect their processes. The initial plan was to take compliance actions for egregious actions or repeated non-compliance. 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 action to bring the company into compliance.

During FY 2000, CVM issued an interactive CD-ROM for use by FDA, state regulatory authorities and the regulated industry that provides training on the BSE feed regulation. In January 2001, FDA held a conference call with other federal and state feed control officials to present inspection data results to date and to discuss prospective assignments and coordination.

To date 10,240 inspections of renderers, FDA licensed and non-licensed feed mills have been completed. Various segments of the feed industry had different levels of compliance. While inspections continue, preliminary data from initial inspections performed by FDA and cooperating states indicate an average compliance rate with FDA's regulation of approximately 75 percent.

- In 1997, the FDA issued a Small Entity Compliance Guide, which provides guidance for compliance with the regulation to all of the affected industries. In February 1998, this guidance was revised to be more readable and understandable for the user. The revision included splitting the document into 4 separate guides, one for renderers, one for feed manufacturers and protein blenders, one for ruminant feeders with on-farm feed mixing and one for ruminant feeders without on-farm feed mixing.

- In June 1998, a satellite teleconference was held for the feed manufacturing industry to provide information on how to comply with the regulation

- In June 1999, CVM presented a BSE workshop 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 actions on repeat violators.

2.4.3 Verification and Validation

An integral part of the FDA continual improvement initiative has been upgrading our data processing and information systems. This includes automation of manual systems and integration of existing systems, which reduces duplication and chances of data entry 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. For example, checks are in place to ensure that the person who enters the data does not audit the data.

In the postmarket area we are working with, and using data from, other governmental agencies such as CDC and USDA. To ensure that our federal partners address our data needs, we have established memorandums of understanding and memorandums of need with other agencies. To accomplish our Food Safety Initiative goal (Performance Goal 9 - 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 that has responsibility to follow-up on violative tissue residues reports from USDA. USDA prepares an annual residue sampling plan with input from FDA. Under the new Hazard Analysis Critical Control Point (HACCP) plan, the requirements for how slaughter plants choose samples for testing 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 developed 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 desktop units, and replaced the twenty units that were not Year 2000 compliant.

2.5 MEDICAL DEVICES & RADIOLOGICAL HEALTH

2.5.1 Program Description, Context and Summary of Performance

Total Program Resources:

	FY 2002 Request	FY 2001 Current Estimate	FY 2000 Actual	FY 1999 Actual
Total $000	**197,676**	**179,791**	**170,257**	**159,008**

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.

FDA is faced with an increasing challenge to maintain parity with an ever-changing industry. The medical device industry has continued to grow at a rate of approximately 8

percent per year over the ten-year period ending in 1996. Since 1996, the number of firms has increased from 9,061 in FY 1997 to 13,428 in FY 2000. The medical device industry of the 21st century is developing more and more devices based on leading-edge technology. FDA has to maintain its ability to make high quality scientific decisions. This is especially critical for areas of emerging technologies such as: 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.

FDA's Center for Devices and Radiological Health (CDRH) is developing a set of key strategies concentrating on ensuring the health of the public throughout the total life cycle of a product. This approach will allow the Center to focus is resources on products that are most likely to improve the effectiveness and safety of medical devices and radiological health no matter what stage of their development (concept development, active marketing, or modification). These strategies are:

1. Total Product Life Cycle (TPCL) -- develop a TPLC model in coordination with stakeholders (Internal, External, and International);
2. Knowledge Management -- manage knowledge to support TPLC (Build a knowledge culture, Exploit Information Technology, and develop CDRH as an e-Center);
3. Magnet for Excellence -- attract and retain people who want help fulfill our public health mission; and
4. Meaningful Metrics -- measure and set targets to assess our continuing impact on public health. FDA has updated review guidance and procedures to ensure safe and effective products reach the market quickly.

FDA intends to leverage its own efforts by working closely with stakeholders to maximize the quality and timeliness of regulatory decisions and interactions with industry and other stakeholders.

To meet these challenges, two key strategic goals have been established for the 21st Century:

- **Provide the medical community with faster access to important, life-saving and health-enhancing medical devices, while assuring 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.**

FY 2000 Performance Highlights

FDA has worked diligently over the past three years 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 2000, CDRH received 9,753 of these major submissions. There were no overdue submissions for the fourth consecutive year. FDA maintained high quality, timely reviews despite increasingly complex device technology.

Medical devices comprise a wide array of products that have become medically and technologically more complex. While the medical device industry is growing and revolutionizing, FDA's inspectional coverage is decreasing and domestic recall rates are increasing. FDA did not meet its FY 2000 domestic inspection coverage goal for higher risk device firms of 22 percent. FDA's actual performance was just 18 percent, the result of an increasing number of firms to inspect and declining field resources. This is far below the statutory requirement of 50 percent. FDA is not able to routinely inspect over 7,000 lower risk firms whose products are mostly exempt from premarket review.

FDA continues to look for ways to reduce preventable deaths and injuries associated with the use of medical device products. FDA moved closer to implementing the Medical Device Surveillance Network (MeDSuN) to reduce public health risks by timely identification of actual or potential problems associated with the use of medical devices. When fully implemented, MeDSuN will reduce the occurrence of medical device related events,; serve as an advanced warning system from the clinical community; and create a two-way communciation channel between FDA and the user-facility community.

In FY 2000, FDA began Phase II of the MeDSuN pilot which will cover 25 hospital facilities. Under a collaborative agreement with the University of Maryland, FDA is developing an internet-based reporting system which will include a web site, database, and search engine.

The quality of mammography services in the United States continues to improve. In FY 2000 the goal of ensuring that mammography facilities meet inspection standards was achieved with a 97 percent rate. This was the third consecutive year of achieving this high standard. Additionally, FDA trained 16 new inspectors on the requirements of the MQSA regulations; issued 27 issues of the Mammography Matters Newsletter; performed 200 audit inspections under the Inspector Quality Assurance program; developed a continuing education video on m image scoring and distributed it to each state and district office; and calibrated testing equipment (369 sensitometers and 363 desensitometers) on a routine basis for use in the MQSA program to ensure the accuracy of measurements and inspections. FDA also drafted final regulations for "States as Certifiers" which will transfer certification authority from FDA to applicant States, as

provided by MQSA. Final regulations will become effective immediately upon publication in the Federal Register sometime in April 2001.

2.5.2 Strategic Goals

Strategic Goal 1:

Provide the medical community with faster access to important, life-saving and health-enhancing medical devices, while assuring their safety and effectiveness.

A. Strategic Goal Explanation

Medical Devices marketed in the United States are subject to rigorous premarket review by FDA. Prior to marketing a device, manufacturers must seek FDA clearance or safety and effectiveness approval of their products using FDA's premarket approval processes. Medical devices vary widely in their complexity and their degree of risk or benefits, and 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 needed to assure product safety and effectiveness.

FDA reviews: Premarket Notifications (510(k)s -- products substantially equivalent to products on the market; Investigational Device Exemptions (IDEs) -- devices used in clinical investigations on human subjects; and, Premarket Approval Applications (PMAs) - post-1976 amendments or not substantially equivalent devices. FDA is charged with review of submissions within the time frames specified by law. FDA strives to support a stable and predictable review process, meet statutory requirements for review times for PMAs and 510(k)s, and increase sponsor interaction. (Performance Goals 1- 4)

FDA received a premarket funding increase in FY 2000 and FY 2001 to improve timely reviews, and for activities in the areas of reuse, genetic testing, and standards recognition. These increases are reducing review times and facilitating new technology review.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Maintain the on-time percentage of Premarket Approval Application (PMA) first actions within 180 days. (15001)	FY 02: 90% FY 01: 90% FY 00: 85% FY 99: 65%	FY 02: FY 01: FY 00: 96% FY 99: 74% FY 98: 79% FY 97: 65%	1999 Update
2. Review and complete 90 percent of PMA supplement	FY 02: 90% FY 01 90% FY 00: 85%	FY02: FY 01: FY 00: 98.7%	1999 Update

final actions within 180 days in FY 2002. (15009)	FY 99: N/A	FY 99: 100% FY 98: 100% FY 97: 65%	
3. Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days in FY 2001. (15002)	FY 02: 95% FY 01: 95% FY 00: N/A FY 99: 90%	FY 02: FY 01: FY 00: 100% FY 99: 100% FY 98: 99.5% FY 97: 98%	1999 Update
4. Review and complete 75 percent of 510(k) (Premarket Notification) final actions within 90 days in FY 2002. (15021)	FY 02: N/A FY 01: N/A FY 00: 65% FY 99: N/A	FY 02: FY 01: FY 00: 78% FY 99: 75% FY 98: 76% FY 97: 70%	1999 Update
5. Complete 100 percent of Investigational Device Exemption (IDE) Agreement" meetings within 30 days in FY 2002. (15015)	FY 02: N/A FY 01: N/A FY 00: 80% FY 99: N/A	FY 02: N/A FY 01: N/A FY 00: N/A FY 99: 23% FY 98: 33%	
6. Complete 95 percent of PMA "Determination" meetings within 30 days in FY 2002. (15024)	FY 02: 95% FY 01: 95% FY 00: 95% FY 99: N/A	FY 02: FY 01: FY 00: 100% FY 99: 100% FY 98: 25%	
7. Initiate development of 20 to 25 new or enhanced standards to be used in application review in FY 2002. (15003)	FY 02: Initiate 20 to 25 new or enhanced standards to be used in application review.	FY 02:	
	FY 01: Initiate 20 to 25 additional application review standards	FY 01: FY 00: 567 Standards recognized	
	FY 00: Review 50 Standards for continued applicability and 50 standards for recognition	FY 99: 450 Standards recognized	

	FY 99: Recognize over 415 standards for use in application review and update the list of recognized standards	FY 98: 370 Standards recognized	
		FY 97: 2 Standards recognized	
8. Conduct 335 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.) (15025)	FY 02: 335 FY 01: 260 FY 00: N/A	FY 02: FY 01: FY 00: 249	
TOTAL FUNDING ($000)	FY 02: $79,391 FY 01: $71,391 FY 00: $64,698 FY 99: $60,423		

C. Goal-By-Goal Presentation of Performance

1. Maintain the on-time percentage of Premarket Approval Application (PMA) first actions within 180 days in FY 2002. (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.
- **Data Sources:** Center for Devices and Radiological Health (CDRH) Premarket Tracking System and Receipt Cohorts
- **Performance:** The original FY 1999 goal, as shown in the FY 1999 Congressional Justification, was revised due to better baseline data. In FY 2000, FDA performance was 96 percent for the applications received in the first six months. The performance strategy is to redirect resources from low-risk to high-risk devices. Also, reinvention efforts such as early meetings with manufacturers, modular review, streamlined reviews, and product development protocols have resulted in faster reviews. Faster reviews give patients quicker access to important new medical devices.

  This goal has been modified to remove HDEs, humanitarian use devices 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. There are very few HDEs

actually submitted to FDA, and these are normally completed within the 75-day timeframe prescribed by FDAMA.

NOTE: PMA submissions will continue to increase in FY 2001 and FY 2002 due to technology advances, increased use of computerized and miniaturized devices. Therefore, it is expected that FY 2002 will not only be a year of more submissions but submissions will require multiple reviewers with different areas of expertise. Reviews will be more complex and take even more science time.

2. Review and complete 90 percent of Premarket Approval Application (PMA) supplement final actions within 180 days in FY 2002. (15009).

Note: workload will continue to increase in FY 2001 and FY 2002 due to increased submissions and advances in technology.

- **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 technology changes or the addition of a new indication. It is essential that FDA complete the review process for these products quickly and thoroughly.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** FY 2000 performance is currently 98.7 percent for the applications received in the first six months. This goal is a new commitment in FY 2000 and FY 2001.

3. Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days in FY 2002. (15002)

- **Context of Goal:** This is an FY 1999 goal, dropped in FY 2000, and picked back up for FY 2001 and FY 2002, as a more meaningful measure of performance in this area. This goal for first actions on 510(k)s within 90 days addresses the statutory requirement to review a 510(k) within 90 days.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** FY 2000 performance is 100 percent. 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, using more consensus standards in its reviews, and using more third party reviews. As a result, 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. In FY 1999, FDA received only 32 510(k)s with a third party review, but more than 1,200 were eligible.

Abbreviated and Special 510(k) Submissions provide 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 1999, 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 percent of 510(k) (Premarket Notification) final actions within 90 days in FY 2000. (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
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** FY 2000 performance is currently 78 percent. This goal is a new commitment in FY 2000, and is being dropped in FY 2001, with time to first actions being determined to be a more meaningful measure of performance in this area.

5. Complete 100 percent of Investigational Device Exemption (IDE) "Agreement" meetings within 30 days in FY 2002. (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 Ill 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 premarket approval actions that deal with devices that are complex and represent new technologies. It is intended that opening a premarket discussion with the manufacturer will greatly improve the quality of IDE and PMA submissions and result in a reduction of the review time required. Although the performance goal in FY 2002 remains at completing these meetings within 30 days, increased resources will be required to update science guidelines used at these meetings in order to keep them current with emerging medical device technologies.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** Performance was 75 percent in FY 2000. This goal is being discontinued for FY 2001.

6. Complete 100 percent of Premarket Approval Application (PMA) "Determination" meetings within 30 days in FY 2002. (15024)

- **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 premarket approval meetings will reduce the premarket review times and result in moving new products to the market faster.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** FY 2000 performance is 100 percent.

7. Initiate development of 20 to 25 new or enhanced standards to be used in application review in FY 2002. (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.
- **Data Sources:** Standard status document reports
- **Performance:** FDA recognized 117 standards in FY 2000 for a cumulative total of 567 at the end of the year. 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.

8. Conduct 335 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.). (15025)

- **Context of Goal:** In FY 2002, FDA plans to initiate the BIMO program by conducting 335 investigational inspections of approximately 1000 active IDEs identified that involve vulnerable populations (e.g., pediatric). This initial effort will provide a better idea of the workload associated with a fully implemented program. Each of the IDE applications may involve 10 to15 clinical Investigators and workload information is needed.

  CDRH has approximately 1000 active Investigational Device Exemptions (IDEs) of high-risk investigational devices (e.g., implantable cardiac defibrillators,

artificial skin, digital mammography diagnostic units). Approximately 10 percent of these cover studies involving vulnerable populations. We are continuing to see an increase in these types of actions.

In FY 2001, FDA is devoting more resources to a BIMO initiative, an area significantly impacting public health research and human subject protection. BIMO device review resources are targeted based on FDAMA requirements for timely and interactive reviews. We are seeing frequent violations of informed consent, undocumented research, and confusion of experimental and control treatments that involve millions of patients. There are an estimated 100 to 300 patients per investigator and 10,000 to 15,000 active clinical investigators in the United States.

- **Data Sources:** CDRH Field Data Systems
- **Performance:** This goal is a new commitment in FY 2002. In FY 2000, 249 BIMO inspections were conducted.

Strategic Goal 2:

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.

A. Strategic Goal Explanation

Medical device risk reduction activities cover four major areas: (1) Inspections; (2) Mammography; (3) Radiation Control; and (4) Adverse Event Reporting. FDA exercises considerable discretion regarding the frequency and comprehensiveness of inspections. For approximately 4,100 high risk device establishments (excluding mammography facilities), the law requires FDA to conduct inspections at least once every two years. In addition, FDA is responsible for Low risk devices to insure that they comply with Quality System Regulations. FDA is not inspecting over 7000 Class I firms whose products are also 510(k) exempt. However, the regulations do not state a mandatory time frame for these inspections. There are also 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; 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 9 - 11)

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 and higher violation rates. Although FDA received an increase of funding in FY 2001, the increase was offset by the need by reprogramming and the lack of an increase to cover current services. In FY 2002, FDA is requesting an appropriated funding increase for domestic inspections and additive user fees for foreign inspections and imports. 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 can not monitor adherence to standards or quality systems conformance at current resource levels.
- Foreign inspection coverage is very low and 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. To date, only 11 percent of the several hundred foreign manufacturers contacted have agreed to participate in the MRA Inspection Program. Foreign manufacturers will not participate in the program unless they believe that FDA inspections are likely to occur. Sufficient funding is needed to assure an inspection level adequate to motivate foreign manufactures to pay for inspections by Conformity assessment bodies. Over the long term, successfully implemented MRAs will reduce the number of foreign firms requiring FDA inspection.
- 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 one of every eight American women will contract breast cancer during their lifetime. When the disease is detected in its early stages, the probability of survival increases significantly. 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)

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 9,200 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

Radiological health resources dropped from 400 FTE in FY 1978 to about 65 FTE in FY 2000. We are seeing a resurgence of problems such as widespread new used for fluoroscopy by relatively untrained practitioners increasing the risk of over exposure. We attribute this to a lack of ability to keep up with the new developments in electronic product technology.

Adverse Event Reporting

A key element in any comprehensive program to regulate medical devices is a postmarket reporting 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. The Medical Device Surveillance Network (MeDSuN) System when fully implemented will reduce the occurrence of untoward medical device related events; serve as an advanced warning system; and create a two way communication channel between FDA and the user-facility community.

In FY 2000, FDA began Phase II of the MeDSuN pilot that will include 25 Hospitals. FDA is using FY 2001 funding to add 75 to 100 new facilities. FDA is developing an internet-based reporting system that includes a Web site, database, and search engine. This pilot will develop methodology to recruit hospitals in MeDSun by obtaining information from hospital experts on organization structure and liability concerns. (Performance Goal 13)

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
9. Provide inspection coverage for Class II and Class Ill domestic medical device manufacturers at 20 percent in FY 2002. (15005.01)	FY 02: 20% FY 01: 17% FY 00: 22% FY 99: 26%	FY 02: FY 01: FY 00: 13% FY 99: 30% FY 98: 33% FY 97: 40%	

10. Assure FDA inspections of domestic medical device manufacturing establishments result in at least 90 percent conformance. (15018)	FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	FY 02: FY 01: FY 00: 92% FY 99: 95% FY 98: 95% FY 97: 96%	
11. Maintain inspection coverage for Class II and Class Ill foreign medical device manufacturers in FY 2002. (15005.02)	FY 02: 9% FY 01: 9% FY 00: 9% FY 99: N/A	FY 02: FY 01: FY 00: 11% FY 99: 10% FY 98: 14% FY 97: 23%	
12. Ensure at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent with Level I (serious) problems in FY 2002. (15007)	FY 02: 97% FY 01: 97% FY 00: 97% FY 99: 97%	FY 02: FY 01: FY 00: 97% FY 99: 97% FY 98: 97% FY 97: 97%	
13. Implement the MeDSuN System. (15012)	FY 02: Recruit 75 to 100 new facilities.	FY 02:	
	FY 01: Recruit 75 to 100 hospitals to report adverse events associated with medical devices.	FY 01:	
	FY 00: Develop MeDSuN based on approximately 75 to 90 user facilities.	FY 00: Implement Phase II Pilot with 25 Hospitals	
	FY 99: NA	FY 99: Pilot completed FY 1998 Recruited 24 pilot facilities	
14. Meet time frames of Reuse Regulatory Strategy (15026)	FY 02: Meet Strategic Timelines FY 01: Reuse Goals Started FY 00: N/A	FY 02: FY 01: FY 00: Guidance Issued in August	
TOTAL FUNDING:	FY 02: $118,667		

($000)	FY 01: $108,400 FY 00: $105,559 FY 99: $ 98,585		

C. Goal-By-Goal Presentation of Performance

9. Provide inspection coverage for Class II and Class III domestic medical device manufacturers at 20 percent in FY 2002. (15005.01)

- **Context of Goal:** This goal includes inspections done by FDA directly, or through state contracts or partnership agreements on Class II and Ill 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 domestic workload is expected to increase by 6 percent from FY 2000 to FY 2002. Due to the workload increase, additional resources will be needed to maintain the domestic coverage rate. No class I manufacturers will be inspected. The FY 1999 goal was added in the FY 2000 Performance Plan as a result of its inclusion in the FDA Plan for Statutory Compliance, published in November 1998. Class II and Ill 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 percent annual coverage rate.
- **Data Sources:** CDRH Field Data Systems
- **Performance:** The FY 2000 performance goal of 22 percent was not met. FY 2000 only produced a 13 percent performance rate. This failure was due to reduced field resources and increased workload.

  Although medical devices and electronic products have become more medically and technologically complex and the industry is growing domestically and internationally, device and radiological health inspection resources have been reduced by 23 percent since FY 1995. The compliance program is focused on the improvement of enforcement actions by redirecting current resources to high-risk devices such as implants. However, limitations on inspection resources have put coverage below critical mass. In addition, 510(k) exemptions for Class I products puts more need for Class I inspections to verify that firms have quality systems in place. In FY 2000, FDA inspected 13 percent of domestic manufacturers in FDA's official establishment inventory compared to 40 percent in FY 1997. Foreign manufacturer inspections also suffered dropping from 23 percent in FY 1997 to in FY 2000. None of the 3,335 Class I domestic manufacturers are being inspected

  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 and electronic 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.

10. 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.
- **Data sources:** CDRH Field Data Systems
- **Performance:** In FY 2000, FDA had a 92 percent conformance rate.

11. Maintain inspection coverage for Class II and Class III foreign medical device manufacturers at 9 percent in FY 2002. (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 7 percent. As the workload increases, coverage percentages are expected to decline. One of the major initiatives introduced to assist in reducing the inspection workload associated with medical device review is the US/European Union (EU) Mutual Recognition Agreement (MRA). In FY 1999, FDA continued to implement the MRA with the EU to 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 US and EU Conformity

Assessment Bodies (CABs) that are participating in confidence building activities. The web-site is: http://www.fda.gov/cdrh/mra/index.html. No Class I manufacturers will be inspected.
- **Data Sources:** CDRH Field Data Systems
- **Performance:** In FY 2000, FDA inspected

Although medical devices and electronic products have become more medically and technologically complex and the industry is growing domestically and internationally, device and radiological health inspection resources have been reduced by 23 percent since FY 1995. The compliance program is focused on the improvement of enforcement actions by redirecting current resources to high-risk devices such as implants. However, limitations on inspection resources have put coverage below critical mass. In addition, 510(k) exemptions for Class I products increases the need for Class I inspections to verify that firms have quality systems in place. Foreign manufacturer inspections suffered, dropping from 23 percent in FY 1997 to 11 percent in FY 2000.

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 and electronic 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.

12. Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level I (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.
- **Data Sources:** Mammography Program Reporting and Information System (MPRIS)
- **Performance:** The FY 2000 goal of ensuring that mammography facilities meet inspection standards was achieved with a 97 percent 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 percent 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. Enhance the MeDSuN System by implementing Drugs and Biologics training in recruited hospitals. (15012)

- **Context of Goal:** FDAMA gives FDA the option to replace universal user facility reporting with the Medical Device Surveillance Network (MeDSuN) surveillance system composed of a network of user facilities that constitute a representative profile of user reports. MeDSuN 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. MeDSuN is FDA's response to FDAMA's provision that universal user facility reporting be replaced with a system that is limited to a subset of user facilities that constitutes a representative profile of user reports. In FY 2002, FDA will continue to recruit new facilities for the MeDSun program. FDA estimates that there may be as many as 300,000 injuries and deaths annually associated with device use. FDA will use additional FY2001 resources to maintain the facilities in the program, expand the program by recruiting 75-100 new user facilities, and extend the program to other types of facilities such as ambulatory care surgical centers. FDA will begin implementing MeDSuN, and when fully implemented, the system will enhance our ability to promote and protect the health and safety of patients, users, and others who use our products. MeDSuN will allow FDA to determine the extent of problems associated with medical device products and to develop appropriate mechanisms for providing feedback to the health care community and the public. The long-term goal of MeDSuN is to expand the system to drug and biological products.
- **Data Sources:** CDRH Adverse Events Reports
- **Performance:** This goal is a new commitment in FY 2000 and FY 2001.

14. Meet timeframes of Reuse Regulatory Strategy (new in FY 2002)

- **Context of goal:** The increase in the reuse medical device market and the increase of eldercare devices for an increasing number of older Americans has brought been to the Agencies attention. The number of problems is on the increase and with the growing patient universe is becoming a major concern of FDA. Therefore, FDA intends to develop legislation to further protect the pubic from contamination or possible disease.
- **Data Sources:** FDA Legislative Tracking System
- **Performance:** This goal is a new commitment in FY 2001.

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.

User Facility Adverse Event Reporting -- FDA's adverse event reporting systems newest component is the MedSun program. MeDSun, the Medical Device Surveillance Network, 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 MedSun 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 adverse events.
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 MeDSuN 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 02 Budget Estimate	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**36,943**	**35,490**	**36,522**	**32,109**

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

FY 2000 Performance Highlights

NCTR accomplishments that highlight the Center's multi-disciplinary capabilities and high-quality research include:

1. Geneticists are developing and validating sensitive and predictive in vitro and in vivo systems to identify, measure and understand how chemicals damage human genes.
2. Biologists are studying gene-nutrient interactions involved in carcinogenesis and birth defects.
3. Epidemiologists are working with academia and industry in the development and validation of DNA microarray technology to identify humans that are at increased risk of cancer and/or adverse drug interactions.

4. Toxicologists, in partnership with industry, other government agencies and FDA centers, are utilizing a knowledge base that will assist in the rapid access to specific research knowledge to aid in making regulatory decisions.
5. Photocarcinogenic tumor studies are continuing that focus on measuring the effects that cosmetics containing a- and b-hydroxy acids have on the induction of edema, cell death, and cell proliferation following exposure to UV and/or simulated solar light.
6. Researchers are developing microbial dose-response models and risk assessment methods for applications in reducing uncertainties associated with dosing, human and animal comparisons, and microbial pathogenicity.
7. The interaction of chemicals and the aging process has been investigated and the knowledge is being used to better understand developmental influences and the pathogenesis of neurotoxicants.
8. Within the Presidential Food Safety Initiative (FSI), NCTR scientists are extending the patented Fresh TagTM concept beyond seafood decomposition to include various food products and other indicators of food quality and are developing new devices for quantitative measurement of decomposition or adulteration of products.
9. Finally, in support of the Presidential Initiative on Antiterrorism, NCTR researchers are using mass spectrometry-based approaches to identify biomarkers of toxicity associated with biological warfare agents and/or foodborne contaminants.

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).

A. Strategic Goal Explanation

One of 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 pre-market application review 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 multi-disciplinary approach to predict human toxicity and to evaluate human risk using appropriate animal and non-animal models.

Toxicology research is moving away from its dependence on whole animal test systems that use large numbers of animals and seek relatively few endpoints. These animal test systems are costly, time-intensive, and do not adequately mimic the human response. Thus, scientists must develop and use alternate systems and tests to better understand chemical toxicity and strengthen the extrapolation from animal models to humans.

Because of America's quest for good health, increasing evidence of adverse drug/chemical reactions in humans, point to a need to identify and protect susceptible subpopulations of people at higher risk from exposure to drugs, contaminated foods, or other regulated products.

The NCTR methods used in the identification of and quantitative measurement of the potency of suspected carcinogens and mutagens are essential to the FDA regulatory process. The systems developed and characterized (Performance Goal 1) are capable of simulating human exposure, and increasing the ability to detect weak carcinogens. Other NCTR programs, through partnerships and collaborative projects with other federal agencies, use human data they have collected to better understand the mechanisms of carcinogenesis and to provide new knowledge on the identification of subpopulations, particularly as they relate to individual susceptibility (Performance Goal 2).

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Introduce the know-ledge of new genetic systems and computer-assisted toxicology (bioinformatics) into the application review process. (16001)	FY 02: Conduct one biologi-cally based mechanistic study combined with pre-dictive modeling to improve extrapolation of animal data to the human condition.	FY 02:	
	FY 01: Provide peer reviewed articles on new genetic and transgenic systems and knowledge to product reviewers.	FY 01:	
	FY 00: Evaluate a new biological assay to measure genetic changes and validate two existing models that predict human genetic damage.	FY 00: Validated the Big Blue Rat and Tk+/- in vivo models by using mutations, micronuclei, apoptotic cells measurements; utilized AHH 1 human lympho-blastoid system to evaluate risk to human genome.	

		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.	
2. Develop, with other organizations, gene chip and gene array technology. (16002)	FY 02: Support at least two multi-disciplined DNA and RNA-based microarray technologies.	FY 02:	
	FY 01: Develop "risk chip" technology to screen large numbers of people for biomarkers simultaneously.	FY 01:	
	FY 00: Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly suscep-tible subpopulations.	FY 00: Established and validated conventional genotyping methods for 28 gene targets and polymor-phisms; 686 colonoscopy individuals were genotyped for all	

		common NAT2 alleles; analysis ongoing on completed case-control colorectal cancer study.	
	FY 99: Complete biochemical and epidemiological 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 of increased risk.	
TOTAL FUNDING: ($000)	FY 02: 18,454 FY 01: 16,680 FY00: 17,160 FY99: 15,084		

C. Goal by Goal Presentation of Performance

1. Introduce the knowledge of new genetic systems and computer-assisted toxicology 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 assessments. NCTR is developing, evaluating and comparing in vivo and in vitro transgenic systems and computer-assisted toxicology knowledge bases for this purpose. Reviewer requests 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 and animal models has been developed, characterized and used to assay phenolphthalein and diphenylhydrazine, proposed human carcinogens, for CDER to assess mutation induction in the human genome. The data generated from the systems provides mechanistic information regarding the mode(s) of certain chemical-mediated diseases and provides a more accurate and rapid assessment of the potential risk to the human population.

2. Develop, with other organizations, gene chip and gene array technology. (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 toxicities, including liver toxicity. Additionally, DNA gene expression microarrays are being developed to better understand interspecies extrapolation. Development of some 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:** Research involving 13 major studies to identify biomarkers of the most frequently occurring pancreatic, colorectal, breast, larynx, ovary, lung, urinary bladder, bone marrow, esophagus, and prostate cancers in highly susceptible sub-populations is continuing as scheduled.

Strategic Goal 2:

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

A. Strategic Goal Explanation

To meet the rapidly changing technology, the Agency needs unique computer-based predictive systems to aid in assessing human toxicity and to improve the safety of human clinical trials. 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.

Estrogen exposure of the human population via plant-derived food is virtually universal and infants consuming soy formula are exposed to the highest doses. Additionally, estrogenic activity is found in environmental products, such as plastics and pesticides, and in FDA-regulated products. Thus, it is important to understand the varying toxicological and pharmacological properties of these compounds as well as their common mechanism of action.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
3. Develop computer-based models and infrastructure to predict the health impact of increased exposure to estrogens and anti-estrogen compounds. (16003)	FY 02: Maintain existing computational databases of estrogenic and androgenic compounds for use by reviewers.	FY 02:	
	FY 01: Validate a predictive model for androgens.	FY 01:	
	FY 00: Validate predictive model for estrogenic or estrogenic-like compounds.	FY 00: The estrogenicity of 150 chemicals was asses-sed using an estradiol receptor-binding assay validating the predictive model. Two additional assays were evaluated for androgen binding.	

	FY 99: Demonstrate a model toxicity knowledge base to support and expedite product review	FY 99: Thirty (30) chemicals for CFSAN and six chemicals for CDER have been used to confirm the predictive value of the computer 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 02: 3,698 FY 01: 4,259 FY00: 4,382 FY 99: 3,853		

C. Goal by Goal Presentation of Performance

3. Develop computer-based models and infrastructure to predict the health impact of increased exposure to estrogens and anti-estrogen compounds. (16003)

- **Context of Goal:** NCTR scientists will identify and predict, using the Endocrine Disrupter Knowledge Base (EDKB), whether the increased exposure to naturally occurring and synthetic estrogens and anti-estrogens can adversely impact public health. Recent recognition that FDA-regulated drugs, food additives, food packaging and EPA-regulated environmental chemicals may have on estrogenic activity has affected the way regulators review human exposures. This raised the level of concern regarding adverse effects on human development/reproduction and contributions to high incidences of cancer and/or toxicity.
- **Data Sources:** Use of the predictive and knowledge-based systems 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 meetings.

- **Performance:** Knowledge base has been used by product centers (CFSAN and CDER) to model estrogen activity. The development of a knowledge base for the binding of chemicals to the estrogen and androgen receptor is continuing. It was reported in medical journals that over 230 chemicals have estrogen-receptor-binding activity and that this activity may be used to predict whether these compounds are hazardous to females at risk for breast or uterine cancer. Studies on androgen receptor binding, involved in prostate cancer are ongoing.

Strategic Goal 3:

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

A. Strategic Goal Explanation

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 strategic goal includes three performance goals that address the Agency strategy for developing science-based product and process standards.

The identification of carcinogens has depended classically upon two approaches, epidemiological studies and lifetime animal exposure studies, each of which has its own strengths and weaknesses. The development of new techniques to assess carcinogenic risk provides the basis for alternative methods of assessing carcinogenic potential that can augment, or perhaps, even replace, the need for expensive animal testing.

Committed to the Food Safety Initiative, the NCTR will continue studies that will identify markers of foodborne pathogens and assess whether these microorganisms undergo change, thus becoming more virulent. Excessive use of antibiotics in medicine and the food industry has led to widespread antibiotic resistance among pathogenic bacteria and is now considered a potentially dangerous health problem.

NCTR scientists will continue to build biologically based dose-response models of microbial infection to assess survival, growth, and infectious components of microbial risk. NCTR is developing research protocols to study the mutagenicity and carcinogenicity of genetically modified foods using in vivo and in vitro transgenic systems that have been evaluated and validated in-house.

product centers; however, industry and academic collaborations are anticipated.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference

4. Study FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity. (16004)	FY 02: Initiate analytical/ biological studies to assess the toxicity of at least one, FDA high priority dietary supplement.	FY 02:	
	FY 01: Study two FDA-regulated compounds.	FY 01:	
	FY 00: Conduct studies to relate how a compound causes damage to the damage itself, thus strengthening the scientific basis for regulation of compounds.	FY 00: Bioassay and mechanistic studies on malachite and leucomal-achite green are ongoing. Animals are being tested to study the effects of hydroxy acids and to determine dose-response for the induction of skin edema on SKH-1 mouse skin as a screen for light-induced phototoxicity.	

	FY 99: Develop faster, more accurate tests based on mechanisms of toxic actions.	FY 99: The experimental portion of the 2-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, an endocrine disrupter, are completed. The chronic 2-year component is ongoing.	
		FY 98: Report presented to regulate fumonisin B1 exposure in foods and long-term chloral hydrate usage.	

		FY 97: Complete dosing regimen for 2-year chronic bioassay on chloral hydrate and fumonisin B1; range- finding studies on genistein, methoxychlor, and nonyl-phenol 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 02: Report at scientific meetings and/or publish preliminary results on the development of new methodologies to identify genetically modified foods, drug residues in foods and antibiotic-resistant strains of bacteria.	FY 02:	
	FY 01: Provide model to replicate bacterial survival in the stomach.	FY 01:	

	FY 00: Develop methods of predicting, more quickly and accurately, the risk associated with such foodborne pathogens as Salmonella spp., Shigella spp., and Campylobacter spp.	FY 00: Studies are con-tinuing on the in vitro model and molecular analysis of competitive exclusion pro-ducts; molecular screening methods have been devel-oped for the determination of vancomycin and fluoroquin-olone resistance in Campylo-bacter sp. isolated from poultry.	
	FY 99: Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants.	FY 99: A project to detect simultaneously 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 and develop standards to establish safety and effectiveness of imaging devices for potential use in the diagnosis of toxicity. (16012)	FY 02: Continue development of solid-phase colorimetric bacterial detection system.		

	FY01: Begin developing solid-phase colorimetric bacterial detection system.		
	FY 00: Begin developing solid-phase colorimetric bacterial detection system.	FY 00: Goal not met due to lack of funding.	
	FY 99: Develop method to identify biomarker proteins; translate method to colorimetric field kit.	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.	
7. Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of toxicity.	FY 02: Publish at least one scientific paper describing one technology for use in reviewing regulated compounds.	FY 02:	
	FY 01: Develop at least three concept papers exploring new technologies for the assessment of toxicity.	FY 01:	
TOTAL FUNDING: ($000)	FY 02: 14,791 FY 01: 14,559 FY00: 14,980 FY99: 13,172		

C. Goal by Goal Presentation of Performance

4. Study FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity. (16004)

- **Context of Goal:** There is a need for expanding the infrastructure for and the conduct of improved comprehensive assessments of FDA-regulated compounds to identify and set new standards of assessment and improve risk decisions impacting public health. 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 submitted by the centers and chosen by an FDA committee for study under the NIEHS/NTP Interagency Agreement which helps both Agencies leverage scarce federal dollars in order to meet both their scientific and regulatory needs.
- **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 and mechanistic studies on food toxicity and endocrine disrupting chemicals are ongoing. The data will be used by the agency to establish regulatory guidelines. Phototoxicity studies continue that will address the effect skin creams containing alpha-hydroxy acids have on the skin of solar-light-exposed mice.

5. Develop methods and build biological dose-response models to replicate bacterial survival in the stomach. (16007)

- **Context of Goal:** The Agency is mandated by the Presidential Food Safety Initiative to assure the American public is eating safe food. Therefore, the Agency must strengthen its scientific basis for food safety policies and regulatory decisions through the development of novel, vigorous risk assessments (models and techniques) and through the use of artificial intelligence and computational science for risk assessments. Concurrently, the Agency must accelerate the identification and characterization of mechanisms and methods development/implementation to support surveillance and risk assessment.
- **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:** NCTR staff developed a project with the CVM for isolation and identification of the bacteria in competitive exclusion cultures, using the most reliable phenotypic and genotypic microbial identification techniques available. Preliminary results have alerted CVM to the possibility that competitive exclusion products can introduce bacteria with undesirable antibiotic resistance into the human food supply.

6. Catalogue biomarkers and develop standards to establish safety and effectiveness of imaging devices for potential use in the diagnosis of toxicity. (16012)

- **Context of Goal:** Identification of biomarkers is important because it will allow rapid identification of and response to potential contamination. These proteins identify specific genes that are potential targets for introduction of foodborne 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:** Mass spectrometry methods developed under this goal are being used nationally and internationally to characterize unknown bacteria. Development of a solid-phase colorimetric bacterial detection system could not be accomplished in FY 2000 due to lack of funding. However, due to increased FY 2001 funding, the target was re-established for this goal.

7. Use new technologies (imaging, proteomics, and metabonomics) for diagnosis of toxicity.

- **Context of Goal:** Staying abreast of new technologies in science is important for the Agency to protect public health. This new goal is designed to establish core competencies within the FDA that can form a foundation for future high technology science. Techniques developed under this goal will utilize the emerging knowledge of the human genome and rapid biological analyses to improve human health, and to insure the safety of marketed products.
- **Data Sources:** NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board and the NTP Scientific Board of Counselors; presentations at national and international scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.
- **Performance:** New Goal.

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 upon 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 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 and Risk Assessment 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 Division staff monitors research progress at the project level on a recurring basis. The Project Management System utilized by the Planning Staff is capable of tracking planned and actual research projects and expenditures in all three strategic goals and in the outlined performance goals. Quality Assurance Staff monitor the experiments that fall within the Good Laboratory Practices (GLP) guidelines. Research 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 02 Budget Estimate	FY 01 Current Estimate	FY 00 Actual	FY 99 Actual
Total ($000)	**0**	**0**	**5,700**	**34,000**

On March 21, 2000, the United States Supreme Court, in a 5-4 decision, affirmed the decision of the U.S. Court of Appeals for the Fourth Circuit that FDA lacks jurisdiction under the Federal Food, Drug, and Cosmetic Act (FDCA or Act) to regulate tobacco products. The Court held that, although premature deaths from tobacco use present "one of the most troubling health problems facing our nation today," FDA lacks the authority to issue and enforce its tobacco regulations. Therefore, as of March 21, 2000, FDA commenced an orderly shutdown of the Office of Tobacco Programs. As a result, there are no performance goals for FY 2001 or FY 2002. Performance reporting for FY 2000 is through March 21, 2000.

FDA asserted jurisdiction over tobacco products because 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 14‡ 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. 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 sought to promote and protect the health of our nation's youth by reducing the number of young people who began to use and become addicted to tobacco products each year. FDA's long-term goal was a 50% decline in young people's use of tobacco within seven years of full program implementation. To help reach this goal, FDA worked 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).

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 granting of the petition continued a stay of the issuance of the Fourth Circuit's mandate while the Supreme Court considered the case. The age and identification provisions of FDA's tobacco rule in effect since February 1997 therefore remained in effect until the United States Supreme Court issued its decision on March 21, 2000.

From February 28, 1997 until March 21, 2000, when the Supreme Court rendered its decision, FDA enforced the age and photo identification restrictions. FDA's role was threefold: enforcement and evaluation, compliance outreach, and product regulation. FDA's overall goals were 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. In just 3 years' time, the Agency designed and implemented an aggressive enforcement program resulting in:

- Nearly 200,000 compliance checks completed nationwide
- Contracts to enforce the age and photo identification restrictions in every State, 2 Territories, and the District of Columbia
- 5,600 complaints for civil money penalties filed against tobacco retailers who had violated the rule at least twice
- More than $1 million in civil money penalties collected from retailers who violated the rule at least twice, some of whom settled their cases for reduced penalties

FY 2000 Performance Highlights

Through March 21, 2000, completed 53,700 compliance checks and conducted follow-up compliance checks of 100% of retailers found to be in violation of the rule.

Through March 21, 2000, conducted a multimedia campaign in 27 media markets; distributed 52,000 retailer kits; and distributed 500 retailer recognition rewards.

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

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 only 3 years, FDA realized significant achievements both in enforcing the age and identification requirements and informing stakeholders about the Tobacco Program.

A key influence on a retailer's decision to comply with the rule was the extent to which the retailer perceived that he or she was likely to be found in violation and the certainty of punishment for that violation. The Agency's enforcement strategy was designed to ensure that every retailer would be inspected and re-inspected if found to be in violation of the rule. Most of the program's enforcement funds were expended for contracts with States and Territories to conduct compliance checks during which minors, accompanied by FDA commissioned officers, attempted to purchase cigarettes or smokeless tobacco at retail establishments.

Under the enforcement plan, retailers who refused to sell tobacco to the minor participating in an FDA inspection received a letter informing them that they were in compliance with the rule. Those who sold to the minor received a letter informing them that they had violated the rule, and that another compliance check could occur in the near future. If on the second purchase attempt the retailer sold to the minor, the Agency sought a $250 civil money penalty and a $1500 civil money penalty for third violations. Penalties were scheduled to escalate further for subsequent violations of the access restrictions, but at the time the Supreme Court ruled, the Agency had not filed complaints for fourth or fifth violations. By the time the Tobacco Program ended, the Agency had filed 5,600 complaints against retailers who had violated the rule two or more times and had collected more than $1 million in civil money penalties.

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

When the Agency shut down the Office of Tobacco Programs, it still was a relatively new program. Nonetheless, there already was an indication that FDA's enforcement program had 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), Ö 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."

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 outreach program was 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 00, the Agency was developing new creative elements for the campaign, including a TV advertisement. FDA had planned to 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 was launched.

FDA used a multitude of media and approaches to ensure the greatest reach and utility of its messages. FDA maintained a toll-free hotline and an Internet site, which provided retailers and the general public with easy access to brochures, materials and answers to frequently asked questions. In FY 2000, through March 21, the hotline received 6,000 calls from retailers and consumers requesting materials, asking questions about the program, or reporting concerns. FDA also received requests for more than 75,000 free in-store materials. In addition, television, radio, newspaper, and billboard ads were running throughout Michigan, Colorado, Tennessee, New Hampshire, and Nevada. Further, 500 rewards were distributed to retailers complying with the regulation.

B. Summary of FY 99 Performance

Performance Goals	Targets	Actual Performance	Reference
1. Conduct 200,000 compliance checks and conduct follow-up compliance checks of 100% of retailers found to be in violation of the rule. (17001)	FY 02: NA	FY 02: NA	
	FY 01: NA	FY 01: NA	
	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 00: Through March 21, 2000, completed 53,700 compliance checks and conducted 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	FY 99: Conducted approximately 9,000 compliance checks per month, totaling 107,200	

	compliance checks each month of retail establishments that sell tobacco products.	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 02: NA	FY 02: NA	
	FY 01: NA	FY 01: NA	
	FY 00: Conduct a multimedia campaign in 40 top media markets; distribute 150,000 retailer kits; and pilot test a retailer recognition program for 3,000 retailers. Maintain retailer awareness at 90%.	FY 00: Through March 21, 2000, conducted a multimedia campaign in 27 media markets; distributed 52,000 retailer kits; and distributed 500 retailer recognition rewards.	
	FY 99: Conduct meetings and a multimedia campaign; educate retailers.	FY 99: Communicated to stakeholders their 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.	
TOTAL FUNDING: ($000)	FY 02: 0 FY 01: 0 FY 00: 5,700 FY 99: 34,000		

C. Goal-By-Goal Presentation of Performance

1. Conduct 200,000 compliance checks and conduct follow-up compliance checks of 100% of retailers found to be in violation of the rule. (17001)

- **Context of Goal:** In FY 00, the Agency intended to expand its enforcement program by arranging to have compliance checks conducted in every State and eligible Territory and by conducting 200,000 compliance checks. In addition, FDA planned to re-inspect each violative retailer within 3 months after notifying the retailer of the violation or after adjudication of civil money penalty.
- **Data source:** FDA Tobacco database
- **Performance:** As of March 21, 2000, the Agency had arranged to have compliance checks conducted in every State, 2 Territories, and the District of Columbia. By the same date, the Agency had completed 53,700 compliance checks. Finally, the Agency had re-inspected 100% of violative retailers within 3 months after notifying the retailer of the violation, or after adjudication of a civil money penalty.

2. Conduct a multimedia campaign in 40 top media markets; distribute 150,000 retailer kits; and pilot test a retailer recognition program for 3,000 retailers. Maintain retailer awareness at 90%. (17003)

- **Context of Goal:** FDA conducted a national advertising campaign aimed at raising retailers' awareness of the tobacco regulations and motivating them to comply. The campaign's primary target audience was 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.

  The revised FY 2000 campaign used a mix of media tools and messages to maximize knowledge of and compliance with the regulations. FDA provided retailers with kits that contained explanations of the requirements, and posters and materials, which helped explain the rules to customers and assist in defusing customer anger or anxiety.

  As part of FY 2000 efforts, FDA intended to 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 planned to pilot-test a retailer recognition program for 3,000 retailers.

- **Data Sources:** FDA sponsored surveys of known retailers of cigarettes and smokeless tobacco.
- **Performance:** Testing not completed during this time.

2.7.3 Verification and Validation

FDA enforced the Age and Photo ID restrictions by training and commissioning state regulatory officials, who conduct unannounced purchase attempts using young people under the age of 18 to determine if retailers sold to minors. The results of these attempts were faxed or mailed to FDA by state officials. FDA 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 contained an inventory of retailers of cigarettes and smokeless tobacco products as they were identified. It allowed 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 permitted FDA to measure the progress of its enforcement program. However, the data was not statistically projectable because it is not based on a random sampling of retailers.

The Agency installed the first increment of an information system that would have greatly enhanced the Agency's 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 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 and territories. Battelle also would have implemented an information technology system to automate all the program's various functions, including contracting, outreach, enforcement, compliance checks, litigation, collection of civil money penalties, etc. The new system was intended to increase the efficiency of the program and improve communications internally as well as with state contractors and with other stakeholders. The various system design components were to be implemented incrementally as they were developed beginning in early 1999. The entire system was scheduled to be operational by 2001. When the Supreme Court rendered its decision, Battelle was ready to pilot-test 2 methods by which commissioned officers would record and submit compliance check results electronically. FDA intends to make available to States its research in this area.

Appendix A

Glossary of Acronyms

Acronym	Definition
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
BIMO	Bioresearch Monitoring
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 Manufaturers 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)
DCC	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	Detention 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	North American Free Trade Agreement Technical Working

TWG	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
NSE	Not substantially equivalent determination
NTP	National Toxicology Program NVPO National Vaccine Program Office
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
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 Nutritional 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	Unites states Department of Agriculture
VFD	Veterinary Feed Directive
VICH	Veterinary International Conference on Harmonization
WHO	United Nations World Health Organization
WTO	World Trade Organization

Appendix B
Disposition of FY 2001 Performance Goals

Goal ID	Original Goal Statement*	Disposition	Revised FY 2001 Targets	Explanation
FOODS				
11001	Complete first action on 50% of food and color additive petitions within 360 days of receipt.	Unchanged		
11003	Complete processing of 80% of GRAS notifications within the time frame established by the final rule.	Unchanged		
11007	Increase to at least 55% the proportion of adults who report changing their decision to buy or use a food product because they read the food label.	Dropped		This goal was dropped in FY99 due to lack of resources. It was in the table of the FY01 CJ mistakenly. The context of goal section in the 01 CJ stated that this goal was discontinued after FY 99.
11010	Achieve adoption of the Food Code by at least 25 states in the USA.	Revised	Achieve adoption of the Food Code by at least one state agency in 25 states in the USA.	The goal language has been changed from "at least 25 states" to "at least one agency in 25 states" to reflect the fact that state agencies are not the only agencies that can adopt

				the Food Code, but Federal, tribal, and local as well.
11011	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 90% - 100% with FDA requirements.	Unchanged	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 to at least 90%.	Made the target more specific based on OMB recommendation.
11020	Increase the percentage of high-risk domestic food establishment inspections to 90 , 100 % once every year.	Revised	Increase the percentage of high-risk domestic food establishment inspections to at least 90% once every year.	Made the target more specific based on OMB recommendation.
11021.02	Increase the number of import exams of high-risk food products to 66,700.	Revised	Increase the number of import exams of food products to 60,000.	The phrase "high-risk" was taken out because imports are not technically tracked by high or low risk. The previous target of 66,700 was too high based on the issuance of the final field plan, planned figures. Therefore, the target was changed to 60,000.

11025	Respond to 90% of notifications for dietary supplements containing "new ingredients" within 75 days.	Unchanged		
11027	Expand monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 11,000 samples.	Revised	Expand monitoring for pesticides and environmental contaminants in foods through the collection and analysis of a targeted cohort of 8000+ samples.	The number was lowered due to reexamination of previous data. This goal was originally set too high. In FY99, FDA analyzed 9400 samples and is setting the goal to 8000+ for 2001 and beyond.
11028	Increase the number of audits and assessments to 10 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.	Unchanged		
HUMAN DRUGS				
12001	Review and act on 90% of standard new drug applications (NDAs) filed within 12 months after receipt (70% within 10 months of receipt); and 90% of priority applications within six months.	Unchanged		

12003	Review and act upon 50% of fileable original generic drug applications within 6 months after submission date.	Unchanged		
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.	Unchanged		
12007	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. 01 Target: Separate data entry and retrieval functions throughout new drug review divisions. Pilot test advanced analytical techniques. Develop and implement special report module.	Revised	Issue Proposed Rule on adverse event reporting requirements. Issue Guidance on electronic submission of adverse event reports. Grant waivers to companies wishing to submit adverse event reports electronically. Continue AERS development (post 2.0 functionality). Roll out AERS datamart to medical officer in new drug review divisions.	Updated to reflect current status of the goal.
12016	Initiate all research programs approved by the PQRI Steering Committee in FY 01 and complete 50% of the projects initiated in	Revised	CDER will initiate laboratory research on at least three projects identified and related to the mission of PQRI.	PQRI is now an independent organization that partners with FDA via a MOU. FDA

	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.			initiated 3 projects that were identified through the PQRI process.
12020	Inspect 28% of registered human drug manufacturers, repackers, relabelers and medical gas repackers.	Revised	Inspect 26% of registered human drug manufacturers, repackers, relabelers and medical gas repackers.	Reduced funding level required lowering target level
12026	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.	Unchanged		
12027	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	Unchanged		

	risk management, analysis, and communication procedures.			
BIOLOGICS				
13001	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.	Unchanged		
13002	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.	Unchanged		
13003	Review and act on 90% of manufacturing supplements within 6 months of receipt, and review act on 70% within 4 months of receipt.	Unchanged		
13004	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.	Unchanged		

13005	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.	Revised	Review and act on 90% of complete blood bank and source PLA/BLA submissions, and 90% of PLA/BLA Major supplements within 12 months after submission date.	The FY 01 performance target has been revised from 85% to 90% because of review initiatives that have been initiated by CBER.
13007	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%)	Unchanged		
13008	Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80%.	Unchanged		
13012	Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing establishments.	Unchanged		

ANIMAL DRUGS AND FEEDS				
14001	Revise and develop 14 guidances for the regulated veterinary industry. 01 Target: 3 manufacturing, 10 new drug approval process and 1 Veterinary International Conference on Harmonization (VICH) guidances.	Unchanged		
14002	Reduce drug development and review time by initiating a process for receiving protocol submissions electronically.	Unchanged		
14003	Develop an antibiotic risk assessment model using FLQ as the antibiotic, Chickens as the animal species and Campylobacter as the bacterial isolate. 01 Target: Perform 2 risk assessments.	Unchanged		
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%) with FDA	Unchanged		

	requirements.			
14005	Increase the overall isolate testing rate for Salmonella in NARMS to 7200 for human and animal isolates.	Revised	Increase isolate testing rate for Salmonella in NARMS to 12,000.	Increased the target level based on latest performance data.
14007	Increase the level of pre-submission conferences with industry sponsors to 80%.	Unchanged		
14009	Improve biennial inspection coverage by inspecting 46% of registered animal drug and feed establishments.	Unchanged		
14017	Review and act on 70% of NADAs/ANADAs within 180 days of receipt.	Revised	Review and act on 75% of NADAs/ANADAs within 180 days of receipt.	Target increase due to Budget increase
14018	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.	Unchanged		
MEDICAL DEVICES AND RADIOLOGICAL HEALTH				
15001	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	Revised	Maintain the on-time percentage of Premarket Approval Application (PMA) first actions within 180 days.	Modified to remove HDEs, humanitarian use devices intended to benefit patients by treating or diagnosing a

	01.			disease or condition that affects fewer than 4,000 invididuals in the U.S. per year. Very few HDEs are actually submitted to FDA, and these are normally completed within the 75-day FDAMA prescribed timeframe.
15002	None	New Goal	Review and complete 95% of 510(k) (Premarket Notification) first actions within 90 days in FY01	This is a FY99 goal, dropped in FY00, and picked back up for FY01 and FY 02, as a more meaningful measure of performance in this area. This goal for first actions on 510(k)s within 90 days addresses the statutory requirement to review a 510(k) within 90 days.
15003	Participate in the development of 20 to 25 standards to be used in application review.	Unchanged		
15005.01	Improve inspection coverage for Class II and Class III domestic medical device manufacturers to 28%.	Revised	Improve inspection coverage for Class II and Class III domestic medical device manufacturers to 17%.	Reduced funding level required lowering target level.

15005.02	Maintain inspection coverage for Class II and Class III foreign medical device manufacturers. 01 Target: 10%	Revised	Maintain inspection coverage for Class II and Class III foreign medical device manufacturers. 01 Target: 9%	Reduced funding level required lowering target level
15007	Ensure that at least 97% of mammography facilities meet inspection standards, with less than 3% of facilities with Level 1 (serious) inspection problems.	Unchanged		
15009	Review and complete 90% of Premarket Approval Application (PMA) supplement final actions within 180 days.	Unchanged		
15012	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.	Revised	Recruit 75 to 100 hospitals report adverse events associated with medical devices.	Reduced funding level required lowering target level
15015	Complete 100% of Investigational Device Exemption (IDE) "Agreement" meetings within 30 days.	Unchanged		
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	Unchanged		

	high rate of conformance (at least 90%) with FDA requirements.			
15021	Review and complete 75% of 510(k) (Premarket Notification) final actions within 90 days in FY 01.	Dropped		First time actions have been determined to be a more meaningful measure of performance in this area.
15024	Complete 95% of Pre-market Approval Application (PMA) "Determination" meetings within 30 days.	Unchanged		
15025	None	New Goal	Conduct 260 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	This is a new goal to reflect the priority for human subjects protection.
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH				
16001	Introduce the knowledge of new genetic systems, specifically transgenic systems and data, into the application review process. 01 Target: Provide peer reviewed articles on new genetic and transgenic systems and knowledge to product reviewers.	Revised	Introduce the knowledge of new genetic systems and computer assisted toxicology (bioinformatics) into the application review process. Target 01: Provide peer reviewed articles on new genetic and transgenic systems and knowledge to product reviewers	Clarify language. Goal statement changed for 01 target did not.

16002	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. 01 Target: Develop, "risk chip" technology to screen large numbers of people for biomarkers simultaneously.	Revised	Develop gene chip and gene array technology. 01 Target: Develop, "risk chip" technology to screen large numbers of people for biomarkers simultaneously.	Clarify language. Goal statement changed for 01 target did not.
16003	Develop a computer based model to predict the impact of increased exposure to estrogens and anti-estrogen compounds on public health. 01 Target Validate a predictive model for androgens.	Revised	Develop computer based models and infrastructure to predict the impact of increased exposure to estrogens and anti-estrogen compounds. 01 Target: Validate a predictive model for androgens.	Clarify language. Goal statement changed for 01 target did not.
16004	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. 01 Target: Study two or more FDA-regulated compounds.	Unchanged	.	

16007	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. 01 Target: Provide model to replicate bacterial survival in stomach.	Revised	Develop methods and build biological dose-response models to replicate bacterial survival in the stomach. 01 Target: Provide model to replicate bacterial survival in stomach.	Clarify language. Goal statement changed for 01 target did not.
16012	Identify biomarkers of toxicity associated with biological warfare agents using innovative new technologies. 01 Target: Publish and disseminate list of biomarkers to FDA product reviewers and other interested scientists.	Dropped		Reduced funding level
16013	Use new technologies (bioinformatics, imaging, proteomics, and metabonomics for diagnosis of toxicity. 01 Target: Publish at least three concept papers exploring new technologies for the assessment of toxicity.	New Goal		
TOBACCO				
17001	Target 50 top media markets; distribute new retailer kit to 200,000 retailers; and increase	Dropped		Program ended on 3/21/00 per order of U.S. Supreme Court

	retailer recognition program to 10,000 retailers. Maintain retailer awareness of FDA tobacco rule at 90% or above.			
17003	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.	Dropped		Program ended on 3/21/00 per order of U.S. Supreme Court

Appendix C

FY 1999 Goals With Updated Reporting Information

Goal # 11001, 11003, 11004, 12001, 12002,12003, 12004, 12005,12007, 13001, 13002, 13003, 13004, 13005, 14005, 15001, 15002,15009, 15021,