FY 2003 Annual Performance Plan
FY 2002 Revised Final Performance Plan
FY 2001 Annual Performance Report

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Part 1: Performance Plan Summary Introduction

FDA's FY 2003 Performance Plan outlines a blueprint for action that will protect U.S. citizens in light of new and ongoing challenges to their health and safety.

The September 11 terrorist attacks and subsequent incidents involving anthrax contamination, raises the prospect that FDA-regulated products--particularly foods - could be used as vehicles to introduce new widespread hazards into the U.S. population. But availability and deployment of FDA-regulated medical products will also minimize the impact of any prospective attack. Because these products represent both threats and opportunities, the American Public will depend on FDA now, more than ever, to safeguard their interests. These new events do not change FDA's 100-year-old public health and safety mission. Rather, they reinforce the magnitude of its importance.

It is critical for FDA to maintain an appropriate balance of strategies that are aimed at addressing terrorist as well as non-terrorist challenges to public health and safety... Although FDA is highly concerned about possible terrorism scenarios, we are also very aware that other major challenges remain. Just to mention a few: New scientific advances continue to generate many complex products that FDA must monitor--not only in the U.S., but also worldwide. Global trade continues to expand and bring an explosion of new products to this country from sources with unknown quality control. To compound this, FDA-regulated industries are using the Internet as a new venue to market their products. This electronic arena poses entirely new challenges to an Agency that has a tradition of regulating in a brick-and-mortar environment.

The Performance Plan Summary will cover the following topics:

- Part One: An overview of FDA: Its mission, responsibilities, key strategic and performance goals, and relation to HHS strategic goals
- Part Two: Highlights of Agency FY 2001 accomplishments
- Part Three: An in-depth description of each strategic goal and associated performance goals and achievements; and
- Part Four: Identifies FDA's partnership and coordination efforts to help make the Plan a reality.

Part One: An Overview

Our Mission and Scope of Responsibilities

FDA has broad responsibilities for protecting the health of American consumers. Although FDA's mission statement clearly outlines these general responsibilities, it does not convey the tremendous scope of activity that we oversee. Decisions made by FDA affect every American every day. To illustrate:

- Last year consumers spent $1 trillion--more than 20 percent of their money--on products that we regulate.
- We judge the safety of an expanding scientific revolution. Public and private entities invest an estimated $50 billion annually in biomedical research and technology.
- We assure the safety of the Nation's manufacturing and processing: FDA is a 10,000 person agency, and is responsible for monitoring over 100,000 U.S. firms that manufacture or process products.
- We also monitor the safety of almost 8 million import shipments that enter this country each year.

FDA: An Overview

1. The public trusts FDA to ensure that:
2. Foods are safe, wholesome, and properly labeled
3. Drugs for both humans and animals, and vaccines for humans, are safe and effective
4. Blood used for transfusions is safe and in adequate supply
5. Medical devices, from scalpels to CAT scans, are safe and effective
6. Transplanted tissues are safe and effective
7. Equipment that uses radiant energy, such as X-ray machines and microwave ovens, is safe
8. Cosmetics are safe and properly labeled.

Prevention--The Cornerstone of FDA Strategic Goals

To successfully accomplish its mission, FDA leadership has identified four strategic goals. Each goal reinforces the importance of prevention as the Agency's primary line of attack on the Nation's health and safety concerns.

Prevention, to FDA, means that we use all means available to minimize health or safety risks facing the American people by correctly assessing the risks and effectively managing them.

Our Strategic Goals:

- **Counter the Terrorist Threat** -- FDA will prepare for the possibility of terrorist attacks on the U.S. population, and respond rapidly and appropriately in the event of an actual attack. This will require: developing a preventive capability for detection, deterrence and interdiction; having adequate supplies of safe and effective medical products to treat victims of an attack; and having in place an emergency preparedness and response plan that will protect U.S. citizens and maintain the internal security of FDA.
- **Maintain a Strong and Effective FDA** -- FDA will maximize return on its human capital by recruiting and adequately compensating the highest caliber scientists and health professionals to carry out its mission. It will also support the President's management objectives to create a streamlined, citizen-centered government agency. Key strategies to achieve this goal include: de-layering the bureaucracy; restructuring Agency functions so that they are more supportive of mission-critical activities; outsourcing traditional government functions where cost efficiencies can be realized; capitalizing on e-government efficiencies; strengthening financial management systems; establishing accountability to the U.S. taxpayer by linking Agency resources to performance; and reconfiguring information technology systems to more effectively support decision making at all levels in the Agency.
- **Assure Medical Product Safety** -- FDA will assure that products are safe by conducting plant and product inspections to ensure that products are manufactured and distributed under safe conditions, and by developing surveillance systems to monitor the safety of the products themselves, their use and consumption.
- **Bring New Technologies to a World-Wide Market** -- FDA will assure that the products of new technologies are available to U.S. consumers. Because of the Agency's timely science-based decisions, millions of Americans can get the medicines and medical devices they need and be assured of safe and effective products.

To effectively carry out these priorities the Agency will adhere to fundamental principles that frame all of its actions and which will lead to more effective public health results. These principles support:

- **Using state-of-the-art science** to make accurate and timely decisions regarding the safety of products and processes;
- **Thinking and acting in a global context**--Since the products we regulate are produced and marketed worldwide, our risk management strategies must also be approached from a global perspective;
- **Making decisions that consider the total product life cycle**--We must use both premarket and postmarket product experience/data in making regulatory decisions. Our practices and regulations must be focused on keeping products safe and effective throughout their entire life cycle; and,

- **Working with partners in all sectors** to strengthen the Agency's prevention efforts. We cannot accomplish our public health mission unless we collaborate with our stakeholders. The table below summarizes FDA's strategic goals, the desired outcomes of these goals, and key performance targets for FY 2003.

FDA Strategic Goals	Desired Outcomes	Key FY 2003 Performance Goals
Counter the Terrorist Threat.	Risks to U.S. citizens posed by potential or real terrorist attacks are minimized.	• Increase the number of physical exams of import entries by 100 percent; focus laboratory analysis on products with suspect histories or origins • Cover an additional 45 ports of entry where there are significant shipments of FDA-regulated products.
Maintain a Strong and Effective FDA	• State-of-the-art scientists and health professionals in position to make critical risk management decisions • Streamlined Agency optimally organized to support mission-critical activities • Cost-effective performance of functions • Citizen-centered agency accountable for results	• Develop and implement a plan to delayer all FDA components • Increase the percentage of electronically purchased transactions to 91 percent. • Increase the percentage of commercial FTE that will be reviewed for outsourcing to a total of 15 percent.
Assure Medical Product Safety	Significant reduction in the annual 100,000 deaths, injuries and illnesses is achieved because an effective safety net has been established which monitors medical products at all stages in the life cycle--from production	• Meet statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments. • Conduct targeted BSE

	through consumption.	inspections of 100 percent of all known renderers and feed mills handling prohibited material. • Ensure at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent with Level I (serious) problems in FY 2002. • Ensure that all international standards and negotiations are based on good science and protect the public health.
Bring New Technologies to a World-Wide Market	Because of the Agency's timely science-based decisions, millions of Americans can get the medicines and medical devices they need and be assured of safe and effective products.	• Review and act on 90 percent of standard original new drug, product licensing and blood licensing (NDA/PLA/BLA) submissions within 10 months of receipt and 90 percent of priority original NDA/PLA/BLA submissions within 6 months. (PDUFA goal) • Review and act upon 75 percent of fileable original generic drug applications within 6 months of submission date. • Complete 95 percent of Premarket Approval Application (PMA) first actions within 180 days.

FDA's Plan is aligned with HHS Strategic Goals

FDA's strategic goals are an integral part of HHS' one department philosophy. In virtually every Department arena FDA's initiatives are aligned with a broader HHS-wide strategy. The table below indicates this alignment.

FDA Strategic Goals	HHS Strategic Goals					
	1. Reduce the major threats to health and productivity of all Americans.	2. Improve the economic and social well-being of individuals, families, & communities in 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 & human services.	5. Improve the nation's public health systems.	6. Strengthen the nation's health sciences research enterprise & enhance its productivity.
Countering the Terrorist Threat	★			★	★	★
Maintaining a Strong and Effective FDA	★			★	★	★
Assuring Medical Product Safety	★			★	★	
Bringing New Technologies to a World-Wide Market				★	★	★

Part Two: Highlights of FY 2001 Accomplishments

Consumers and patients have traditionally placed a high level of trust in FDA to safeguard their interests. Surveys have repeatedly demonstrated this fact. FDA's significant successes during FY 2001 reinforce why the Public's confidence in FDA is well justified.

- FDA continues to review and approve medical products on a timely basis. For new drug and biologics applications received during FY 2000, the Agency met or exceeded all 15 performance review goals agreed upon. New drugs are approved in the U.S. as fast or faster than anywhere in the world, with the same high standards Americans expect. During the past year, several new therapies were approved including:
    - Gleevec, a new oral treatment for patients with chronic myeloid leukemia was reviewed and approved in two and half months;
    - The Given Diagnostic Imaging System, a new swallowable capsule containing a tiny camera that can facilitate early detection of colon cancer; and,
    - Xigris, the first biologic treatment for the most serious life threatening forms of sepsis, which claims 225,000 lives in the U.S. each year.
- FDA also approved and labeled nine drugs for pediatric use. As of October 2001, over 47,000 children have participated in clinical trials as a result of the studies FDA requested under the exclusivity provision.
- While new products continue to be approved in record times, the Agency also took steps to safeguard the interests of human subjects in clinical trials prior to products reaching the commercial review stage. In the medical device area alone, FDA conducted 238 domestic and foreign inspections under the bioresearch monitoring program. FDA relies heavily on the integrity of data generated from clinical trials in making many of its review decisions.
- FDA took steps to increase assurances that products imported into this Country will be safe. The Agency published a proposed rule that will require marking, prior to exportation, all foods refused for safety reasons. The proposed rule will assure that marked products are exported and not re-entered into the U.S. marketplace. The Agency also worked with USDA to strengthen the ban on feed, food products, dietary supplements and cosmetics that contain bovine materials from BSE-identified countries, so that these products do not enter the United States.
- Well before the events of September 11, several Agency components were engaged in the development of new regulatory models to accommodate the need for preparedness in the case of an emergency attack. For example, protocols were examined to guide the use of experimental medical products that might be used to counter the effects of an anthrax outbreak. FDA also participated in the U.S. Office of Foreign Disaster Assistance tabletop exercise with other federal, state and local governments to prepare for the eventuality of a terrorist attack.
- Finally, FDA's scorecard on FY 2001 performance goals indicates that the Agency met or exceeded almost 90 percent of the goals established at the beginning of the fiscal year.

Part Three: FDA Strategic Goals, FY 2002 and 2003 Performance Goals, and FY 2001 Performance Accomplishments

In Part Two of FDA's Performance Plan, each of the Agency's four strategic goals will be explained in greater depth. This Part is organized into four sections--one corresponding to each strategic goal. In each section, the following topics will be covered:

Desired Outcome--What impact does FDA hope to achieve?

Why FDA's Contribution is Important--What role does the Agency play in achieving the end result?

Key Strategies--What are the major elements of FDA's approach to achieve the strategic goal?

Current Status and Barriers to Future Progress--What is FDA's current performance in this area, what is the gap between actual and ideal performance, and what is preventing us from narrowing the gap?

Summary of Performance Goals and Accomplishments--This table will report on the status of FY 2001 performance goals; identify final FY 2002 performance goals based on Congressional appropriations; and indicate FY 2003 performance goals that are achievable with the President's budget proposal.

Strategic Goals

Counter the Terrorist Threat

Maintain a Strong and Effective FDA

Assure Medical Product Safety

Bring New Technologies to a World Wide Market

Countering the Terrorist Threat

Desired Outcome

Ensure that U.S. citizens are protected from public health threats posed by unexpected and potentially widespread terrorist attacks.

Why FDA's Contribution Is Important

The terrorist attacks of September 11 have required FDA to play a critical role in the national effort to combat future threats.

There is little experience in this country with deliberate terrorist incidents aimed at the civilian population. FDA must be vigilant in assessing and then quickly and effectively reducing risk associated with unexpected and potentially widespread health and safety threats to the U.S. public. Preparedness and response to potential terrorism acts are complicated by the unpredictable and multi-faceted nature of these hazards.

A combination of public health and law enforcement responsibilities requires FDA's involvement in a number of aspects of the preparedness for and response to terrorist activities. FDA's responsibilities encompass both the civilian and military sectors of the population, broadening the scope of the Agency's counter terrorism activities.

Key Strategies

FDA has developed an integrated strategic approach to address the threat of terrorism in the U.S. These strategies have the following characteristics:

- They build upon existing Agency capacities to manage health and safety risks;
- They leverage the strengths of health, scientific and law enforcement agencies to create a potent counter attack against terrorism; and,
- They create intelligence synergies by bringing the right combination of information to crucial decision points.

The total effect is creation of a safety net that significantly reduces the probability that terrorists will ever achieve their aims; and minimizes the impact of these threats if they do occur.

This safety net consists of four strategies:

- Protect regulated products: Deter, detect, investigate and interdict terrorist threats before they become a reality;
- Develop medical counter measures to minimize the impact of attacks on the population;
- Sharpen the Agency's emergency preparedness and response capability so that FDA is poised to protect the Nation and itself in the event of an attack; and,

- Ensure that radiation devices used to diagnose or treat terrorist-related incidents are safe and effective.

Each of these strategies is described in detail below.

Protect Regulated Products: Deterrence, Detection, Investigation, and Interdiction--This strategy focuses on decreasing the threat of contamination of the food supply, drug tampering or counterfeiting, sabotage of critical medical products, and contamination of animal feed. To be successful, FDA must monitor products from their source of production through the entire distribution system to the point of consumption. Three primary objectives are to:

1. Ensure Import Security--minimizing the threat at the country of origin before products are exported to the U.S.; and at the border so that hazardous products never enter the country. The latter will require greatly enhanced manpower and analytical capability at ports of entry;
2. Ensure Domestic Product Security--strengthening inspection coverage of domestic plants, augmenting product and pathogen testing, and closely monitoring product consumption to detect any pattern of adverse events that may stem from terrorist-related incidents; and,
3. Integrate Information to support risk management decisions--gathering, synthesizing and performing critical analysis of intelligence information and providing that information to those responsible for minimizing threats to the U.S. public health.

Medical Countermeasures--The purpose of this strategy is to assure drugs, vaccines, blood, medical devices and other medical products are available to prevent, diagnose or treat illnesses or injuries resulting from terrorist attack or battlefield injury. Key objectives are to:

1. Facilitate medical product development--stewarding the development of safe and effective drugs, vaccines and medical devices that can be promptly available to protect the public health and safety in the event of a attack;
2. Ensure availability of medical products-- working with federal health and defense agencies to maintain and manage the stockpile of medical products so that they are available in sufficient quantities to address public health emergencies; and,
3. Maintain the balance of public health needs and legal mandates to ensure safety--both interests must be satisfied in monitoring and controlling medical product use at the various stages of the medical product life cycle.

Emergency Preparedness and Response--Pivotal among FDA's strategies is to adequately prepare for, and promptly and effectively respond to terrorist attacks. Key objectives are to:

1. Enhance the Agency's emergency preparedness plan to establish protocols for responding to terrorist attacks;
2. Develop and implement, as needed, emergency contingency plans for specific terrorist incidents;
3. Establish a plan for continuity of FDA operations in an emergency; and,
4. Ensure the safety and security of FDA's most important assets--FDA personnel, physical assets, and information.

Radiation Safety--This country has long overlooked the criticality of radiation safety in day to day operations. FDA's fourth strategy focuses on radiation-emitting devices that are used to: detect potential security threats--e.g. in airports; destroy pathogens that may be released in a terrorist incident; and treat victims of terrorist-generated radiation incidents. This strategy also addresses the efficacy of devices that are used to detect the presence of radiation associated with terrorist events. Within this strategy key objectives are to:

1. Ensure that radiation-emitting products used for security screening or irradiation are safe both for human operators and human subjects;
2. Facilitate development and efficient distribution of medical counter measures to address radiation incidents; and,
3. Develop a radiological health emergency preparedness program.

Current Status and Barriers to Future Progress

The President's proposed budget for counter terrorism significantly strengthens FDA's ability to counter the terrorist threat. The proposal narrows the gap between the ideal and the actual state of affairs in three areas in particular:

1. Food Safety;
2. Medical Product Availability and Safety; and,
3. Internal Security.

In the area of **Food Safety,** the President's Budget annualized the FY 2002 Budget Supplemental for Counter Terrorism; and this will enable FDA to enhance inspection and analytical coverage of imported products. This will have the effect of more than doubling the Field import staff and substantially increasing the number of physical exams and laboratory analyses conducted at the border.

The Operational and Administrative System for Import Support (OASIS) will be enhanced to provide improved targeting of intelligence about suspected terrorism activities that might affect imports.

In addition, the Agency will be developing a Continuity of Operations Plan (COOP) which will allow the Agency to keep its major programs functioning in the event of a disabling attack.

High Performance Liquid Chromatography (HPLC) equipment will be purchased for rapid analysis of suspect foods for Select Agents toxins and other agents that could be used in a terrorist event.

On the domestic front, the Electronic Laboratory Exchange Network (eLEXNET) will be expanded to include more state health laboratories. The Network will also expand its capability to exchange data on select biological agents (possibly including anthrax, botulinum toxin, brucellosis and other potential infectious diseases.

This system is the first Internet-based food safety system that consolidates and shares pathogenic findings among Federal, State, and local government labs;

Additional increases are proposed to enhance **medical product availability.** Increased funds will be used to develop drugs, vaccines and medical devices that will counteract the intentional use of biological, chemical, or nuclear agents.

Internal security of FDA's facilities will be enhanced by proposed funding to:

- Increase physical security and provide for increased guard services, improved security systems, and physical barriers at the entrances to the Agency's buildings and parking lots;
- Secure storage for select agents, including lockable storage cabinets, refrigerators and freezers to prevent unauthorized use or theft;
- Develop and Validate rapid test methods for the detection of agents that could be deliberately introduced into the food supply; and,
- Upgrade designated laboratory facilities at NCTR (located in the Jefferson Laboratories of the FDA in Jefferson Arkansas) to a BioSafety Level 3 (BSL-3) to support BSE/TSE and microbial counter terrorism research.

FDA has developed a FDA five-year strategic plan to counter terrorism. This Plan proposes a staged solution that will ultimately bring the Agency to an ideal state of readiness in addressing the terrorist threat to this Nation. Strategies outlined for FY 2002 and FY 2003 are first steps toward the long-term solution.

Specific performance commitments for FY 2002 and FY 2003 and actual performance from FY 2001 are outlined in the table that follows.

Performance Goals Summary

FY 2001 Performance Report			FY 2002 - 2003 Performance Goals	
Program	**FY 2001 Goal**	**FY 2001 Status**	**FY 2002 Goal**	**FY 2003 Goal**
Deterrence, Detection, Investigation and Interdiction -- Focus on Food Safety				
Foods Goal 1	Complete the safety evaluation of 55 percent of the number of food and color additive petitions that were under review for more than 360 days at the beginning of the Fiscal Year.	FY 2001: 10/02	For the petition receipt cohort of FY 2001, complete within 360 days of filing, the safety evaluation of 60 percent of food and color additive petitions that do not qualify for expedited review.	For the petition receipt cohort of FY 2002, complete within 360 days of filing, the safety evaluation of 65 percent of food and color additive petitions that do not qualify for expedited review.
Foods Goal 2	Respond to 90 percent of notifications for dietary supplements containing "new dietary ingredients" within 75 days.	FY 2001: 100 percent	Respond to 95 percent of notifications for dietary supplements containing "new dietary ingredients" within 75 days.	Respond to 95 percent of notifications for dietary supplements containing "new dietary ingredients" within 75 days.
Foods Goal 4	NA	NA	Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days).	Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days).
Foods Goal 5	NA	NA	NA	Publish a final rule to require premarket notification for bioengineered foods.
Foods	Achieve adoption	FY 2001:	Achieve adoption of	Achieve adoption of

Goal 6	of the Food Code by at least one state agency in 25 states in the USA.	28	the Food Code by at least one state agency in 28 states in the USA.	the Food Code by at least one state agency in 33 states in the USA.
Foods Goal 7	Inspect 95 percent of high-risk domestic food establishments once every year.	FY 2001: 74 percent	Inspect 95 percent of high-risk domestic food establishments once every year.	Inspect 95 percent of high-risk domestic food establishments once every year.
Foods Goal 11	NA	12,169 physical exams conducted on food imports	Increase food import surveillance by hiring 300 new investigators and analysts who will increase the number of physical exams by 97 percent to 24,000 and conduct sample analyses on products with suspect histories.	Increase the number of physical exams by 100% (48,000 exams) and conduct sample analyses on products with suspect histories.
Foods Goal 12	NA	NA	Extend import coverage to an additional 45 ports that handle significant quantities of FDA-regulated products.	Enhance productivity at the additional ports through focused training
Foods Goal 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.	FY 2001: 10/02	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.	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.
NCTR Goal 6	NA	NA	Acquire high-resolution mass spectrometer for use with protein from bacteria, food toxins and genomics studies.	NA
NCTR Goal 6	NA	NA	Upgrade existing laboratory facilities to BSL-3 to support BSE/TSE and	Outfit upgraded laboratory, provide for supplies (agents, chemicals/pathogens)

			microbial bioterrorism work.	and construct library databases of proteins and test to find toxin related markers.
NCTR Goal 6	NA	NA	Recruit additional expertise in Computational Science, Chemistry and Microbiology.	Recruit additional expertise in Computational Science, Chemistry and Microbiology.
Medical Product Availability and Safety				
Human Drugs Goal 5	NA	NA	Publish a Guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure).	NA
Human Drugs Goal 6	NA	NA	Facilitate the initiation of research in a non-human primate model of pneumonic plague	NA
Human Drugs Goal 7	NA	NA	Expedite the review of protocols for investigational new drugs (INDs) to treat organophosphorous nerve agents in the event of a chemical attack. Encourage sponsors of these new drug applications (NDAs) to update current labeling for Antidote Treatment - Nerve Agent, Autoinjectors (ATNAA).	NA
Human Drugs Goal 8	NA	NA	NA	Identify and begin to address labeling gaps in the therapeutic armamentarium for the prevention, mitigation, and treatment of illnesses cases by chemical and biological

				attacks, including the needs for special populations, such as pregnant women, pediatric, and geriatric populations.
Human Drugs Goal 9	NA	NA	NA	Develop a Guidance for Industry on developing antiviral drugs for the mitigation of complications associated with vaccinia immunization.
Human Drugs Goal 10	NA	NA	NA	Facilitate human clinical trials in pneumonic plague for antimicrobial drugs that are not yet labeled for this treatment indication.
Human Drugs Goal 11	NA	NA	NA	Develop a Guidance for Industry on developing antiviral drugs for the treatment of smallpox.
Human Drugs Goal 12	NA	NA	Publish a final rule that allows the Agency to approve new drug and biological products for the treatment of chemical, biological, radiological, or nuclear substances based on animal efficacy studies when adequate and well-controlled studies in humans cannot be ethically conducted and field studies are not feasible.	NA
Human Drugs Goal 19	NA	NA	Publish a Notice of Proposed-Rulemaking to establish a web-	Finalize rulemaking to establish a web-based electronic drug registration and listing

			based electronic animal and human drug and biologics registration and listing database to allow for complete and up-to-date data on all regulated drug products.	database to allow for complete and up-to-date data on all regulated drug products, and follow this finalization with launch of the electronic database.
Human Drugs Goal 20	NA	NA	Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax.	NA
Biologics Goal 6	NA	NA	NA	Expedite review of product specific lot release and extension of dating submissions for the Anthrax Vaccine Absorbed (AVA).
Biologics Goal 7	NA	NA	NA	Provided guidance to the CDC, DOD and the Anthrax Vaccine Absorbed manufacturer regarding clinical studies to support proposed changes in the immunization schedule and routes of administration.
Biologics Goal 8	NA	NA	NA	Facilitate expedited development and review of new vaccines for protection and/or treatment against bioterrorism related threat diseases (e.g., smallpox and anthrax vaccines).
Biologics Goal 9	NA	NA	NA	Facilitate expedited development and review of new gamma globulins for protection and/or

				treatment against bioterrorism related threat diseases.
Biologics Goal 10	NA	NA	NA	Evaluate the need for guidance documents to assist in the development of products such as immunoglobulins and select vaccines.
Emergency Preparedness and Response-- Focus on Internal Security				
Administrative Management Goal 7	NA	NA	Develop a continuity of operations plan (COOP) for FDA, and participate with PSC in development of a Parklawn COOP	Finalize and implement the Plan.
Administrative Management Goal 8	NA	NA	Enhance the Agency Emergency Preparedness plan to establish protocols for responding to terrorist attacks	NA
Radiation Safety				
Human Drugs Goal 13	NA	NA	NA	Expedite the review of protocols for investigational new radioprotectant drugs (including heavy metal chelators) for use in the event of a radiation emergency.
Human Drugs Goal 21	NA	NA	Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies.	NA
Medical Devices Goal 4	NA	NA	NA	Expedite review for 100 percent of Bio-terrorism Diagnostic medical device applications.

Medical Devices Goal 14	NA	NA	Develop Emergency Counter Terrorism Preparedness and Response Plan for radiation.	Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation.
Medical Devices Goal 15	NA	NA	NA	Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places.

Maintaining a Strong and Effective FDA

Desired Outcome

- Ensure that state-of-the-art scientists and health professionals are recruited and retained so that the American people can benefit from scientifically sound risk management decisions;
- Operate a streamlined Agency that is optimally organized to support mission-critical activities;
- Maximize cost-effective performance of functions by achieving a rational balance of in-house and outsourced activities; and,
- Maintain FDA's high standards as a citizen-centered agency accountable for results.

Why is FDA's Contribution Important?

A strong and effective FDA is a core element of the Nation's ability to deal with large, complex and unpredictable risks. The Agency is positioned at crucial decision making points day in and day out, which involve the health and safety of millions of citizens. The recent terrorist events only serve to accentuate the point that if FDA is not scientifically well-armed and able to move quickly and efficiently, then our Country stands on shaky ground. A weakened FDA can only move slowly and with uncertainty. Consumer confidence in the Agency suffers, and real health and safety risks may grow.

Key Strategies

Each of the strategies outlined below are aligned with the President's management objectives to make all Federal government agencies more streamlined and citizen-centered. They are intended to produce greater returns

on human capital investments; more effective systems, structures and processes; and greater responsiveness to the needs of the American people.

Recruit, reward and retain state-of-the-art scientists and health professionals--FDA will continue to aggressively recruit the highest caliber professionals and utilize web-based recruiting strategies to broaden reach and accelerate access. Both monetary and non-monetary incentives are critical in rewarding the top performers in FDA's workforce.

Improve management systems--FDA continues to focus on improving the effectiveness of a wide range of systems that support Agency decisions. These include financial management, procurement, information management security, and workforce planning and performance. The Agency has embarked on several initiatives that include redesigning its financial management system, accelerating movement toward electronic procurements, integrating Agency information systems, and establishing a "continuity-of-operations" plan in the event of an emergency.

Design Effective Organizational Structures--The objective of a well-designed organization structure should be to support the mission of the organization. In FDA's case, several efforts are underway to improve organizational alignments. In response to the OMB Directive of May 8, 2001, FDA submitted a restructuring plan, based on a workforce analysis, to make the agency more streamlined and "citizen-centered." The Agency has also awarded a contract to determine the most effective configuration of administrative functions, and will be implementing contractor recommendations during FY 2002 and FY 2003.

Achieve cost-effective performance of traditional government activities--FDA has committed to examining its' commercial FTE to determine which activities would be more cost-effective if outsourced. The aim is to arrive at a rational balance of in-house and outsourced activities that will maximize overall cost-effectiveness.

Respond to citizens' needs--In 1997, Congress enacted the FDA Modernization Act, which reaffirmed the Agency's long tradition of collaboration with our constituents. Section 406(b) of the Modernization Act directed the Agency to consult with our constituencies to ensure that we fulfill our statutory mandates and that we communicate clearly with our stakeholders. FDA continues to hold frequent meetings with its stakeholders to gather views on regulatory issues and discuss a variety of public health issues. FDA has worked very hard to ensure that everyone affected by the Agency's actions has a voice, and that each voice is heard. While all of these voices may not share the same viewpoint, we have found that this open discourse can engender confidence.

The latest Pew Foundation study reported that over three quarters of consumers, health professionals, patients, and industry representatives say they trust FDA to make the right decisions--more than twice the approval rate for government as a whole.

However, despite these positive signs, FDA must work to remain vigilant in its responsibilities to the American public. FDA's collaborative efforts with other Federal and State governmental agencies, regulated industry and the American public, will ensure that the safest and most effective products are made available in a timely manner, and that critical product safety information is relayed to the American public and health care professional quickly.

Current Status and Barriers to Further Progress

Human Capital --Progress varies. In terms of recruiting and retaining the necessary skill base, FDA is faced with the challenge of replacing its critical knowledge base as a large aging segment of its workforce reaches retirement age. Monetary incentives continue to challenge FDA and other federal agencies because we simply cannot match private sector salaries. In order to enhance competitiveness with industry, FDA would need greater flexibility in recruitment strategies and in pay incentives. While appointment mechanisms in the excepted service, i.e., Title 42 of the Public Health Service Act, offer some relief, they are not appropriate for all hiring situations.

Congress funded pay increases in FY 2002. The provision of pay increases as part of the FY 2003 budget request to Congress will go a long way toward re-establishing incentives among both manager and employees.

On the other hand, FDA has initiated non-monetary, quality of work life incentives that are having a major positive impact. This is reinforced by recent surveys of federal employees, where FDA respondents gave their agency a 72 percent favorable rating in employee job satisfaction--highest of the 49 agencies surveyed.

Management Systems--There is also mixed progress in the area of management systems. There are a few bright signs. FDA has realized $14 million in cost avoidance in FY 2000 through innovative procurement methods. But there are also major issues. Cyber security remains a critical IT management challenge for FDA in FY 2002 and beyond. In light of anticipated terrorist threats, FDA has established a goal to develop a continuity-of-operations plan in FY 2002.

Organization structure--Some common challenges are also being addressed across all of the Agency's organizational structures. These include: determining the appropriate degree of centralization vs. decentralization; maintaining alignment with the mission and strategies of the Agency; arriving at a

reasonable balance between system stabilization and system adaptation--particularly to new technologies; and determining cost-effective approaches to streamlining.

FDA also continues to implement its plan to consolidate headquarters facilities with the aim of improving the cost effectiveness of headquarters operations. Facilities that are now scattered among many locations will be concentrated in two locations in White Oak and College Park, Maryland. Currently, FDA Headquarters is located in 40 buildings in 18 locations. As a part of the FDA Revitalization Act, FDA has embarked on a five-year plan to relocate the major portion of its headquarters personnel to White Oak Maryland. This project, coupled with ongoing efforts to reduce supervisory ratios and delayer headquarters staff will afford FDA maximum flexibility to move resources closer to the day-to-day "front line" programmatic work of the Agency.

Specific performance commitments for FY 2002 and FY 2003 and actual performance from FY 2001 are outlined in the table that follows.

Performance Goals Summary

FY 2001 Performance Report			2002 - 2003 Performance Goals	
Program	**FY 2001 Goal**	**FY 2001 Status**	**FY 2002 Goal**	**FY 2003 Goal**
Organization structure improvements				
Administrative Management Goal 1	Increase supervisory ratio to increase span of control among management to 1:7.28	FY 2001: 1 : 7.69	Develop and implement a plan to delayer FDA components (3 per fiscal year) starting with NCTR, CVM, and CDRH.	Develop and implement a plan to delayer FDA components for CBER, CFSAN, and ORA.
Administrative Management Goal 1	N/A		Plan for the transfer of Legislative and Public Affairs functions to the Department.	Implement the transfer of Legislative and Public Affairs functions to the Department.
Administrative Management Goal 2	N/A	Merged Management, Information Systems, and Evaluation Staff.	Award contract for study of administrative functions to be completed by 9/02 (except for HR function which is to be completed by 5/02).	Implement contractor’s recommendations in the following areas: Personnel, Finance, Budget, Procurement, Grants, and Information

			Requirements and alternative analysis for IT consolidation in Centers and Agency.	Technology.
System Improvements				
Administrative Management Goal 3	N/A	N/A	Increase the percentage of commercial FTE that will be reviewed for outsourcing to 5 percent.	Increase the percentage of commercial FTE that will be reviewed for outsourcing to a total of 15 percent.
Administrative Management Goal 4	Increase the percentage of electronically purchased transactions to 87 percent.	FY 2001: 90.5 percent	Increase the percentage of electronically purchased transactions to 89 percent.	Increase the percentage of electronically purchased transactions to 91 percent.
Administrative Management Goal 5	Maintain a clean (or unqualified audit opinion with no material weakness.	FY 2001: Yes	Maintain a clean (or unqualified audit opinion with no material weakness.	Maintain a clean (or unqualified audit opinion with no material weakness.
Administrative Management Goal 6	N/A	FY 2001: 23.6 percent	Achieve a total of 25 percent of contract dollars to performance based contracts.	Achieve a total of 30 percent of contract dollars to performance based contracts.
Enhanced Science Base				
Human Drugs Goal 15	Conduct laboratory research on at least three projects identified as related to the mission of PQRI	Initiated 3 laboratory research programs (Oral Biopharmaceutics, Drug Product, and Drug Substance programs) And performed the corresponding research in connection with the mission of PQRI.	Conduct laboratory research on at least 3 projects	CDER will continue with significant progress (defined as 25 percent toward completion for each project) on the three projects identified by the PQRI.
Animal Drugs and Feeds	Initiate the development of	Initiated the development of a	Plan and design the option selected	Expansion of content and

Goal 5	a Staff College (Phase I: further needs assessment, feasibility studies, and analysis of alternatives).	Staff College (Phase I).	in Phase I.	developmental components & integration w/Center & Agency IT infrastructure.
Animal Drugs and Feeds Goal 7	Develop an antibiotic risk assessment model using fluoroquinolone, chickens and Campylobacter. Perform 2 risk assessments.	Performed risk assessments for Campylobacter and Synercid™.	N/A	N/A
NCTR Goal 1	Provide peer reviewed articles on new Genetic and transgenic systems and knowledge to product reviewers.	Publications submitted to peer reviewed journals: (1) describing methodology damage to mitochondria and (2) providing a review of the possibility of using new genotypic selection for risk assessment.	Conduct one biologi-cally based mechanistic study combined with pre-dictive modeling to improve extrapolation of animal data to the human condition.	Provide an evaluation of the new molecular technology for detecting alterations in multiple genes.
NCTR Goal 2	Develop "risk chip" technology to screen large numbers of people for biomarkers simultaneously.	Risk chip used to screen population resulted in initiation of negotiations to extend the use of biomarkers and other subpopulations for further investigation.	Support at least two multi-disciplined DNA and RNA-based microarray technologies.	Present one finding and publish one result of the microarray technology polymorphism study.

Assuring Medical Product Safety

Desired Outcome

Assure the safety of medical products at all stages in the life cycle--production, distribution and consumption.

Why FDA's Contribution is Important

Consumers spend $326 billion annually in the U.S. on medical products. An estimated 1.3 million people are accidentally injured by medical therapy in the U.S. each year, and as many as 100,000 die as a result of preventable medical errors. FDA must be vigilant in monitoring the production, distribution and use of these products because FDA's presence raises the likelihood that public health and safety problems associated with these products will be addressed and because it is critical to citizen safety.

To ensure that these products are safe the Agency must oversee their entire life cycle--from production through distribution, and consumption/use. In the production and distribution phases of the cycle FDA must monitor over 40,000 establishments that manufacture these products. FDA is also responsible for ensuring the safe operation of some 10,000 mammography facilities. In addition, FDA must monitor over 2 million line entries of imported drugs, biologics, animal drugs and feeds, and medical devices that cross our borders annually.

Key Strategies

FDA's three primary strategies for ensuring medical product safety are to: a) enhance global vigilance over product manufacturing and distribution; b) strengthen and focus domestic industry monitoring; and, c) expand and automate the systems which report on adverse events associated with the use of medical products.

In the **global** arena, FDA plans to enhance the automated import monitoring system (OASIS) to improve cost effectiveness in screening unacceptable imports; and expand import coverage at ports. The Agency will also increase criminal investigations of fraudulent medical product imports. To improve public confidence in the safety of foreign medical products at the source, FDA will implement the European Mutual Recognition Agreement; participate in international standard setting forums such as the International Conference on Harmonization (ICH) to continue to advocate for rigorous standards; and increase the number of foreign inspections.

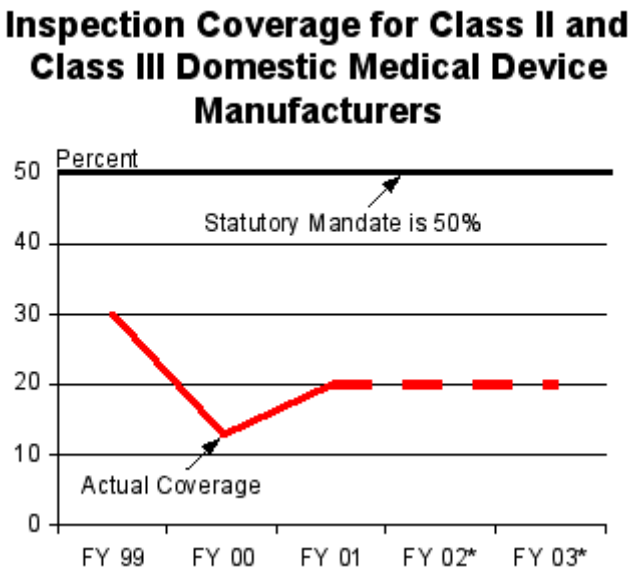
On the **domestic** front, FDA will continue to make the most effective use of limited inspection resources by implementing four key strategies: 1) Leveraging through contracts with the states, other third parties and outreach to small firms; 2) Focusing resources on the highest risk firms and medical products--areas which will bring the greatest health benefit; 3) Ensuring that inspectors have the scientific and technological support necessary to make quick and valid judgements about medical device compliance; and, 4) Reengineering the inspection process by implementing quality system inspections that will significantly reduce inspection time and increase effectiveness.

FDA's **adverse event reporting** strategies are intended to: develop a comprehensive adverse event reporting capability; analyze problems surfaced by these reports so that appropriate interventions can be designed; and educate both health professionals and patients about problems and solutions associated with appropriate product use. Two examples of strategies designed to develop more complete reporting are the Medical Device Surveillance Network (MeDSuN) System and the HHS Patient Safety Task Force. The MeDSuN System is a pilot program that educates and encourages hospital personnel to accurately identify and report injuries and deaths associated with medical products. This year FDA will implement the third phase of the (MeDSuN) to include drug products. FDA is also coordinating with the Department's Patient Safety Task Force to gain synergies from existing systems that are already collecting data on patient safety.

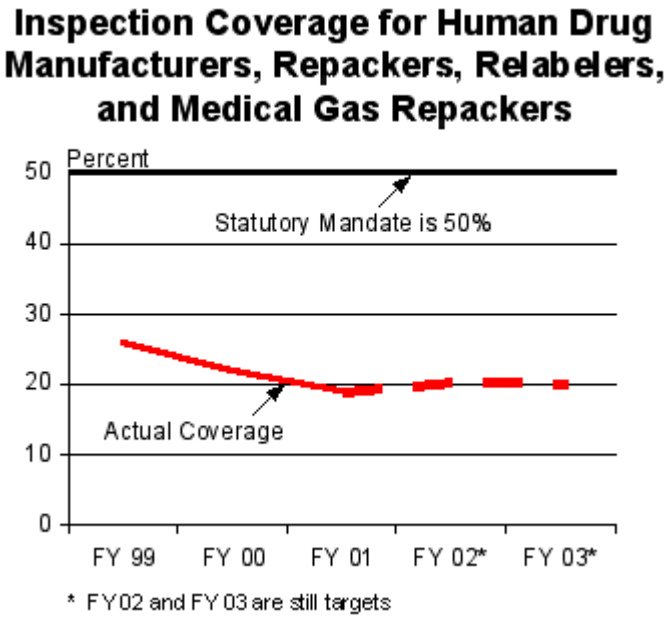
Current Status and Barriers to Future Progress

Global Vigilance -- Imports of all FDA regulated products have been increasing over the last several years--growing at an annual rate of 10 to 12 percent. In FY 2001, FDA physically examined less than one percent of all entries offered for import into the United States. A highly integrated web-enabled import monitoring system is required to allow the Agency to prevent unsafe import entries on a cost-effective basis. The proposed FY 2003 budget will fund the first steps toward establishing such a system. Alternatively, FDA would need restructured regulatory authority that would place more responsibility on exporters to assure that products entering the U.S. are safe.

Domestic Industry Monitoring -- The law requires that FDA inspect certain biologics, human and animal drug and feed, and medical device manufacturers at least once every 2 years. Although at least 50 percent of statutory establishments should be inspected annually, only 22 percent of human drug, and 13 percent of medical device statutory establishments were inspected in FY 2000. FDA will still fall far short of its statutory inspection requirements given current funding levels.

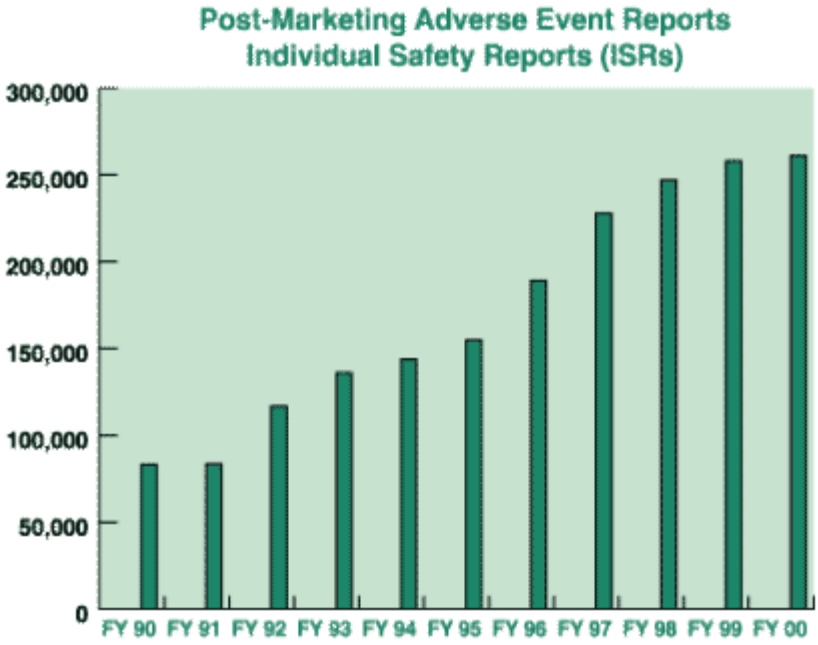


* FY 02 and FY 03 are still targets



Adverse Event Reporting -- 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 how to use the new labeling. But the adverse event reporting system must be significantly strengthened. Although we do not know the actual number of adverse events associated with medical

products, just the reports we receive have more than doubled in the past ten years.



FDA needs more expertise in medical epidemiology and statistical analysis to evaluate adverse events associated with increasingly complex medical products, and more educational efforts to correct these problems.

Specific performance commitments for FY 2002 and FY 2003 and actual performance from FY 2001 are outlined in the table that follows.

Performance Goals Summary

FY 2001 Performance Report			FY 2002 - 2003 Performance Goals	
Program	**FY 2001 Goal**	**FY 2001 Status**	**FY 2002 Goal**	**FY 2003 Goal**
Global Vigilance				
Medical Devices Goal 11	Inspect 9 percent of Class II and Class III foreign medical device manufacturers.	Completed: 11 percent of foreign device manufacturers were inspected during FY 2001.	Inspect 9 percent of Class II and Class III foreign medical device manufacturers.	Inspect 9 percent of Class II and Class III foreign medical device manufacturers.

Domestic Industry Monitoring				
Human Drugs Goal 16	Inspect 26 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.	Not Completed: 18 percent of drug establishments were inspected during FY 2001. Resources were diverted to high-risk inspection situations — particularly monitoring clinical trials with vulnerable populations.	Inspect 26 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.	Inspect 26 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.
Human Drugs Goal 17	Assure that 90 percent of drug industry is in conformance with FDA requirements.	Completed: 95 percent conformance rate is an estimate based on limited baseline data.	NA	NA
Biologics Goal 11	Assure that 90 percent of biologics industry is in conformance with FDA requirements.	Completed: 99 percent conformance rate is an estimate based on limited baseline data.	NA	NA
Biologics Goal 12	Maintain the percentage of plasma fractionator establishments in compliance at 80 percent.	Not Completed: 69 percent of these establishments were in compliance in FY 2001. Inspections continue to find compliance discrepancies.	NA	NA
Biologics Goal 13	Meet statutory requirement by inspecting 50 percent of blood banks, source plasma operations and biologics manufacturing	Exceeded: 57 percent of the blood banks were inspected during FY 2001.	Inspect 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments.	Inspect 50 percent of registered blood banks, source plasma operations and biologics manufacturing

	establishments.			establishments.
Animal Drugs and Feeds Goal 8	Maintain statutory requirement by inspecting 50 percent of registered animal drug and feed establishments.	Not Completed: 37 percent of establishments inspected. Resources were redirected to perform BSE inspections in order to minimize risk of BSE introduction into the U.S.	Maintain statutory requirement by inspecting 50 percent of registered animal drug and feed establishments.	Maintain statutory requirement by inspecting 50 percent of registered animal drug and feed establishments.
Animal Drugs and Feeds Goal 9	Assure that 90 percent of animal drug industry is in conformance with FDA requirements.	Completed: 99 percent conformance rate is an estimate based on limited baseline data.	NA	NA
Animal Drugs and Feeds Goal 10	Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.	CY 2001: Data not available until March 2002. CY 2000: Total: 11,000 Salmonella isolates	Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.	Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.
Animal Drugs and Feeds Goal 11	N/A	N/A	Conduct targeted BSE inspections of 100 percent of all known renderers and feed mills handling prohibited material.	Conduct targeted BSE inspections of 100 percent of all known renderers and feed mills handling prohibited material.
Medical Devices Goal 8	Inspect 17 percent of Class II and III domestic medical device manufacturers.	Completed: 20 percent	Inspect 20 percent of Class II and Class III domestic medical device manufacturers.	Inspect 20 percent of Class II and Class III domestic medical device manufacturers.
Medical Devices Goal 9	Assure that 90 percent of medical device industry is in conformance with FDA	Completed: 96 percent conformance rate is an estimate based	NA	NA

	requirements.	on limited baseline data.		
Medical Devices Goal 12	Ensure at least 97 percent of mammography facilities meet FDA standards	Completed: 97 percent of the mammography facilities met this requirement.	Ensure at least 97 percent of mammography facilities meet inspection standards.	Ensure at least 97 percent of mammography facilities meet inspection standards.
Adverse Event Reporting				
Human Drugs Goal 14	Issue guidance on electronic submission of adverse drug event reports. Roll out AERS datamart to medical officer in new drug review divisions.	Completed: Guidance issued. AERS datamart is now being utilized by medical officers in drug review divisions.	Accept electronic submissions from drug companies, and code information consistent with internationally accepted standards.	Major reporting companies will submit adverse drug reports electronically for all types of reports.
Medical Devices Goal 13	Implement MedSun System by recruiting 75 hospitals.	Not Completed: Only 25 hospitals were recruited, more effort than expected was needed for software development, and increased IT security requirements.	Build a medical device surveillance network of 80 facilities.	Extend network to 180 facilities.

Bringing New Technologies To A World-Wide Market

Desired Outcome

To provide quick and safe access to products of new technologies and to enhance U.S. consumer access to these new products, as well as to less expensive generic drugs.

Key Performance Goals

	PDUFA Goal	Actual Performance

FY 1997	90%	100%
FY 1998	90%	100%
FY 1999	90%	100%
FY 2000	90%	100%
FY 2001	90%	
FY 2002	90%	
FY 2003	90%	

	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%	56%	96%
FY 2001	100%	50%*	97%
FY 2002	100%	65%*	95%*
FY 2003	100%	75%*	95%*
* Targets			

Why is FDA's contribution important?

Pre Market Review

FDA's signature activity and a prime service to the American public is to review the safety and effectiveness of drugs, biologics, feeds, 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.

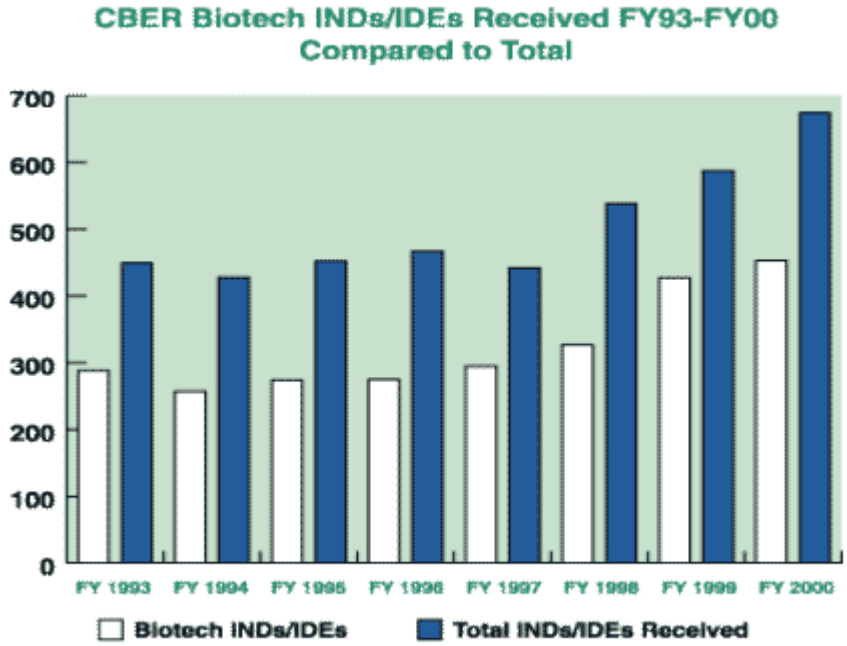
FDA's primary goal is to reduce the time required for review of new product applications without sacrificing standards of performance and safety. Since 1990, FDA review times for new drugs have been cut in half--from 24 months

to less than 12 months. In addition to the obvious health benefits of getting needed drugs to the public much more quickly, faster reviews have also resulted in significant savings to the pharmaceutical industry.

FDA has also approved several thousand generic drugs and medical devices that are used successfully by millions of patients.

Although FDA does place emphasis on expedited review of new products, it is also responsible for overseeing all of the activities that span new product development--from initial research to final market approval. Among the factors that must be monitored and well managed are:

- **New technologies** -- FDA must have a state-of-the-art understanding of the new science and technology that fuels these new products--particularly developments in the biotechnology field--so that review decisions on such products can be based on rigorous science-based standards;



- **Special population needs**--FDA must carefully monitor research and development activities as they progress through the clinical trial stage in order to guide safe and effective products toward populations that need these products, particularly children and the elderly; and
- **Human Subject Protection**--FDA, in cooperation with other health and safety overseers, must ensure that human subjects are adequately protected during clinical trials. There is heightened concern for the rights

and welfare of volunteers, given 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.

Key Strategies

Pre Market Review

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

- Continue the Prescription Drug User Fee Act (PDUFA) Program. This initiative has been extremely successful, and serves as a model for reinventing government with all stakeholders working together to achieve performance goals that make a difference to the Nation;
- Develop standards for new products of emerging technologies, such as novel drugs and biologics, to facilitate product development, expedite reviews and move products to market faster;
- Strengthen external ties. Expeditious medical product review is dependent upon enhanced collaboration and cooperation with industry, academia, professional societies and health care professionals;
- Implement a comprehensive quality control system to ensure the Agency's premarket review processes are held to the highest standards. FDA is working with stakeholders to implement this in the least burdensome way;
- Continue to prioritize products to increase the efficiency of "fast track" review processes in order to address the most urgent needs for new medical products first; and,
- Improve the generic drug review program to reduce review backlogs and review all application within six months.

New Technologies

FDA will continue to increase its expertise in and understanding of new technologies that shape new products submitted for approval. For example, it is anticipated that drug development in the future will be based increasingly on an understanding of the sequencing in the human genome. FDA will have to maintain parallel expertise. At the same time, the Agency must take steps to ensure the safety of these products. For example, 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.

Special Populations--Pediatric Medicine

FDA will also implement strategies targeted toward serving special populations with needed new products--particularly children. These strategies stem from provisions contained in The FDA Modernization Act of 1997 (FDAMA). The provisions established economic incentives for industry to conduct pediatric studies in the form of 6 months of 'exclusivity' to be attached to any existing exclusivity or patent protection on a drug for which FDA has requested pediatric studies and where the manufacturer has conducted such studies in accordance with the requirements of FDAMA.

Human Subject Protection

To protect volunteers in clinical research 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 (IRBs); and enhance follow-up compliance activities.

Current Status and Barriers to Further Progress

Pre Market Review 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, in 25 percent less time than in FY 1997.

In the area of generic drugs, recent increases have enabled the program to raise performance targets. Currently, review times are running three times longer than the statutory limit, but the review staff has been augmented to shorten review time.

Animal drug reviews are facing major hurdles because accelerating science and technology associated with these new products require more intensive evaluations. A strongly funded user fee program would help lower these hurdles.

	FY 1990	FY 1995	FY 2000
	Months	Months	Months

Drugs (PDUFA)	23.8	18.7	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

Pediatric Medicine

The pediatric exclusivity provision has done more to generate clinical studies and useful prescribing information for the pediatric population than any other regulatory or legislative process to date. As a result of this provision, FDA has issued 191 Written Requests as of May 1st asking for over 300 studies that would potentially involve well over 20,000 pediatric patients. The Agency has also issued 31 grants of pediatric exclusivity. However, because of the anticipated significant increase in application supplements requesting exclusivity, the proposed expansion of PDUFA user fees is needed. In addition, the exclusivity provision in FDAMA does not apply to drugs with no remaining exclusivity or patent life. Thus, a number of drugs are on the market for which clinical trials tailored to children have not been conducted.

Specific performance commitments for FY 2002 and FY 2003 and actual performance from FY 2001 are outlined in the table that follows.

Performance Goals Summary

FY 2001 Performance Report			FY 2002 - 2003 Performance Goals	
Program	**FY 2001 Goal**	**FY 2001 Status**	**FY 2002 Goal**	**FY 2003 Goal**
Premarket Review				
Human Drugs Goal 1	Review and act on 70 percent of standard original NDA submissions within 10 months of receipt and 90	FY 2001: Data available 1/2003 FY 2000: 79 percent of Standard NDAs and 97 percent of	Review and act on 90 percent of standard original NDA submissions within 10 months of receipt and 90	Review and act on 90 percent of standard original NDA submissions within 10 months of

	percent of priority original NDA submissions within 6 months.	Priority NDAs	percent of priority original NDA submissions within 6 months.	receipt and 90 percent of priority original NDA submissions within 6 months.
Biologics Goal 1	Review and act on 70 percent of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90 percent of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt.	FY 2001: Data available 9/2002 and 5/2002 FY 2000: 100 percent of Standard NDA/PLA/BLAs and 100 percent of Priority NDAs/PLA/BLAs	Review and act on 90 percent of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90 percent of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt.	Review and act on 90 percent of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90 percent of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt.
Biologics Goal 2	Review and act on 70 percent of standard PDUFA efficacy supplements within 10 months; and review and act on 90 percent of priority PDUFA efficacy supplements within 6 months of receipt.	FY 2001: Data available 9/2002 and 5/2002 FY 2000: 100 percent of Standard efficacy supplements and 100 percent of Priority efficacy supplements	Review and act on 90 percent of standard PDUFA efficacy supplements within 10 months; and review and act on 90 percent of priority PDUFA efficacy supplements within 6 months of receipt.	Review and act on 90 percent of standard PDUFA efficacy supplements within 10 months; and review and act on 90 percent of priority PDUFA efficacy supplements within 6 months of receipt.
Biologics Goal 3	Review and act on 90 percent of PDUFA manufacturing supplements within 6 months of receipt, and review and act on 90 percent of PDUFA manufacturing	FY 2001: Data available 5/2002 FY 2000: 100 percent of Standard manufacturing supplements and 100 percent of Priority manufacturing	Review and act on 90 percent of PDUFA manufacturing supplements within 6 months of receipt, and review and act on 90 percent of PDUFA manufacturing	Review and act on 90 percent of PDUFA manufacturing supplements within 6 months of receipt, and review and act on 90 percent of PDUFA

	supplements requiring prior approval within 4 months of receipt.	supplements	supplements requiring prior approval within 4 months of receipt.	manufacturing supplements requiring prior approval within 4 months of receipt.
Biologics Goal 4	Review and act on 90 percent of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90 percent of Class 2 resubmitted original PDUFA applications within 6 months of receipt.	FY 2001: Class 1 — 100 percent Class 2 - Data available 5/2002 FY 2000: Class 1 — 100 percent Class 2 — 100 percent	Review and act on 90 percent of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90 percent of Class 2 resubmitted original PDUFA applications within 6 months of receipt.	Review and act on 90 percent of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90 percent of Class 2 resubmitted original PDUFA applications within 6 months of receipt.
Biologics Goal 5	Review and act on 90 percent of complete blood bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA supplements within 12 months after submission date.	FY 2001: Data available 11/2002 FY 2000: Complete Submissions — 100 percent Supplements — 100 percent	Review and act on 90 percent of complete blood bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA supplements within 12 months after submission date.	Review and act on 90 percent of complete blood bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA supplements within 12 months after submission date.
Animal Drugs and Feeds Goal 1	Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80 percent.	Completed FY 2001: 80 percent	Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80 percent.	Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80 percent.
Animal Drugs and	Review and act on 75 percent of NADAs/ANADAs within 180 days of receipt.	Not Completed: FY 2001 --50 percent. Review resources were shifted in order to reduce the	Review and act on 50 percent of NADAs/ANADAs within 180 days of receipt.	Review and act on 90 percent of all new animal drug applications and

Feeds Goal 2		backlog of pending overdue applications.		supplements within 275 days and review and act on 90 percent of all investigational new animal drug data submissions (type P) within 325 days.
Animal Drugs and Feeds Goal 3	N/A	N/A	Reduce pending overdue Animal Drug applications by 15 percent.	Reduce pending overdue Animal Drug applications by 15 percent.
Animal Drugs and Feeds Goal 4	Continue to pilot and validate procedures to receive protocol submissions electronically. Initiate the development of a method for receiving protocol submission electronically	Changed focus of protocol submission to hard media (e.g., tapes, cd-rom, hard drives). Implemented automated logging/routing of e-mail electronic submissions. Posted standards on dockets for submission of electronic information in support of NADAs. On-going contract to develop CVM-specific guidance for file organization and format for hard media submissions. Expanded electronic archive to accept hard media submissions.	Pilot and validate the procedure for receiving protocol submissions electronically.	Receive protocols and ADE active form.
Animal Drugs and	Revise and develop 14 guidances. FY	FY 2001: Completed 7 final and 7 draft	FY 2002: NA	FY 2003: NA

Feeds Goal 6	2001: 3 manufacturing, 10 new drug approval process and 1 Veterinary International Conference on Harmonization (VICH) guidances.	manufacturing, new animal drug approval process and VICH guidances.		
Medical Devices Goal 1	Review and Complete 90 percent of Premarket Approval Application (PMA) first actions within 180 days.	Completed FY 2001: 97 percent	Review and Complete 90 percent of Premarket Approval Application (PMA) first actions within 180 days.	Review and Complete 95 percent of Premarket Approval Application (PMA) first actions within 180 days.
Medical Devices Goal 2	Review and complete 90 percent of PMA supplement final actions within 180 days.	Completed FY 2001: 98.4 percent	Review and complete 90 percent of PMA supplement final actions within 180 days.	Review and complete 95 percent of PMA supplement final actions within 180 days.
Medical Devices Goal 3	Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.	Completed FY 2001: 100 percent	Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.	Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.
Medical Devices Goal 5	Complete 95 percent of PMA Determination meetings within 30 days.	Completed FY 2001: 100 percent	Complete 95 percent of PMA "Determination" meetings within 30 days.	Complete 95 percent of PMA "Determination" meetings within 30 days.
Medical Devices Goal 6	Recognize 20 new or enhanced standards to use in application review.	Completed FY 2001: 30 additional standards recognized.	Recognize 20 new or enhanced standards to use in application review.	Recognize 20 new or enhanced standards to use in application review.
Pediatric Medicine				
Human	Implement,	FY 2001:	Implement,	Implement,

Drugs Goal 2	evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule	Written requests issued 43; Exclusivity determinations 19; As of October 2001, over 47,000 children have participated in clinical trials as a result of FDA requested studies under the exclusivity provision. Nine drugs approved and labeled for pediatric use based on studies in response to Written Requests.	evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.
Generic Drugs				
Human Drugs Goal 3	Review and act upon 50 percent of fileable original generic drug applications within 6 months after submission date.	FY 2001: Data available 1/2003 FY 2000: 55.6 percent	Review and act upon 65 percent of fileable original generic drug applications within 6 months after submission date.	Review and act upon 75 percent of fileable original generic drug applications within 6 months after submission date.
Human Subject Protection				
Human Drugs Goal 4	N/A	FY 2001: 553 inspections completed	Protect human research subjects who participate in drug studies and assess data quality from these studies by conducting approximately 780 onsite inspections and data audits annually.	Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting approximately 780 onsite inspections and data audits

				annually.
Medical Devices Goal 7	Conduct 250 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Not Met: 238 BIMO inspections conducted	Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)

Part Four: 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 2003 Performance Plan. Examples of these initiatives are described in the following paragraphs.

Collaborative Institutes:

FDA is proposing in FY 2003 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 patients 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 among the 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 2003 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 reporting facilities with highly trained staff can provide high

quality, informative reports representative of user facility device problems in general.

The National Antimicrobial Resistance Monitoring System (NARMS), initiated by FDA, CDC and the 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 more accurately 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 Conference 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 percent 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 2: Performance Plan and Report presents updated FY 2003 and final FY 2002 performance goals, along with the FY 2001 Performance report and an update on performance for some FY 2000 goals for each of FDA's programs.

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 2000 results.
- A verification and validation section which addresses sources and quality of data used in the plan.

The following sections will be covered:

Administrative Management -- Ensures that FDA provides the highest quality of service possible to the public by managing its resources effectively and efficiently in alignment with the Departmental Plan.

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

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

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

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.

2.1 ADMINISTRATIVE MANAGEMENT

2.1.1 Program Description, Context and Summary of Performance

Total Program Resources:

	FY 2003 Current Estimate	FY 2002 Current Estimate	FY 2001 Actual	FY 2000 Actual	FY 1999 Actual
Total $000	91,824	91,267	80,126	78,120	84,639

FDA's Administrative Management Performance Goals are aligned with the Departmental Plan and focus on making the FDA more citizen-centered and efficient. These performance goals will help the agency produce quality services in the most cost-efficient manner possible.

2.1.2 Strategic Goals

Strategic Goal 1: Provide for a streamlined and efficient hierarchy within the Agency that is more efficient and effective and ties in with Department goals.

A. Strategic Goal Explanation

Outlined below are five performance goals that focus on flattening the workforce and increasing the span of control for managers, consolidating administrative functions across the Agency, increasing the percent of FTE that are reviewed for outsourcing to private industry, increasing the percent of electronic purchases made in the agency and maintaining the highest possible financial audit levels attainable. These administrative management

performance goals listed below will help FDA provide more effective and efficient services to the public and regulated industry but will help the Programs accomplish their performance.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Increase supervisory ratio to increase the span of control among management personnel. (19001)	FY 03: Develop and implement a plan to delayer CBER, CFSAN and ORA; Transfer Legislative and Public Affairs function to DHHS FY 02: Develop and implement a plan to delayer NCTR, CVM and CDRH.; Plan to transfer Legislative and Public Affairs function to DHHS FY 01: 1 : 7.28	FY 03: FY 02: FY 01: 1 : 7.69 FY 00: 1 : 7.31 FY 99: 1 : 7.61	
2**. Consolidate administrative functions in the agency.** (19002)	FY 03: Personnel, Finance, Budget, Procurement, Grants, Information Technology, Legislative & Public Affairs FY 02: Award contract of administrative functions to be completed by 9/2002 with the	FY 03: FY 02: FY 01: Merged Management Information Systems Staff and Evaluation Staff FY 00:	

	Human Resources portion completed by May 2002. FY 01: N/A	Abolished three OC Offices: OEA/IO, ISCAS, and OHA. FY 99: Consolidated ten OEA offices across four allowances to fall under one allowance allowing for greater operating efficiencies.	
3. Increase the percentage of Commercial FTE that will be reviewed for outsourcing. (19003)	FY 03: 15 percent FY 02: 5 percent FY 01: N/A	FY 03: FY 02: FY 01: N/A	
4. Increase the percentage of electronically purchased transactions.* (19004)	FY 03: 91 percent FY 02: 89 percent FY 01: 87 percent	FY 03: FY 02: FY 01: 90.5 percent FY 00: 93.6 percent FY 99: 93.5 percent	
5. Maintain a clean (or unqualified) audit opinion with no material weakness. (19005)	FY 03: Yes FY 02: Yes FY 01: Yes	FY 03: FY 02: FY 01: Yes FY 00: Yes FY 99: Yes FY 98: Yes FY 97: No	
6. Increase percentage of contract dollars to performance based contracts from 30 percent.	FY 03: 30% FY 02: 25% FY 01: N/A	FY 03: FY 02: FY 01: 23.6 percent	

(19006)			
7. Assure continuity of FDA operations in case of an emergency. (19007)	FY 03: Implement Agency Continuity of Operations Plan FY 02: Develop Agency Continuity of operations plan; Participate with PSC to develop COOP FY 01: N/A	FY 03: FY 02: FY 01: N/A	
8. Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks. (19008)	FY 03: N/A FY 02: Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks. FY 01: N/A	FY 03: FY 02: FY 01: N/A	
TOTAL FUNDING: **($ 000)**	FY 03: 91,824 FY 02: 91,267 FY 01: 80,126 FY 00: 78,120 FY 99: 84,639		

*This goal refers to the percentage of purchases that are eligible to be purchased electronically. Not all FDA purchases are eligible to be purchased electronically.

C. Goal-By-Goal Presentation of Performance

1. Increase supervisory ratio to increase span of control among management personnel. (19001)

- **Context of Goal:** FDA is making significant efforts to de-layer the agency further and allow for a more effective structure and a streamlined organization, as well as increase the span of control for managers across the Agency. FDA is a knowledge-based organization, which utilizes complex scientific systems and overseas research activities, which complicate increasing the span of control too much.

Large spans of control are generally more appropriate for production and transaction-based organizations. FDA managers are frequently managing research and development or scientific activities, where large spans of control are not possible or desired.

- **Data Sources:** FDA Personnel databases
- **Performance:** The FY 2000 supervisory ratio was 1: 7.31 Agency wide. This is a slight decrease from FY 1999, due to critical managerial hiring needs in the scientific components in the Agency. In FY 2001 the Agency exceeded the goal of 1:7.28 because of consolidation within the field force.

2. Consolidate administrative functions in the Agency. (19002)

- **Context of Goal:** FDA is aligning itself with Departmental guidelines for the consolidation of administrative functions across the Agency. As the Departmental consolidation and streamlining plan progresses, the FDA consolidation effort can be further clarified. FDA has already taken major steps towards the consolidation of administrative functions across the agency in FY 2000 and FY2001. In FY 2002 and FY 2003, FDA is tying in further administrative management consolidation efforts with the Department's Plan. These are listed below.

FY 2003

Consolidate the following administrative management functions:

- Personnel
- Finance
- Budget
- Procurement
- Grants
- Information Technology
- Legislative Affairs
- Public Affairs

FY 2002

- Eliminated a Deputy Commissioner position
- Moved all remaining components under Deputy Commissioner to current senior managers

FY 2001

- Merged the Management Initiatives Staff with the Evaluation Staff

FY 2000

- Abolished the Office of External Affairs.
- Eliminated two Deputy Commissioner positions
- Eliminated the Office of Industry, Small Business and Constituent Affairs Staff
- Eliminated the Office of Health Affairs

FY 1999

- Consolidated 10 OC offices in External Affairs across four allowances to fall under one allowance. Consolidated the budget process for these offices to allow for greater efficiencies.
    - **Data Sources:** FY 2001 FDA Workforce Restructuring Plan
    - **Performance:** FDA has combined the Management Initiatives Staff with the Evaluation Staff and has also reduced the number of Deputy Commissioners from four to two. By the end of FY 2001, FDA will have met its FY 2003 schedule of elimination of all targeted positions except the Principal Deputy Commissioner, as the Deputy Commissioner for International and Constituent Relations plans to retire in September 2001. FDA is currently taking steps to consolidate the personnel, information technology, budget, finance, procurement, grants, legislative affairs and public affairs functions within the Agency by FY 2003.

3. Increase the percentage of Commercial FTE that will be reviewed for Outsourcing. (19003)

- **Context of Goal:** FDA has outsourced many of its functions to the commercial sector and will review the Percentage of Commercial FTE for these years for additional possible outsourcing. In FY 2002, FDA has committed to review the following functions: graphic design, library and web design development. In each of FY 2003, FY 2004 and FY 2005, FDA will review an additional 10 percent of the Agency's Commercial FTE for possible outsourcing. In FY 2006, FDA plans to review an additional 15 percent of its Commercial FTE for possible outsourcing. This brings the total Commercial FTE FDA will review for outsourcing by FY 2006 to 50 percent.
- **Data Sources:** FY 2001 FDA FAIR Act Inventory
- **Performance:** For the past few years, FDA has been converting many of its activities to be commercially outsourced. In particular, FDA has outsourced animal husbandry services, building operations and maintenance, mail service and certain IT activities. FDA is committed to reviewing the above listed additional Commercial FTE for possible outsourcing in the out-years.

4. Increase the percentage of electronically purchased transactions. (19004)

- **Context of Goal:** The targets for FDA for FY 2001, FY 2002 and FY 2003 are departmentally mandated targets for HHS. FDA expects to significantly exceed these targets in all years. The percentages are not representative of all purchases, but reflect the percentages of purchases made electronically that were eligible for electronic purchase. The figures represented above also reflect the percentages of transactions and not the percentages of dollar purchases. In examining the departmental definitions for these categories, we discovered that the FY 2000 Target is defined differently than the targets in the other years (FY 2001, FY 2002, and FY 2003). It is also defined differently than the Actuals for FY 2000, thereby making it non-comparable. The definitions for the FY 2000 Actuals and the Targets for FY 2001, FY 2002, and FY 2003 are the same.
- **Data Sources:** FDA Small Purchase System, statements from bank card company
- **Performance:** Ninety four percent of eligible transactions were purchased electronically in FY 2000. FDA expects this figure to grow and also expects to significantly exceed the departmental targets given to FDA. The Agency is conscientiously seeking to use the Impact Card instead of a purchase order for buying items with low overhead costs. By using the Impact Card, the Agency lowers the $90.00 overhead cost for each purchase. This then has led to the Agency exceeding its goal for FY 2001 as expected.

5. Maintain a clean (unqualified) audit opinion, with no material weakness. (19005)

- **Context of Goal:** An unqualified audit opinion is a statement by the auditors that an entity's financial statements present fairly, in all material respects, the financial position, its net costs, changes in net position, budgetary resources, and reconciliation of net cost to budgetary obligations for the year ended, in conformity with generally accepted accounting principles. A financial statement material weakness is a significant finding which, in the opinion of the auditors, poses a risk or threat to the internal control systems of an audited entity.

The table listed below shows additional relevant historical information regarding FDA's prior financial performance and reflects the results of the steps FDA took to get to its current condition. In FY 1997, FDA had 5 reportable conditions, 3 material weaknesses, did not have an unqualified audit opinion and was timely. Since then, FDA has managed to progressively perform at a higher level.

	FY 1997	**FY 1998**	**FY 1999**	**FY 2000**	**FY 2001**

Timely audit opinion	No	Yes	Yes	Yes	Yes
Clean (Unqualified) audit opinion	No	Yes	Yes	Yes	Yes
Number of material weaknesses	3	0	0	0	0
Number of reportable conditions	5	3	3	1	1
Number of instances of non-compliance with laws and regulations including non-compliance with the Federal Financial Management Improvement Act (FFMIA)	1	1	1	1	1

- **Data Sources:** Fiscal Year 2000 FDA Chief Financial Officer's Annual Report.
- **Performance:** FY 2000 Performance is at 100 percent. Since FY 1997, the performance has steadily improved due to FDA taking many corrective actions, including establishing a branch organization in the Division of Accounting to prepare financial statements and to interact with the auditors. As a result, FDA went from not having an unqualified opinion with three material weaknesses and five reportable conditions in FY 1997 to having an unqualified opinion with no material weakness and one reportable condition in FY 2000. The remaining reportable condition deals with the information systems controls of FDA's financial management systems. FDA is actively taking corrective actions to resolve this condition. The sole instance of non-compliance with laws and regulations dealt with FFMIA compliance. To achieve compliance with FFMIA and the Secretary's directive, FDA is working with HHS and other HHS components in the implementation and development of the Unified Financial Management System (UFMS), which will meet federal system requirements. Where possible the Agency has improved its performance as seen in the chart above. In those areas where the FDA has remained stable, it is anticipated that the UFMS will lead to improvements.

6. Increase percentage of contract dollars to performance based contracts from 30 percent.

- **Context of Goal:** This goal is based on three key policy decisions to enhance performance-based contracts. First, Policy Letter 91-2 commits the Federal Government Policy to use performance-based contracting to the maximum extent practical when acquiring services.

This was followed by a March 9, 2001 memorandum OMB's Deputy Director directing agencies to use performance-based technique in at least 20 percent of all service contracts worth more than $25,000 in FY 2002. Finally, on June 14, 2001 Secretary Tommy Thompson directed all OPDIVs to submit implementation plans for achieving OMB's goal of awarding 20 percent of eligible contract dollars using PBC by FY 2002.

- **Data Sources:** The Agency will rely on the data system developed and maintained by the Department of Health and Human Services. This database classifies contracts based on whether they use performance contracting. The Agency receives periodic reports that classify the percentage of contracts that are performance based.
- **Performance**: The Agency has historically set the example for HHS OPDIVs implementing performance based contracts; therefore FDA was able to meet the Department's goal. FDA reviews each contract to determine if it is a candidate for performance based contracting. If so, the Agency provides the contract's objectives and requests the contractor to provide the method(s) to meet the objective. Once the Agency and contractor agree, FDA personnel regularly evaluate the contractor's performance. If necessary, the Agency invokes a previously negotiated financial penalty against the contractor for failing to meet the objective(s). This allows the Agency and contractor to assure high performance.

7. Assure continuity of FDA operations in case of an emergency.

- **Context of Goal:** In light of the September 11, 2001 events, the Agency decided to develop a Continuity of Operations Plan (COOP) to allow it to keep its major programs functioning in the event of a disabling attack. Executive Order 12656, Presidential Decision Directive 67 and Federal Preparedness Circular 65 reinforced this objective.
- **Data Sources:** Success will be measured based upon awarding the contract during FY 2002.
- **Performance:** N/A

8. Enhance the Agency Emergency Preparedness plan to establish protocols for responding to terrorist attacks.

- **Context of Goal:** The events of September 11, 2001 and subsequent incidents involving anthrax contamination raise the frightening prospect that FDA-regulated products could be used as vehicles to cause widespread harm to U.S. citizens. FDA's Counter Terrorism Plan outlines a strategic blueprint for protecting U.S. citizens in the event of future terrorist attacks. One of the key goals of the Plan is to sharpen the Agency's emergency preparedness and response capability so that FDA is poised to protect the Nation and itself in the event of an attack. In order to address these kinds of threats, the Agency must anticipate

which FDA-regulated products are the most likely weapons; which harmful agents are the strongest candidates for weaponization; and which points in the pipeline are the most vulnerable to attack. Then steps must be taken to reduce the vulnerabilities at these points. If any part of the system is breached, FDA must have the appropriate medical products and emergency response plans in place to minimize harmful impacts.

- **Data Sources:** Development of protocols for responding to terrorist attacks.
- **Performance:** N/A

2.1.3 Verification and Validation

FDA will ensure consistency in the tracking and reporting of the administrative management performance goals. In addition, FDA is taking steps to routinely monitor this data and take appropriate actions as needed. Data is from a variety of sources for these performance goals including the Annual Chief Financial Officer's Report, Civilian and Commission Corps personnel databases, monthly and annual full-time equivalent (FTE) reports and data-runs, the FDA FAIR Act Inventory and the FY 2001 FDA Workforce Restructuring Plan, monthly statements from bank card companies and the FDA Small Purchase System.

2.2 FOODS

2.2.2 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 2003 Current Estimate	FY 2002 Current Estimate	FY 2001 Actual	FY 2000 Actual	FY 1999 Actual
Total ($000)	412,097	404,599	287,504	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.

2.2.2 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 premarket notifications for food contact substances within the statutory time frame (Performance Goal 3-11034)
- Respond to dietary supplement notifications within 75 days (Performance Goal 2-11025)
- Give priority to those additives that are intended to decrease the incidence of foodborne illness
- 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 the safety evaluation of 65 percent of the number of food and color additive petitions that were under review for more than 360 days at the beginning of the Fiscal Year. (11001)	FY 03: 65 percent FY 02: 60 percent FY 01: 50 percent FY 00: 40 percent FY 99: 30 percent	FY 03: FY 02: FY 01: 10/02 FY 00: 91 percent FY 99: 77 percent	
2. Respond to 95 percent of notifications for dietary supplements containing "new dietary ingredients" within 75 days. (11025)	FY 03: 95 percent FY 02: 95 percent FY 01: 90 percent FY 00: 90 percent FY 99: N/A	FY 03: FY 02: FY 01: 100 percent FY 00: 100 percent FY 99: 100 percent	
3. Complete processing of 80 percent of GRAS notifications within 180 days. (11003)	FY 03: N/A FY 02: N/A FY 01: 80 percent FY 00: Finalize GRAS Rule late in year or early 01 FY 99: Finalize the rulemaking creating a premarket notification process for independent GRAS determinations.	FY 03: FY 02: FY 01: 06/02 FY 00: made progress toward finalizing GRAS rule FY 99: rule not completed, no measurement	
4. Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days). (11034)	FY 03: 95 percent FY 02: 95 percent FY 01: N/A FY 00: N/A	FY 03: FY 02: FY 01: 3/02 FY 00: 99 percent	
5. Publish a final rule to require premarket notification for bioengineered foods.	FY 03: Publish final rule FY 02: N/A FY 01: N/A	FY 03: FY 02: FY 01: N/A FY 00: N/A	

(11035)	FY 00: N/A		
TOTAL FUNDING: ($000)	FY 2003: 57,693 FY 2002: 56,643 FY 2001: 39,850 FY 2000: 39,661 FY 1999: 25,196		

C. Goal-by-Goal Presentation of Performance

1. Complete the safety evaluation of 65 percent of the number of food and color additive petitions that were under review for more than 360 days at the beginning of the Fiscal Year. (11001)

- **Context of Goal:** In this goal, a first action is defined 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. "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.
  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 this goal of completing the safety evaluation of 65 percent of food and color additive petitions within 360 days. The most important of these factors is the implementation of the new premarket notification process. With the full implementation of the premarket notification program, many of the simpler food additive petitions that could have been completed within 360 days are being filed under the notification program, thus decreasing 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. 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 2002.
- **Data Sources:** CFSAN's electronic workflow system
- **Performance:** In FY 2000, FDA exceeded its goal of completing the review of 40 percent, respectively, of food and color additive petitions

with 360 days. The high performance figures in 1999 and 2000 do not presage similar numbers in later years. This is primarily because Congress passed, under the FDA Modernization Act of 1997, and implemented in FY 2000, the Food Contact Substance Premarket Notification Program. As a result, we are now receiving far fewer petitions in total than in previous years, and those that we do receive are for direct food additive uses of greater potential public health significance; in general, these take more time and effort per petition to complete. In addition, as the new PMN program was being implemented, many pending petitions for food contact materials were withdrawn, leading to "completed actions" on many petitions. This artifact led to the increased performance figures for the receipt cohorts of FY 1999 and FY 2000. This is, however, a one-time phenomenon. We have done a careful analysis of these trends in recent years. Based on all available data, including receipt of far fewer (but generally far more labor intensive) petitions than in previous years, we project that completing review of 65 percent of food and color additive petitions in 360 days for the 2002 receipt cohort is a fair and challenging level of performance. FY 2001 data is expected in October 2002.

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

- **Context of Goal:** Within 75 days, FDA reviews premarket notifications for new dietary ingredients (NDI) of dietary supplements. The Agency anticipates that in the future these notifications will become more complex and that the volume of such notifications submitted to the FDA will increase. Nevertheless, the Agency has increased its review goal target from 90 percent to 95 percent for both FY 2002 and FY 2003. Since the Agency does not know precisely what the workload will be in any given year, the 95 percent target is considered full performance the next two fiscal years.
- **Data Sources:** CFSAN's Correspondence Tracking System and manual tracking
- **Performance**: Since the beginning of this premarket notification program, FDA has completed 100 percent of its reviews of NDI notifications within the 75-day deadline. Due to the overlapping nature of a 75-day period, a notification review may be completed during the same or following fiscal year in which it was received. In addition, a notification may be received prior to the fiscal year in which the review was completed. Based upon this scenario, the following data represents the actual number of NDI notification reviews completed within the stated fiscal year: 20 in FY 1998; 23 in FY 1999; 25 in FY 2000; and 22 in FY 2001.

3. Complete processing of 85 percent of GRAS notifications within 180 days. (11003)

- **Context of Goal:** (Goal Dropped for FY 2002 and 2003). GRAS notification is a new program and the final rule creating a premarket notification process for independent GRAS determinations is planned for publication soon. 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:** FY 2001 Performance data will be available in June 2002. CFSAN evaluated a cohort of GRAS notices (GRNs) received in FY 2000. For this cohort, CFSAN responded to 59 percent of GRAS notices received within 180 days. A total of 27 GRNs were received in FY 2000; 16 of 27 (59 percent) were completed in less than 180 days; 4 of 27 (15 percent) were completed in less than 220 days. The nature of the Agency's response was as follows: FDA had no questions - 19 of 27 (70 percent); notice that did not provide a basis for GRAS - 4 of 27 (15 percent); notifier stopped process - 3 of 27 (11 percent); and one GRN is still pending. In FY 2000, 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.

4. Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days). (11034)

- **Context of Goal:** The data for FY 2001 will be available March 2002. 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 2000, the Agency completed review of 82 of 83 notifications for food contact substances within 120 days. FY 2001 data is expected in March 2002.

Publish a final rule to require premarket notification for bioengineered foods. (11035)

- **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. As of March 2001, FDA has received more than 40,000 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 publish the final rule by the end of FY 2003.

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 received in FY 2001, 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
6. Achieve adoption of the Food Code by at least one state agency in 33 states in the USA. (11010)	FY 03: 33 FY 02: 28 FY 01: 25 FY 00: 18 FY 99: 13	FY 03: FY 02: FY 01: 28 FY 00: 20 FY 99: 15	
7. Inspect 95 percent of high-risk domestic food	FY 03: at least 95 percent once	FY 03:	

establishments once every year. (11020)	every year FY 02: at least 95 percent once every year FY 01: at least 90 percent once every year FY 00: 90 —100 percent Once every one to two years FY 99: NA	FY 02: FY 01: 74 percent FY 00: 91 percent FY 99: NA	
8. Assure that FDA inspections of domestic food establishments result in a high rate of conformance (at least 90 percent) with FDA requirements. (11011)	FY 03: NA FY 02: NA FY 01: at least 90 percent FY 00: 90-100 percent FY 99: 90-100 percent	FY 03: FY 02: FY 01: 99 percent FY 00: 97 percent FY 99: 98 percent	
9. Increase the number of import exams of food products. (11021.02)	FY 03: N/A FY 02: N/A FY 01: 60,000 FY 00: 60,600 FY 99: N/A	FY 03: FY 02: FY 01: 29,751 FY 00: 28,275 FY 99: 32,000	
10. 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 03: N/A FY 02: N/A FY 01: 10 FY 00: N/A FY 99: N/A	FY 03: FY 02: FY 01: 0 FY 00: N/A FY 99: 4	

11. Increase the number of physical exams by 100% to 48,000 exams and conduct sample analyses on products with suspect histories. (11036)	FY 03: 100% (48,000 exams) FY 02: Increase food import surveillance by hiring 300 new investigators and analysts who will increase the number of physical exams by 97% to 24,000 exams and conduct sample analyses on products with suspect histories. FY 01: NA	FY 03: FY 02: FY 01: 12,169	
12. Enhance productivity at the 45 additional ports through focused training. (11037)	FY 03: Enhance productivity at the 45 additional ports through focused training. FY 02: Extend import coverage to an additional 45 ports that handle significant quantities of FDA-regulated products. FY 01: NA FY 00: NA FY 99: NA	FY 03: FY 02: FY 01: NA FY 00: NA FY 99: NA	
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 03: 8,000 + FY 02: 8,000 + FY 01: 8,000 + FY 00: N/A FY 1999: N/A	FY 03: FY 02: FY 01: 7,300 total (2,475 domestic and 4,900 imported) FY 00: 7,400 total (2,500 domestic and 4,900	

		imported) FY 99: 9,400 total pesticide and chemical contaminant samples: 3,400 domestic and 6,000 imports.	
TOTAL FUNDING: ($000)	FY 03: 354,404 FY 02: 347,954 FY 01: 247,699 FY 00: 240,044 FY 99: 209,972		

C. Goal-by-Goal Presentation of Performance

6. Achieve adoption of the Food Code by at least one state agency in 33 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 1999, 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 2000, agencies in 20 states have adopted the Food Code. In FY 2001, at least one state agency in 28 states adopted the Food Code.

7. Inspect 95 percent of high-risk domestic food establishments once every year. (11020)

- **Context of Goal:** 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 2001, 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 2002, the entire high-risk establishment inventory is expected to increase and thus the target for FY 2002 has been changed from 90 -100 percent to at least 95 percent, to anticipate the level of increase in the number of high-risk establishment inspections.
- **Data Sources:** Field Data Systems
- **Performance:** In FY 2000, the number of high-risk food inspections was approximately 5700, of the identified possible inventory of high-risk product/process domestic firms. In FY 2001, the Agency accomplished only 74 percent of the identified possible inventory of high-risk product/process domestic firms. The reason FDA missed this goal was because the Agency purposefully diverted resources for these inspections to focus on an even greater threat of BSE that was breaking out in Europe at the time.

8. 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 percent) with FDA requirements. (11011)

- **Context of Goal:** (Goal Dropped for FY 2002 and 2003) In previous FDA performance plans, goals were established for maintaining the level of industry conformance to FDA requirements at 90 percent or above for each of the Agency product-oriented programs. This year we are recommending that these goals be deleted from the Plan. This is our rationale: Inspections are the Agency's method for determining whether an establishment is in or out of compliance with FDA requirements. Because of resource constraints, the Agency must allocate a significant proportion of its inspections to high risk situations, such as food firms who are producing high risk foods, or to emergency situations such as BSE. The number of remaining inspections each year is not adequate to draw a statistically valid inference about the compliance status of an entire industry at a reasonably high level of confidence.
  It is the Agency's professional judgement that the majority of firms in the regulated industries are in conformance with FDA's requirements. Based on the Agency's experience over several years, that percentage in general, has remained at 90 percent or above. Thus, establishing a performance goal that simply describes the stable state of the industry does not provide useful new information; nor does it serve as a management tool to drive the overall industry to a higher level of conformance.
- **Data Sources:** Field Data Systems
- **Performance:** In FY 1997, 1998 and 1999, FDA inspections of domestic food establishments (excluding the domestic seafood industry) resulted in a 98 percent 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 percent rate of conformance in FY 2000. In FY 2001, actual conformance was 99 percent.

9. Increase the number of import exams of food products. (11021.02)

- **Context of Goal:** (Goal Dropped for FY 2002 and 2003). This goal has been dropped because it is too coarse a measure of the effort FDA is expending to reduce the threat from imports. The planned 60,600 "import exams" is actually a catch all category that includes counts of several different kinds of activity at the border, including: physical exams, sample analyses, examination of paper manifests and product detentions. FDA has determined that the most important measure for import safety is the number of physical exams, and our new import coverage goal focuses on those (Goal 11).

- **Data Sources:** Field Data Systems
- **Performance:** The actual performance figures reported in the table for FY 1999, 2000 and 2001, are the combined totals of *only* the number of physical exams and laboratory samples analyzed, not the combination of additional activities initially envisioned. In FY 2001, 29,751 import exams were conducted. This includes 17,582 sample analyses in addition to the 12,169 physical exams mentioned in the new import exam performance goal (Goal 11). Our new Goal 11 focuses on physical exams exclusively. It is a more sensitive measure of the effort dedicated to reducing risk at the border, and it is a performance area where rapid improvements can be shown as a result of budget increases received in FY 2002 and 2003.

10. 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:** (Goal Dropped for FY 2002 and 2003). 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 percent of the U.S. food supply, and for some commodities, such as many fresh fruits and vegetables, 40 percent 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 percent by FY 2002. 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 1998, FDA completed food safety system assessments in two countries: Honduras and Trinidad & Tobago. In FY 1999, 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 was a new commitment in FY 2001. The Agency did not complete any audits and assessments of foreign food safety systems due to a redirection of resources to other international issues.

11. Increase the number of physical exams by 100 % to 48,000 exams and conduct sample analyses on products with suspect histories. (11036)

- **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 percent of the U.S. food supply, and for some commodities, such as many fresh fruits and vegetables, 40 percent 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. Currently, FDA receives five million line imports and therefore surveillance needs to be increased. In FY 2002, 400 additional people will be hired to carry out border activities. Of these 400, 300 will be directly used to conduct physical examinations and follow up leads on suspicious products. The remaining 100 people will be used to conduct laboratory analyses. Additional duties will include:
    - pursuing compliance case work, including carrying out criminal investigations;
    - ensuring the quality of filer reviews of import entries;

- expediting the triage process through use of the OASIS system; and
- acting as liaisons between firms and FDA to explain the purpose of sample collection, the time frame for collecting and notifying firms of the results in a timely manner. This function is critical to importers and brokers who must have timely information to determine appropriate business decisions.

A 100% increase in physical exams over planned FY 2002 figures is estimated. This percentage increase is based on the productivity expected from 300 additional investigators. The productivity increase of 100% is based on a number of calculations, including: timing of recruitment, training time required, workload modules for physical exams and time allowed for follow-up investigation of suspicious products. Also factored into the productivity increase is the estimated import workload increase of 10% a year. Because of the increased emphasis on the potential for terrorist threats, the workload module for physical exams, and the time required to follow up on suspicious products has been increased. It should be noted that even with more rapid recruitment through the Agency's 'quick hire' program, and focused training of new recruits [both accomplished through web-based improvements], the field investigator requires time to reach full productivity. The ramp-up is 10% productivity at the end of the training period, 50% productivity one year after training and 100% productivity after two years. In addition, the time of seasoned investigators must be partially diverted to provide hands-on training to new investigators that will be coming on board in large numbers over the next two years. Significant increases in productivity should be realized after new investigators have been on board for a year.

- **Data Sources:** Field Data Systems
- **Performance:** This goal is new for FY 2002 and FY 2003, so there was no FY 2001 performance target, but the FY 2001 baseline was 12,169 physical exams. It should be noted that the measure being used for this performance goal - 'physical exams' - is different than the measure used in Goal # 9 which is now being dropped. Goal #9 used the measure 'import examinations,' which was a catch all category that includes counts of several different kinds of activity at the border. That is why the total number of 'import examinations' envisioned in Goal 9 is much higher than the number of physical exams alone. The baselines are not comparable. FDA believes that the measurement of physical exams - which is 'hands-on' examination of the product - is a more relevant measure of the Agency's attempt to address potentially high risk products at the border.

12. Enhance productivity at the 45 additional ports through focused training. (11037)

- **Context of Goal:** The President's Budget annualized the FY 2002 Budget Supplemental for Counter Terrorism, which will enable FDA to enhance inspection and analytical coverage of imported products. This will have the effect of more than doubling the Field import staff and substantially increasing the number of physical exams and lab analyses conducted at the border. In FY 2002, FDA will be able to extend import coverage to an additional 45 ports that handle significant quantities of FDA regulated products. In FY 2003, focused training should increase productivity of the new investigators at these ports.
- **Data Sources:**
- **Performance:** This is a new goal for FY 2002 and FY 2003.

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 acquires data on particular commodity/pesticide combinations and carries out its market basket survey, called the Total Diet Study. In conducting the Total Diet Study, 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 residues and environmental contaminants. The levels of pesticides found will be used in conjunction with USDA food consumption data to estimate the dietary intake of the pesticide residues.
  Under the regulatory monitoring program, 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 2001, FDA expects to analyze 8,000 plus. In FY 2002, FDA expects to analyze 8,000 plus samples for pesticide residues and 1,750 samples for dioxin. FDA must maintain resource levels devoted to the sampling and analyses of pesticide and environmental contaminants, specifically dioxin, not only to ensure that the U.S. food supply is safe, but also to reduce dietary exposure.

- **Data Sources:** FACTS, CFSAN website
- **Performance:** FY 1998 - 8,500 samples (3,600 domestic and 4,900 imports); FY 1999 - 9,400 samples (3,400 domestic and 6,000 imports); FY 2000 - 7,400 samples (2,500 domestic and 4,900 imports). FY 2001 - 7375 samples (2,475 domestic and 4,900 imports.)

2.2.3 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 nine 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 1998, 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 1999, 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 2001. 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 2001, 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 2001, the Agency began 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 2002, 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 2000, 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 1999, 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.

2.3 HUMAN DRUGS

2.3.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 03 Current Request	FY 02 Current Estimate	FY 01 Actual	FY 00 Actual	FY 99 Actual
Total ($000)	457,979	366,897	322,480	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 by thoroughly analyzing scientific data submitted to the Agency on prescription and over-the counter (OTC) drug products. Once drugs are approved, they may be marketed and distributed for use. At that time, Agency postmarket surveillance assures the quality of drugs on the market and strives to minimize adverse events associated with their use. To accomplish its premarket and postmarket responsibilities, 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, 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 its 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 associated with the evaluation of investigational new drugs (INDs), new drug applications (NDAs), generic drug applications (abbreviated new drug applications - ANDAs), efficacy supplements, and manufacturing supplements. Review of OTC labeling and pediatric study requests is also an integral part of our premarket review process. Postmarket surveillance performance goals include: assessing risk to identify adverse events; 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.

2.3.2 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. These include reduced drug development time, increased and quicker access to new drug products, and an increased number of therapeutic options for health professionals. 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. The timely performance of high-quality drug reviews in recent years reflects the importance of managerial reforms and additional resources provided under the Prescription Drug User Fee Act (PDUFA). The law, first enacted in 1992, was renewed for an additional five years in the 1997 FDA Modernization Act (FDAMA). Under the law, the drug industry pays user fees for NDAs, efficacy supplements, and some other activities. User fees helped the Agency hire additional scientists to perform reviews.

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 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30% Standard NDAs within 12 months: FY 03: NA FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90% Priority NDAs within 6 months: FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90%	FY 03: FY 02: FY 01 Final data available 01/03 FY 00: 79% FY 99: 66% FY 03: FY 02: FY 01: Final data available 01/03 FY 00: 97% FY 99: 100% FY 03: FY 02: FY 01: Final data available 01/03 FY 00: 97%	
2. Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule. (12026)	FY 03: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule FY 02: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	FY 03: FY 02: FY 01: 43 Written Requests issued;19 Exclusivity Determinations;	

	FY 01: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	Over 47,000 children have participated in clinical trials as of October 2001 as a result of the studies FDA requested under the exclusivity provision. Nine drugs were approved and labeled for pediatric use based on studies conducted in response to Written Requests. FY 00: **Exclusivity:** 39 Proposed Pediatric Study Requests reviewed 62 Written Requests issued 59 Amended Written Requests' issued 19 Exclusivity determinations 16 Exclusivities granted 7 Labels changed Ped Rule: Pediatric Assessments Deferred = 76 Pediatric Assessments Waived = 91	
3. Review and act upon fileable original generic drug applications within 6 months after submission date. (12003)	FY 03: 75% FY 02: 65% FY 01: 50% FY 00: 45% FY 99: 60%	FY 03: FY 02: FY 01: Final Data available 4/02 FY 00: 55.6% FY 99: 28%	

4. Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting approximately 780 onsite inspections and data audits annually. (12032)	FY 03: 780 FY 02: 780 FY 01: NA FY 00: NA FY 99: NA *Note*: The number of inspections completed each year is dependent on the number of applications received.	FY 03: FY 02: FY 01: 553 inspections completed FY 00: 697 inspections completed FY 99: 683 inspections completed	
5. Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure). (12033)	FY 03: NA FY 02: Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure). FY 01: NA	FY 03: FY 02: FY 01: NA	
6. Facilitate the initiation of research in a non-human primate model of pneumonic plague. (12034)	FY 03: NA FY 02: Facilitate the initiation of research in a non-human primate model of pneumonic plague. FY 01: NA	FY 03: FY 02: FY 01: NA	
7. Expedite the review of protocols for investigational new drugs (INDs) to treat organophosphorous nerve agents in the event of chemical attack. Encourage sponsors of these new drug application (NDAs) to update current labeling for Antidote Treatment Nerve	FY 03: NA FY 02: Expeditite the review of protocols for investigational new drugs (INDs) to treat organophosphorous nerve agents in the event of chemical attack. Encourage sponsors of these new drug application (NDAs) to update current labling for Antidote	FY 03: FY 02: FY 01: NA	

Agent, Autoinjectors (ATNAA). (12035)	Treatment Nerve Agent, Autoinjectors (ATNAA). FY 01: NA		
8. Identify and begin to address labeling gaps in the therapeutic armamentarium for the prevention, mitigation, and treatment of illnesses cases by chemical and biological attacks, including the needs for special populations, such as pregnant women, pediatric, and geriatric populations. (12036)	FY 03: Identify and begin to address labeling gaps in the therapeutic armamentarium for the prevention, mitigation, and treatment of illnesses cases by chemical and biological attacks, including the needs for special populations, such as pregnant women, pediatric, and geriatric populations. FY 02: NA FY 01: NA	FY 03: FY 02: FY 01: NA	
9. Develop guidance for Industry on developing antiviral drugs for the mitigation of complications associated with vaccinia immunization. (12037)	FY 03: Develop guidance for Industry on developing antiviral drugs for the mitigation of complications associated with vaccinia immunization. FY 02: NA FY 01: NA	FY 03: FY 02: FY 01: NA	
10. Facilitate human clinical trials in pneumonic plague for antimicrobial drugs that are not yet labeled for this treatment indication. (12038)	FY 03: Facilitate human clinical trials in pneumonic plague for antimicrobial drugs that are not yet labeled for this treatment indication.	FY 03: FY 02: FY 01: NA	

	FY 02: NA FY 01: NA		
11. Develop guidance for Industry on developing antiviral drugs for the treatment of smallpox. (12039)	FY 03: Develop guidance for Industry on developing antiviral drugs for the treatment of smallpox. FY 02: NA FY 01: NA	FY 03: FY 02: FY 01: NA	
12. Publish a final rule which allows the agency to approve new drug and biological products for the treatment of chemical, biological, radiological, or nuclear substances based on animal efficacy studies when adequate and well-controlled studies in humans cannot be ethically conducted and field studies are not feasible. (12040)	FY 03: NA FY 02: Publish a final rule which allows the agency to approve new drug and biological products for the treatment of chemical, biological, radiological, or nuclear substances based on animal efficacy studies when adequate and well-controlled studies in humans cannot be ethically conducted and field studies are not feasible. FY 01: NA	FY 03: FY 02: FY 01: NA	
13. Expedite the review of protocols for investigational new radioprotectant drugs (including heavy metal chelators) for use in the event of a radiation emergency. (12041)	FY 03: Expedite the review of protocols for investigational new radioprotectant drugs (including heavy metal chelators) for use in the event of a radiation emergency. FY 02: NA FY 01: NA	FY 03: FY 02: FY 01: NA	

TOTAL FUNDING: ($000)	FY 03: 343,484 FY 02: 275,173 FY 01: 257,984 FY 00: 233,425 FY 99: 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 given to the review of new drugs 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:** CDER met its FY 2000 performance goal (see Table 1 below).

Table 1
Fiscal Year 2000 Cohort (as of 12/31/01)

Submission Type	Number of Submissions Filed	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
NDAs -- Priority	29	90% in 6 mo.	28	97%
NDAs -- Standard	92	90% in 12 mo. 50% in 10 mo.	89 73	97% 79%

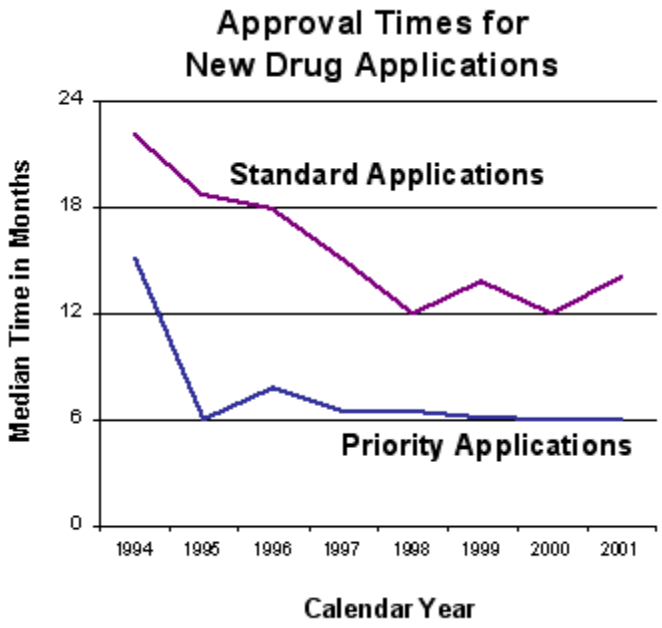
Several important new drugs were also approved by FDA in FY 2001 (see Table 2 below).

Table 2
Significant NDAs Approved in FY 2001

Drug	Purpose
Combination of Xeloda (capectitabine) and Taxotere (docetaxel)	Treatment of metastatic breast cancer that has progressed after treatment with anthracycline cancer therapy (such as Adriamycin and doxorubicin)
Natrecor® (nesiritide) Injection	Treatment of acute congestive heart failure (CHF).
Gleevec (imstinib mesylate, also known as STI-571)	Treatment of chronic myeloid leukemia --a rare life-threatening form of cancer
Cancidas (caspofungin acetate) Intravenous Infusion	New anti-fungal medication for patients who are unresponsive to or cannot tolerate standard therapies for the invasive form of aspergillosis
Femara (letrozole)	First-line treatment for postmenopausal women with hormone receptor positive or hormone receptor unknown, advanced or metastatic breast cancer

The graph below (figure 1) illustrates that approval time in months for priority applications has decreased from 15 months in 1994 to 6 months in 2001, and approval time for standard applications have decreased from 22.1 months to 14 months. Approval time represents the total review time at the Agency plus industry response time to the Agency's requests for additional information.

Figure 1



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 for pediatric studies if the Agency determines that information related to the use of a 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 population 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. The April 1, 1999 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.
  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 245 Proposed Pediatric Study Requests (PPSR), issued 197 Written Requests (WR) asking for over 421 studies to be conducted in the pediatric population and has granted exclusivity to 32 products. Nineteen of the 32 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.
  On January 4, 2002, the President signed into law the "Best Pharmaceuticals Act for Children," which is the final version of the pediatric exclusivity reauthorization legislation. The signing of this important piece of legislation ensures that pediatric studies of drugs will continue to be conducted, providing useful new information in product labeling concerning safety and effectiveness. Pediatric supplements that require clinical data for approval will now be considered Priority supplements under PDUFA and are subject to the performance goals that apply to Priority drugs, which is currently a six-month review. The fourth Pediatric Advisory Subcommittee occurred on April 23 and 24, 2001. Pediatric drug development in two diseases/conditions was discussed: chronic hepatitis C infection in children and drooling in pediatric patients with cerebral palsy and other neurologic disorders. 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.
  Ethical issues and concerns have been raised regarding the increase in the enrollment of children in clinical trials. The increase is due to the Pediatric Rule and the pediatric provisions of FDAMA. In October 2000, the Children's Health Act (Pub. L. 106-310) was signed into law. As mandated by the Act, the Agency incorporated Subpart D of the DHHS regulations into FDA regulations. The interim rule, *Additional Safeguards for Children in Clinical Investigations of FDA-Regulated Products* (66 Federal Register 20589), was published on April 24, 2001 and effective on April 30, 2001.
  The Agency contracted out development of an inpatient pediatric database that will be used to accumulate information on the use of drugs in children in the inpatient care setting, e.g., children's hospitals, community hospitals, and chronic care facilities. The information is critical to the Agency as it determines the potential health benefit for drugs to be issued Written Requests or to comply with the Pediatric Rule.

3. Review and act upon 75% of fileable original generic drug applications within 6 months after submission date. (12003)

- C**ontext of Goal:** FDA continues to support an active generic drugs program with a focus on expanding the availability of high quality generic drug products to the public. A generic drug product is one that is comparable to the reference listed drug product in dosage form, strength, route of administration, quality, performance characteristics, and intended use. Generic drug applications are termed "abbreviated" in that they generally do not require preclinical (animal) and clinical (human) data to establish safety and effectiveness. These parameters were established upon the approval of the innovator drug product. A Congressional Budget Office report estimates "that the purchase of generic drugs reduced the cost of prescriptions (at retail prices) by roughly $8 to $10 billion in 1994."[1]
  [[1] Congressional Budget Office, A CBO Study: *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* (ftp://ftp.cbo.gov/6xx/doc655/pharm.pdf, July 1998), p. 13.]
- **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 met its goal for FY 2000 acting on 55.6 percent of original applications within 6 months after the submission date. This is an increase of more than 27 percent over FY 1999.
  Of these applications, several represent the first time a generic was approved for a product. Examples of important first time approvals are listed in Table 3 below.

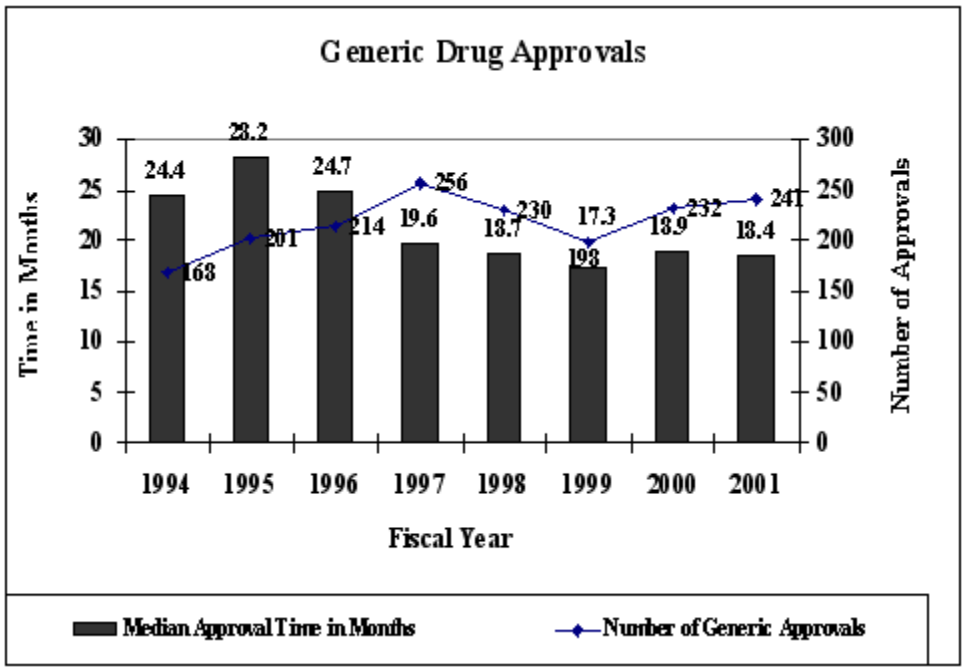
Table 3
Notable First Time Generic Approvals

Drug	Purpose
Buspirone Hydrochloride	Management of anxiety disorders or short-term relief of symptoms of anxiety (generic for Buspar by Bristol Myers Squibb)
Famotidine	Prevention and treatment of heartburn (generic for Pepcid AC by Merck)
Fluoxetine	Treatment of depression (generic for Prozac by Lilly)
Butorphanol Tartrate	Management of pain (generic for Stadol NS by Mead Johnson)

Levocarnitine	Treatment of primary systemic carnitine deficiency (generic for Carnitor by Sigma Tau)

The FY 2001 18.4-month median approval time compares to 18.9 months in FY 2000 and 17.3 months in FY 1999 (see Figure 2 below).

Figure 2



CDER used a $1.2 million dollar increase in FY 2001 to fully annualize the positions added in FY 2000 and add several additional FTE. Several of these staffers are already on-board, fully trained, and demonstrating high levels of productivity. With this additional increase, all chemistry reviewer vacancies are currently filled. This in itself will hopefully improve performance, as chemistry reviews were a source of delay.

The Office of Generic Drugs (OGD) continues to refine the review process to increase efficiency with the $1.2 million increase and increases in past years. It is also evaluating ways to increase resources devoted to information technology. As the backlog of applications is addressed, it is hoped OGD can close the gap between actions so that the first action is taken within the statutory time frame. There are certain factors outside the control of OGD that may prevent complete adherence to the 180-day time frame. These include the need to adhere to the review queue structure, timeliness of inspections of the manufacturing plants, and legal issues raised late in the review process. In addition to these factors, the Agency continues to examine every aspect of the review process to try to identify problem areas that need to be addressed.

OGD also plans to revise the current system for amendment designation, major versus minor, to improve total review times.

4. Protect human research subjects who participate in drug 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:** FDA approves drug products only after the manufacturers/sponsors provide 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, clinical investigators, contract research organizations, monitors, institutional review boards, and non-clinical/analytical laboratory facilities 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. PDUFA mandates specific deadlines for review of manufacturers'/sponsors' submissions.
- **Data Source and Issues:** COMIS, Field Accomplishments and Compliance Tracking System (FACTS), and ACCESS databases are used to track assignments and results of inspections/data audits.
- **Performance:** The Agency completed 683 BIMO inspections in FY 1999, 697 in FY 2000, and 553 in FY 2001. The number of inspections conducted and completed each year is dependent on the number of applications received.

5. Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure). (12033)

- **Context of Goal:** Issuance of a Guidance for Industry on inhalational anthrax post-exposure prophylaxis will facilitate drug manufacturers' ability to expeditiously develop new drugs or already marketed drugs for this indication.
- **Data Sources and Issues:**
- **Performance:**

6. Facilitate the initiation of research in a non-human primate model of pneumonic plague. (12034)

- **Context of Goal:** At present, only streptomycin and doxycycline are FDA-approved for the treatment of plague. However, no drug is specifically approved for inhalational pneumonic plague. Animal models are needed to

address whether certain drugs are effective (or ineffective) in the treatment of human pneumonic plague.
- **Data Sources and Issues:**
- **Performance:**

7. Expeditite the review of protocols for investigational new drugs (INDs) to treat organophosphorous nerve agents in the event of chemical attack. Encourage sponsors of these new drug application (NDAs) to update current labling for Antidote Treatment Nerve Agent, Autoinjectors (ATNAA). (12035)

- **Context of Goal:** In the event of a nerve agent attack, a vulnerability to the public health exists if limited drugs options are available. Increasing the number of drugs approved for this specific usage improves the Nation's preparedness including the CDC's National Pharmaceutical Stockpile (NPS).
- **Data Sources and Issues:**
- **Performance:**

8. Identify and begin to address labeling gaps in the therapeutic armamentarium for the prevention, mitigation, and treatment of illnesses cases by chemical and biological attacks, including the needs for special populations, such as pregnant women, pediatric, and geriatric populations. (12036)

- **Context of Goal:** In the Federal Government's response to various agents of mass destruction, drugs will be mobilized from the CDC's National Pharmaceutical Stockpile (NPS). However, not all drugs in the NPS are FDA-approved for counter-terrorism uses. Identification of these deficits including development of a plan to address these deficits will move the Public Health Service closer to a goal of labeling all drugs that reside in the NPS for counter-terrorism uses.
- **Data Sources and Issues:**
- **Performance:**

9. Develop guidance for Industry on developing antiviral drugs for the mitigation of complications associated with vaccinia immunization. (12037)

- **Context of Goal:** In the event that the public receives vaccinia immunization as protection against a smallpox threat, it is estimated that some vaccine recipients will experience serious complications due to the vaccine. Drug therapies are needed to mitigate the risks associated with vaccinia immunization. No drug is currently FDA-approved to mitigate the complications associated with vaccinia immunization.
- **Data Sources and Issues:**

- **Performance:**

10. Facilitate human clinical trials in pneumonic plague for antimicrobial drugs that are not yet labeled for this treatment indication. (12038)

- **Context of Goal**: At present only streptomycin and doxycycline are FDA-approved for the treatment of plague. However, no drug is specifically approved for inhalational pneumonic plague. Human clinical trial data experience is needed to demonstrate safety and efficacy for this specific treatment indication and to identify new therapeutic drug options.
- **Data Sources and Issues:**
- **Performance:**

11. Develop guidance for Industry on developing antiviral drugs for the treatment of smallpox. (12039)

- **Context of Goal:** If smallpox was intentionally released on the American pubic, the effects could be devastating. One response to this threat includes mass vaccinia immunization. However, depending on the patient population, safe and effective drug therapies may be preferred to vaccinia immunization. No drug is currently FDA-approved for the treatment of smallpox.
- **Data Sources and Issues:**
- **Performance:**

12. Publish a final rule which allows the agency to approve new drug and biological products for the treatment of chemical, biological, radiological, or nuclear substances based on animal efficacy studies when adequate and well-controlled studies in humans cannot be ethically conducted and field studies are not feasible. (12040)

- **Context of Goal:** To date FDA approvals of drugs and biological products require that prior to licensing, safety and efficacy must be substantiated in adequate and well-controlled *human* clinical trials. Issuance of a final "animal rule" *(Evidence Needed to Demonstrate Efficacy of New Drugs When Efficacy Studies in Humans are not Ethical or Feasible)* will permit the Agency's determination of substantial evidence for *efficacy* be based on animal surrogates. This is particularly germane for drugs to prevent, mitigate, or treat the effects of a bioterrorist agent that can't be ethically studied in humans today (e.g., smallpox infection).
- **Data Sources and Issues:**
- **Performance:**

13. Expedite the review of protocols for investigational new radioprotectant drugs (including heavy metal chelators) for use in the event of a radiation emergency. (12041)

- **Context of Goal:** Although potassium iodide (KI) is FDA approved as a thyroid blocking agent in a radiation emergency, it's protective effects are limited to the thyroid gland. Additional drug options (e.g., heavy metal chelators) are needed to mitigate the effects of an intentional radiation emergency.
- **Data Sources and Issues:**
- **Performance:**

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 determine everything about a drug's safety before it is approved. 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. FDA also must be vigilant to protect Americans from injuries and deaths caused by unsafe, illegal, fraudulent, substandard or improperly used products.

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, AERS, contains approximately 2 million adverse event reports from health care professionals (see goal 12007). In calendar year 2000, over 275,000 individual safety reports (ISRs) were received into entry into AERS of which over 30% represented serious and unexpected events. The first quarter data for calendar year 2001 projects over 300,000 reports for the full year. FDA evaluates spontaneous reporting data from 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 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. Manufacturers of human drugs must register their establishment(s) with the FDA and also submit a listing of every product they market in the US. The Agency uses this information to swiftly communicate with these manufacturers in cases of product emergencies.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
14. Streamline adverse drug event reporting system. (12007)	FY 03:Major reporting companies will be submitting Adverse Drug Reaction (ADR) reports electronically for all types of ADR reports. FY 02: Accepting electronic submissions from companies and be current with MedDRA coding versions. FY 01: Issue Proposed Rule on adverse event reporting requirements. Issue Guidance on electronic submission of	FY 03: FY 02: FY 01: AERS version 2.1 completed. 11,000 ISRs submitted electronically. AERS version 2.2 implemented. FY 00: Development and roll-out of AERS 2.0 was completed. Pilot program to increase	

	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 officers in new drug review divisions. FY 00: Develop next generation of AERS to enhance functionality. FY 99: Implement AERS for the electronic receipt and review of voluntary and mandatory ADR reports.	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: The AERS was successfully implemented and has been operational for nearly three years.	
15. CDER will conduct laboratory research on at least three projects identified as related to the mission of PQRI. (12016)	FY 03: CDER will continue with significant progress (defined as 25% toward completion for each project) on the three projects identified by the PQRI. FY 02: Conduct laboratory research on at least 3 projects FY 01: Initiate laboratory research	FY 03: FY 02: FY 01: Initiated 3 laboratory research programs (Oral Biopharmaceutics, Drug Product, and Drug Substance programs) and performed the	

	on at least 3 projects FY 00: 25% Goal metric changed for FY 01 and 02. See Context Section	corresponding research in connection with the mission of PQRI. FY 00: 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.	
16. Inspect registered human drug manufacturers, repackers, relabelers and medical gas repackers.[1] (12020)	FY 03: 20% FY 02: 20% FY 01: 26% FY 00: 22% FY 99: 22%	FY 03: FY 02: FY 01: 19% FY 00: 22% FY 99: 26% FY 98: 24% FY 97: 26%	
17. Assure that FDA inspections of domestic drug manufacturing and repacking establishments result in a high rate of conformance (at least 90%) with FDA requirements. (12006)	FY 03: NA FY 02: NA FY 01: at least 90% FY 00: at least 90%	FY 03: FY 02: FY 01: 95% FY 00: 93%	
18. Give consumers and health professionals more easily understandable	FY 03: NA FY 02: NA FY 01: Give consumers and health professionals more easily	FY 03: FY 02: FY 01: The OTC label education campaign was further developed and	

prescription and OTC drug information. (12027)	understandable prescription and OTC drug information. FY 00: Make new drug approval information increasingly available via the Internet. Develop partnerships with national organizations to disseminate educational information to consumers.	implemented and additional emerging consumer risk-management issues were addressed such as those surrounding bioterrorism. FY 00: The CDER Internet site posted consumer drug information sheets for new drugs, as well as the approval letter, physicians drug label, and the reviews of the drug. OTC label education campaigns were targeted to grassroots consumers and key health professional organizations.	
19. Finalize rulemaking to establish a web-based electronic drug registration and listing database to allow for complete and up-to-date data on all regulated drug products, and follow this finalization with launch of the electronic database. (12042)	FY 03: Finalize rulemaking to establish a web-based electronic drug registration and listing database to allow for complete and up-to-date data on all regulated drug products, and follow this finalization with launch of the electronic database. FY 02: Publish a Notice of Proposed-Rulemaking to establish a web-based electronic animal and human drug and biologics registration and listing database to	FY 03: FY 02: FY 01: NA	

	allow for complete and up-to-date data on all regulated drug products. FY 01: NA		
20. Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax. (12043)	FY 03: NA FY 02: Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax. FY 01: NA	FY 03: FY 02: FY 01: NA	
21. Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies. (12044)	FY 03: NA FY 02: Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies. FY 01: NA	FY 03: FY 02: FY 01: NA	
TOTAL FUNDING: ($000)	FY 03: 114,495 FY 02: 91,724 FY 01: 64,496 FY 00: 77,809 FY 99: 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

14. 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:** 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

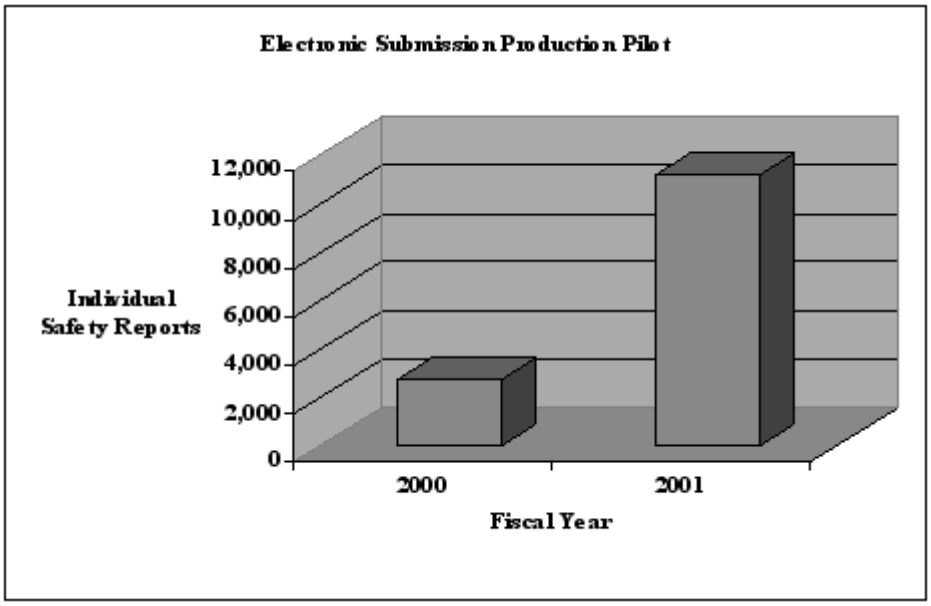
format for electronic submission of the reports from the manufacturers. Features include on-screen review of reports, searching tools, and various output reports in support of postmarketing drug surveillance and compliance activities. AERS contains approximately 2 million individual safety reports (ISRs). FDA evaluates spontaneous reporting data from 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.

In FY 2003, the Agency will conduct additional risk management and risk communication research, including pilot initiatives to minimize preventable adverse drug reactions and medication errors. The Agency will also implement a regulation related to Bar Coding of pharmaceutical products.

- **Data Sources and Issues:** AERS
- **Performance:** AERS has been operational for nearly four years. In calendar year 99, over 275,000 ISRs were received for entry into AERS of which over 82,000 (30%) represented serious and unexpected events (30%). In calendar year 2000, over 270,000 individual safety reports (ISRs) were received for entry into AERS with almost 3000 electronic submitted test reports. To date, AERS has received 105,000 ISRs, and it is anticipated that AERS will receive over 280,000 for the calendar year 2001, which will include electronic submitted reports (over 10%).

  AERS version 2.1, completed in February 2001, enhanced the compliance and Freedom of Information portions of AERS by making it more accessible to compliance staff and improving compliance-related search capabilities. CDER implemented an Electronic Submission Product Test Pilot for AERS in October 2000. This pilot provided a mechanism for companies to test and send electronic submissions of expedited reports via physical media or gateway directly into AERS. Over 11,000 individual case safety reports were submitted electronically under the pilot program in FY 2001 (see Figure 3 below).

Figure 3



AERS version 2.2 was implemented in May 2001, enhancing the ability of the system to accept electronic submissions. Also in May 2001, a draft guidance for industry, *"Providing Regulatory Submissions in Electronic Format - Postmarketing Expedited Safety Reports"* was released.

The Electronic Submission Product Test Pilot for AERS is part of a step-level implementation program for the electronic submission of postmarketing surveillance information. The pilot allows FDA to identify and resolve several process issues while regulatory and infrastructure changes are implemented. Electronic submissions provide CDER, FDA, and the public with several tangible benefits. Specifically, automating the receipt and processing of safety reports will allow FDA to: be more responsive to public health issues, reduce resources associated with data management, and apply better data and better science to the drug regulatory process. The proposed rule on ADR reporting and guidance on electronic submissions is in the process of being finalized.

15.CDER will conduct laboratory research on at least three projects identified and approved by the Product Quality Research Institute. (12016)

- **Context of Goal:** The Product Quality Research Institute (PQRI) is a first-ever collaboration among FDA, 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; "Proposed Operating Principles for the PQRI"; PQRI Technical Committee, Steering Committee, and Board of Directors meeting minutes.
- **Performance:** In FY 2001, FDA initiated three laboratory research programs and performed the corresponding research in connection with the mission of PQRI: Oral Biopharmaceutics, Drug Product, and Drug Substance. The Oral Biopharmaceutics program completed the validation of the BCS system suitability of a cell culture system, performed two food effect clinical studies, established the Biopharmaceutics Classification System database (initial phase), and developed novel models of using *in vitro* methods to predict *in vivo* bioavailability and bioequivalence. The Drug Product program accomplished the design, manufacturing, and characterization of over 40 furosemide tablet formulations. The Drug Product program also evaluated the regulatory acceptability of using Near-IR to monitor the blend uniformity and assessed particle size technology. These programs are expected to contribute to developing/revising bioavailability/bioequivalence, SUPAC, and drug substance regulations for product quality.

16. Inspect 20% 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 2001 goal of 26% was not 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 2002 actuals.

17. Assure that 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:** (Goal dropped for FY 02 and 03) In previous FDA performance plans, goals were established for maintaining the level of industry conformance to FDA requirements at 90% or above for each of the Agency product-oriented programs. This year we are recommending that these goals be deleted from the Plan. This is our rationale: Inspections are the Agency's method for determining whether an establishment is in or out of compliance with FDA requirements. Because of resource constraints, the Agency must allocate a significant proportion of its inspections to high risk situations, such as food firms who are producing high risk foods, or to emergency situations such as BSE. The number of remaining inspections each year is not adequate to draw a statistically valid inference about the compliance status of an entire industry at a reasonably high level of confidence. It is the Agency's professional judgement that the majority of firms in the regulated industries are in conformance with FDA's requirements. Based on the Agency's experience over several years, that percentage in general, has remained at 90% or above. Thus, establishing a performance goal that simply describes the stable state of the industry does not provide useful new information; nor does it serve as a management tool to drive the overall industry to a higher level of conformance.
- **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.

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

- **Context of Goal:** (Dropped for FY 02 and 03) 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. This goal has been dropped for FY 2002 and 2003 because performance goals that can be verified-- either through quantitative measures or milestones -- have

not been specified. As specific goals are developed, this goal may be reinstated.

- **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:** In cooperation with its leveraging partners in FY 2001, FDA continued to develop the Over-the-Counter Medicine Label Campaign in anticipation of full implementation by manufacturers in FY 2002. FDA also addressed other emerging and high-priority risk-management issues for consumers such as those surrounding bioterrorism. Additional outreach for the Over-the-Counter Medicine Label Campaign resulted in an ad for movie theaters that reached six million viewers, refrigerator magnets distributed to 20,000 marathon runners and a grocery bag stuffer used by a large West Coast grocery chain. The Agency developed a consumer friendly brochure on medication risk management called "Be a Member of Your Health Care Team." The accompanying print public service announcement appeared in 212 newspapers nationwide with a combined readership of 30 million. A public service announcement outlining the risks and benefits of buying medications online has appeared in 646 newspapers with a readership of 27 million and aired on 233 radio stations with six million listeners. A risk management outreach program to reduce and eliminate death and injury from medical gas mixups used leveraging with professional societies and health organizations as well as public health advisories and printed posters, flyers and stickers.

The Agency worked on expanding the prototype Dockets Comments Management System for the proposed regulation to improve the format and content of prescription drug labeling to allow easy electronic public comments linked with an internal networked comments review system. An outreach campaign to individual physicians was launched to gain their input and opinion about the proposed rule.

Also in FY 2001, the Agency posted consumer-oriented risk management information on its Web site on these specific topics: the new risk-management plan for Accutane to reduce fetal exposure to the drug; the withdrawal of Baycol for safety concerns; the counter terrorism recommendations on using three specific drugs to treat exposure to anthrax; and strengthened warnings and precautions about the pain medication Oxycontin. The Agency's Web site has more than 38,000 drug information pages and documents plus three Web-enabled databases (Orange Book, National Drug Code Directory, and Oncology Tools). FDA has begun focusing on user-focused "sense-making" and content management by designing Web pages that pull information together in a way that will help solve users information problems. All pages are tested for both accessibility compliance and for usability. In FY 2001, FDA's Web site increasingly focused on consumer information, building sense-making introductory pages on drug safety, bioterrorism drugs, and risk management. An initial step in synchronizing the Agency's consumer information campaigns with Web sites included Over-the-Counter labeling and food-drug interactions. Development was begun on a one-stop catalog of drug information that will link a drug's labeling, its reviews, MedWatch alerts, and other information such as shortages. The one-stop catalog is being designed to replace four existing tables and indexes on the current site. FDA began obtaining cost estimates on Web casting drug advisory committee meetings with piloting expected in FY 2002. Public use of the Agency's drug information Internet site averaged more than half a million visitors each month, and each visitor viewed on average 17 pages of information including menus. The FDA's Consumer Drug Information Sheets received an average of more than 200,000 hits a month.

In FY 2001, the Agency responded to more than 31,000 individual inquiries from consumers about their medications and nearly 8,000 similar inquiries from physicians and other health care professionals.

19. Finalize rulemaking to establish a web-based electronic drug registration and listing database to allow for complete and up-to-date data on all regulated drug products, and follow this finalization with launch of the electronic database. (12042)

- **Context of Goal:** In the event of a terrorist attack, various drugs may be utilized in response to the attack. Rapid access to accurate and timely information pertaining to the manufacturers and their respective drugs is

critical to surge manufacturing production needs and to reduce the risk of drug shortages.
- **Data Sources and Issues:**
- **Performance:**

20. Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax. (12043)

- **Context of Goal:** At the time of the anthrax attacks, only one drug, ciprofloxacin, was approved for inhalational anthrax post-exposure prophylaxis. Issuance of this notice effectively approves two other drug options for this indication.
- **Data Sources and Issues:**
- **Performance:**

21. Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies. (12044)

- **Context of Goal:** In the event of an intentional radiation emergency, in addition to evacuation, potassium iodide would be indicated to decrease the risk of thyroid cancer. Issuance of a final KI dosing guidance will provide clear dosing recommendations to the public and facilitate Federal, State, and local preparedness.
- **Data Sources and Issues:**
- **Performance:**

2.3.3 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 functionality of AERS. Because pharmacovigilance is a constantly changing field and the volume of postmarketing safety information continues to increase annually, AERS will need modifications and improvements to maintain its usefulness to the FDA users.

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. The full-scale implementation requires CDER to develop processes for both electronic data management and pharmacovigilance. 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. This program allows CDER to work with manufacturers who voluntarily submit safety reports electronically. Besides AERS resources being used for the users, AERS resources are used

for this pilot program to work with the manufacturers for the implementation of the electronic submissions program of the safety reports. In conjunction with the pilot, proposed rulemaking is being written to require that manufacturers submit suspected adverse drug reaction reports electronically.

As we gain more experience with the pilot electronic submissions program with the manufacturers, maintenance and improvements will be needed to make it more functional and successful. AERS was designed to accommodate electronic submission of adverse event reports from the manufacturers based on ICH specifications. Periodically, these specifications are modified and updated. Therefore some of the AERS maintenance will be due to changing ICH specifications. For example, currently, there is a new version that needs to be implemented. The manufacturers' participation in the pilot program is delayed until the new version is in place. This maintenance also includes MedDRA version upgrades in AERS. This is to assure that the electronic submissions utilizing the current version of MedDRA from the manufacturers are compatible with the version utilized in AERS.

The ultimate goal of the electronic submissions program is to be able to exchange safety reports with other regulators and manufacturers. Currently, we are only able to receive reports electronically. Some of the pilot program manufacturers are able to send reports electronically and are working with their affiliates to be able to receive reports too. We need to be able to share and send reports electronically with other regulators and industry.

In summary, the AERS database in the FDA assures that postmarketing adverse event reports are completely and accurately entered, quality controlled and reviewed to monitor product safety and to protect the public health. The data are valid for this goal because they measure the required performance indicator of expediting the process and evaluation of adverse drug events.

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.

The document room enters the date on which a Proposed Pediatric Study Request (PPSR) is received and when the Agency issues a Written Request (WR). Then the pediatric team enters the information pertaining to the types of studies to be conducted. Once the final pediatric studies are submitted to the Agency, the document room enters the receipt date into the database. The project manager for the Pediatric Team enters any additional information

pertaining to the granting or denial of exclusivity. The data is quality controlled each month by the pediatric team when they complete their monthly statistics update.

The major strength of this database is that it captures all data relative to exclusivity. Maintaining the database is time consuming for the pediatric team, i.e., entering the data on the studies. However, the document room staff are not trained to recognize what types of studies are requested in the WRs so it is not feasible for them to enter this data themselves.

The Pediatric Page Database was redesigned, piloted, and implemented in July 2000. This database was designed to capture data pertaining to the Pediatric Final Rule, i.e., whether or not pediatric studies required under the rule were completed, the number of waivers and deferrals granted, and the age ranges that may be waived, deferred, or have actually been completed. The project managers consult with the medical officers to determine whether pediatric studies are necessary, waived, or deferred and what ages should be included in the study. Then the project manager enters the information into the database. This information must be entered prior to the approval of an NDA or supplement. The pediatric page, with all relevant pediatric data, is then printed from the database and included with the action package. The action package is then forwarded to various people, i.e., the appropriate reviewer, project managers, team leader, deputy division director, division director, and office director (for NDAs only) who verify the pediatric data and sign off on the package.

The previous version of the database required a password and was not user friendly. Therefore, many project managers did not use the system resulting in incomplete data for a number of applications. The database has been updated, no longer requiring a password, and is now web-based. Training has been provided to the divisions on the new version. The number of pediatric patients being requested to be involved in studies and the types of studies being requested are tracked manually and maintained by individuals in separate databases on their computers or on common drives. Alternatives are being considered to make this an electronic process as well.

The Pediatric Inpatient Database is still being negotiated. Once this information is available to the pediatric team it will be able to determine exactly what drugs are being used in the pediatric population for unlabeled indications and then focus on requesting the studies that are necessary in order to get the products properly labeled.

This information demonstrates that the data in the Pediatric Exclusivity Database and the Pediatric Page Database are complete and accurate and that appropriate quality control practices are in place. The data are valid for this goal because they measure the required performance indicators.

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) and abbreviated new drug application (ANDA) portions of COMIS contain information about investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs), 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 on any restricted field, the task leader or senior task leader must send a written change request to the Records Management Team (RMT), Office of Information Technology (OIT). 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) has three Technical Information Specialists (TIS) assigned to the document rooms in Parklawn, Woodmont II, Corporate Boulevard, Metro Park North II and Wilkins Avenue who oversee the daily activities within their building document rooms. Quality control checks are done on application jackets, outgoing letters, memoranda and reviews, procedure and programming changes and all other activities that take place in their document rooms.

Overall, the data in COMIS are complete and accurate, and appropriate quality control practices are in place. A limited number of people in RMT and the Division of Applications Development Services (DADS), OIT, have authority to input data into COMIS, which helps to protect the integrity of the data. Once entered into the system, data are immediately accessible to users..

Meetings are held on a weekly basis to discuss any and all issues related to COMIS data entry, document rooms, and procedure changes to ensure that COMIS reflects changes in policy and legislative requirements. Attendees at these meetings include two members of the Document Control Room contract management staff in RMT, a Chief Project Manager review division representative from Parklawn, WOCII and Corporate Boulevard, a programmer from DADS, and representatives from the Division of Drug Marketing, Advertising, and Communications, the Office of Generic Drugs, and the Reports and Data Management Team, ORM.

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.

2.4 BIOLOGICS

2.4.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 2003 Current Estimate	FY 2002 Current Estimate	FY 2001 Actual	FY 2000 Actual	FY 1999 Actual
Total ($000)	209,323	175,675	147,230	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 31 percent from FY 1996 to FY 2001. INDs and IDEs are an

indication of future license application 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 facilitating the maintenance of 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.

2.4.2 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 and use.

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 Agency and industry representatives have begun negotiations to renew PDUFA legislation beyond FY 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. The PDUFA performance goals for FY 2003 and beyond, will have to be negotiated with industry.

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 14million 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

Performance Goals	Targets	Actual Performance	Reference
1. Review and act on 90 percent of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90 percent of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt. (13001)	Standard Applications within 12 months: FY 2003: N/A FY 2002: N/A FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent Standard Applications within	Standard Applications within 12 months: FY 2001: 11/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 100 percent FY 1997: 100 percent Standard Applications within	

	10 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 70 percent FY 2000: 50 percent FY 1999: 30 percent Priority Applications within 6 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent	10 months: FY 2003: FY 2002: FY 2001: 09/2002 FY 2000: 100 percent FY 1999: 80 percent Priority Applications within 6 months: FY 2003: FY 2002: FY 2001: 05/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 100 percent FY 1997: 100 percent	
2. Review and act on 90 percent of standard PDUFA efficacy supplements within 10 months; and review and act on 90 percent of priority PDUFA efficacy supplements within 6 months of receipt. (13002)	Standard Applications within 12 months: FY 2003: N/A FY 2002: N/A FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent Standard Applications within 10 months: FY 2003: 90	Standard Applications within 12 months: FY 2001: 11/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 100 percent FY 1997: 100 percent Standard Applications within 10 months:	

	percent FY 2002: 90 percent FY 2001: 70 percent FY 2000: 50 percent FY 1999: 30 percent Priority Applications within 6 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent	FY 2003: FY 2002: FY 2001: 09/2002 FY 2000: 100 percent FY 1999: 100 percent Priority Applications within 6 months: FY 2003: FY 2002: FY 2001: 05/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 100 percent FY 1997: 100 percent	
3. Review and act on 90 percent of PDUFA manufacturing supplements within 6 months of receipt, and review and act on 90 percent of PDUFA manufacturing supplements requiring prior approval within 4 months of receipt. (13003)	Within 6 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent Within 4 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 70 percent FY 2000: 50	Within 6 months: FY 2003: FY 2002: FY 2001: 05/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 99 percent FY 1997: 98 percent Within 4 months: FY 2003: FY 2002: FY 2001: 03/2002 FY 2000: 100 percent FY 1999: 93 percent	

	percent FY 1999: 30 percent		
4. Review and act on 90 percent of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90 percent of Class 2 resubmitted original PDUFA applications within 6 months of receipt. (13004)	Class 1 resubmissions within 2 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 70 percent FY 2000: 50 percent FY 1999: 50 percent Class 2 resubmissions within 6 months: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent	Class 1 resubmissions within 2 months: FY 2003: FY 2002: FY 2001: 100 percent FY 2000: 100 percent FY 1999: 100 percent FY 1998: 100 percent Class 2 resubmissions within 6 months: FY 2003: FY 2002: FY 2001: 05/2002 FY 2000: 100 percent FY 1999: 100 percent	
5. Review and act on 90 percent of complete blood bank and source plasma PLA/BLA submissions, and 90 percent of PLA/BLA supplements within 12 months after submission	Complete Submissions: FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 85 percent	Complete Submissions: FY 2003: FY 2002: FY 2001: 11/2002 FY 2000: 100 percent FY 1999: 100 percent FY 1998: 85	

date. (13005**)**	FY 1999: 60 percent Supplements FY 2003: 90 percent FY 2002: 90 percent FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent	percent FY 1997: 83 percent Supplements FY 2003: FY 2002: FY 2001: 11/2002 FY 2000: 100 percent FY 1999: 99 percent FY 1998: 97 percent FY 1997: 98 percent	
6. Expedite review of product specific lot release and extension of dating submissions for the Anthrax Vaccine Absorbed (AVA). (13013)	FY 2003: Expedite review of product specific lot release and extension of dating submissions for the Anthrax Vaccine Absorbed (AVA). FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001:	
7. Provided guidance to the CDC, DOD and the Anthrax Vaccine Absorbed manufacturer regarding clinical studies to support proposed changes in the immunization schedule and routes of administration. (13014)	FY 2003: Provided guidance to the CDC, DOD and the Anthrax Vaccine Absorbed manufacturer regarding clinical studies to support proposed changes in the immunization schedule and routes of administration. FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001:	

8. Facilitate expedited development and review of new vaccines for protection and/or treatment against bioterrorism related threat diseases (e.g., smallpox and anthrax vaccines). (13015)	FY 2003: Facilitate expedited development and review of new vaccines for protection and/or treatment against bioterrorism related threat diseases (e.g., smallpox and anthrax vaccines). FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001:	
9. Facilitate expedited development and review of new gamma globulins for protection and/or treatment against bioterrorism related threat diseases. (13016)	FY 2003: Facilitate expedited development and review of new gamma globulins for protection and/or treatment against bioterrorism related threat diseases. FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001:	
10. Evaluate the need for guidance documents to assist in the development of products such as immunoglobulins and select vaccines. (13017)	FY 2003: Evaluate the need for guidance documents to assist in the development of products such as immunoglobulins and select vaccines. FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001:	
TOTAL FUNDING ($000)	FY 2003: 166,752 FY 2002: 134,374 FY 2001: 114,849 FY 2000: 111,968 FY 1999: 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. The PDUFA performance goals for FY 2003 and beyond will have to be negotiated with industry. "N/A" means the goal is not applicable in that fiscal year.

1. Review and act on 90 percent of standard original PDUFA NDA, PLA, and BLA submissions within 10 months; and review and act on 90 percent 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 2001 data for standard applications within 12 months will be available after November 2002. The FY 2001 data for standard applications within 10 months will be available after September 2002.

2. Review and act on 90 percent of standard PDUFA efficacy supplements within 10 months; and review and act on 90 percent 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 2001 data for standard applications within 12 months will be available after

November 2002. The FY 2001 data for standard applications within 10 months will be available after September 2002.

3. Review and act on 90 percent of PDUFA manufacturing supplements within 6 months of receipt, and review act on 90 percent 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.

4. Review and act on 90 percent of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90 percent 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
- **Performance:** These applications are tracked by year of receipt, which is the cohort year. FDA's FY 2001 performance for review of class 1 resubmissions within 2 months was 100 percent.

5. Review and act on 90 percent of complete blood bank and source plasma PLA/BLA submissions, and 90 percent 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
- **Performance:** These applications are tracked by year of receipt, which is the cohort year. The cohort-year review performance is not available until the prescribed review time, i.e., 12 months after receipt, is expired. The FY 2001 data for review of complete submissions and for major supplements will be available after November 2002.

6. Facilitate expedited development and review of new vaccines for protection and/or treatment against bioterrorism related threat diseases (e.g., smallpox and anthrax vaccines). (13013)

- **Context of Goal:** An essential element of the Counter Terrorism initiative includes the expeditious development and licensing of products to diagnose, treat or prevent outbreaks from exposure to the pathogens that have been identified as bioterrorist agents. These products must be reviewed and approved prior to the large-scale productions necessary to create and maintain a stockpile. Staff must guide the products through the regulatory process, including the manufacturing process, pre-clinical testing, clinical trials, and the licensing and approval process. Experts in these areas must expedite the licensing and approval process for these products. Pathogens that have been identified as potential biological warfare agents include those that cause smallpox and anthrax. CBER is responsible for the review of biologic products including vaccines, blood and blood products, as well as therapeutic biologic products.
- **Data Sources:** Not applicable
- **Performance:** New goal/not available

7. Facilitate expedited development and review of new gamma globulins for protection and/or treatment against bioterrorism related threat diseases. (13014)

- **Context of Goal:** Gamma globulin products may be useful as a treatment or as protection against certain bioterrorism related threat diseases. These products must be reviewed and approved prior to the large-scale productions necessary to create and maintain a stockpile. Staff must guide the products through the regulatory process, including the manufacturing process, pre-clinical testing, clinical trials, and the licensing and approval process. Experts in these areas must expedite the licensing and approval process for these products.
- **Data Sources:** Not applicable

- **Performance:** New goal/not available

8. Expedite review of product specific lot release and extension of dating submissions for the Anthrax Vaccine Absorbed (AVA). (13015)

- **Context of Goals:** Biologic products are derived from living organisms and are sometimes made in living organisms, therefore their manufacture presents difficulties not encountered in drug manufacturing. Biologics consist of delicate substances or cells that are sensitive to heat, light, and to being shaken when in liquid form, and are easily susceptible to contamination. Manufacturers must submit samples of product lots and results of their own tests for potency, safety and purity to the Agency before release of the product. Tests generally include those for bacterial and fungal sterility, general safety, purity, identity, suitability of constituent materials and potency.
- **Data Sources:** Not applicable
- **Performance:** New goal/not available

9. Provided guidance to the CDC, DOD and the Anthrax Vaccine Absorbed manufacturer regarding clinical studies to support proposed changes in the immunization schedule and routes of administration. (13016)

- **Context of Goals:** Sponsors must obtain approval for proposed changes related to approved products. Guidance documents assist the Center staff and regulated industry in specifying issues and areas where more specific direction can be outlined and thus contribute to expediting the review process. The review process is facilitated by identifying areas in the regulatory process where more specific direction regarding requirements are needed.
- **Data Sources:** Not applicable
- **Performance:** New goal/not available

10. Evaluate the need for guidance documents to assist in the development of products such as immunoglobulins and select vaccines. (13017)

- **Context of Goals:** Guidance documents assist the Center staff and regulated industry in specifying issues and areas where more specific direction can be outlined and thus contribute to expediting the review process. The review process is facilitated by identifying areas in the regulatory process where more specific direction regarding requirements are needed.
- **Data Sources:** Not applicable
- **Performance:** New goal/not available

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.

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
11. Assure that FDA inspections of domestic biologics manufacturing, repacking and blood banks establishments result in a high rate of conformance (at least 90 percent) with FDA	FY 2003: N/A FY 2002: N/A FY 2001: at least 90 percent FY 2000: at least 90 percent FY 1999: at least 90 percent	FY 2003: FY 2002: FY 2001: 99 percent FY 2000: 96 percent FY 1999: 98 percent FY 1998: 98 percent FY 1997: 98 percent	

requirements (13007)			
12. Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80 percent. (13008)	Currently 26 foreign and Domestic Plasma Fractionator establishments FY 2003: N/A FY 2002: N/A FY 2001: 80 percent FY 2000: 80 percent FY 1999: 80 percent	FY 2003: FY 2002: FY 2001: 67 percent, 16 out of 24 in compliance FY 2000: 69 percent, 18 out of 26 in compliance FY 1999: 62 percent, 16 out of 26 in compliance FY 1998: 54 percent, 13 out of 24 in compliance	
13. Meet the biennial inspection statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments.[1] (13012)	FY 2003: 50 percent FY 2002: 50 percent FY 2001: 50 percent FY 2000: 50 percent FY 1999: 43 percent	FY 2003: FY 2002: FY 2001: 57 percent FY 2000: 57 percent FY 1999: 64 percent FY 1998: 46 percent FY 1997: 46 percent	
TOTAL FUNDING ($000)	FY 2003: 42,571 FY 2002: 41,301 FY 2001: 32,381 FY 2000: 28,749 FY 1999: 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

11. 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 percent) (13007)

- **Context of Goal:** (Goal dropped for FY 2002 and 2003) In previous FDA performance plans, goals were established for maintaining the level of industry conformance to FDA requirements at 90 percent or above for each of the Agency product-oriented programs. This year we are recommending that these goals be deleted from the Plan. This is our rationale: Inspections are the Agency's method for determining whether an establishment is in or out of compliance with FDA requirements. Because of resource constraints, the Agency must allocate a significant proportion of its inspections to high risk situations, such as food firms who are producing high risk foods, or to emergency situations such as BSE. The number of remaining inspections each year is not adequate to draw a statistically valid inference about the compliance status of an entire industry at a reasonably high level of confidence. It is the Agency's professional judgement that the majority of firms in the regulated industries are in conformance with FDA's requirements. Based on the Agency's experience over several years, that percentage in general, has remained at 90 percent or above. Thus, establishing a performance goal that simply describes the stable state of the industry does not provide useful new information; nor does it serve as a management tool to drive the overall industry to a higher level of conformance.
- **Data Sources:** FDA Field Information System (FIS)
- **Performance:** Performance for this goal in FY 2001 was 99 percent. Conformance rates for FY 1997 through FY 2001 have been adjusted to reflect the observed average correction rate for each year.

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

- **Context of Goal:** (Goal dropped for FY 2002 and 2003) Plasma fractionator establishment compliance with CGMP's is beyond the control of FDA. FDA can determine their CGMP compliance through inspections. Since Goal 13009 pertains to biennial CGMP inspections for all biologics manufacturing establishments, including plasma fractionator establishments, this goal is deleted. There are currently 24 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 24 foreign and domestic plasma fractionator establishments. In FY 2000, 69 percent, or 18 establishments of 26 were in compliance. In FY 2001, 67 percent or 16 establishments of 24 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.

13. Meet the biennial inspection statutory requirement by inspecting 50 percent 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 and FY 2001, FDA inspected 57 percent of the establishments in the Official Establishment Inventory, exceeding the goal of 50 percent. The drop in inspection coverage from 64 percent in FY 1999 to 57 percent 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.

2.4.3 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-Biologics License Application (RMS-BLA). The RMS-BLA is CBER's new VAX-based, Oracle database that is used to track all biologics license applications, 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-

BLA records application review information on each license application and supplement received and filed by the Center. The RMS-BLA 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-BLA.

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 by 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-BLA, 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.

2.5 ANIMAL DRUGS AND FEEDS

2.5.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 03 Current	FY 02 Current	FY 01 Actual	FY 00 Actual	FY 99 Actual

	Estimate	Estimate			
Total ($000)	88,972	86,467	64,070	49,593	43,253

The mission of the Animal Drugs and Feeds Program is to protect the health and safety of all food producing, companion or other non-food animals; and, to assure that food from animals is safe for human consumption. To support this mission, the Center for Veterinary Medicine (CVM) focuses on two strategic goals:

1. **Increase the availability and diversity of safe and effective animal drugs and feeds.**
2. **Reduce the risks associated with marketed animal 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. The premarket program is using several initiatives to expedite the animal drug review process including pre-submission conferences, development of electronic submissions, and the revision and development of guidance documents. On the postmarket side, CVM compliance inspection and surveillance monitoring activities manage public health risks such as Bovine Spongiform Encephalopathy (BSE) and antibiotic resistance. CVM's approach to achieving the strategic goals and summary of the key performance goals are explained in the following sections.

2.5.2 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 to ensure the health of companion animals. 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. Also, the availability of safe and effective drugs ensures companion and guide animals (used to assist individuals with disabilities) live healthier and longer lives.

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. CVM's practice of "Phased Review" provides industry sponsors with timely feedback on product applications, and may detect application deficiencies early in the drug approval process. Pre-submission conferences (Performance Goal 1) and guidance documents (Performance Goal 5) increase industry efficiency. The Agency is committed to improving the review time for new animal drug applications (NADAs) (Performance Goal 2). Development of an enhanced information system for electronic submission of applications and data will allow FDA to perform application review activities more efficiently (Performance Goal 3). To ensure that FDA has the science capability and intellectual capital necessary to assess data and make regulatory decisions, a staff college is being developed (Performance Goal 5). Risk assessment models will evaluate the risk to human health from resistant foodborne pathogens associated with consumption of antimicrobials in food producing animals (Performance Goal 7).

These premarket 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 human 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 healthier 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 03: 80% FY 02: 80% FY 01: 80% FY 00: 73% FY 99: NA	FY 03: FY 02: FY 01: 80% FY 00: 75% FY 99: 73%	
2. Review and act on 90% of all new animal drug applications and supplements within 275 days and review and act on 90% of all	FY 03: Review and act on 90% of all new animal drug applications and supplements within 275 days FY 03: Review and	FY 03:	

investigational new animal drug data submissions (type P) within 325 days. (14017)	act on 90% of all investigational new animal drug data submissions (type P) within 325 days. FY 02: Review and act on 50% of NADAs/ANADAs within 180 days of receipt. FY 01: 75% FY 00: 73% FY 99: NA	FY 02: FY 01: 50% FY 00: 74% FY 99: 73%	
3**. Reduce pending overdue Animal Drug applications by 15%.** (14019)	FY 03: 15% FY 02: 15% FY 01: NA FY 00: NA FY 99: NA	FY 03: FY 02: FY 01: NA FY 00: NA FY 99: NA	
4. Continue to pilot and validate procedures to receive protocol submissions electronically. (14002)	FY 03: Receive protocols and ADE active form. FY 02: Pilot and validate the procedure for receiving protocol submissions electronically. FY 01: Initiate the development of a method for receiving protocol submission electronically FY 00: Completed an additional 4 phases -	FY 03: FY 02: FY 01: Changed focus of protocol submission to hard media (e.g., tapes, cd-rom, hard drives). Implemented automated logging/ routing of e-mail electronic submissions. Posted standards on dockets for submission of electronic information in support of NADAs. On-going contract to develop CVM-specific guidance	

	Notices of Slaughter; Notices of Animal Final Disposition; Meeting Agendas; USDA Slaughter Reports FY 99: Complete 1 phase — Notices of Claimed Investigational Exemptions (NCIE)	for file organization and format for hard media submissions. Expanded electronic archive to accept hard media submissions. FY 00: Wrote guidance on 4 phases. Developed technology for logging/routing of electronic submissions. FY 99: 1 phase completed (NCIE).	
5. Begin to design and implement a Staff College. (14018)	FY 03: Expansion of content and developmental components & integration w/Center & Agency IT infrastructure. FY 02: Plan and design the option selected in Phase I. FY 01: Initiate the development of a Staff College (Phase I: further needs assessment, feasibility studies, and analysis of alternatives). FY 00: NA FY 99: NA	FY 03: FY 02: FY 01: Initiated the development of a Staff College (Phase I). FY 00: NA FY 99: NA	

6. Revise and develop 14 guidances. (14001)	FY 03: NA FY 02: NA FY 01: 3 manufacturing, 10 new drug approval process and 1 Veterinary International Conference on Harmonization (VICH) guidances. FY 00: Update 12 guidelines (original target was 7 documents which was 10 % of animal drug review guidances). FY 99: Update 1 guideline (1% of animal drug review guidances).	FY 03: FY 02: FY 01: Completed 7 final and 7 draft manufacturing, new animal drug approval process and VICH guidances. FY 00: Published 19 draft and/or final guidances (including 7 VICH documents). FY 99: 8 guidelines: including 3 FDAMA and 5 VICH.	
7. Develop an antibiotic risk assessment model using fluoroquinolone, chickens and Campylobacter. (14003)	FY 03: NA FY 02: NA FY 01 Goal: Perform 2 risk assessments. FY 00 Goal: Generalize the model by performing risk assessments related to other antibiotics and other animal/bacterial species. FY 99 Goal: Increase Risk Assessments by 10% FY 99: (Baseline-FY 01) Develop an antibiotic risk assessment model	FY 03: FY 02: FY 01: Performed risk assessments for campylobacter and Synercid™. FY 00: Draft FQRA published/comments received. Model broadened to include virginiamycin use in food animals & indirect transfer of Enterococcus faecium. FY 99: 1 Risk Assessment completed.	

	using fluoroquinolone as the antibiotic, Chickens as the animal species and Campylobacter as the bacterial isolate		
TOTAL FUNDING: ($ 000)	FY 03: 30,169 FY 02: 29,336 FY 01: 26,624 FY 00: 21,117 FY 99: 18,522		

C. Goal-by-Goal Presentation of Performance

1. Maintain the level of requested pre-submission conferences conducted with industry sponsors at 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 goal was met for FY 00 and FY 01. Based on current data, 80% is a reasonable target for FY 02 and FY 03.

2. Review and act on 90% of all new animal drug applications and supplements within 275 days and review and act on 90% of all investigational new animal drug data submissions (type P) within 325 days. (14017)

- **Context of Goal:** In FY 03, CVM is changing this performance goal to a new measure that is a more useful for both Center management and industry. Key industry stakeholders have told us that 'how long an application takes to get reviewed' is more meaningful to them than 'what percent is reviewed on time'. CVM has also introduced a new performance goal (Goal 3) to emphasize its commitment to reducing the current backlog in applications. FDA is taking steps to move closer to statutory requirements in future years.

- **Data Sources**: Submission Tracking and Review System (STARS).
- **Performance:** The performance reporting for FY 99 through FY 02 pertains to the review and action on NADAs and ANADAs within 180 days of receipt. In FY 99, CVM updated its tracking system to be consistent with procedures under ADAA achieving a 73% performance rate. CVM slightly exceeded the FY 00 target with a performance rate of 75%. In FY 2001, CVM reviewed and acted on approximately 50% of New Animal Drug applications (NADAs) and Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt.
  CVM found it necessary to shift focus in its performance regarding animal drug application review in FY 2001. The Office of New Animal Drug Evaluation (ONADE) needed to reduce the backlog of overdue documents. This required working on the oldest, already overdue documents. Decreasing the backlog was necessary in order to move CVM back on track towards meeting statutory and stakeholder requirements for new animal drug application review. By taking the step of closing out the most overdue documents, CVM's on time completion rate for NADAs and ANADAs was adversely affected this year. Although approximately 50% of NADAs and ANADAs were reviewed on time in FY 2001, CVM reduced its backlog of pending overdue documents by 1,334, from 2,234 to 900.
  The goal for FY 02 has been revised to review and act on 50% of NADAs/ANADAs within 180 days of receipt. The goal was revised from 80% to 50% because the Center has changed priorities and redirected resources to clear the large backlog of animal drug applications.

3. Reduce pending overdue Animal Drug Applications by 15%. (14019)

- **Context of Goal:** During FY 2001, the Center conducted an evaluation of our performance in the new animal drug review process and determined that our priorities needed to shift in order to eliminate the backlog in pending new animal drug submissions. This goal was created for FY 02 and FY 03 to facilitate that process and to provide the needed emphasis on this strategic goal of making more animal drugs available.
- **Data Sources**: Submission Tracking and Review System (STARS).
- **Performance:** The Animal Drugs and Feeds program will reduce the backlog of pending overdue animal drug applications by 15% in both FY 02 and FY 03.

4. Continue to pilot and validate procedures to receive 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 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 several electronic submission processes for use by the animal industry. 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.

- **Data Sources:** CVM's priority project tracking system.
- **Performance:** In FY 99, 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. In FY 00, CVM published Federal Register Notices on four (4) draft guidance documents pertaining to electronic submissions.
  In FY 01, all sponsors receiving instructions on submissions are advised of the availability of using the e-mail method for some submissions and directed to our website for instructions. A workshop was held to highlight new and improved systems and forms available for electronic information transfer. System modifications made smart form available to increase quality control of information input by submitters, and automated login to the Center's tracking system and forwarding for review.
  Use of the Center's email to submit electronic information expanded to 15 sponsors from 13. Currently available forms and types of submissions on the Agency's Electronic submission docket: Notices of Claimed Investigational Exemptions; Notice of Intent to Slaughter for Human Food Purposes; Notice of Final Disposition of Animals Not Intended for Immediate Slaughter; and Request for a Meeting or Teleconference. These are all supported by guidance documents and smart forms released February 2001. Information is available through our web page.
  Protocal Submissions: CVM has delayed electronic receipt of Protocol Submissions until automation requirements of a more complicated business review process have been fully developed.
  In July, 2001, CVM increased the automation of the NCIE, Intent to Slaughter, Notice of Final Disposition, and Meeting Request by providing the sponsors with a PDF fill-in form for submission by e-mail, allowing a higher degree of automated processing at CVM by uploading data in the STARS tracking database. The time required for verification of receipt to the sponsor has been decreased to a few minutes from a potential high of three days. In 2001, the Center posted a reference on the electronic dockets that allows submission of data in electronic format in support of New Animal Drug Applications. This allows interested parties, with the concurrence of the Center to submit more extensive data electronically. The Center is working toward a draft of CVM-specific guidance for file organization and format for hard media submissions. The Center is also expanding its current electronic archive to accept hard media submissions. The Center has also become active in coordinating the Agency effort to harmonize standards in the Agency, and has participated in the Agency-wide General Consideration Document that will publish for

comment early in 2002. CVM will participate in the Agency guidance and acceptance of submission to the Agency of Manufacturing Stability data in XML format. The Center will also participate in an Agency Panel at the Drug Information Association Meetings in February 2002. Work has also begun on the guidance and smart form design for the submission of Adverse Drug Experience reports - both by form and XML data sets. Additional phases of electronic submissions will be initiated in FY 02 and FY 03 in support of this goal.

5. 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 99: Identify need to enhance and maintain scientific expertise. FY 00: Develop a strategy to establish a Staff College in CVM. FY 01: Initiated Phase I - conduct further needs assessment, feasibility studies, and analysis of alternatives:
    - Contract awarded to perform needs assessment and begin building the Staff College infrastructure necessary for a competency based learning management system to enhance the science-base.
    - Began the research and design of a training facility to support the infrastructure of the CVM Staff College. Awarded a facilities and equipment contract and construction of the training facility began late in FY01.
    - Recruited a FDA/CVM Search Team to conduct a nationwide search for a qualified Staff College Director who could continue building the Staff College infrastructure. Review of the 130 candidates was completed late in FY 01.
    - Conducted in-house development and implementation of seminars, professional meetings and courses that increased the science-based knowledge of the FDA's review staff which can help reduce review times and backlogs of pending applications.

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

- **Context of Goal:** Reform legislation and reinvention initiatives, such as the Results Act (RA) and FDAMA, require input from our customers and stakeholders. Input from customer surveys, stakeholder meetings, and

other interactions with regulated industry helped FDA target resources toward developing guidance documents that will accurately reflect the current veterinary medicated feed and drug approval/monitoring processes. Guidance documents reflect changes in the approval processes resulting from enactment of the ADAA, FDAMA, and CVM's efforts to reinvent its new animal drug approval processes. The availability of guidance documents facilitates 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 99 and will continue into FY 00 and FY 01. 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. (Goal dropped for FY 2002.)

- **Data Sources:** CVM's priority project tracking system.
- **Performance:** 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 VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products). 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). In FY 01, 14 draft and/or final guidances were completed: 3 manufacturing, 10 new animal drug approval process, and 1 VICH.
  This goal is dropped in FY 02 since CVM can not directly measure the number of (increased) drug approvals tied to the revision/development of guidance documents. Guidance documents improve the efficiency of phased review (applications are submitted with complete forms that contain required information); however, the number of submissions from industry will not necessarily increase due to issuance of guidance documents.

7. 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:** Improved 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. (Goal dropped for FY 2002.)

- **Data Sources:** The NARMS database mentioned later in this report, surveillance systems of other government organizations (e.g. CDC and USDA), and published literature.
- **Performance:** The Center has used the principles of risk assessment to determine that the microbial safety of antibiotics used in food animals be assessed prior to approval. The assessment modeled the risk of having a resistant Campylobacter infection attributable to the use of fluoroquinolones in chickens and being treated with a fluoroquinolone. The draft risk assessment report on Campylobacter was made available on the CVM homepage and was discussed at a workshop held December 9-10, 1999. The final document was released in October 2000. Based partly on the results of the Campylobacter risk assessment, CVM proposed to withdraw approval of the new animal drug application for use of the fluoroquinolone antimicrobial drug enrofloxacin in poultry. One of the two sponsors, Abbott has voluntary withdrawn the product. Bayer is requesting a hearing. If the approval is withdrawn, this drug would no longer be legally marketed for this indication. Other approved uses of fluoroquinolones in cattle, dogs, and cats are not affected by this proposal. On April 5, 2001, FDA/CVM announced that a feasibility study had been completed for a risk assessment on the link between the use of virginiamycin in animals and Synercid™ resistance in humans. Based on the feasibility study, the Center for Veterinary Medicine determined that sufficient data did exist or was forthcoming to support a quantitative risk assessment of the human health impact from the use of virginiamycin in food-producing 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.
  This goal was dropped for FY 02 because the risk assessment on fluoroquinolone resistance in Campylobacter has been completed.

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. This involves inspections, sample collections and analysis, investigations, and other activities (Performance Goals 8 and 9). Regulatory actions are taken as needed to control violative goods and firms.

CVM surveillance systems identify potential human and/or animal health hazards. The surveillance systems also help develop 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 withdraw marketed drugs as necessary to protect human and animal health). The desired outcome is to assure that marketed animal drugs and food additives provide safe food products derived from animals and ensure quality health care of animals.

The National Antimicrobial Resistance Monitoring System (NARMS), part of the President's Food Safety Initiative, was developed to provide an effective early-warning system that can detect food illness outbreaks early and prevent their spread. NARMS (Performance Goal 10), developed in conjunction with USDA and CDC, 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 prevention efforts.

Another critical FDA goal is to prevent the introduction and spread of Bovine Spongiform Encephalopathy (BSE) into the U.S. herd and human food chain. There is strong scientific evidence (epidemiological and laboratory) that the agent that causes BSE in cattle is the agent that causes variant Creutzfeldt-Jakob Disease (vCJD) in people. If BSE emerged in the U.S. it could pose a serious health risk to humans and be financially devastating to the U.S. beef industry. CVM plans to conduct 100% inspections of all known renderers, FDA licensed and non-licensed feed mills in order to maintain compliance with the BSE feed regulation. (Performance Goal 11).

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
8. Maintain biennial inspection coverage by inspecting 50% of registered animal drug and feed establishments. (14009)	FY 03: 50% FY 02: 50% FY 01: 50% FY 00: 27% FY 99: 27%	FY 03: FY 02: FY 01: 37% FY 00: 39% FY 99: 25%	
9. Assure that FDA inspections of domestic animal drug and feed	FY 03: NA FY 02: NA FY 01: at least 90% FY 00: at least 90%	FY 03: FY 02: FY 01: 99% FY 00: 97%	

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%	
10. Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000. (14005)	CY* 03: Total 12,000 Salmonella isolates CY 02: Total: 12,000 Salmonella isolates CY 01: Total: 12,000 Salmonella isolates CY 00: Total: 6,000 Salmonella isolates - 2,000 (human), 4,000 (veterinary) CY 99: Total: 6,000 Salmonella isolates - 2,000 (human), 4,000 (veterinary)	CY 03: CY 02: CY 01: Data not avail- Able until March 2002. CY 00: Total: 11,000 Salmonella isolates — 2,000 (human), 9,000 (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)	
11. Conduct targeted BSE inspections of 100% of all known renderers and feed mills handling prohibited material.	FY 03: 100% FY 02: 100% FY 01: NA	FY 03: FY 02: FY 01: NA	

(14006)			
TOTAL FUNDING: ($ 000)	FY 03: 58,803 FY 02: 57,131 FY 01: 37,446 FY 00: 28,476 FY 99: 24,731		
* CY = Calendar Year			

C. Goal by Goal Presentation of Performance

8. 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 medicated 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. The increase in the inspection coverage target from 27 percent to 50 percent in FY 2001 through FY 2003 is attributed to the ability to hire up to the number of inspectors to assist toward accomplishment of this goal.
- **Data Sources:** Field Accomplishment Compliance Tracking System (FACTS) [formerly known as the Program Oriented Data System (PODS)], Official Establishment Inventory.
- **Performance:** FY 99 = 25%; FY 00 = 39%; FY 01 = 37%. In FY 99, 25% of registered animal drug and feed establishments were inspected. The FY 99 actual performance fell short of the 27% target based on the fact that the initial inspection percentages were estimates, due to the complexity and number of inspections, and re-inspections.
  In FY 00, 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. The goal was not met in FY 2001. The program did accomplish 37% biennial inspection

coverage of registered animal drug and feed establishments. The need to perform BSE inspections became a higher priority in FY 2001 because of the increase in reported cases of BSE in Europe. To minimize the risk of BSE introduction into US cattle herds and to protect the health of American citizens, the program received contingency funding. After re-establishing priorities within the field portion of the Animal Drugs and Feeds Program, BSE inspections were instituted to ensure that 100 percent of renderers, protein blenders, and feed mills were inspected; and to conduct sample analysis to assure compliance with the BSE regulation. The BSE crisis in England and Europe made it apparent that 100 percent of renderers, protein handlers, and feed mills handling prohibited material would need to be inspected every year to continue to protect US cattle herds from BSE and the health of American citizens.

9. 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 at least 90% conformance with FDA requirements. (14004)

- **Context of Goal:** (Goal dropped for FY 02 and 03) In previous FDA performance plans, goals were established for maintaining the level of industry conformance to FDA requirements at 90% or above for each of the Agency product-oriented programs. This year we are recommending that these goals be deleted from the Plan. This is our rationale: Inspections are the Agency's method for determining whether an establishment is in or out of compliance with FDA requirements. Because of resource constraints, the Agency must allocate a significant proportion of its inspections to high risk situations, such as food firms who are producing high risk foods, or to emergency situations such as BSE. The number of remaining inspections each year is not adequate to draw a statistically valid inference about the compliance status of an entire industry at a reasonably high level of confidence. It is the Agency's professional judgement that the majority of firms in the regulated industries are in conformance with FDA's requirements. Based on the Agency's experience over several years, that percentage in general, has remained at 90% or above. Thus, establishing a performance goal that simply describes the stable state of the industry does not provide useful new information; nor does it serve as a management tool to drive the overall industry to a higher level of conformance.
- **Data Sources:** FDA Field Data Systems.
- **Performance:** FY 97 = 97%; FY 98 = 98%; FY 99 = 99%; FY 00 = 97%; FY 01 = 99%. 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 a given year. As the statistical model and industry coverage is improved, the rates will better represent the conformance status of the overall industry.

10. Maintain isolate testing rate for Salmonella in National Antimicrobial Resistance Monitoring System (NARMS) at 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:** National Antimicrobial Resistance Monitoring System.
- **Performance:** In FY 99 = collected 8,510 animal and 1,706 human isolates; FY 00 = collected 9000 animal and 2000 human isolates. We will increase the goal to 12,000 isolates per year for 2001-2003, which we will continue to send for serotyping, susceptibility testing, and quality control testing. Reports will continue to be generated and analyzed.
  The performance data for FY 01 will not be available until March 2002.

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. A pilot study was conducted with medical microbiologists from hospitals 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 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.

11. Conduct targeted BSE inspections of 100% of all known renderers and feed mills handling prohibited material. (14006)

- **Context of Goal:** CVM sought to protect the public through the development of a comprehensive strategy of education, inspection and enforcement action on industry. These activities were initiated to ensure compliance with the Bovine Spongiform Encephalopathy (BSE) regulations. Using an inventory of all known renderers and FDA licensed and non-licensed feed mills, FDA will conduct inspections to determine compliance with the BSE feed rule. Inventories of these firms may vary from year to year based on changes at the firm such as consolidations, business closures, relocations, etc. FDA will continue to update and improve the inventory of firms with information from states and other sources.
- **Data Sources:** FDA Field Data Systems.
- **Performance:** On August 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. FDA has developed a three-pronged aproach in its efforts to realize 100% compliance with the 1997 feed rule--education, a strong and visible inspection presence, and enforcement action. More than 12,000 inspections have been done since 1997 at over 10,000 firms including renderers, feed mills, ruminant feeders, protein blenders, feed haulers and distributors.
  Based on the change in priorities, the goal has been changed to include re-inspection of 100 percent of firms found to be out of compliance, 100 percent of renderers, protein handlers, and feed mills, handling prohibited material, and as many other firms in these businesses, as resources allow, that we currently have listed as not handling prohibited materials, and to conduct sample analysis as needed to assure compliance with the BSE regulation. The need to perform BSE inspections became a higher priority in FY 2001 because of the increase in reported cases of BSE in Europe. To minimize the risk of BSE introduction into US cattle herds and to protect the health of American citizens, the program received contingency funding.

2.5.3 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 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 entered into Interagency Agreements for the development of databases. Therefore, we are dependent 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. Since 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.

2.6 MEDICAL DEVICES & RADIOLOGICAL HEALTH

2.6.1 Program Description, Context and Summary of Performance

Total Program Resources:

	FY 2003 Current Estimate	FY 2002 Current Estimate	FY 2001 Actual	FY 2000 Actual	FY 1999 Actual
Total $000	206,640	196,425	177,565	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, medical ultrasound equipment, and x-ray machines. In addition, FDA is taking on new priorities to support the Administration's fight against terrorism. For the Device and Radiological Health program, Counter-terrorism activities include expedited review of bioterrorism diagnostics, managing product shortages, supporting the safe and effective development and use of battlefield and emergency devices, working to ensure safe use of people scanners in airport and other security systems, and increased monitoring of imports.

FDA is faced with an increasing challenge to maintain parity with an ever-changing, rapidly growing industry. The number of device firms domestically and internationally has increased from 9,061 in FY 1997 to 13,701 in FY 2001 and projected to increase to over 15,000 in FY 2003. The medical device industry of the 21st century is developing more and more devices based on leading-edge technology. FDA is responsible for regulating 10,000 mammography facilities under the MQSA and over 4,000 radiological health firms under RCHSA. The device program is also responsible for oversight of 15,000 active clinical investigators. FDA has to maintain its regulatory mission by making 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; device-drug combination products; and pioneering organ replacement and patient assist devices. FDA's premarket functions support the Department's Prevention Priorities, and the postmarket functions support the Department's Medical Errors/Healthcare Quality Priorities. In addition, many devices are used by the elderly and directly relate to the Department's priorities for patient diagnostic care. CDRH also regulates diabetes diagnostics.

FDA's Center for Devices and Radiological Health (CDRH) has developed *key strategies* to more directly promote and protect the public health through the total life cycle of a product. This will allow CDRH to focus regulatory resources on products in a least burdensome way no matter what their stage of development; from concept development to active marketing or modification.

- Total Product Life Cycle (TPLC) -- Apply TPLC model in coordination with stakeholders;
- Magnet for Excellence -- Attract and retain a diverse workforce to accomplish our public health mission;
- Meaningful Metrics -- Measure and communicate our impact on the public health; and
- Knowledge Management -- Manage knowledge to support TPLC in the information age.

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 information exchange. 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.

The Center is working toward improving areas that are not working well in the following scorecard by using the elements of the Strategic Plan:

Program Area	Working Well	Working But Facing Challenges	Not Working Well
Device Review	✓		
Regulatory Science		✓	
Device Inspection			✓
Device Post-Market Surveillance			✓
Mammography	✓		

Radiation Safety			✓

2.6.2 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

In the FY 2003 budget, FDA requests cost of living increases that will be needed to meet FY 2003 device review performance targets. FDA is also proposing to use part of its Counter-terrorism funding to expedite review of diagnostics to detect bioterrorism agents like anthrax in humans. Due to competing priorities, FDA is not requesting any other program increases to improve device review in the FY 2003 budget. FDA also requested cost of living increases in FY 2002, which will be needed to meet FY 2002 device review performance targets.

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 device review 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. Under the FDCA places all medical devices into one of three regulatory classes based on the level of control needed to provide reasonable assurance 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 that are considered safe and effective; and, device types (no "s") developed after the 1976 Device Amendments for which safety and effectiveness data must be submitted by the sponsor to the FDA for review. 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 1-5)

In measuring device review performance, CDRH follows Agency standards in measuring and reporting review time, defining statutory review time requirements, and setting performance goals. FDA's device review

performance goals follow the Agency standards of using receipt cohorts to measure the percentage of FDA reviews completed within the number of days specified by the statute, for the "cohort" of applications received in a particular year. Some device-specific review time definitions follow to help stakeholders interpret device review data.

For 510(k)s, section 510(k) of the Federal Food, Drug and Cosmetic Act establishes a 90-day timeframe for the review of a premarket notification. In addition, 21 CFR 807.81(a) and 21 CFR 807.87(1) reference the 90-day benchmark for 510(k)s. If a final decision on the notification cannot be made on the basis of the information supplied by the manufacturer, it is placed on hold and a new 90-day review (cycle) begins when the requested information is received.

For premarket approval applications (PMAs), section 515(d)(1)(A) of the Federal Food, Drug and Cosmetic Act establishes a 180-day review benchmark for Agency action on a PMA. In addition, 21 CFR 814.37(c)(1) and 21 CFR 814.40 reference a 180-day review period (cycle) for a PMA. A new 180-day review period begins when a major amendment (containing significant new or updated data, detailed new analyses, or information previously omitted) is received. FDA works collaboratively with manufacturers to make the total review time less than 180 days.

The total review time for rendering a decision (either approval or disapproval, clearance or not substantially equivalent decisions) on a premarket application includes both FDA time and non-FDA time. The FDA time includes the number of days FDA took to review the application that led to a final approval decision. The non-FDA time is the time spent by the manufacturer responding to FDA's requests for information.

FDA cannot control the amount of time a manufacturer takes to respond back to FDA's concerns about deficient applications (other than deleting the applications after a certain amount of hold time has elapsed). FDA continues to work with industry to make applications more complete and scientifically sound when they are submitted to FDA. FDA's goal is to streamline the internal review process and improve the quality of premarket submissions received from manufacturers so the total review time is within FDAMA statutory requirements.

B. Summary of Performance Goal

Performance Goals	Targets	Actual Performance	Reference
1. Review and Complete 95 percent	FY 2003: 95 percent FY 2002: 90 percent	FY2003: FY 2002:	

of Premarket Approval Application (PMA) first actions within 180 days. (15001)	FY 2001: 90 percent FY 2000: 85 percent FY 1999: 65 percent	FY 2001: 97 percent FY 2000: 96 percent FY 1999: 74 percent	
2. Review and complete 95 percent of PMA supplement final actions within 180 days. (15009)	FY 2003: 95 percent FY 2002: 90 percent FY 2001 90 percent FY 2000: 85 percent FY 1999: N/A	FY 2003: FY 2002: FY 2001: 98.4 percent FY 2000: 98.7 percent FY 1999: 100 percent	
3. Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days. (15002)	FY 2003: 95 percent FY 2002: 95 percent FY 2001: 95 percent FY 2000: N/A FY 1999: 90 percent	FY 2003: FY 2002: FY 2001: 100 percent FY 2000: 100 percent FY 1999: 100 percent	
4. Expedite review for 100 percent of Bioterrorism Diagnostic Medical Device Applications. (15028)	FY 2003: 100 percent FY 2002: N/A FY 2001: N/A FY 2000: N/A FY 1999: N/A	FY 2003: FY 2002: FY 2001: FY 2000: FY 1999:	
5. Complete 95 percent of PMA "Determination" meetings within 30 days. (15024)	FY 2003 95 percent FY 2002: 95 percent FY 2001: 95 percent FY 2000: 95 percent FY 1999: N/A	FY 2003: FY 2002: FY 2001: 100 percent FY 2000: 100 percent FY 1999: 100 percent	

6. Recognize 20 new or enhanced standards to use in application review. (15003)	FY 2003: Recognize 20 new or enhanced standards to use in application review. FY 2002: Recognize 20 new or enhanced standards to be used in application review. FY 2001: Recognize 20 additional application review standards FY 2000: Review 50 Standards for continued applicability and 50 standards for recognition FY 1999: Recognize over 415 standards for use in application review	FY 2003: FY 2002: FY 2001: 597 Standards recognized FY 2000: 567 Standards recognized FY 1999: 450 Standards Recognized	
7. Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.) (15025)	FY 2003: 290 FY 2002: 290 FY 2001: 250 FY 2000: N/A	FY 2003: FY 2002: FY 2001: 238 FY 2000: 249	
TOTAL FUNDING ($000)	FY 2003: $78,523 FY 2002: $74,641 FY 2001: $67,475 FY 2000: $64,698 FY 1999: $60,423		

C. Goal-By-Goal Presentation of Performance

1. Review and Complete 95 percent of Premarket Approval Application (PMA) first actions within 180 days. (15001)

- **Context of Goal:** PMAs involve potentially high-risk devices with most chance 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. Workload is expected to increase in FY 2003.

- **Data Sources:** Center for Devices and Radiological Health (CDRH) Premarket Tracking System and Receipt Cohorts
- **Performance:** In FY 2001, FDA performance was 97 percent for the applications received in FY 2001. The performance strategy is to redirect resources from low-risk to high-risk devices. Reengineering of the PMA process to include early meetings with manufacturers, modular review, streamlined reviews, and product development protocols have speeded reviews. Faster reviews give patients quicker access to important new medical devices.

2. Review and complete 95 percent of Premarket Approval Application (PMA) supplement final actions within 180 days. (15009).

Note: workload will continue to increase in FY 2003 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.
  Real-time PMA Supplement review is a regulatory tool that gives sponsors the option of participating in "real-time" reviews that are conducted by teleconference or face-to-face. This gives manufacturers a chance to discuss all of FDA's review issues at one time. Last year, sponsors of over 25 percent of the 545 PMA supplements submitted to FDA chose real-time reviews, mostly by teleconference.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts
- **Performance:** FY 2001 performance was 98.4 percent for the applications received in FY 2001.

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

- C**ontext of Goal:** This is an FY 1999 goal, dropped in FY 2000, and picked back up for FY 2001, FY2002, and FY 2003, 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 2001, 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 optimize how critical FDA and industry resources are used. The two efforts below illustrate FDA device review improvements. FDA encourages firms to use these regulatory options.

Third Party 510(k) Reviews are consistent with FDAMA's intent to encourage use of outside scientific and technical expertise, and provide an alternative to FDA review. During FY 2001, FDA received 107 510(k)s reviewed by third parties.

- a. 510(k)s reviewed by Accredited Persons received FDA marketing clearance 29 percent faster than comparable 510(k)'s reviewed entirely by FDA. An added bonus is that most Accredited Persons have specialized expertise in areas that may be helpful to 510(k) submitters, such as device testing, standards, or foreign regulatory requirements. In an effort to encourage greater use of the Third Party Program, FDA implemented an expansion pilot in 2001 that allowed Accredited Persons to review many Class II devices that were not previously eligible. The pilot allows, subject to certain conditions, Accredited Persons to review Class II devices for which there are no device-specific guidance documents. FDA's website is at http://www.fda.gov/cdrh/thirdparty/.
- **b. Special and Abbreviated 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 2001, As of September 30TH the Agency has received 717 Special 510(k) applications and 174 Abbreviated (510(k). 685 Special 510(k)s were processed within 32 days and all of the Abbreviated 510(k)s were acted on within the required 90 days, FDA expects to receive an estimated 1000 Special and Abbreviated 510(k) submissions in 2002.

4. Expedite review for 100 percent of Bioterrorism Diagnostic Medical Device Applications. (15028)

- **Context of Goal:** This performance goal deals with a new area for FY 2003 (Bioterrorism). FDA will review diagnostic test devices and test kits that detect or measure bioterrorism agents like anthrax in humans that are being marketed within the U.S. Currently there are no approved commercial diagnostics for this purpose, and FDA is working with industry on applications. The review work on diagnostics started in FY 2002, and is a new performance goal for FY 2003.
- **Data Sources:** CDRH Premarket Tracking System and Receipt Cohorts.
- **Performance:** This is a new goal for FY 2003 and therefore, has no performance history.

5. Complete 100 percent of Premarket Approval Application (PMA) "Determination" meetings within 30 days. (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 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 2001, performance was 100 percent.

6. Recognize 20 new or enhanced standards to be used in application review. (15003)

- **Context of Goal:** Science, technology and standards activities are directed to improve science support related to the device review process. FDA works on other standards expected to benefit the entire medical device industry to improve premarket approval times. Use of standards also helps to expedite reviews of 510(k)s and in certain cases to fill a standard void. As example: No standardized protocol for the cleaning of devices after use but prior to sterilization is available. FDA requested the Association for the Advancement of Medical Instrumentation (AAMI) to initiate standards development in that area. The AAMI Sterilization Standards Committee has initiated the development of such a protocol. When completed, this protocol will be useful to hospitals and others who clean medical devices prior to their being placed back into service.
- **Data Sources:** Standard status document reports
- **Performance:** FDA recognized 30 standards in FY 2001 and 117 standards in FY 2000 for a cumulative total of 597 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.

7. Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.). (15025)

- **Context of Goal:** In FY 2003, FDA plans to conduct 290 BIMO Inspections, the same number as in FY 2002. 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. CDRH is continuing to see an increase in these types of actions.

- **Data Sources:** CDRH Field Data Systems
- **Performance:** This goal is a new reporting commitment in FY 2002. In FY 2001, 238 BIMO inspections were conducted. FDA did not achieve it's performance goal of 250 device bioresearch inspections because the absence of a cost of living increase reduced the number of Field staff available to do device bioresearch inspections.

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 include: (1) Device Inspections; (2) Mammography Program (3) Radiation Safety; and (4) Adverse Event Reporting. In addition, FDA is setting new performance goals for Counter-terrorism, including implementing an emergency preparedness and response plan for radiation contamination incidents, and beginning to develop radiation safety standards for expanded use of people scanners in airports and other security systems.

FDA estimates the number of domestic and international device firms will grown to over 15,000 in FY 2003. For approximately 5,500 domestic higher risk device establishments and over 3,000 foreign higher risk device firms (excluding mammography facilities), the law requires FDA to conduct inspections at least once every two years. FDA is also responsible for regulating over 7,000 lower risk devices to insure they comply with Quality System Regulations. FDA does not routinely inspecting about 4,000 domestic and 3,000 foreign Class I firms. Most of their Class I products are also 510(k) exempt. However, the regulations do not establish a mandatory time frame for lower risk inspections. There are also approximately 10,000 mammography facilities, which must be inspected at least once each year. FDA is also responsible for regulating about 4,350 radiological health firms domestically and internationally. FDA is responsible for regulating these firms but the law does not specify how frequently inspections or product testing should be done. The inspection performance goals for devices, MQSA and radiological health focus on statutory coverage requirements.

Device Inspections

FDA enforces numerous regulations to protect the public from unsafe or ineffective medical devices or radiological products. FDA also confirms 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 7 - 10)

Medical devices and electronic products are increasingly complex, and industry is growing domestically and internationally. This growth and reduced inspection resources have reduced inspection coverage with the result that when manufacturers are inspected, they have increased violation rates. In FY 2002, FDA requested an appropriated funding increase for domestic inspections and additive user fees for foreign inspections and imports, but these increases will not enable FDA to meet statutory inspection requirements. FDA's inadequate device inspection coverage impairs product safety and FDA's ability to meet the following responsibilities:

FDAMA reduces reliance on premarket clearance for many low and medium risk devices favor 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.

Domestic higher risk inspection coverage was only 20 percent in FY 2001 compared to the statutory requirement of 50 percent, and violation rates were high.

Foreign higher risk inspection coverage was only 11 percent in FY 2001 equal to the 11 percent rate in FY 2000. Additionally, 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. To date, less than 25 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 firms to pay for inspections by Conformity Assessment Bodies. Over the long term, successfully implemented MRAs will reduce the number of foreign firms FDA needs to inspect but until the MRA is fully implemented it is unlikely that devices will satisfactory have an inspection presence with foreign firms.

Emerging device product safety assurance issues 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.

Radiation Safety

Radiological health resources dropped from 400 FTEs in FY 1978 to less than 50 FTEs in FY 2001. We are seeing a resurgence of problems in both the medical and consumer product area. For examples, FDA issued a public health notification to emphasize the importance of radiation doses during CT procedures. The Agency is extremely concerned because the overexposure of children or small adults during computed tomography (CT) procedures can easily go unrecognized since medical personnel can not simply tell that a patient has been over exposed. FDA also monitored cases of unnecessary radiation emitted during fluoroscopy. Principal risks to patients from over-exposure include long term possibilities for cancer induction and a short term potential for skin burns. FDA is proposing new regulations that it estimates would save lives from over-exposure by requiring more restrictive specifications for new equipment. FDA has also partnered with the American College of Cardiology to address user issues through education.

FDA's radiological health program is challenged with working with all the new technology that is currently available and on the horizon, and solving problems that were solved years ago but are coming back with a new twist. Radiation-induced skin burns are an example of a resurgence of an old radiation issue. Reports in the MDR database and the medical literature shows that these injuries result from the use of fluoroscopy in conjunction with interventional procedures. FDA is also dealing with the expanding overseas facilities, which contribute roughly 335 million foreign made products.

FDA is concerned that projected coverage falls to low to ensure FDA can effectively regulate radiation safety. FDA will do what it can with available resources to address the expanding problems being reported. (Performance Goal 9).

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. Final regulations for "States as Certifiers", which will transfer certification authority from FDA to applicant States, were published in the Federal Register. In FY 2001, FDA ensured that 97 percent of mammography facilities met inspection standards, with 3.4 percent with Level 1 (serious) problems. The slight increase above the GPRA goal of 3 percent for this element was likely due to the fact that under the final regulations, which became effective in April 1999, several citations were elevated to Level I. (Performance Goal 11).

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 device-related medical errors; serve as an advanced warning system; and create a two way communication channel between FDA and the user-facility community. MeDSuN is also FDA's pilot for establishing a network of user facilities that will require user reporting for only a subset of facilities. During FY 2001, FDA began feasibility testing with 25 hospitals and worked on software changes needed for website health data security. In FY 2002, FDA is adjusting the performance goal downward from 125 facilities to 80 facilities. Concerns and problems with development timing, unanticipated program changes, and increased information technology security requirements. FDA projects recruiting up to 80 facilities by the end of FY 2002, and, depending on funding, up to 125 facilities by the end of FY 2003. (Performance Goal 12)

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
8. Provide inspection coverage for Class II and Class III domestic medical device manufacturers at 20 percent. (15005.01)	FY 2003: 20 percent FY 2002: 20 percent FY 2001: 17 percent FY 2000: 22 percent FY 1999: 26	FY 2003: FY 2002: FY 2001: 20 percent FY 2000: 13 percent FY 1999: 30 percent	

	percent		
9. Assure FDA inspections of domestic medical device manufacturing establishments result in at least 90 percent conformance. (15018)	FY 2003: N/A FY 2002: N/A FY 2001: 90 percent FY 2000: 90 percent FY 1999: 90 percent	FY 2003: FY 2002: FY 2001: 96 percent FY 2000: 92 percent FY 1999: 95 percent	
10. Provide inspection and product testing coverage of Radiological Health industry at 10 percent (15027)	FY 2003: 10 percent FY 2002: N/A FY 2001: N/A	FY 2003: FY 2002: FY 2001: 10 percent FY 2000: 10 percent	
11. Provide inspection coverage for Class II and Class III foreign medical device manufacturers at 9 percent for FY 2003. (15005.02)	FY 2003: 9 percent FY 2002: 9 percent FY 2001: 9 percent FY 2000: 9 percent FY 1999: N/A	FY 2003: FY 2002: FY 2001: 11 percent FY 2000: 11 percent FY 1999: 10 percent	
12. Ensure at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent with Level I (serious) problems. (15007)	FY 2003: 97 percent FY 2002: 97 percent FY 2001: 97 percent FY 2000: 97 percent FY 1999: 97 percent	FY 2003: FY 2002: FY 2001: 97 percent; but with 3.4% with level I (serious) problems. FY 2000: 97 percent FY 1999: 97 percent	
13. Implement the MeDSuN System by expanding the network to 180 facilities. (15012)	FY 2003: Build a MedSun hospital network of 180 facilities FY 2002: Implement	FY 2003: FY 2002:	

	MedSuN by recruiting a total of 80 facilities for the network FY2001: Recruit a total of 75 hospitals to report adverse medical device events FY 2000: Develop MeDSuN based on approximately 25 user facilities FY 1999: Implement Pilot	FY 2001: FDA began feasibility testing with 25 hospitals and worked on software changes needed for website health data security . FY 2000: Develop MeDSuN Phase II Pilot based on approximately 25 user facilities. FY 1999: Pilot Completed	
14. Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation. (15029)	FY 2003: Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation. FY 2002: Develop Emergency Counter Terrorism Preparedness and Response Plan for radiation. FY 2001: N/A	FY 2003: FY 2002: FY 2001: N/A	
15. Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places. (15030)	FY 2003: Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports	FY 2003: FY 2002: FY 2001: N/A	

	and other places. FY 2002: N/A FY 2001: N/A		
TOTAL FUNDING: ($000)	FY 2003: $128,117 FY 2002: $121,784 FY 2001: $110,090 FY 2000: $105,559 FY 1999: $ 98,585		

C. Goal-By-Goal Presentation of Performance

8. Provide inspection coverage for Class II and Class III domestic medical device manufacturers at 20 percent. (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. Class II and Ill manufacturers are required by statute to be inspected at least once every two years. Reuse inspections have been incorporated into the domestic higher risk inventory, which is projected to increase from 5,000 to 5,500 in FY 2003. FDA plans to conduct 200 reuse hospital inspections in FY 2003, and these will need to be conducted with base resources. In FY 2002, inspections of hospitals reprocessing class I devices will be educational in nature. Formal GMP inspections will be reserved for those hospitals reprocessing higher risk class II and III devices. The approximately 4,000 class I lower risk domestic firms will not be inspected on a routine basis: only "for cause" to follow up on problems identified in recalls or reported by the public. During FY 2002, FDA plans to use base resources to inspect a sample of Class I firms to monitor Quality Systems conformance.
- **Data Sources:** CDRH Field Data Systems
- **Performance:** In FY 2001, FDA exceeded its FY 2001 performance target (17 percent) by inspecting 20 percent of 4,900 domestic higher risk Class II and Class III manufacturers. FDA's statutory performance requirement is 50 percent. With the exception of those inspected for cause, many manufacturers of low risk Class I devices have never been inspected. To develop a better understanding of their compliance rate a small number of such firms were inspected.
  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 inspection coverage is not

keeping pace with the new device firms, and domestic recall rates are increasing. Medical devices and radiological health inspection resources have been reduced by 23 percent since FY 1995 and these resource limitations have put coverage below critical mass.
FDAMA exempts many lower risk devices from pre-market approval, and relies instead on 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 routinely monitor quality systems conformance for lower risk at current resource levels. In FY 2002, FDA plans to inspect a sample of these firms.

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

- **Context of Goal:** (Goal Dropped for FY 2002 and 2003) In previous FDA performance plans, goals were established for maintaining the level of industry conformance to FDA requirements at 90 percent or above for each of the Agency product-oriented programs. This year we are recommending that these goals be deleted from the Plan. This is our rationale: Inspections are the Agency's method for determining whether an establishment is in or out of compliance with FDA requirements. The Agency must allocate a significant proportion of its inspections to high risk situations, such as firms who are producing high risk medical devices, or where the technology is rapidly evolving and must be more closely monitored. The number of remaining inspections each year is not adequate to draw a statistically valid inference about the compliance status of an entire industry at a reasonably high level of confidence.
  It is also the Agency's judgement that the majority of firms in the regulated industries are in conformance with FDA's requirements. Based on the Agency's experience over several years, that percentage in general, has remained at 90 percent or above. Thus, establishing a performance goal that simply describes the stable state of the industry does not provide useful new information; nor does it serve as a management tool to drive the overall industry to a higher level of conformance.
- **Data sources:** CDRH Field Data Systems.
- **Performance:** In FY 2000, FDA had a 92 percent conformance rate. In FY 2001, FDA had a 96 percent conformance rate.

10. Provide inspection coverage and product testing coverage of the Radiological Health industry.

- **Context of Goal:** Radiological health resources have continued to drop from 400 FTEs in FY 1978 to less than 50 FTEs in FY 2001. FDA is seeing a resurgence of problems in both the medical and consumer

radiological product area such as widespread new uses for fluoroscopy by relatively untrained practitioners increasing the risk of over exposure and high emission rates from consumer products. We attribute this to a lack of coverage of industry shipments and the fact that FDA is not able to keep up with the new developments in electronic product technology. FDA has monitored cases of unnecessary radiation emitted during fluoroscopy. Principal risks to patients from over-exposure include long term possibilities for cancer induction and a short term potential for skin burns. FDA is proposing new regulations that would require more restrictive specifications for new equipment. FDA estimates the new regulations can spare 723 lives per year from radiation-induced cancer, recognizing it averages 30 years for the long-term radiation-induced cancer to emerge after exposure. FDA has also established a working collaborative with the ACC, (cardiologists being a most frequent user to educate other users.) FDA also receives approximately 5000 electronic product reports yearly. Since FDA can't review these on a one-by-one basis, FDA plans to select product areas which require immediate attention by testing specific automatic screening criteria for electronic reports.

- **Data sources:** CDRH Rad Health Data Systems. FDA estimates there is almost no overlap between the device inspection coverage goals and this radiological health coverage goals because the device inspections and radiological health inspections examine different things and require different inspector training. FDA works in partnership with the states.
- **Performance:** In FY 2001, FDA estimates there were approximately 4,350 active radiological health firms FDA is responsible for regulating domestically and internationally. In FY 2001, FDA was only able to provide coverage for about 10 percent of these firms. To conserve resources, FDA initiated activities to prioritize and leverage its radiation protection efforts with state governments, professional societies, and other federal agencies. Additionally, in FY 2001, FDA initiated a working group to develop an electronic reporting system for laser products, which account for three-quarters of the reports submitted on radiation-emitting electronic products.

11. Provide inspection coverage for Class II and Class III foreign medical device manufacturers at 9 percent in FY 2003. (15005.02)

- **Context of Goal:** The foreign higher risk Class II and III inventory is expected to increase from 2,550 in FY 2002 to 3,000 in FY 2003. As workload increases, inspection coverage is expected to be only 9 percent in FY 2002 and 9 percent in FY 2003. The approximately 3,000 Class I lower risk foreign manufacturers will not be routinely inspected, only for cause. This goal includes joint inspections of high-risk device manufacturers with European Union Conformance Assessment Bodies. 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, if the MRA is successfully implemented, it could reduce the number of foreign firms that FDA will need to inspect. FDA supports a web site 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.

- **Data Sources:** CDRH Field Data Systems
- **Performance:** In FY 2001, FDA foreign inspection rate was 11 percent and 266 inspections were conducted compared to 261 inspections conducted in FY 2000. 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 far below critical mass. FDA cannot maintain foreign inspections or successfully implement the MRA with current resources.

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. In the Mammography Quality Standards Reauthorization Act (MQRSA) of October 1998, Congress authorized the FDA to undertake a demonstration program to assess the results of conducting mammography inspections less frequently than annually for the highest performing facilities. The program implementation date is May 2002. The MQSA is also up for reauthorization this year.
  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 do 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 web site, collaboration with NIH to provide a list of MQSA-certified facilities, a

consumer brochure, meetings with consumer groups, and interactive teleconferencing for facilities.

- **Data Sources:** Mammography Program Reporting and Information System (MPRIS)
- **Performance:** During FY 2001, FDA ensured that 97 percent of mammography facilities met inspection standards, with 3.4 percent with Level 1 (serious) problems. The slight increase above the GPRA goal of 3 percent for this element was likely due to the fact that under the final regulations, which became effective in April, 1999, several citations were elevated to Level I, and some new Level I citations were added. Additionally, FDA Performed 169 audit inspections under the Inspector Quality Assurance program and trained 26 new inspectors on the requirements of the MQSA regulations.
  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.

13. Build the MeDSuN System by Expanding the Network to 180 Facilities. (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. FDA estimates that there may be as many as 300,000 injuries and deaths annually associated with device use and misuse. MeDSuN will give FDA the health information it needs to identify and address some of those problems. 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. FDA is adjusting the performance goal downward from 125 facilities to 80 facilities. The reason for this is that in FY 2001, FDA delayed implementing feasibility testing due to extended software development and unanticipated program changes and increased information technology security requirements. FDA began feasibility studies with only 25 facilities instead of the 75 facilities originally projected for FY 2001. FDA expects to add more facilities to the network throughout FY 2002. FDA projects recruiting up to 80 facilities by the end of FY 2002, and, depending on funding, up to 180 facilities by the end of FY 2003. 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 and to reduce mandatory reporting requirements for most user facilities. 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:** In FY 2001, FDA did not meet the goal of recruiting 75 hospitals because most of the effort was focused on extended software development for the Internet-based reporting system (interactive web-based form and database), unanticipated program changes and increased information technology security requirements. FDA did recruit 25 hospital facilities. Throughout FY 2002, FDA will add more facilities, and projects recruiting a total of 80 facilities for the network. The long-term goal is to expand the program to include different types of health care facilities and to include drug and biologic products.

14. Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation.

- **Context of Goal:** CDRH is updating an emergency response plan used in the past to respond to radiation contamination incidents like Three Mile Island. With part of its Counter-terrorism funds, CDRH will update the radiation emergency response plan to include counter terrorism events. In FY 2003, CDRH will implement as much of the plan as resources will allow. CDRH's radiological health resources for emergency preparedness have been severely reduced in past years, and the requested increase for Counter-terrorism funds will not be enough to fully staff the radiation emergency response teams.
- **Data Sources:** CDRH's radiation emergency preparedness response plan.
- **Performance:** This is a new goal for FY 2003 and therefore, has no performance history.

15. Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places.

- **Context of Goal:** In response to recent terrorist attacks, the increase of scanners in airports and other security systems has increased exponentially. But the increased use of security scanners also increases risks of radiation exposure. The health effects of expanded use of people scanners haven't been adequately tested, and standards need to be set for their safe use. FDA is responsible for working with FAA and industry and other standard setting stakeholders to set radiation safety standards. FDA will work to update standards within a portion of its requested Counter-terrorism resources. FDA does not have enough resources to

aggressively conduct extensive testing in this area, and must work with the other stakeholders.
- **Data Sources:** CDRH standard setting documents.
- **Performance:** This is a new goal for FY 2003 and therefore, has no performance history.

2.6.3 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 and 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 system's newest component is the Medical Device Surveillance Network, MedSuN program. MeDSuN is an initiative designed both to educate all health professionals about the critical importance of being aware of, monitoring for, and reporting adverse events, medical errors and other 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.

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.

2.7 NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

2.7.1 Program Description, Context, and Summary of Performance

Total Program Resources:

	FY 2003 Current Estimate	FY 2002 Current Estimate	FY 2001 Actual	FY 2000 Actual	FY 1999 Actual
Total ($000)	40,688	42,882	36,248	36,248	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.

2.7.2 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 03: Provide an evaluation of the new molecular technology for detecting alterations in multiple genes. FY 02: Conduct one biologically based mechanistic study combined with pre-dictive modeling to improve extrapolation of animal data to the human condition. FY 01: Provide peer reviewed articles on new Genetic and transgenic systems and knowledge to product reviewers. FY 00: Evaluate a new biological assay to measure genetic changes and validate two existing models that predict	FY 03: FY 02: FY 01: Publications submitted to peer reviewed journals: (1) describing methodology damage to mitochondria and (2) providing a review of the possibility of using new genotypic selection for risk assessment. FY 00: Validated the Big Blue Rat and $Tk^{+/-}$ *in vivo* models by using mutations, micronuclei, apoptotic cells measurements;	

	human genetic damage. FY 99: Develop better Biological assays to measure genetic changes and predict human genetic damage	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 03: Present one finding and publish one result of the microarray technology polymorphism study. FY 02: Support at least two multi-disciplined DNA and RNA-based microarray technologies. FY 01: Develop "risk	FY 03: FY 02: FY 01: Risk chip used to screen population resulted in initiation of negotiations to	

	chip" technology to screen large numbers of people for biomarkers simultaneously. FY 00: Conduct molecular epidemiology studies to Identify biomarkers of the most frequently occurring cancers in highly suscep-tible subpopulations. FY 99: Complete biochemical and epidemiological studies to define the basis of susceptibility of humans to the toxicity of regulated products	extend the use of biomarkers and other subpopulations for further investigation. 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: 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 03: 25,242 FY 02: 29,361 FY 01: 23,271 FY 00: 17,160 FY 99: 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:** Collaboratively with the Center for Drug Evaluation and Research (CDER), NCTR researchers will determine if animal data required for pre-market approval of drugs can adequately predict possible developmental toxicity risks in humans. Data collection began from both literature and the FDA files on various drugs. Scientists developed a new animal test for the evaluation of genetic change. The test was modeled after a similar rodent lymphoma test already used internationally for hazard identification. The test, which studies the chemical basis of genetic damage, is shown to detect most, if not all, of the mutational events leading to human cancer. The data generated from the animal and cell culture systems provide a more accurate and rapid assessment of the potential risk to the human population. These findings were submitted for review and will be published in scientific journals.

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 focus is on the foodborne heterocyclic amines, environmental aromatic amines, and poylcyclic aromatic hydrocarbons, on widely used drugs including selected benzodiazepines, antihistamines, drugs inducing peroxisomal proliferation or oxidative stress, on estrogens, antiestrogens and endocrine disruptors, as well as tobacco usage. Projects ongoing include the etiology of human cancers of the colon/rectum, pancreas, larynx, breast, ovary, prostate, lung, urinary bladder, and bone marrow. Implementation of conventional genetic compositions was completed and validation studies carried out. Increasing evidence of adverse drug and chemical reactions in sub-populations (specific classifications such as race, gender, geographic location, common disease (inflicted) of humans, point t a need to identify and protect groups of people at higher risk from exposure to specific drugs, contaminated food, or other FDA-regulated products. The human data produced with utilization of this technology will provide FDA with a better understanding of how some individuals react adversely to drugs and regulated products.

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 03: Maintain existing computational databases of estrogenic and androgenic compounds for use by reviewers. FY 02: Maintain existing computational databases of estrogenic and androgenic compounds for use by reviewers. FY 01: Validate a predictive model for androgens. FY 00: Validate predictive model for estrogenic or estrogenic-like compounds. FY 99: Demonstrate a model toxicity knowledge base to support and expedite product review	FY 03: FY 02: FY 01: Predictive model for androgen receptors was developed and assessment of 204 chemicals completed. 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: 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 03: 15,466 FY 02: 13,521 FY 01: 12,977 FY 00: 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 and the EPA to model estrogen activity. The development of the knowledge base for the binding of chemicals to the estrogen and androgen receptor; and, studies on androgen receptor (AR) binding continue. Scientists validated a predictive computer model for estrogenic or estrogen-like compounds. Replicate tests are now complete for 204 chemicals that bind

to the male hormone receptor, thus potentially influencing the development of the male reproductive system.

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.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
4. Study FDA-regulated	FY 03: Continue toxicological	FY 03:	

compounds to relate the mechanism(s) by which a chemical causes toxicity. (16004)	evaluations of anti-HIV therapeutics and photoactive compounds. FY 02: Initiate analytical/ biological studies to assess the toxicity of at least one, FDA high priority dietary supplement. FY 01: Study two FDA-regulated compounds. FY 00: Conduct studies to relate how a compound causes damage to the damage itself, thus strengthening the scientific basis for regulation of compounds. FY99: Develop faster, more accurate tests based on mechanisms of toxic actions.	FY 02: FY 01: Developed protocols to conduct comprehensive toxicological evaluations of *Aloe vera* and mixtures of anti-HIV therapeutics. Conducted literature review of retinyl palmitate. 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: 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 B_1 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 03: Identify and characterize the role antibiotic resistance plays in emerging and evolving foodborne diseases. 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	FY 03: FY 02: FY 01: Performed pre-validation studies that examines the efffect of low-level antibiotic residues on	

	strains of bacteria. FY 01: Provide model to replicate bacterial survival in the stomach. FY 00: Develop methods of predicting, more quicklyand accurately, the risk associated with such foodborne pathogens as Salmonella spp., Shigella spp., and Campylobacter spp. FY 99: Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants.	the human intestinal microflora by using a chemostat to model the human intestinal tract. 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: 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	FY 03: Develop one instru-mental rapid sensor detection method. Outfit upgraded laboratory, provide for supplies (agents, chemicals/pathogens) and construct library databases of proteins	FY 03: FY 02: FY 01:Application/extension of Fresh Tag® technologies for detection of nitrogen-based explosives began. FY 00:	

the diagnosis of toxicity. (16012)	and test to find toxin related markers; Recruit additional expertise in Computational Science, Chemistry and Microbiology FY 02: Continue development of solid-phase colorimetric bacterial detection system. Acquire high-resolution mass spectrometer for use with protein from bacteria, food toxins and genomics studies. Upgrade existing laboratory facilities to BSL-3 to support BSE/TSE and microbial bioterrorism work. Recruit additional expertise in Computational Science, Chemistry and Microbiology. FY01: Begin developing solid-phase colorimetric bacterial detection system. FY 00: Begin developing solid-phase colorimetric . bacterial detection system. FY 99: Develop method to identify biomarker proteins; translate method to colorimetric field kit.		

7.Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of toxicity. (16013)	FY 03: Evaluate, for use Agency-wide, one new technology such as proteomics or genomics for determining liver damage by regulated products. FY 02: Publish at least one scientific paper describing one technology for use in reviewing regulated compounds. FY 01: Develop at least three concept papers exploring new technologies for the assessment of toxicity.	FY 03: FY 02: FY 01: Three concept papers were submitted and approved: 1) design and analysis of gene array expression data; 2) development of glass-slide based oligonucleotide microarrays for rat and human genes; 3) two-dimensional micro-LC-proteonomics using stable-isotope affinity tags for differential display of toxicity-induced biomarkers.	
TOTAL FUNDING: ($000)	FY 03: 16,263 FY 02: 14,791 FY 01: 14,559 FY 00: 14,980 FY 99: 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**: In addition to providing basic information on toxicological endpoints, such as cancer, the studies being performed also form the basis for mechanistic studies to ascertain if the response detected in the experimental model is pertinent to humans. Major efforts are continuing in the area of phototoxicity with emphasis on the potential interaction between ultraviolet (UV) light and substances found in over-the-counter cosmetics. Scientists have studied alpha and beta hydroxy acids, glycolic and salicylic acids. Studies demonstrated that acids found in many skin cosmetics, when applied to the skin of mice in conjunction with ultraviolet (UV) radiation, induced skin tumors. Results suggest that the compound in sun-skin-care preparations may enhance the damage caused by the sun.

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:** Researchers at the NCTR and the Center for Veterinary Medicine (CVM), are continuing to perform pre-validation studies on an *in vitro* system that examines the effect of low-level antibiotic residues on the human intestinal microflora by using a chemostat to model the human intestinal tract. Other essential research ongoing includes the elucidation of the mechanisms of resistance to antimicrobial agents among bacteria from the human gastrointestinal tract. Three different concentrations of the fluoroquinolone antibiotic ciprofloxacin were tested. Studies clearly indicate that the *in vitro* system can be a valuable tool to evaluate the effects on the human intestinal microflora of low levels of antimicrobial agents in food.

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. NCTR has the capabilities of rapidly developing a BL3/BL4 containment laboratory that would be capable of doing high containment biological research on a wide variety of animal species. The BL3/BL4 laboratory will enable FDA to perform critical research in a relatively risk-free environment with a highly trained staff. Scientists will be able to expand a novel approach pioneered at the NCTR to rapidly identify biomarkers of toxicity associated with biological warfare agents. These types of agents used by bioterrorists would be difficult to detect using existing technology. The research conducted in collaboration with the Center for Disease Control (CDC), the Department of Defense (DoD), Naval Research Labs, the Joint Institute for Food Safety Applied Nutrition (JIFSAN) and the Center for Food Safety and Applied Nutrition (CFSAN).
- **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:** For FY 2000, NCTR's goal was not met due to lack of funding. Chemical sensor technology for the assessment of food quality was further developed and the concept evolved into both a commercial version and a consumer version. The research extended to detect other endpoints that are measures of product quality and freshness. As an extension of this work, an interagency agreement was established with the Federal Aviation Administration (FAA). For FY 01, NCTR used its unique Fresh Tag accomplishments to detect nitrogen-based explosives. This meant that NCTR refined its Fresh Tag technology which was originally developed to detect and identify deteriorating food to prevent consumption in the early stages of spoilage. This is a good example of NCTR's nimble reaction to current events to aid in the nation's fight against terrorism.

7. Use new technologies (imaging, proteomics, and metabonomics) for diagnosis of toxicity. (16013)

- **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:** Researchers are developing new molecular technologies to be used in evaluating structural and functional changes in the genome of both rodents and humans. NCTR scientists are developing a new research focus area in these technologies and applying them to fundamental risk assessment questions. The concept papers developed include: 1) developing statistical and computational procedures for the design, analysis and interpretation of gene expression data from microarray experiments; 2) developing, printing, and establishing the methodology for using a "rat chip" containing approximately 4000 genes and a "human chip" containing approximately 8300 genes; and 3) addressing the need to develop biomarkers of toxicity, disease progression/regression, and efficacy of drug treatment. The techniques developed will further utilize the emerging knowledge of the human genome and rapid biological analyses to improve human health and to insure the safety of marketed products.

2.7.3 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.

GLOSSARY OF ACRONYMS

510(k)	Premarket notification for medical devices substantially equivalent to products already on the market
AADA	Abbreviated Antibiotic Drug Application
ADE	Adverse Drug Event
ADAA	Animal Drug Availability Act of 1996
ADR	Adverse Drug Report
AERS	Adverse Events Reporting System
AHI	Animal Health Institute
AIDS	Acquired Immune Deficiency Syndrome
ANDA	Abbreviated New Drug Application
ANSI	American National Standards Institute
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 TWG	North American Free Trade Agreement Technical Working Group
NARMS	National Antimicrobial Resistance Monitoring System
NASS	National Agricultural Statistics Survey
NCI	National Cancer Institute
NCIE	Notice of Claimed Investigational Exemptions
NCTR	FDA National Center for Toxicological Research
NDA	New Drug Application
NDE/MIS	New Drug Evaluation Management Information System
NIAID	National Institute of Allergy and Infectious Diseases

NIDA	National Institute on Drug Abuse
NIEHS	National Institute for Environmental Health Sciences
NIH	National Institute of Health
NLEA	Nutrition Labeling and Education Act
NME	New Molecular Entity
NPR	National Partnership for Reinventing Government
NRC	National Research Council
NSE	Not substantially equivalent determination
NTP	National Toxicology Program
NVPO	National Vaccine Program Office
OASIS	Operational and Administrative System for Import Support
OBRR	Office of Blood Research and Review
OPA	CFSAN, Office of Premarket Approvals
ORA	FDA Office of Regulatory Affairs
ORISE	Oak Ridge Institute for Science and Education
OSHA	Occupational Safety and Health Administration
OTC	Over-the-counter
OTR	Office of Testing and Research (CDER)
PAS	FDA Public Affairs Specialist
PDPs	Product Development Protocols
PDUFA	Prescription Drug User Fee Act of 1992
PIFSI	Produce and Food Safety Initiative
PLA	Product License Application
PMA	Premarket Approval (Application to market medical device that requires premarket approval)
PODS	Project-Oriented Data System
PQRI	Product Quality Research Initiative
QSIT	Quality System Inspection Technique
RA	Rheumatoid Arthritis

RCHSA	Radiation Control for Health and Safety Act
REGO	Reinventing government initiative
RIMS	Regulatory Information Management Staff
RVIS	Residue Violation Information System
SAB	Science Advisory Board
SAMHSA	Substance Abuse and Mental Health Services Administration
SE	Salmonella Enteriditis
SN/AEMS	Special 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

Disposition of FY 2002 Performance Goals

Goal ID	Original Goal Statement as Stated in FY 02 Congressional Justification	Disposition	Revised FY 2002 Targets	Explanation
FOODS				
11001	Complete first action on 65% of food and color additive petitions within 360 days of receipt.	Revised	Complete first action on 60% of food and color additive petitions within 360 days of receipt	Target revised to a slightly lower level because of implementation of the Food Contact Substance Premarket Notification Program which changed the way these applications are submitted. Fewer but more complex applications are now expected.
11002	Reduce the number of remaining overdue food and color additive petitions by 50%.	Dropped		This backlog goal was dropped and assumed under the primary review goal for food and color additive petitions. (goal 11001)
11025	Respond to 95% of notifications for dietary supplements containing "new dietary ingredients" within 75 days.	Unchanged		
11003	Complete processing of 85%	Dropped		This goal was dropped

	of GRAS notifications within the time frame established by the final rule.			because there is no final rule and no statutory authority for this goal. It is strictly voluntary.
11034	Complete review of 100% of premarket notifications for food contact substances within 120 days.	Revised	Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days).	Target was lowered to 95% because 100% was an unrealistic target.
11035	Issue final rule to require premarket notification for bioengineered foods.	Dropped		The comments from the proposed rule have been received and analyzed, but no reaction has been received from the department or administration so publishing this in FY 2002 is unrealistic. However, this goal can be accomplished in FY 2003.
11010	Achieve adoption of the Food Code by at least one state agency in 28 states in the USA.	Unchanged		
11020	Increase the percentage of high-risk domestic food establishment inspected once every year at least 95%.	Unchanged		
11011	Assure that FDA inspections of domestic food establishments result in a high	Dropped		This goal was dropped from each program because it was confusing and

	rate of conformance (at least 90%) with FDA requirements.			not a useful measure for performance. (See the context section for this goal in the Performance Plan for more details.)
11021.02	Increase the number of import exams of food products to 60,000.	Dropped		Import exams are now measured by a new goal (goal 11036) which measures physical exams only and not the combination of physical and analytical exams like this one.
11028	Increase to 10 the number of audits and assessments of foreign food safety systems, with an emphasis on high volume exporters to the U.S.	Dropped		This goal was dropped because resources are not available to conduct the in-depth audits necessary to assess the efficacy of the entire foreign food safety system.
11027	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.	Unchanged		
11036	None	New Goal	Increase food import surveillance by hiring 300 new investigators and analysts who will increase the	Goal added to reflect additional Agency Counter Terrorism

			number of physical exams 97% (24,000 exams) and conduct sample analyses on products with suspect histories.	efforts developed in response to the September 11 terrorism attack.
11037	None	New Goal	Extend import coverage to an additional 45 ports that handle significant quantities of FDA-regulated products.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
DRUGS				
12001	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.	Unchanged		
12003	Review and act upon fileable original generic drug applications within 6 months after submission date.(55%)	Revised	Review and act upon fileable original generic drug applications within 6 months after submission date.(65%)	Target raised due to resource increase for the Generic Drug Program.
12032	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.	Unchanged		
12007	Streamline adverse drug event reporting	Revised	Accepting electronic submissions from	Updated to reflect current status of goal.

	system. (Issue final rules on ADRs and electronic submissions)		companies and be current with MedDRA coding versions.	
12016	CDER will initiate laboratory research on at least three projects identified and related to the mission of PQRI.	Unchanged		
12020	Inspect registered human drug manufacturers, repackers, relabelers and medical gas repackers. (26%)	Revised	Inspect registered human drug manufacturers, repackers, relabelers and medical gas repackers. (20%)	The target decreased due to problems resulting from the transition to a new database (FIS to FACTS) in FY 2000, which caused some adjustments in the way inventory and inspectional coverage were calculated. FY 2001 actual performance data was 19%, not the expected 26%.
12006	Assure that FDA inspections of domestic drug manufacturing and repacking establishments result in a high rate of conformance (at least 90%) with FDA requirements.	Dropped		This goal was dropped from each program because it was confusing and not a useful measure for performance. (See the context section for this goal in the Performance Plan for more details.)
12026	Implement, evaluate, track and report on the clinical trials FDA is requesting	Unchanged		

	under FDAMA or requiring under the Pediatric Rule			
12027	Give consumers and health professionals more easily understandable OTC drug information.	Unchanged		
12033	None	New Goal	Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure).	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12034	None	New Goal	Facilitate the initiation of research in a non-human primate model of pneumonic plague.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12035	None	New Goal	Expeditite the review of protocols for investigational new drugs (INDs) to treat organophosphorous nerve agents in the event of chemical attack. Encourage sponsors of these new drug application (NDAs) to update current labling for Antidote Treatment Nerve Agent, Autoinjectors (ATNAA).	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12040	None		Publish a final rule	Goal added to

			which allows the agency to approve new drug and biological products for the treatment of chemical, biological, radiological, or nuclear substances based on animal efficacy studies when adequate and well-controlled studies in humans cannot be ethically conducted and field studies are not feasible.	reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12042	None	New Goal	Publish a Notice of Proposed-Rulemaking to establish a web-based electronic animal and human drug and biologics registration and listing database to allow for complete and up-to-date data on all regulated drug products.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12043	None	New Goal	Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
12044	None	New Goal	Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism

				attack.
BIOLOGICS				
13001	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.	Unchanged		
13002	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	Unchanged		
13003	Review and act on 90% of PDUFA manufacturing supplements within 6 months of receipt, and review and act on 90% of PDUFA manufacturing supplements requiring prior approval within 4 months of receipt.	Unchanged		
13004	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	Unchanged		

	receipt.			
13005	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.	Unchanged		
13007	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	Dropped		This goal was dropped from each program because it was confusing and not a useful measure for performance. (See the context section for this goal in the Performance Plan for more details.)
13008	Maintain the percentage of plasma fractionator establishments in compliance with CGMPs at 80%.	Dropped		This goal was dropped for two reasons: 1) Plasma fractionator establishment compliance with CGMP' s is beyond the control of FDA. FDA can determine their CGMP compliance through inspections, but it cannot maintain their compliance for them. 2) The biennial inspection goal for biologic establishments (Goal 13012) includes

				inspections of plasma fractionator establishments.
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				
14007	Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80%.	Unchanged		
14017	Review and act on 80% of NADAs/ Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt.	Revised	Review and act on 50% of NADAs/ANADAs within 180 days of receipt.	The goal was revised from 80% to 50% because the Center has changed priorities and redirected resources from new reviews to clear the large backlog of animal drug applications. Decreasing the backlog was necessary in order to move CVM back on track towards meeting statutory and stakeholder requirements for new animal drug application review.
14019	None	New Goal	Reduce pending overdue Animal	This goal was added to reflect

			Drug applications by 15%.	the center' s commitment to reducing its backlog. Decreasing the backlog was necessary in order to move CVM back on track towards meeting statutory and stakeholder requirements for new animal drug application review.
14002	Pilot and validate the procedure for receiving protocol submissions electronically.	Unchanged		
14018	Begin to design and implement a Staff College. FY 02: Plan and design the option selected in Phase I	Unchanged		
14009	Maintain biennial inspection coverage by inspecting 50% of registered animal drug and feed establishments.	Unchanged		
14004	Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers result in at least 90% conformance.	Dropped		This goal was dropped from each program because it was confusing and not a useful measure for performance. (See the context section for this goal in the Performance Plan for more details.)
14005	Increase isolate	Revised	Maintain isolate	

	testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.		testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.	
14006	Assure 100% compliance with the BSE feed regulation through inspections and compliance actions.	Revised	Conduct targeted BSE inspections of 100% of all known renderers and feed mills handling prohibited material.	The scope of this goal was revised from "Assuring compliance" to "Conducting inspections" although the target of 100% remains the same. Realistically, assuring 100% compliance is too difficult to measure or attain.
MEDICAL DEVICES AND RADIOLOGICAL HEALTH				
15001	Maintain the on-time percentage of Premarket Approval Application (PMA) first actions within 180 days. (90%)	Unchanged		
15009	Review and complete 90 percent of PMA supplement final actions within 180 days in FY 2002	Unchanged		
15002	Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days in FY 2002.	Unchanged		
15024	Complete 95 percent of PMA "Determination" meetings within 30 days in FY 2002.	Unchanged		
15003	Initiate	Unchanged		

	development of 20 to 25 new or enhanced standards to be used in application review in FY 2002.			
15025	Conduct 335 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Revised	Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Target level was decreased due to decrease in resources.
15005.01	Provide inspection coverage for Class II and Class Ill domestic medical device manufacturers at 20 percent in FY 2002.	Unchanged		
15018	Assure FDA inspections of domestic medical device manufacturing establishments result in at least 90 percent conformance.	Dropped		This goal was dropped from each program because it was confusing and not a useful measure for performance. (See the context section for this goal in the Performance Plan for more details.)
15005.02	Maintain inspection coverage for Class II and Class Ill foreign medical device manufacturers in FY 2002. (9%)	Unchanged		
15007	Ensure at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent with Level I (serious)	Unchanged		

	problems in FY 2002.			
15026	Meet time frames of Reuse Regulatory Strategy	Dropped		This goal was included in the FY 02 CJ by mistake. It was intended to be a placeholder while a more specific goal was developed for this important issue, but it was inadvertently left in the goal table after the idea was dropped.
15012	Implement the MeDSuN System. 02: Recruit 75 to 100 new facilities	Revised	Implement MedSuN by recruiting a total of 80 facilities for the network	Target more specific
15029	None	New Goal	Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH				
16001	Introduce the knowledge of new genetic systems and computer-assisted toxicology (bioinformatics) into the application review process.	Unchanged		
16002	Develop, with other organizations, gene chip and gene array	Unchanged		

	technology.			
16003	Develop computer-based models and infrastructure to predict the health impact of increased exposure to estrogens and anti-estrogen compounds.	Unchanged		
16004	Study FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity.	Unchanged		
16007	Develop methods and build biological dose-response models to replicate bacterial survival in the stomach.	Unchanged		
16012	Catalogue biomarkers and develop standards to establish safety and effectiveness of imaging devices for potential use in the diagnosis of toxicity.	Revised	Continue development of solid-phase colorimetric bacterial detection system. Acquire high-resolution mass spectrometer for use with protein from bacteria, food toxins and genomics studies. Upgrade existing laboratory facilities to BSL-3 to support BSE/TSE and microbial bioterrorism work. Recruit additional expertise in Computational Science, Chemistry and Microbiology.	Additional three targets added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.

16013	Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of toxicity.	Unchanged		
ADMINISTRATIVE MANAGEMENT				
19001	None	New Goal	Develop and implement a plan to to delayer NCTR, CVM and CDRH.; Plan to transfer Legislative and Public Affairs function to DHHS	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19002	None	New Goal	Award contract of administrative functions to be completed by 9/02 with the Human Resources portion completed by May, 2002.	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19003	None	New Goal	Increase the percentage of Commercial FTEs that will be reviewed for outsourcing. (5%)	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19004	None	New Goal	Increase the percentage of electronically purchased transactions (89%)	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19005	None	New Goal	Maintain a clean (or unqualified) audit opinion with no material weakness. (yes)	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19006	None	New Goal	Increase percentage of contract dollars to	Goal added to reflect the Agency' s

			performance based contracts from 23.6% to 25%	commitment to the Department' s Management Goals
19007	None	New Goal	Develop Agency Continuity of operations plan; Participate with PSC to develop COOP	Goal added to reflect the Agency' s commitment to the Department' s Management Goals
19008	None	New Goal	Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks.	Goal added to reflect additional Agency Counter Terrorism efforts developed in response to the September 11 terrorism attack.