FY 2004 Annual Performance Plan
FY 2003 Revised Final Performance Plan
FY 2002 Annual Performance Report

January 2003

Contents

Part 1: Performance Plan Summary Introduction

TO: Tommy Thompson
Secretary of Health and Human Services

FROM: Commissioner of Food and Drugs

SUBJECT: FY 2004 Annual Performance Plan

I am pleased to submit the Food and Drug Administration's FY 2004 Performance Plan. The Plan outlines actions we will undertake to ensure the safety and, where applicable, efficacy of FDA-regulated products throughout their entire life cycle - from initial research and development through their ultimate use/ consumption. This Plan will point out the crucial role that FDA plays in improving the health of the Nation. We steward innovative new medical technologies to the market. We monitor the safety of medical products and foods throughout the manufacturing and distribution chain, and we track the use of these products by consumers and use this feedback to reduce risks to the American Public.

FDA will continue to carry out these roles in an environment characterized by both challenges and opportunities. A major and continuing challenge is the prospect of terrorist attacks on the U.S., particularly via our food supply. But additional challenges face the Agency. To name a few: Import shipments of regulated products continue to grow at 10 to 12 percent annually. These products must be carefully monitored to prevent hazards from entering the country.

Another challenge is the occurrence of adverse events and medical errors associated with the use of medical products. According to an Institute of Medicine estimate, nearly 100,000 Americans die each year as a result of medical mishaps. These incidents, many of which could be reduced by FDA interventions, must be addressed. FDA must also be vigilant about the particular safety concerns of special populations, such as children and the elderly. Under provisions of the "Best Pharmaceuticals for Children Act of 2002, FDA is taking action to encourage the availability of accurate dosing, efficacy and safety information regarding the use of medications in children. FDA also recognizes that the cost of drugs can present a potential barrier to patient access to medicine. To help address this situation, FDA has committed to expand efforts to increase availability of generic drugs and support increases in the number of conversions from prescription to over-the-counter drugs. The Agency will continue to take the opportunity to help millions of

Americans enjoy the benefits of innovative medical technologies and nutritious, safe foods by making timely science-based decisions to facilitate their entry into the market.

To address the above challenges and opportunities, the Agency has established five strategic goals:

Risk Management - FDA will continue to effectively manage product risks throughout their life cycle- from research and development through use/ consumption. Risk management decisions will be supported by rigorous scientific analysis that weighs, when appropriate, not on the risk-to-benefit profile of the product itself, but also the risk versus the benefit associated with Agency actions.

Strong FDA - FDA will maintain a strong science-based organization to support its risk management responsibilities by: attracting and retaining the most talented scientists; operating a streamlined and cost-effective agency that is optimally organized to support mission-critical activities; and implementing the President's Management Agenda to deliver value to our constituents. A more complete discussion of Agency efforts to link our programs to favorable public health outcomes is included in the 'Outcomes Appendix' to the Performance Plan.

Counterterrorism - FDA will assist in countering the terrorism threat by: 1) preparing for the possibility of attacks on the U.S. population through a strengthened product monitoring infrastructure and emergency preparedness plans; and 2) responding rapidly and appropriately in the event of an actual attack with effective medical countermeasures and product disposal actions.

Consumer Information - FDA will provide information to consumers, health professionals, and other constituencies that will enable them to make prudent decisions regarding the use of FDA-regulated products. A well-informed constituency will raise the likelihood that product risks will be reduced and improved health outcomes will be realized.

Adverse Events and Medical Errors - FDA will contribute to the reduction of adverse events and medical errors through enhanced reporting capability, strengthened problem analysis, and appropriate risk management strategies to address the problems.

In conclusion, I believe that implementation of this Plan, in collaboration with FDA's health and regulatory partners, will help to ensure that Americans will continue to enjoy the safest foods, medicines, and medical devices of any country in the world, and have more rapid access to new and promising therapies. The combination of safe and, when applicable, effective products that have been validated by rigorous risk analysis, and a well-informed

constituency that can use these products wisely should lead to substantially improved health outcomes for the Nation.

I thank you for your support of FDA's FY 2004 Performance Plan,

Mark B. McClellan, M.D., Ph.D.

Executive Summary

Our Mission and Scope of Responsibilities

As part of the Department of Health and Human Services, FDA has broad responsibilities for promoting and protecting the health of American consumers.

FDA's Mission

The public trusts FDA to ensure that:

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

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 almost $1.5 trillion - more than 20 percent of their money on products that we regulate.
- We judge the safety and often the efficacy of an expanding scientific revolution. Public and private entities invest an estimated $50 billion annually in biomedical research and technology.
- We assure the compliance of the Nation's manufacturing and processing with FDA regulations: FDA is a 10,000-person agency, and is responsible for monitoring over 100,000 U.S. firms that manufacture or process FDA regulated products.
- We also monitor the safety of 8 million import shipments that enter this country each year.

To successfully accomplish its mission, FDA leadership has identified five strategic goals. Each goal reinforces the importance of risk management as the Agency's primary tool to address the Nation's health and safety concerns. Progress towards these goals will be made using both FDA's base resources and those additional resources requested in the FY 2004 Budget request.

Risk management, to FDA, means that we use all means available to minimize health or safety risks facing the American people by:

1. Correctly assessing the risks based on scientific understanding and rigorous risk analysis;
2. Establishing risk priorities based on this analysis; and,
3. Effectively managing risks with the appropriate intervention - beginning with the most critical risks.

Our Strategic Goals:

- **Risk Management -** FDA will minimize risk to U.S. consumers throughout the product life cycle - from research and development through production, distribution and use. Rigorous science-based assessment of hazards and thorough risk analysis will provide the foundation for effective risk management decisions. Because of the Agency's timely science-based decisions, millions of Americans will have access to the medicines and medical devices they need, and can be assured that these products are safe and effective.
- **A Strong 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 Agenda 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;
    - Reconfiguring information technology systems to more effectively support decision making at all levels in the Agency;
    - Outsourcing traditional government functions where cost efficiencies can be realized;
    - Capitalizing on e-government efficiencies;
    - Strengthening financial management systems; and,
    - Establishing accountability to the U.S. taxpayer by linking Agency resources to performance and public health outcomes.

FDA leadership is currently in the process of exploring possible outcome indicators that could be linked to Agency program efforts, as well as data sources that would provide valid and reliable measures of these indicators. This progress is described in Appendix B of the Performance Plan entitled "Progress Toward Developing Outcome Measures."

- **Counterterrorism -**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:

    - Detection, deterrence and interdiction of potentially dangerous foods and medical products overseas, at our borders and throughout domestic commerce;
    - Having adequate supplies of safe and effective medical products to protect or treat victims of an attack;
    - Sharpen FDA's emergency preparedness and response plan that will protect the American Public and maintain the internal security of FDA; and,
    - Minimizing threats from radiological sources.
- **Consumer Information -** FDA will engage in a variety of activities designed to provide the best available information to consumers, patients and health professionals to make them full participants in managing risks associated with FDA-regulated products.
- **Adverse Events and Medical Errors -** FDA will accomplish this health care goal by collaborating to establish a comprehensive reporting capability with the cooperation of the health care community; analyzing and quantifying the risks revealed in adverse event reports and other data sources; and taking appropriate actions to prevent future harm.

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 rigorous science and risk analysis** to make accurate and timely decisions regarding the safety of products and processes;
- **Thinking and acting in a global context -** Since the products FDA regulates are produced and marketed worldwide, the Agency's risk management strategies must also be approached from a global perspective;
- **Making decisions that consider the total product life cycle -** FDA must use both premarket and postmarket product experience/ data in making regulatory decisions. Agency 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. FDA cannot accomplish its vital public health mission without stakeholder collaboration.

The following page summarizes FDA's strategic goals, the desired outcomes of these goals, and key performance targets for FY 2004. Table 2 summarizes the specific results that will be achieved as a direct result of each FY 2004 Increase request.

Summary of FDA's FY 2004 Strategic and Performance Goals

Risk Management
Desired Outcomes: Because of the Agency's timely science-based decisions prior to market entry, and close monitoring of products after they enter the market, millions of Americans can be assured of safe and effective products. Safe products and judicious use of these products are key elements leading to positive health outcomes.

Key Performance Goals:

- Complete Review and Action on 90% of standard original new drug, product licensing and biologic licensing (NDA/PLA/BLA) submissions within 10 months of receipt and 90% of priority original NDA/PLA/BLA submissions within 6 months. (PDUFA goal)
- Complete Review and Action on 90% of generic drug applications within 6 months
- Complete Review and Action on 100% of Rx to OTC switch applications within 10 months of receipt.
- Increase the number of drugs that are adequately labeled for children.
- Complete Review and Action on 90% of NADAs & reactivations of such applications within 295 days; 90% of investigational animal drug study submissions within 320 days; and review 90% of investigational animal drug submissions consisting of protocols, without substantial data within 125 days.
- Complete Review and Action on 90% of Device Premarket Approval Application (PMA) first actions within 180 days.
- Inspect 55% of high risk drug establishments.
- Inspect 50% of registered blood banks, source plasma operations and biologics manufacturing establishments.
- Ensure at least 97% of mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems in FY 2004.

A Strong FDA
Desired Outcomes: 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

Key Performance Goals:

- Streamline Agency administrative management functions by establishing a shared services organization.

- Expand application of enterprise IT architecture.
- Increase the percentage of commercial FTE that will be reviewed for outsourcing.
- Complete systems preparation to implement Financial Enterprise Solutions
- Increase the proportion of contract dollars allocated to performance-based contracts
- Reduce the number of review levels in the Agency
- Increase the percentage of electronically purchased transactions
- Maintain a clean (unqualified) audit opinion

Counterterrorism
Desired Outcomes: Risks to the American Public posed by potential or real terrorist attacks are minimized.

Key Performance Goals:

- Significantly expand eLEXNET system participation [federal and state labs sharing food hazard analysis results.
- Focus the 48,000 annual import physical exams on the most suspect problem areas.
- Perform at least 1,000 Filer Evaluations under new procedures.
- Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported.
- Inspect 95% of high risk domestic food establishments.
- Incorporate information on pneumonic plague into drug product labeling; review and analyze data from animal studies conducted on inhalational anthrax; publish a revised guidance on potassium iodide for use in special populations.
- Expedite review for 100% of Bioterrorism Diagnostic Medical Device Applications.

Adverse Events and Medical Errors
Desired Outcomes: Risks to the American Public posed by potential or real terrorist attacks are minimized.

Key Performance Goals:

- Enhance the postmarketing drug safety system.
- Increase the receipt of Periodic Safety Update Reports (PSURs) electronically into CDER's electronic document room. (Receipt of reports is voluntary.)
- Publish final guidance to Industry on good risk assessment and risk management, and pharmacovigilance practices.
- Enhance AERS to support medication error capture and analysis.

- Submit majority of Adverse Drug Reaction (ADR) reports electronically.
- Expand implementation of the MeDSuN System to a network of 240 facilities.

Consumer Information
Desired Outcomes: A well informed constituency is a major component of the solution to preventable deaths, illnesses and injuries in the U.S.

Key Performance Goal:

- Enhance the transparency of the NARMS program to stakeholders, the public, and other interested parties by increased reporting and communicating of NARMS results and program information.

Table 2: Performance Results from FY 2004 Increase Requests

Department/FDA Strategic Goal	FY 2004 Increase	What the Increment Buys (from the Budget)	Related Performance Goals
Risk Management	$1 mil. -OTC drugs & drug monographs	Increase Rx to OTC switches by 50% Improve OTC review process Complete unfinished monographs - e.g., analgesics, antiseptics, laxatives and sunscreens	Complete Review and Action on 100% of Rx to OTC switch applications within 10 months of receipt
	$13mil. -generic drugs	Faster reviews Research on bioequivalence methods & standards IT enhancement	Move from 80% to 90% reviewed within 6 mos.
	$5 mil. - Best Pharmaceuticals for Children's Act	Facilitate & guide studies Science to address pediatric/neonatal issues Work w/NIH on off-patent drugs	Faster reviews of supplements; more written requests for off-patent studies
	$5 mil. - New animal drug review user fees	Reduce review backlog Expand review	New review goal supported by industry

		capacity in science & support areas Expand IT Continue Staff College development Update industry guidance	Increase from 15% to 25% reduction in review backlog
	$5.065 mil - Medical device review[$4.065 mil user fees $1 mil approp.]	Sustain performance on review goals Increased time for reviewer training Updated guidance to industry Enhanced IT More pre-approval inspections	03 review performance sustained for 04 New 'decision' and 'cycle goals initiated in conjunction w/user fee implementation [beginning in FY 05 or beyond]
A Strong FDA	$2.29 mil - Unified Financial Mgmt System	Plan to implement new financial system beginning with General Ledger & progressing to Accounts Payable, Small Purchases and Accounts Receivable	Complete system preparation of Financial Enterprise Solutions, FDA's version of UFMS.
	$3.5 mil.Arkansas Laboratory	Complete Phase III - enables effective collaborations w/Agency programs	

	$6 mil. -CDER Move	Consolidate CDER office and lab functions into one complex at White Oak, Md.	
Counterterrorism	$10.5 mil. - Food Registration System	The Food Registration and Listing System & the Prior Notice System will be operational • Registrations and prior notifications will be processed automatically 24 hours a day, 7 days a week • System in place to process 'paper' registrations and notifications • Drug facility registration and listing system will be in place	
	$5 mil. - lab preparedness	eLEXNET expansion Intramural research Food Lab Accreditation	Expand state participation in eLEXNET from 54 to 79 laboratories
	$5 mil. - state	Enhance states'	

	grants	laboratory capacity Increase number of risk-based inspections	
Adverse Events and Medical Errors	$3 mil. -Adverse Event Reporting System	More electronic reporting Risk-based guidance to industry Greater analytic capability	Automate Periodic Safety Update Reports Final guidance to industry on risk assessment, management & pharmacovigilance Electronic submission of most ADR reports
	$1 mil. - Medical Product Surveillance Network	Expand facility participation Enhance error monitoring, electronic reporting Special reporting for in vitro diagnostics	Increase the number of participating facilities from 180 to 240
Consumer Information			

Risk Management

Problem | Desired Outcomes | Key Strategies | FY 2004 Goal Highlights | Current Status | FY 2002 Performance Goals | FY 2001-2002 Highlights

Problem

FDA oversees the public health standards of an industry that produces almost $1.5 trillion worth of regulated products. The products include the entire food supply, except for meat and poultry; over-the-counter and prescription medications; blood products; vaccines; tissues for transplantation; medical equipment and implantable devices; devices that emit radiation; animal drugs and feeds; and cosmetics.

FDA faces two challenges in assuring that U.S. citizens fully reap the health benefits of modern medical technology, and enjoy a safe and nutritious food supply:

1. FDA must assure the safety and effectiveness of drugs, biologics, food additives, medicated animal feeds, and medical devices before they are allowed on the market. This challenge means keeping pace with the increasing scientific complexity of products that emerge from a $50 billion a year research and development effort. FDA scientists must accurately judge the readiness of these products to be marketed, and help these innovative products reach the market as quickly as possible.

There must also be a sufficient number of reviewers to handle the product review workload to provide timely feedback to application sponsors to identify and address deficiencies. Any delays might:

- Postpone critically needed disease prevention and treatment, especially for a growing population of elderly and immune-compromised patients;
- Increase the cost of bringing a new product to market by lengthening the time a product is in development; and,
- Result in fewer low-cost alternatives for patients (including children and the elderly).

4. FDA must also monitor the safety of products once they are on the market. U.S. consumers spend an estimated $326 billion annually on medical products that are produced world-wide, and make their way to the market throughout a wide variety of distribution channels.

To ensure that these products are safe, the Agency must oversee their entire life cycle - from production through distribution, and use/ consumption.

Desired Outcome

FDA's long-term goal is to contribute to improving the health status of U.S. citizens by minimizing the risks associated with use of medical products and the consumption of food in the U.S. This becomes more likely when informed consumers and health professionals make wise choices concerning the dissemination and use of these products. FDA is examining specific outcome measures that will reflect progress towards this goal, and will be working to identify data sources to accurately measure this progress.

Key Strategies

FDA recognizes that improvements in U.S. public health will only be possible through a coordinated effort on the part of many partners in the public and private sectors, as well as the consumer. In this joint effort, FDA makes a significant contribution in several ways:

- Thorough, science based scrutiny prior to market entry assures that only safe and effective products are used to treat and prevent disease and promote health.
- Efficient product review processes make life saving new technologies available to the market on a timely basis so that they begin to make a difference earlier.
- Inspection of facilities ensures that products are being manufactured according to Good Manufacturing Practices (GMPs), and that these standards are based on rigorous science and sound quality control principles. This reduces the probability that defective or hazardous products will ever enter the distribution system.
- Effective collaborations with health and regulatory partners will leverage the use of FDA's standards through a wider domain at the international, state and local levels of governance.
- Rigorous risk analysis will help the Agency focus on the highest risks at all points in the product life cycle; and it will lead to a cost-effective deployment of FDA resources.
- FDA's educational efforts are directed at consumers, health professionals and all those who can ensure safe use of products - e.g., correct use of medications, healthy eating habits, etc This, in turn, contributes to better treatment outcomes and improved health status for U.S. citizens. Collaborative educational efforts with outside organizations further strengthen this influence.

These multiple roles will contribute greatly to the availability and appropriate use/ consumption of FDA-regulated products. Although product availability and safe use are still only part of the equation they are necessary ingredients that must be present to improve public health outcomes.

The discussion that follows outlines specific strategies that FDA is embarking on in the areas of premarket review, postmarket inspection and enforcement; and risk analysis that underpin the entire effort:

1. Premarket Strategies

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

- Increase the number of inspections and target high-risk clinical trials - e.g., vulnerable populations such as mentally impaired, pediatric, etc.; and increase training for investigators; improve the inspection process for Institutional Review Boards (IRBs); and enhance follow-up compliance activities.
- Develop disease indication-specific guidance on clinical evidence to support premarket applications.
- Continue the Human Drug Review Program supported by the reauthorization of the Prescription Drug User Fee Act (PDUFA) to keep pace with the review of increasingly complex new drugs and vaccines.
- Continue the Medical Device Review Program supported by the Medical Device User Fee and Modernization Act (MDUFMA) to keep pace with the increasingly complex medical device review process.
- Increase efforts to promote safe and effective over-the-counter (OTC) drug products in the United States.
- Develop standards for new products of emerging technologies, including new drugs, biologics, medical devices and bioengineered foods, to facilitate safe product development guided by current science.
- Implement a comprehensive quality control systems approach to medical product review, and ensure the Agency's premarket review processes are consistent, high-quality and efficient. FDA is working with stakeholders to implement this in the least burdensome way.
- **Pediatrics**
    - Increase the number of drugs that are adequately labeled for children.
    - Provide incentives for the effective development and dissemination of information on how to properly use therapies in children.
- **Premarket Generic**
    - Improve the generic drug review program to reduce review backlogs and expedite the review of new applications; and implement improved regulations governing generic drug competition.
- **Dietary Supplements**
    - Continue prompt review and evaluation of premarket notifications for dietary ingredients.

2. Inspection and Enforcement Strategies

- **Import Strategies**
  - Enhance the automated import monitoring system (OASIS) to improve cost effectiveness in screening imports and expand coverage at ports.
  - Increase criminal investigations of fraudulent medical product imports.
  - Implement the European Mutual Recognition Agreement; and participate in international standard setting forums such as the International Conference on Harmonization (ICH) to continue to advocate for rigorous standards.
- **Domestic Strategies**
  - Leverage inspection efforts through contracts and grants with the States, other third parties and outreach to small firms.
  - Review Human Drug, Biologics and Animal Drug GMPs to emphasize science-based risk management and quality control.
  - Ensure that inspectors have the scientific and technological support necessary to make quick and valid judgments about medical product and food compliance.
  - Focus resources on the highest risk firms for food and medical product areas, which will bring the greatest health benefit.

3. Risk Analysis Strategies

- Identify statistical analysis and modeling methods, such as computer simulation and monitor best practices that could potentially be applied or extended in Agency risk management.
- Armed with appropriate information and analytical tools, apply principle of "reasonable certainty of no harm" in making risk management decisions.
- Assess opportunities for more standardized methods and approaches to risk analysis in support of risk management decisions.
- Introduce the knowledge of new genetic systems and computer-assisted toxicology (toxicoinformatics) into the risk management process.

Performance Goal Highlights for FY 2004

Premarket

- **Meet PDUFA III commitments for the review of original New Drug Application (NDA), Product License Application (PLA), and Biologic Licensing Application (BLA) submissions.**
- **Complete Review and Action upon 90 percent of fileable original generic drug applications within 6 months after submission date.**
- **Complete Review and Action on 90 percent of prescription-to over-the-counter switch applications within 10 months of receipt.**

- **Increase the number of drugs that are adequately labeled for children.**
- **Complete the safety evaluation of 75 percent of food and color additive petitions within 360 days of receipt.**
- **Complete Review and Action on 90 percent of New Animal Drug Applications and reactivations of such applications within 295 days; 90 percent of investigational animal drug study submissions within 320 days; and review 90 percent of investigational animal drug submissions consisting of protocols, without substantial data within 125 days.**
- **Complete Review and Action on 90 percent of Device Premarket Approval Application (PMA) first actions within 180 days.**
- **Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting onsite inspections and data audits under FDA's Bioresearch Monitoring Program.**
- **Respond to at least 95 percent of premarket notifications for new dietary ingredients within the statutory time frame (75 days);**

Postmarket

- **Inspect 55 percent of an estimated 630 registered high-risk human drug manufacturers.**
- **Meet the biennial inspection statutory requirement by inspecting 50 percent of the approximately 2,700 registered blood banks, source plasma operations, and biologics manufacturing establishments to reduce the risk of product contamination.**
- **Utilize risk management to target inspection coverage for Class II and Class III domestic medical device manufacturers at 20 percent. [Class II Devices require standards to be developed prior to marketing. Class III Devices are considered to be higher risk devices, such as heart valves].**
- **Utilize risk management to target inspection coverage for Class II and Class III foreign medical device manufacturers at 20 percent.**

Current Status

Premarket Review

Human Drugs and Biologics: 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 as 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 supplement appropriated funds.

Generic Drugs: In the area of generic drugs, recent increases have enabled the program to raise performance targets.

OTC Drugs: For over-the-counter (OTC) drugs, the FDA has finalized 52 monographs or "recipes" for marketing these drug products without the need for FDA preclearance. The monographs save manufacturers costs and reduce barriers to competition, as they allow both large and small companies to enter the market place with OTC drug products that have to meet the same, uniform criteria. By the end of FY 2004, the Agency expects to have initiated the review process (e.g. submit as advance notice of proposed rulemaking (ANPR)) for as many as 110 major drug category monographs. In the next 10 years, FDA expects to review and complete approximately 25 monographs, a number of which are major product categories (e.g. internal and external analgesic, and health care antiseptics). The road from ANPR to when a monograph is finalized is a complex and time-consuming rule-making process and can take several years.

Pediatric Medicine: The original pediatric exclusivity provision of FDAMA 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 worked with NIH to develop off-patent drugs and to elicit study proposals from industry. FDA has issued over one hundred written requests for studies that could affect thousands of pediatric patients. The Agency has also issued a number of grants of pediatric exclusivity. The Best Pharmaceuticals for Children Act (BPCA), enacted on January 4, 2002, will continue to provide incentives for the effective development and dissemination of information on how to properly use therapies in children.

Postmarket

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. Plans for a highly integrated web-enabled import monitoring system are being developed to allow the Agency to prevent unsafe import entries on a cost-effective basis. 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 drugs and feeds, and medical device manufacturers at least once every two years. Although at least 50 percent of statutory establishments should be inspected annually, only 19 percent of human drug, and 20 percent of medical device statutory establishments were inspected in FY 2001. However, the Agency did exceed its goal in inspecting

over 50 percent of registered blood banks, source plasma operations, and biologics manufacturing establishments in FY 2001. Beginning in FY 2003, FDA has developed a new high risk performance goal to inspect the highest risk drug manufacturers.

FY 2002 Performance Goals

Program	Final FY 2002 Goal Statement	Was the target met?	Explanation
Foods	Complete review and action on 60% of food and color additive petitions within 360 days of receipt.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 360 days after the end of the fiscal year.
Foods	Respond to 95% of notifications for dietary supplements containing "new dietary ingredients" within 75 days.	***Yes***	
Foods	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.	***Yes***	
Human Drugs	Complete review and action on 90% of Standard NDAs within 10 months and 90% of Priority NDAs within 6 months.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6 and 10 months after the end of the fiscal year.
Human Drugs	Complete review and action on 65% of fileable original generic drug applications within 6 months after submission date.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6 months after the end of the fiscal year.

Human Drugs	Improve the capability and efficiency of pharmaceutical development and manufacturing by conducting laboratory research on at least 3 projects.	***Yes***	
Human Drugs	Inspect 20% of registered human drug manufacturers, repackers, relabelers and medical gas repackers.	***Yes***	
Human Drugs	Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting 780 onsite inspections and data audits annually.	***No***	In FY 2002, there was a reduction in the number of NDAs submitted and this reduced the number of completed inspections.
Human Drugs	Increase the number of drugs that are adequately labeled for children by implementing, evaluating, tracking and reporting on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	***Yes***	
Biologics	Complete review and action on 90% of standard PDUFA NDA/ PLA/ BLAs within 10 months and 90% of priority PDUFA NDA/ PLA/ BLAs within 6 months.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6 and 10 months after the end of the fiscal year.
Biologics	Complete review and action on 90% of standard PDUFA efficacy supplements within 10	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6

	months and 90% of priority PDUFA efficacy supplements within 6 months.		and 10 months after the end of the fiscal year.
Biologics	Complete review and action on 90% of PDUFA manufacturing supplements within 6 months of receipt and 90% of PDUFA manufacturing supplements requiring prior approval within 4 months of receipt.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6 and 10 months after the end of the fiscal year.
Biologics	Complete review and action on 90% of Class 1 resubmitted original PDUFA applications within 2 months and 90% of Class 2 resubmitted original PDUFA applications within 6 months of receipt.	***Data Not Yet Available***	Although we met the 2 month target, and we expect to meet the 6 month target for this review goal, the final data won't be in until at least 6 months after the end of the fiscal year.
Biologics	Complete review and action on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90% of PLA/BLA supplements within 12 months after submission date.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until at least 6 and 10 months after the end of the fiscal year.
Biologics	Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing establishments to reduce the risk of product contamination.	***Yes***	
Animal	Maintain the level of	***Yes***	

Drugs and Feeds	requested pre-submission conferences conducted with industry sponsors at 80%.		
Animal Drugs and Feeds	Pilot and validate the procedure for receiving protocol submissions electronically.	***Yes***	
Animal Drugs and Feeds	Conduct targeted BSE inspections of 100% of all known renderers and feed mills processing products containing prohibited material.	***Yes***	
Animal Drugs and Feeds	Maintain biennial inspection coverage by inspecting 50% of registered animal drug and feed establishments.	***Yes***	
Animal Drugs and Feeds	Complete Review and Action on 50% of NADAs/ANADAs within 180 days of receipt.	***Yes***	
Animal Drugs and Feeds	Reduce pending overdue Animal Drug submissions by 15%.	***Yes***	
Animal Drugs and Feeds	Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.	***Data Not Yet Available***	Although we expect to meet the target for this review goal, the final data won't be in until March 2003.
Medical Devices	Complete 95% of PMA "Determination" meetings within 30 days.	***Yes***	
Medical Devices	Review and Act on 90% of Premarket Approval Application of an estimated 80 (PMA) first	***Yes***	

	actions within 180 days.		
Medical Devices	Review and Act on 95% of an estimated 4,500 510(k) (Premarket Notification) first actions within 90 days.	***Yes***	
Medical Devices	Recognize 20 new or enhanced standards to be used in application review.	***Yes***	
Medical Devices	Utilize Risk management to target inspection coverage for Class II and Class Ill domestic medical device manufacturers at 20%.	***Yes***	
Medical Devices	Utilize Risk management to target inspection coverage for Class II and Class Ill foreign medical device manufacturers at 9%.	***No***	The international climate after the terrorist attacks of September 11, adversely impacted foreign travel until well into the 1st quarter of FY 2002. As a result, only 209 out of a planned 225 inspections were completed.
Medical Devices	Ensure at least 97% of an estimated 8749 domestic mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems.	***Yes***	
Medical Devices	Review and Act on 90% of PMA supplement final actions within 180 days.	***Yes***	
Medical Devices	Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired,	***Yes***	

	pediatric, etc.)		
NCTR	Conduct one biologically based mechanistic study combined with pre-dictive modeling to improve extrapolation of animal data to the human condition.	***Yes***	
NCTR	Support at least two multi-disciplined DNA and RNA-based microarray technologies.	***Yes***	
NCTR	Maintain existing computational databases of estrogenic and androgenic compounds for use by reviewers.	***Yes***	
NCTR	Initiate analytical/ biological studies to assess the toxicity of at least one, FDA high priority dietary supplement.	***Yes***	
NCTR	Report at scientific meetings and/or publish preliminary results on the development of new methodologies to identify genetically modified foods, drug residues in foods and antibiotic-resistant strains of bacteria.	***Yes***	
NCTR	Publish at least one scientific paper describing one technology for use in reviewing regulated compounds.	***Yes***	

Highlights of FY 2001-2002 Accomplishments

Premarket

Medical Product Research Oversight

- 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 issued an interim rule to provide additional safeguards for children participating in clinical studies. The new rule provides specific criteria, such as an assurance of informed consent by the children and their parents that have to be maintained by the Institutional Review Boards that supervise the trials.

Human Drugs and Biologics

- FDA successfully negotiated the reauthorization of the Prescription Drug User Fee Act, which will give the Agency access to resources necessary to effectively support human drug development and expedite premarket application review.
- 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 committed to. New drugs are approved in the U.S. as fast as 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; 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 has also made progress in increasing the number of drugs that are adequately labeled for children. Before FDA can approve such labels, Agency-requested studies must be conducted. As of July 2002, FDA had requested 588 studies that address dosing, safety and use of drugs for children. Over 34,000 patients are projected as participants in these studies. As of May 2002 over 30 pediatric labels have been approved. Accurate dosing and safety information is now available for children who are being treated for allergies, diabetes, heartburn, high blood pressure and many other conditions. In January 2002, the President signed the "Best Pharmaceuticals for Children Act" which reauthorized the pediatric exclusivity provisions of the 1997 "FDA Modernization Act" and provided new approaches for assuring the appropriate study of drugs that were not

being studied under the exclusivity provisions. FDA, in conjunction with NIH, has initiated the various steps needed to implement this legislation.

Medical Devices

FDA successfully negotiated the authorization of the Medical Device User Fee and Modernization Act (MDUFMA), which will give the Agency access to resources necessary to effectively support medical device development and expedite premarket application review.

In 2002, several new products were approved including:

- The Given Diagnostic Imaging System, a new swallowable capsule containing a tiny camera that can facilitate early detection of colon cancer;
- Expanded use of defibrillators to treat heart patients; new drugs to treat rare pediatric liver disease (nitisinone); and broader use of a brain implant to treat Parkinson's disease.

Foods

- FDA has completed 100 percent of its reviews for "new dietary ingredients" notifications within the 75-day deadline, which exceeds its 95 percent target. The Agency also completed review of all 80 notifications received in 2001, which also exceeds its 95 percent target.

Postmarket

Human Drugs and Biologics

- FDA met its statutory requirements by inspecting 50 percent of registered blood banks, source plasma operations, and biologics manufacturing establishments to reduce the risk of product contamination.
- The Agency ensured that recipients of blood products will be better protected thanks to licensing of the first nucleic acid test systems intended for screening of plasma donors. These systems are expected to further ensure the safety of plasma-derived products by permitting earlier detection of HIV and HCV infections in donors.
- In FY 2001, FDA became part of a coordinated HHS-wide effort to establish common reporting portal that will simplify the task for those who are submitting adverse events information for medical products, and for the Federal agencies that are collecting it.
- FDA made progress in automating the receipt and processing of drug safety reports that will allow the Agency 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.

Medical Devices

- FDA continued to improve reporting of adverse events associated with medical device use by recruiting several additional hospitals into the Medical Product Surveillance Network. This reporting network is intended to reduce the estimated 300,000 injuries and deaths associated with medical device use and misuse.

Foods

FDA took further steps to understand and manage the risk associated with dietary supplements, including the following:

- Implemented the Cooperative Agreement with the National Center for Natural Products Research at the University of Mississippi. Work done by the National Center to identify and analyze specific components in dietary supplement ingredients, including botanical ingredients, is an essential component to FDA's research and regulatory programs directed at ensuring the safety and effectiveness of dietary supplements.
- Developed "Tips for the Savvy Supplement User," to assist consumers in making informed decisions and evaluate information about dietary supplements.
- Reviewed 43 of 44 notifications for new dietary ingredients within the 75-day statutory timeframe.

BSE Risk Management

FDA participated in the USDA sponsored training of risk analysts to use and continue developing the Harvard Center for Risk Analysis (HCRA) BSE simulator. The simulator has been installed in FDA's Center for Veterinary Medicine (CVM) to run computationally-intense risk assessment and risk management models. FDA's Risk Analysis Team is running the simulator to test the impact on risk of BSE infectivity in cattle under alternative compliance strategies. The risk management approach to BSE risks in the U.S. enables FDA to make difficult resource allocation decisions under the scientific uncertainty attendant health risk issues.

A Strong FDA

Problem | Desired Outcomes | Key Strategies | FY 2004 Goal Highlights | Current Status | FY 2002 Performance Goals | FY 2001-2002 Highlights

Problem

In addition to the terrorist threat, other major environmental forces are exerting a major influence on how FDA must operate: globalization of trade and regulation, increasing industry use of the Internet and continuing innovations in science and technology.

These forces for change coincide with the direction of the Administration's leadership through the President's Management Agenda. Following this agenda, the Agency seeks to achieve excellence in management practices by becoming more streamlined, cost-effective, oriented toward strategic alliances, Internet-based and citizen-centered.

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.
- Enhance capacity to produce program performance data and management control systems that allow the Agency to maximize performance relative to targeted public health outcomes.
- Maintain FDA's high standards as a citizen-centered Agency accountable for results.

Key Strategies

Each of the strategies outlined below are aligned with the President's Management Agenda to make all Federal government agencies more streamlined and citizen-centered.

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. The Agency must also

assure that scientists maintain state-of-the-art expertise by training them in emerging technologies. Without understanding the science underpinning new products we cannot make credible regulatory decisions.

Improve Management Systems - FDA continues to focus on achieving excellence in management practices by improving the effectiveness of a wide range of systems that support Agency decisions. These include financial management (including travel and procurement), information management, and security. The Agency has embarked on several initiatives that include implementing a new financial management system, upgrading the current Legacy systems, 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 2003.

Achieve Cost-effective Performance of Traditional Government Activities - FDA has committed to examining its commercial FTEs to determine which activities would be more cost-effective to implement if outsourced. The aim is to arrive at a rational balance of in-house and outsourced activities that will maximize the overall cost-effectiveness of Agency resources.

Focus on Performance and Accountability 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 we communicate clearly with our stakeholders. The President's Management Agenda reinforces the importance of being a citizen-centered government; strive for long term outcome goals that meet citizens' needs; and identify the resources necessary to achieve those goals through effectively integrating performance and budgetary planning.

FDA strategies are aligned with the President's Management Agenda. Agency leadership is committed to the establishment of long-term outcome goals that make a difference to the U.S. taxpayer. To this end, we are developing the capacity to produce program data to better monitor, measure and manage Agency activities and resources to maximize performance relative to targeted public health outcomes. We will also strive for closer integration of

performance and budget by establishing systems that will provide the necessary information to identify the performance-resource linkage. Finally, a system of performance contracts will be implemented to establish the linkage between individual and organizational accountability for performance results.

Demonstrate enhanced capacities of FDA website for providing information to industry on FDA-enforced regulations - FDA recognizes the need for innovative methods to communicate important public health information to the public. FDA is currently creating and implementing effective communication methods to give consumers the information they need to make better health decisions. One improvement is enhancing the FDA website. FDA is continuing to increase the percentage of applications submitted electronically and enhanced electronic capacities for domestic food inspections and imports.

Performance Goal Highlights for FY 2004

- **Reduce the number of review levels in the Agency to help streamline operations.**
- **Increase the percentage of commercial FTEs that will be reviewed for outsourcing.**
- **Expand the use of Agency-wide Enterprise IT architecture in accordance with the Department of Health and Human Services Plan.**
- **Complete system preparation to implement Financial Enterprise Solutions, FDA's version of UFMS.**

Current Status

Human Capital - FDA is faced with the challenge of replacing its critical knowledge base as a large segment of its workforce reaches retirement age. Because federal salaries cannot match industry salaries, FDA needs greater flexibility in recruitment strategies and in pay incentives. Using initiatives such as Quick Hire, over 800 Investigators and Analysts are on board to increase surveillance of products at the border. FDA has used appointment mechanisms in the excepted service, i.e., Title 42 of the Public Health Service Act. However, special hiring authorities 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 equity among both managers and employees.

FDA has initiated non-monetary, quality of work life incentives that maintain a highly motivated workforce. In recent federal employee surveys FDA respondents gave the Agency a 72 percent favorable rating in employee job satisfaction - highest of the 49 agencies surveyed.

FDA has also aligned its workforce planning efforts with the Department's Strategic Workforce Plan. This initiative will enhance FDA ability to recruit and retain a diverse workforce; implement strategies that allow for replacement of our aging workforce; and attract high quality professional employees needed for the Agency to address the complex challenges it will face in the future.

Management Systems - FDA is initiating the first steps in implementing a Financial Enterprise Solutions System that will be aligned with the HHS Unified Financial Management System. This will provide qualitative and quantitative benefits to FDA because it will achieve improved business processes and provide more accurate and timely information to better support FDA's and DHHS' mission.

In the area of information technology (IT), FDA will establish an Agency-wide enterprise architecture. Top priorities focus on Counterterrorism and establishing an Agency-wide registration system for all regulated establishments and their products. PDUFA III information demands will also be greatly facilitated by enterprise IT architecture supporting that arena of decisions.

Major IT challenges remain, including Cyber security. FDA is meeting this challenge by assessing the security readiness of all of its major IT system components. In FY 2003, FDA is expected to assess 100 percent of the IT infrastructure and one third of the major systems for compliance with provisions of the Government Information Security Reform Act (GISRA) and perform any needed corrections.

Organization structure - FDA is in the process of streamlining its organizational structure by: flattening the hierarchy; consolidating administrative functions and locations; and implementing a customer-responsive "shared services" system.

Flatten the hierarchy - FDA is striving to reduce the number of review levels for decision making within the Agency to no greater than four, which is consistent with the President's Management Agenda and Departmental guidelines. Reducing review levels will allow for a more effective structure and a streamlined organization, as well as increase the span of control for managers across the Agency.

Consolidation - FDA is consolidating administrative functions across the Agency, and 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.

Shared Services - During FY 2003 FDA will develop detailed plans for the shared services organization, following completion of the contract for analysis of FDA's administrative services. In FY 2004, FDA will begin the actual implementation of the shared service organization. This will be a customer-focused organization in which business units establish service priorities and services which will be tailored to meet the individual needs of the business units (programs). Service level agreements will be drawn between administrative service providers and the customers.

The shared service organization will be governed by a group which will include representatives of both providers and customers. Performance will be monitored against 'best practices' in internal and external organizations. The shared services model will help FDA focus on its 'core business'; create satisfied customers and employees; leverage technology and information; and more effectively manage costs.

Change Management - Because many of the management improvement initiatives represent major Agency-wide efforts, and are occurring simultaneously, they have the potential to significantly impact the work life of many employees. In order to make the conversion as smooth and as productive as possible, a Change Management Integration Team of FDA senior personnel has been established. The purpose of this team is to assist the Agency in managing the communication, information sharing, data gathering, and implementation associated with each of the management improvement initiatives.

FY 2002 Performance Goals

Program	Final FY 2002 Goal Statement	Was the target met?	Explanation
Animal Drugs and Feeds	Plan and design the Staff College.	***Yes***	
Agency Wide	Reduce the number of review levels in the Agency to help streamline	***Yes***	

	operations by developing and implementing a plan to delayer NCTR, CVM and CDRH; and planning to transfer Legislative and Public Affairs function to DHHS.		
Agency Wide	Implement 'shared services' concept and consolidate selected functions in the agency by awarding contract of administrative functions to be completed by 9/2002 with the Human Resources portion completed by May.	***Yes***	
Agency Wide	Increase the percentage of Commercial FTE that will be reviewed for outsourcing to 5%.	***No***	Due to the HHS and FDA IT consolidation, FDA decided to postpone a study of web design and development. FDA still expects to complete this study in time to meet its FY 03 target.
Agency Wide	Increase the percentage of electronically purchased transactions to 89%.	***Yes***	
Agency Wide	Maintain a clean (or unqualified) audit opinion with no material weakness.	***Yes***	
Agency Wide	Increase percentage of contract dollars allocated to performance based contracts to 25%.	***Yes***	
Agency Wide	Develop Agency Continuity of operations plan; Participate with PSC to develop COOP.	***Yes***	

Agency Wide	Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks.	***Yes***	

Highlights of FY 2001-2002 Accomplishments

- FDA finalized and published its Strategic Workforce Plan and provided it to all employees via the Internet. Key strategies addressed: recruitment and retention; workforce leveraging; workforce skills; scientific workforce development; and, leadership development.
- FDA and GSA have begun construction of CDER laboratories at the White Oak facility, which will result in approximately 114,000 square feet of laboratory, animal holding, and office space that will be occupied by approximately 200 CDER employees by September 2003.
- FDA's Website has received a Bronze Award in the "Health Promotion/Disease & Injury Prevention Information" category of the latest WWW Health Awards competition. This twice-yearly contest is sponsored by the Health Information Resource Center, which holds the competition to provide "a seal of quality for electronic health information." A panel of health experts judges entries for content, format and overall quality.
- FDA has begun streamlining the structure of the Agency. Efforts are underway to reduce the number of reporting layers to no more than four and initial steps have been taken to consolidate selected functions - in particular human resources and information technology.
- FDA initiated performance-based contracts for all senior executives. These contracts were used to align individual leadership commitments with key Departmental and Agency Performance Goals. The contracts were also used to evaluate end-of-year performance, and make appropriate adjustments for FY 2003.

Counterterrorism

Problem | Desired Outcomes | Key Strategies | FY 2004 Goal Highlights | Current Status | FY 2002 Performance Goals | FY 2001-2002 Highlights

Problem

A combination of public health and law enforcement responsibilities defines FDA Counterterrorism activities. Regardless of the circumstances, FDA must uphold its responsibility for ensuring the safety of approximately 80 percent of the Nation's food supply, as well as ensuring the availability of safe and effective drugs, vaccines, blood products, medical devices, and animal drugs and feed. The scope of the Agency's Counterterrorism activities includes both the civilian and military sectors of the population. The Office of Crisis Management (OCM) has been created to provide an umbrella office of three programs, Office of Counterterrorism Programs, Office of Emergency Operations and Office of Physical Security, which coordinate the majority of internal and external FDA activities to meet these responsibilities.

There is little experience in this country with terrorist agents targeting the U.S. civilian population. The possibility of food products being used as a vehicle for attack is particularly worrisome because such an event potentially affects every U.S. citizen. FDA must have the capability to be vigilant in assessing, and then quickly and effectively reducing risks associated with unexpected and potentially widespread health and safety threats to the U.S. public. The unpredictability and wide variety of ways that potential acts of terrorism can be launched complicate preparedness and the ability to quickly and effectively respond to just such an attack.

The challenge for FDA is being prepared to safeguard products in light of the possibility that terrorists could strike at any point in the product pipeline - from production through distribution and use/ consumption; and in both import and domestic arenas.

Desired Outcome

Ensure that U.S. citizens are protected from public health threats posed by unexpected and potentially widespread terrorist attacks by enhancing the ability of the Nation's health care system to effectively respond to Counterterrorism and other public health challenges. A key outcome of this effort is that all Americans continue to enjoy a safe and secure food supply.

Key Strategies

FDA has developed an integrated **strategic approach** to address the Counterterrorism threat in the U.S. and protect the citizens of our homeland. These strategies are complementary to DHHS' Strategic Goal "To Protect Our Homeland" and have the following characteristics. They:

- Build upon existing Agency capacities to manage health and safety risks.
- Leverage the strengths of health, scientific, and law enforcement agencies to create a powerful and effective response to terrorism.
- Magnify the benefits of various streams of knowledge by bringing the right combination of information to crucial decision points.

The total effect is the 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. Because FDA is responsible for such a large segment of the nation's food supply, food safety is a significant component of this strategy.
- Develop medical countermeasures 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.
- 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 these products from their source of production through the entire distribution system to the point of use/ consumption. This strategy encompasses all FDA-regulated products; and because threats to the food supply are such a major concern, the Agency is placing a high priority on this area. Three primary objectives are to:

1. Ensure Import Security - FDA's efforts will focus on minimizing the threat of imported foods and medical products at different stages of their life cycle:
    - At the country of origin before products are exported to the U.S.;

    - At the border to minimize the chance that hazardous products ever enter the U.S.; and,
    - Throughout the pathway that imports take in domestic commerce. Ensuring the safety of imports will require greatly enhanced information systems; laboratory analysis capability; and, a continued strong presence at the border.
2. Ensure Domestic Product Security - FDA will strengthen inspection coverage of domestic product manufacturers and product distribution; and augment product and pathogen testing.
3. Information Integration - Integrate information that is necessary to target suspected products, processes and actors to support risk management decisions; and closely monitoring product use/ consumption to detect any pattern of adverse events that may stem from terrorist-related incidents. With the passage of the Public Health Security & Bioterrorism Preparedness and Response Act of 2002, and with the requested budget increase, FDA is well on its way to establishing a National Food Registration System. This system will allow the Agency the ability to comprehensively monitor the domestic and imported food industry. With this information, FDA can more quickly and accurately follow through on high risk situations.

Medical Countermeasures - The purpose of this strategy is to ensure safe and effective drugs, vaccines, blood, medical devices and other medical products are available to prevent, diagnose or treat illnesses or injuries resulting from a 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 an attack.
2. Facilitate the availability of necessary medical products - working with industry, Federal agencies, and foreign governments to ensure the safety and effectiveness of stockpiled medical products so that they are available in sufficient quantities to address public health emergencies.
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.
4. Maintain the scientific infrastructure to ensure the availability of approved medical products.
5. Ensure the availability of specialized equipment and facilities for containment.
6. Establish and disseminate the necessary guidance/ standards.

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

1. Enhance the Agency's emergency preparedness plan to establish protocols for responding to Counterterrorism threats.
2. Establish emergency operations and laboratory networks that integrate critical information, procedures, key personnel and decisions in order to minimize impacts of Counterterrorism threats.
3. Enhance emergency preparedness and response.
4. Ensure the safety and security of FDA's most important assets - FDA personnel, physical assets, and information.
5. Establish a plan for continuity of FDA operations in an emergency.

Radiation Safety - 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 during a terrorist incident.
- 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 countermeasures to address radiation incidents.
3. Develop a radiological health emergency preparedness program.

Performance Goal Highlights for FY 2004

Premarket

FDA is committed to bring the Agency to a state of readiness in addressing the Counterterrorism threat to this Nation. The strategies begun in FY 2002 and FY 2003 were steps toward a long-term solution. In FY 2004, goals have been developed to further strengthen the Agency's capability to respond to a Counterterrorism emergency. Examples of FY 2004 goals include:

- **Expand Federal/State/local involvement in FDA's eLEXNET system by having 79 laboratories participate in the system.**
- **Inspect 95 percent of high-risk domestic food establishments once every year.**

- **Perform 48,000 physical exams and conduct sample analyses on imported products with suspect histories.**
- **Perform at least 1,000 Filer Evaluations under new procedures.**
- **Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported.**
- **Enhance states' laboratory analysis (8 new participating laboratories); and inspection capabilities (1,200 more inspections)**

Current Status

The President's FY 2003 budget for bioterrorism significantly strengthened FDA's ability to counter the terrorist threat at the border through personnel enhancements. However, FDA still has limited capacity to monitor or control the flow of imported foods, inspect domestic manufacturers, and detect foodborne pathogens before they cause human illness. When these limitations are combined with the possibility of a deliberate attempt to contaminate the food supply at any point along the food production, processing and distribution chain, the risk associated with a potential Counterterrorism incident are greatly increased.

In FY 2004, FDA will strengthen the import information systems to improve targeting of suspect products, and to enhance links between import and domestic information systems, so that imported products can be traced in domestic commerce. FDA believes that by coordinating a laboratory response network, it will enhance the Agency's ability to identify and contain outbreaks associated with deliberate attempts to contaminate the food supply.

The Agency is continuing to make strides in each of the major Counterterrorism goal areas:

Protect Regulated Products: Deterrence, Detection, Investigation, and Interdiction - FDA has assigned a cadre of field investigators at the border that will increase by 100 percent the number of import physical exams conducted during FY 2003. Targeted inspections of food entries and high-risk domestic food inspections continue to be the focus of effort in this area of protecting regulated products.

Additionally, in FY 2004, FDA will bolster its existing Foods Domestic Retail and Interstate Travel Programs (ITP). The Foods Retail works cooperatively with state and local governments to ensure that their resources expended for this program are directed towards activities producing the greatest degree of consumer protection. The ITP inspects passenger conveyances (planes, busses, trains, water vessels) and support facilities (watering points, food caterers, and waste facilities) involved in interstate commerce to ensure safe drinking water and food.

During FY 2003, FDA will develop a more robust imported products physical examination approach that merges the assessment of information integrity with the safety and security of the product. The Agency will also develop better estimates of time required for the new augmented examination so that appropriate resources can be matched with the revised approach.

Passage of bioterrorism legislation in FY 2002 provided FDA with greater regulatory authority to detain and refuse entry to suspect products; to require that accurate records be maintained by shippers and importers of food products; and, to require that all establishments register with FDA in order to ascertain those firms that are shipping products to the U.S.

Medical Countermeasures - 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 medical countermeasures. The ultimate goal is that regulated products in the NPS will be approved as safe and effective and will be appropriately labeled to treat the medical consequences of biological, chemical or radiation attacks. In addition, FDA is preparing guidance for industry on the development of products that can be used as medical countermeasures. The guidance will provide information regarding the development of antiviral drugs and post exposure anti-microbial drugs for inhalational anthrax. Further, the Agency is expediting the review of protocols and facilitating the conduct of human clinical trials for new investigational radioprotectant drugs, and drugs to treat organophosphorous nerve agents.

The Food and Drug Administration is requesting grant applications to support clinical trials on the safety and effectiveness of drug products for the treatment of human plague (bubonic, pneumonic, meningitic, or septicemic) caused by Yersinia pestis. FDA anticipates awarding up to three awards each for a total of up to $700,000 for two years. These grants are available to any foreign or domestic, public or private nonprofit entity (including State and local units of government) and any foreign or domestic, for-profit entity that waives its fees. This program is part of FDA's Counterterrorism efforts.

On January 31, 2002, FDA took the final actions necessary to allow the BioPort Corporation to begin routine distribution of licensed anthrax vaccine from its renovated facility. Due to the complex nature of biological products, the Public Health Service Act and FDA regulations require approval of a supplement for major changes made to a facility in which a licensed product is manufactured. In addition, each lot of anthrax vaccine undergoes thorough testing for purity, potency, identity and sterility. No lot of anthrax vaccine can be distributed from the renovated facility until FDA's Center for Biologics Evaluation and Research releases it based on the results of these tests. This process, called lot release, helps assure product safety by providing yet another quality control check on product specification.

A radioprotectants team was created to increase the availability of products to prevent and treat radiotoxicity. The following drugs are currently under development as heavy metal chelators: Prussian Blue, Calcium DTPA, and Zinc DTPA. In addition, FDA's Division of Radiopharmacolgical Drug Products has worked extensively with the sponsors of these drugs in providing advice and assistance. It has also conducted numerous literature searches, reviewed published information, and worked with external groups to gather additional information on these products.

Emergency Preparedness and Response - FDA has developed a Continuity of Operations Plan (COOP) which will allow the Agency to keep its major programs functioning in the event of a disabling attack.

To facilitate the sharing of laboratory results, particularly during a terrorist incident, the Electronic Laboratory Exchange Network (eLEXNET), a federally coordinated effort, will be expanded to include more State health laboratories in both FY 2003 and FY 2004. This system is the first Internet? based food safety system that consolidates and shares pathogenic findings among Federal, State, and local government laboratories.

FY 2002 Performance Goals

Program	Final FY 2002 Goal Statement	Was the target met?	Explanation
Foods	Achieve adoption of the Food Code by at least one state agency in 28 states in the USA.	***Yes***	
Foods	Inspect 95% of estimated 7,000 high-risk domestic food establishments once every year.	***Yes***	
Human Drugs	Facilitate the initiation of research in a non-human primate model of pneumonic plague.	***Yes***	
Human Drugs	Expedite the review of protocols for investigational new drugs (INDs) to treat	***Yes***	

	organophosphorous nerve agents in the event of chemical attack. Encourage sponsors of these new drug applications (NDAs) to update current labeling for Antidote Treatment Nerve Agent, Autoinjectors (ATNAA).		
Human Drugs	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.	***Yes***	
Human Drugs	Publish guidance for industry on developing antimicrobial drugs for inhalational anthrax (post-exposure).	***Yes***	
Human Drugs	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.	***No***	Focus was shifted on drafting a barcoding rule. In addition, because of changes anticipated as a result of the barcoding rule, the draft proposed rule on drug registration and listing had to be revised.
Human Drugs	Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing	***Yes***	

	recommendations for inhalational anthrax.		
Human Drugs	Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies.	***Yes***	
Medical Devices	Develop Emergency Counterterrorism Preparedness and Response Plan for radiation.	***Yes***	
NCTR	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.	***Yes***	
Agency Wide	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.	***Yes***	

Highlights of FY 2001-2002 Accomplishments

Protect Regulated Products: Deterrence, Detection, Investigation, and Interdiction -

- Hired and began training 655 new investigators, analysts and other support personnel as authorized by the FY 2002 Counterterrorism Supplemental Appropriation. These personnel improve the Agency's capacity to respond to Counterterrorism threats and attacks and augment domestic food safety and security. Many are investigators and analysts who closely monitored the highest risk imports entering the country, and allowed FDA to increase border presence by doing more field exams, sample collection and analysis, domestic inspections and laboratory analysis. FDA increased physical exams by 100 percent in FY 2002, and projecting to do so again in FY 2003.
- Conducted intense threat assessments of risks of different products and agents that could be used for a Counterterrorism attack involving intentional contamination during various stages of food production and distribution.
- Developed rapid methods for detecting microbial and viral food contaminants. FDA has leveraged this expertise with public and private sector partners to operate national rapid identification systems used to control outbreaks of foodborne diseases.
- Published guidance for domestic food producers and importers on preventive measures to increase their preparedness and enhance the security of their products (67 FR 1224; January 2, 2002).
- Took steps to increase assurances that products imported into this Country will be safe. Published a proposed rule that would have required marking, prior to exportation, of all foods refused for safety reasons, and would have assured that marked products were exported and not re-entered into the U.S. marketplace. This rule has been withdrawn, as the proposed marking provisions of the rule were incorporated into the recent bioterrorism legislation.
- Contributed to the development of methodology for the detection of biological agents with Counterterrorism threat potential.
- Upgraded designated laboratory facilities to a BioSafety Level 3 (BSL-3) to support microbial Counterterrorism research. BSL-3 facilities have containment capability that allows work with indigenous or exotic agents that may cause serious or potentially lethal disease.
- Obtained High Performance Liquid Chromatography equipment needed for rapid analysis of suspect foods to assay for biological or chemical agents that could be introduced into food products.
- Outfitted upgraded laboratory facilities with infrastructure to include containment hoods and appropriate filtering and monitoring devices. This will allow researchers to characterize multiple strains, construct a library/ database of constituent proteins and query the library/ database to find toxin related markers.

Medical Countermeasures - The Office of Crisis Management is the "portal of entry" to FDA for any inquiries regarding existing regulatory mechanisms for enhanced product availability, and Counterterrorism initiatives and programs across the Agency. The Office coordinated a number of efforts to serve emergency public health needs. These included the following:

- Coordination to provide expedited regulatory guidance to CDC during the administration of post exposure anthrax vaccine and antibiotics to Capitol Hill and Postal Service employees.
- Coordination to respond to an inquiry from U.S. Special Forces regarding the availability of medical countermeasures to assist in the deployment of airborne hospital facilities for the evacuation of battlefield casualties.
- Response to inquiry from Joint Chiefs of Staff regarding availability of critical medical product for combat readiness.
- Response to hundreds of inquiries from product developers-small and large companies, academic investigators, other federal agencies, concerned citizens- regarding access to FDA, questions of regulatory jurisdiction, liaison with product centers to develop Counterterrorism-related medical products.
- Launched an internship program with DoD to facilitate understanding of the regulatory needs of military programs conducting research, developing medical countermeasures, planning combat readiness, and caring for military personnel. The first intern reported in July 2002 for a 12-month tour.
- Engaged in the development of new regulatory models to support preparedness in the case of an emergency attack - e.g., anthrax. 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.
- Launched the Counterterrorism Tracking System (CTTS), an electronic database used throughout the Agency for real-time status reports on counterterrorism activities. The system was developed with the Office of Information Resources Management. The Office of Crisis Management maintains and monitors the system and trains system users.

FDA took the initiative to clarify that the antibiotics, doxycycline and penicillin G procaine, are effective and approved for use in treating all forms of anthrax infections. This notice included explicit dosing based on FDA's review of scientific literature and data from the same rhesus monkey study that had been used to support the August 2000 approval of ciprofloxacin for the treatment of anthrax. The assurance that the three drugs are effective against all forms of anthrax infection eased the public's concerns about a potential shortage of medication for the victims of the mailed anthrax powder.

Worked closely with industry and other government agencies to assure adequate supply of products for immunization against anthrax, botulism, smallpox and other substances that might be used by terrorists, and to evaluate adverse experiences reported after administration of anthrax vaccine to optimize the safe use of this vaccine.

On May 31, 2002, the Agency published a rule which allows approval of 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.

FDA collaborated with the National Institutes of Health in developing a guidance on the use of potassium iodide to reduce the risk of thyroid cancer in radiation emergencies.

Emergency Preparedness and Response - Strategic Plan/Action Plan: The attacks of September 11, 2001, the subsequent anthrax outbreak, U.S. military deployment in Central Asia, and the need to respond to a possible anthrax contamination of our own facilities broadened and intensified the Agency's Counterterrorism activities. A comprehensive update of the existing FDA Counterterrorism Strategic Plan was completed early in 2002 to meet the Agency's need to coordinate this greatly expanded area. This was followed by the drafting of the Agency Action Plan to identify specific activities needed to meet the goals of the Strategic Plan.

- Worked hand-in-hand with CDC's Public Health Information Network, and in very close coordination and cooperation with CDC. FDA will continue to work to make the Electronic Laboratory Exchange Network (eLEXNET) an integral component of the Public Health Information Network.
- Expanded existing service contracts for obtaining additional guards for a number of FDA facilities.
- Secured storage for select agents to prevent unauthorized use or theft.
- Opened the FDA Emergency Operations Center in FDA Headquarters Building in Rockville, Maryland.
- Managed, tracked and investigated over 150 significant incidents and emergencies involving FDA regulated products.
- Managed the National Consumer Complaint System that collects information on the condition of FDA regulated products on the market with which consumers are dissatisfied for reasons such as violation of the law, or for causing injury or death. This information can be compiled and evaluated to highlight current problems and long term trends, and can be used as background data in the development of FDA programs. Processed 6066 complaints in FY 2002.

- Planned, developed and conducted emergency response exercises for FDA personnel, to prepare for potential BSE and Bioterrorism emergencies.
- Provided planning, coordination and support for the HHS Command Center during the Winter Olympics.
- Drafted and issued the FDA Radiological Emergency Response Plan.
- Drafted and issued the FDA Chemical and Biological Emergency Response Plan.
- Awarded the contract to design and develop the FDA Emergency Operations Network (3 to 4 year project) to create functional and technological infrastructure for a seamless emergency preparedness and response system.

Adverse Events and Medical Errors

Problem | Desired Outcomes | Key Strategies | FY 2004 Goal Highlights | Current Status | FY 2002 Performance Goals | FY 2001-2002 Highlights

Problem

The prevalence of avoidable health complications that involve the use of FDA-regulated products, presents a challenge for the Agency. A 1999 Institute of Medicine (IOM) report estimated that as many as 100,000 Americans die each year as a result of medical errors, which are projected to rank as the eighth leading cause of death in the United States. Misuse of pharmaceuticals is associated with about 3 million hospital admissions a year. Drug-related adverse events in the ambulatory population cost Americans approximately $75 billion annually.

FDA's central public health role is to ensure that medical products (drugs, biologics, and devices) are proven safe and efficacious prior to marketing, and that these products continue to be safely used once approved and marketed. FDA must monitor over 40,000 manufacturing establishments and almost 10,000 mammography facilities. In addition, FDA examines drugs, biologics, animal drugs and feeds, and medical devices that cross our borders annually. FDA vigilance in overseeing the production, distribution and use of these products, means FDA can respond to safety problems quickly to mitigate the impact associated with these products, which is critical to public safety.

The risks associated with medical products are never fully revealed during the premarket review process. New safety findings may emerge after approval, when a wider patient population uses products under a broader range of clinical circumstances. In some of these cases, preventable complications and adverse events may occur that were not observed before product approval. Thus, FDA must assure a postmarket system operate effectively to protect the American public.

There is a significant need for more data from health care providers who prescribe or use medical products. FDA must identify alternative methods to obtain safety data to reduce the public's risk of unsafe products, or in many cases, receiving the wrong dose or product. Automatic data collection on medication errors and adverse events will enable the Agency to limit adverse health outcomes associated with FDA regulated products. To address this opportunity, FDA will look to partner with provider networks and organizations and continue to work with other government agencies to obtain a more consistent stream of safety data.

Virtually all medical therapies have side effects. It is important for these side effects to be well understood so that we can be sure a product's benefits outweigh its risks. But, preventable adverse events are a different health hazard: they are avoidable medical complications that need not and should not occur. FDA continues to help health professionals avoid medical errors that lead to adverse events.

Desired Outcome

Reduce adverse events related to FDA-regulated products by improving postmarketing surveillance and helping to prevent adverse outcomes related to medical errors.

Key Strategies

FDA uses a risk-based approach to adverse event reporting that harmonizes efforts across the three medical centers (drugs, biologics and medical devices):

1. Establish Reporting Capability.
2. Develop analytical capability to identify and quantify medical product risk and to investigate, analyze and understand these risks and their consequences based on adverse information that is captured (risk analysis/assessment).
3. Increase communication of risks to educate both health professionals and patients about problems and solutions associated with appropriate product use (risk management decisions).

Performance Goal Highlights for FY 2004

FDA is committed to reducing preventable adverse events associated with medical product use and medical errors. The Agency has placed greater emphasis on inspecting medical products with highest risk, and is committed to devoting scarce resources to highest risk areas.

Examples of FY 2004 goals include:

- **Enhance the postmarketing drug safety. (Formerly, streamline adverse drug event reporting system.**
    - **Increase the receipt of Periodic Safety Update Reports (PSURs) electronically into CDER's electronic document room. (Receipt of reports is voluntary.)**
    - **Publish final guidance to Industry on good risk assessment and risk management, and pharmacovigilance practices.**
    - **Enhance AERS to support medication error capture and analysis.**

    - **Submit majority of Adverse Drug Reaction (ADR) reports electronically.**
- **Expand implementation of the MeDSuN System to a network of 240 facilities.**

Current Status

Establish Reporting Capability - FDA has developed and is improving a system of voluntary reporting of adverse events associated with the use of Agency-approved products. The Agency's MedWatch program receives about 25,000 adverse event and medical product problem reports annually, mostly from health care professionals and consumers. The MedWatch data are entered into FDA's Adverse Events Reporting System, which also receive 270,000 manufacturers' reports. The manufacturers' reports, which must be filed periodically, are based on information provided by physicians and other health care providers.

Another important FDA program is the Vaccine Adverse Events Reporting System (VAERS). VAERS received more than 14,000 reports of adverse reactions in FY 2002, most of which were volunteered by health care providers, patients and their parents. To ensure the safety of the blood supply, the Center for Biologics Evaluation and Research (CBER) requires all blood banks to promptly report fatalities connected with blood transfusions and donations. In addition, the Center operates a web-based voluntary reporting system for rapid identification of supply shortages affecting blood, blood components and reagents.

FDA is also currently expanding the Medical Product Surveillance Network (MeDSuN) System. MeDSuN, a pilot program that requires rapid adverse event reporting on medical devices by selected hospitals and nursing homes. The system is designed to train hospital personnel to accurately identify and report injuries and deaths associated with medical products. MeDSuN advances the public's health by giving FDA quicker and more detailed information, without identifying specific individuals, on potential problems with health care products in actual medical practice. This is a rapidly growing network that also provides health care organizations with fast feedback about lessons learned by the FDA.

The MeDSuN model, currently only designed to track and analyze adverse events due to medical devices, will be expanded to include drug products. Initial work includes a feasibility and acceptability assessment of a small regional group of hospital pharmacists about incorporating MeDSuN into their reporting of adverse drug effects and medication errors.

The Agency is also working on a proposed rule regarding suspect adverse drug reactions (SADRs). Currently, only manufacturers, repackers, and

distributors are required to report adverse effects relating to their medical products. The rule will require that any companies that have contracts with the manufacturers, repackers, or distributors also report adverse drug reactions and medication errors. This is intended to eliminate many of the adverse reactions that go unreported. It is primarily focused on medication errors, which occur when a patient is giving the wrong drug, but does not necessarily have an adverse event.

Risk Analysis/Assessment -FDA is currently working to publish draft guidance to industry on good risk analysis, risk assessment, and pharmacovigilance practices. The Agency puts substantial effort into reviewing adverse event and medication error reports to identify serious or potentially serious outcomes that might be avoided by modifying the labeling or packaging or other means. AERS is an important risk assessment database essential for identifying and monitoring the incidence of adverse effects. FDA evaluates spontaneous reporting data from AERS to identify 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.

Risk Management Decisions - FDA is also increasing risk communication to different audiences. The Agency may decide to disseminate risk information through Dear Healthcare Professional letters, MedWatch alerts and partners programs, and may initiate regulatory action.

The Agency has developed new standards for over-the-counter drug product labeling to increase patient knowledge about medication and decrease errors in use. FDA is using a nationwide media campaign to inform consumers how to use the new labeling. In addition, FDA has proposed regulations to enhance the information on prescription drug labeling for professionals. Despite these initiatives to improve drug product labeling, millions of Americans experience adverse events associated with drug use each year.

FDA will publish a final rule to require a barcode be placed on human drugs and biological products. FDA anticipates that 40 percent of medication errors related to administration and dispensing may be eliminated by application of the barcode on drug, biologic and blood packaging and could reduce the yearly rate of medication errors by millions.

The Agency is also working to finalize a rule to amend its regulations governing the format and content of labeling for human prescription drug and biologic products. This proposal would revise current regulations to require modifications that would make it easier for health care practitioners to access, read, and use information in prescription drug labeling and would enhance the safe and effective use of prescription drug products. This proposal would also

amend prescription drug labeling requirements for older drugs to require that certain types of statements currently appearing in labeling be removed if they are not sufficiently supported. Finally, the proposal would eliminate certain unnecessary statements that are currently required to appear on prescription drug product labels and move other, less important information to labeling. These changes would simplify drug product labels and reduce the possibility of medication errors. This is one step in moving towards an electronic labeling format.

FDA's adverse event reporting system must be significantly strengthened. Although the actual numbers of adverse events associated with medical products are not known, the reports FDA receives 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 prevent these problems.

FY 2002 Performance Goals

Program	Final FY 2002 Goal Statement	Was the target met?	Explanation
Human Drugs	Streamline adverse drug event reporting system by accepting electronic submissions from companies and be current with MedDRA coding versions.	***Yes***	
Medical Devices	Implement MedSuN by recruiting a total of 80 facilities for the network	***Yes***	

Highlights of FY 2001-2002 Accomplishments

- FDA continued to improve reporting of adverse events associated with medical device use by recruiting several additional hospitals into the Medical Product Surveillance Network. This reporting network is intended to reduce the estimated 300,000 injuries and deaths associated with medical device use and misuse.

- In FY 2001, FDA became part of a coordinated HHS-wide effort to establish common reporting portal that will simplify the task for those who are submitting adverse events information, and for the Federal agencies that are collecting it.
- FDA made progress in automating the receipt and processing of drug safety reports that will allow the Agency 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.

Consumer Information

Problem | Desired Outcomes | Key Strategies | FY 2004 Goal Highlights | Current Status | FY 2001-2002 Highlights

Problem

Clear and effective communication between FDA and its constituents is vital to FDA's mission as a public health agency. Consumers and health professionals need timely information in order to make informed decisions regarding diet, nutrition, and safe and effective health care.

Desired Outcome

Ensure that consumers, health professionals and other FDA stakeholders have accurate and timely information about potential benefits and health consequences associated with the products regulated by FDA; and a transparent view of FDA processes. Substantially improved public health outcomes should be achieved when well informed consumers and health professionals use safe, high quality products.

Key Strategies

Four key strategies are necessary for effective communication with Agency constituents:

1. Develop a thorough understanding of what information constituents need in order to make wise product choices;
2. Develop and implement appropriate communication vehicles and content to satisfy the needs of different constituent segments;
3. Assure that information communicated to constituents is based on sound scientific evidence; and,
4. Determine the impact of FDA communications on constituent understanding, behavior and ultimately on health outcomes. This fourth strategy provides the necessary feedback to adjust future communication strategies.

FDA's communication approach must consistently factor in the technical complexity, uncertainty of information, urgency of decisions, different levels of scientific understanding and perceptions of risk.

Although FDA interacts with many different constituencies, the following illustrations identify planned FDA initiatives that target consumers. In each of these initiatives, FDA's four key strategies will be addressed.

Working With Other Federal Agencies to Clarify Consumer Information

FDA will take advantage of opportunities to work with other public sector agencies to build effective communication strategies. For example, FDA will:

- Partner with the Federal Trade Commission (FTC) to best determine how to improve the quality and impact of information disseminated through direct to consumer advertising and other communication forums;
- Work with the FTC to identify an efficient and reliable review process for new health claims on food products;
- Coordinate with the National Institutes of Health (NIH) regarding the development of "off patent" drugs for use in children, and negotiate labeling concerns with listed drug holders and if necessary identify product labels requiring appeal activity and present to the Advisory Subcommittee; and,
- Hold meetings with other federal agencies, including: FTC, CDC, EPA and NIH to design inter-agency communication approaches that will enhance the effectiveness of FDA consumer strategies.

Providing Timely Information on Product Recalls to Consumers

FDA is in the process of developing and implementing an internet-based Recall System (RES) that will allow both industry and consumers faster and more accurate access to information.

Performance Goal Highlights for FY 2004

FFDA is committed to improving the way information is shared between the Agency and its constituents. Beginning in FY 2004, goals will be developed to further strengthen the Agency's capability to provide more effective consumer information. FDA's existing goal in this area is:

- **Enhance the transparency of the National Antimicrobial Resistance Monitoring System (NARMS) program to stakeholders, the public, and other interested parties by increased reporting and communicating of NARMS results and program information.**

Current Status

Dietary Supplement Health and Education Act (DSHEA) - FDA is in the process of using a nationwide media campaign to inform consumers how to use new food and nutrition labeling. This initiative has three related actions: Issuing guidance on qualified health claims for conventional foods and dietary supplements; Strengthening enforcement of dietary supplement rules of 1994, Dietary Supplement Health and Education Act (DSHEA) and establishing an

FDA task force on Consumer Health Information for Better Nutrition. This task force will develop a framework to help consumers obtain accurate, up-to-date and science-based information about conventional food and dietary supplements.

Best Pharmaceuticals for Children Act (BPCA) - On January 4, 2002, Congress enacted the Best Pharmaceuticals for Children Act (BPCA), Public Law 107-109, to continue providing incentives for the effective development and dissemination of information on how to properly use therapies in children. One of FDA's roles following review of pediatric studies is to disseminate appropriate information to health care professionals.

Work With Other Public Sector Agencies - The Division of Federal-State Relations (DFSR) within the Office of Regulatory Affairs participates in cooperative and educational efforts designed to inform, interact with, and serves as the focal point for cooperating state and local officials, and associations of these state officials, to promote cohesive and uniform policies and activities in food and drug-related matters.

Highlights of FY 2001-2002 Accomplishments

To ensure successful public health outcomes, FDA leadership continued to encourage FDA programs to engage their stakeholders in formulating ways to accomplish the Agency's mission. FDA programs have been involved in various collaborations and initiatives. Some of these are provided below:

- Risk Management Communication and Education - FDA partnered with the National Association of Chain Drugstores and 80 national organizations to distribute million of copies of the brochure, "My Medicines," to women to educate themselves and their families about using medicines wisely.
- Targeted Collaboration on Critical Health Issues - FDA along with the National Institutes of Health, Centers for Disease Control and Prevention (CDC), American Red Cross, American Association of Blood Banks, and state agencies participate in setting standards and developing health education.
- Shared Surveillance Networks - FDA partnered with CDC and the U.S. Department of Agriculture to develop the National Antimicrobial Resistance Monitoring System. This system helps to detect whether foodborne pathogens are developing resistance to drug treatment.
- Cooperative International Standard Setting - FDA participated in the International Committee for Harmonization, International Standards Organization, Codex Alimentarius, and the World Health Organization to ensure that U.S. interests are upheld in establishing standards for products under the Agency's regulatory purview.

- FDA's web-site has received a Bronze Award in the "Health Promotion/Disease & Injury Prevention Information" category of the latest WWW Health Awards competition. This twice yearly contest is sponsored by the Health Information Resource Center, which holds the competition to provide "a seal of quality for electronic health information." A panel of health experts judge entries for content, format and overall quality.
- FDA's CDRH Division of Communication Media received the 2002 OMNI - BRONZE award for "Communication Skills for Regulators".
- FDA Conducted three laboratory research programs and performed the corresponding research in connection with the mission of Product Quality Research Institute (PQRI); Oral Biopharmaceutics, Drug Product, and Drug Substance.
- FDA issued and posted the Draft Guidance for Industry: *Inhalational Anthrax (Post-Exposure) - Developing Antimicrobial Drugs* (dated March 18, 2002).

Summary of Program Assessment Rating Tool (PART) Evaluation of FDA Centers

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The Office of Management and Budget (OMB) developed a program assessment process in preparation for the FY 2004 budget review. The program assessment flows from the Administration's efforts to link program performance with the budget process, and was seen in the FY 2003 President's Budget when it included explicit assessments of program performance. Twenty percent of all federal programs were selected for evaluation.

A common analytic tool, "*Program Assessment Rating Tool (PART)*," was created to develop information that would enable OMB to evaluate the effectiveness of Agency's programs and their budget request. The PART instrument examines the program purpose, strategic planning, program management, and program results.

OMB reviewed the five FDA programs: Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Medical Devices and Radiological Health. OMB's numerical scores for the five programs ranged from 54.8 to 58.9. While the five programs scored well on the program purpose section, OMB identified strategic planning, program management, and program results as areas for improvement. The results have enabled FDA to begin exploring various possibilities for developing long term outcome goals, examining potential program strategies and various mechanisms to achieve the goals, and strengthening the linkage between the budget and performance plan.

Based on feedback from the OMB on FDA's responses to the PART, FDA leadership has begun to explore the possibility of developing long term outcome goals in the areas of expanding national laboratory capacity; medical countermeasures; and, Bovine Spongiform Encephalophy (BSE). While these may not be the actual areas where FDA finally commits to positive long term outcomes, these areas are candidates being examined.

With the recent appointment of a new Commissioner, FDA leadership is developing a long-range strategic plan to formulate ways in which Agency activities can contribute to positive public health outcomes. These efforts include developing Agency and program strategies that will improve the likelihood that long-term outcomes will be achieved, identifying intermediate outcome measures which could serve as good leading indicators of ultimate health outcomes, identifying databases that will serve as valid and reliable sources of information in selected areas and, conducting analyses and

evaluations to strengthen our understanding of the relationship between FDA program efforts and intermediate and long term public health outcomes.

There is still much work to be done. The Agency strategies for pursuing these goals are included in FDA's FY 2004 Performance Plan submission to Congress.

Program Performance Report Summary

The following table provides summary information on FDA's Performance Goals from FY 1999 through FY 2004.

Year	Measures in Plan	Results Reported	Results Met	Unreported
1999	70	70	55	0
2000	60	60	54	0
2001	64	64	54	0
2002	67	53	49	14
2003	79	NA	NA	NA
2004	75	NA	NA	NA

Part 2: Performance Plan and Report

Introduction

Part 2: Performance Plan and Report presents new FY 2004 and updated FY 2003 performance goals, along with the final FY 2002 performance goals and an update on performance for some FY 2001 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 2001 results.

The following sections will be covered:

- ***Agency Wide -*** Ensures the Agency is streamlined for more cost-effective operations, establishes a strong emergency response capability in the event of terrorist attacks, and establishes global product safety and security.
- ***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 AGENCY-WIDE

2.1.1 Program Description, Context and Summary of Performance

Total Program Resources: *

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	116,360	107,675	94,086	80,126	78,120

* The resources in the Agency-Wide program section correspond to the Other Activities budget line, but it also includes several crosscutting goals with resources allocated across programs that are reflected as part of program resource totals.

Three strategic goal components are identified in the Agency-Wide Section of the Performance Plan. These goal components address: streamlining the Agency for more cost-effective operations; establishing a strong emergency response capability in the event of terrorist attacks; and establishing global product safety and security. These three strategic goal components are labeled as such because they are critical elements of two broad Agency strategic goals described in Part One of the Plan [see table below].

Agency Strategic Plans	Strategic Goal Components
Improved Agency Management	Streamline FDA
Homeland Security	Emergency Preparedness & Response Global Product Safety & Security

These particular strategic goal components have been selected for discussion in this section because they set the context for unique performance goals that have agency-wide relevance.

2.1.2 Strategic Goal Components

Strategic Goal Component 1:
Streamline FDA operations to make it a more cost-effective and citizen-centered Agency.

A. Strategic Goal Explanation

FDA's Administrative Management Goals are aligned with the President's Management Agenda to modernize all Executive Branch agencies so that they are more efficient and responsive to the needs of the American Public. This will also align FDA goals with the Department's "One HHS" philosophy. These performance goals outlined below will help the Agency produce quality services in the most cost effective manner possible. This should lead to improvement in the way Agency programs serve the needs of the American Public.

Outlined below are five performance goals that focus on: reducing unnecessary reporting levels in the organization; 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; improved financial management and maintaining the highest possible financial audit levels attainable. The performance goals listed below will help FDA provide more effective and efficient services to the public and regulated industry and will help the Programs accomplish their performance goals.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Reduce the number of review levels in the Agency to help streamline operations. (19001)	FY 04: ORA to be completed by the end of 1st quarter. Accomplishment summary due to HHS by January 2004. FY 03: Develop and implement a plan to delayer CBER, CFSAN, CDRH, OC and ORA. FY 02: Develop and implement a plan to delayer NCTR, and CVM.	FY 04: FY 03: FY 02: Developed and implemented a plan to de-layer NCTR, CVM and OC.	Strategic Management of Human Capital Efficiancy Goal
2. Implement 'shared services' concept	FY 04: Implement the	FY 04:	Strategic Management of

and consolidate selected functions in the agency. (19002)	Shared Service organization for those functional areas transferred to the organization. FY 03: Begin implementation of shared services concept in accordance with the BAH Administrative Consolidation Study. FY 02: Award contract of administrative functions to be completed by September 2002 with the Human Resources portion completed by May 2002. FY 01: NA	FY 03: FY 02: Completed Agency-wide assessment of administrative services. FY 01: Merged Management Initiatives Staff and Evaluation Staff within the Office of Planning FY 00: Abolished three OC Offices: OEA/IO, ISCAS, and OHA.	Human Capital Efficiancy Goal
3. Increase the percentage of Commercial FTE that will be reviewed for outsourcing.(19003)	FY 04: 10% or 146 FTE FY 03: 10% or 145.7 FTE FY 02: 5% or 72.7 FTE	FY 04: FY 03: FY 02: 4% or 57.7 FTE	Competitive Sourcing Efficiancy Goal
4. Increase the percentage of electronically purchased transactions.* (19004)	FY 04: 92% FY 03: 91% FY 02: 89% FY 01: 87%	FY 04: FY 03: FY 02: 93.5% FY 01: 90.5% FY 00: 93.6% FY 99: 93.5%	Expanded ElectronicGovernment Efficiancy Goal

5. Maintain a clean (or unqualified) audit opinion with no material weakness. (19005)	FY 04: Yes FY 03: Yes FY 02: Yes FY 01: Yes	FY 04: FY 03: FY 02: Yes FY 01: Yes FY 00: Yes FY 99: Yes	Improved Financial Management Efficiancy Goal
6. Increase percentage of contract dollars allocated to performance based contracts (19006)	FY 04: 40% FY 03: 30% FY 02: 25%	FY 04: FY 03: FY 02: 25.5% FY 01: 23.6%	Budget & Performance Integration Efficiancy Goal
7. Establish an Agency-wide Enterprise Architecture (EA). (19009)	FY 04: Complete next phase (i.e., critical business and data process that is next in line in priority) of the EA, leveraging outcome of EA developed for CT, Administrative and PDUFA business processes. FY 03: Complete EA for identified CT and PDUFA business purposes; implement Agency-wide EA governance. FY 02: Obtain FDA leadership buy-in; award contract for EA development support; initiate the	FY 04: FY 03: FY 02: Completed all goals	Expanded Electronic Government Efficiancy Goal

	establishment of an EA framework.		
8. Expand the Agency-wide IT security program to ensure all of Agency's IT assets that support the Agency's business processes are in compliance with the Government Information Security Reform Act (GISRA). (19010)	FY 04: Continue to ensure 100% compliance of the FDA IT infrastructure and assess the next third of the major systems for GISRA compliance, and perform appropriate risk mitigation. FY 03: FDA is expected to assess 100% of the FDA IT infrastructure and one third of the major systems for GISRA compliance and provide any needed corrections. FY 02: NA	FY 04: FY 03: FY 02: 100% - The FDA performed comprehensive assessments of OC and NCTR, as well as GISRA compliance reviews of selected major applications and critical IT services	Expanded Electronic Government Efficiancy Goal
9. Implement Financial Enterprise Solutions, FDA's version of UFMS. (19017)	FY 04: Complete systems preparation to implement Financial Enterprise Solutions starting with General Ledger, payroll, Travel Manager FY 03: Begin data cleanup	FY 04: FY 03: FY 02: 100% - The FDA performed comprehensive assessments of OC and NCTR, as well	Improved Financial Management Efficiancy Goal

	and preparation for conversion of existing systems to new financial system FY 02: Prepare for consolidation of accounting operations in the ORA regions reducing the number of payment centers from 15 to 1; standardize on financial system use throughout FDA for accounts payable and Travel.	as GISRA compliance reviews of selected major applications and critical IT services	
TOTAL FUNDING:* ($ 000)	FY 04: 116,360 FY 03: 104,752 FY 02: 94,086 FY 01: 80,126 FY 00: 78,120	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

* These goals are crosscutting goals with resources allocated across programs that are reflected as part of program resource totals.

C. Goal-By-Goal Presentation of Performance

1. Reduce the number of review levels in the Agency to help streamline operations. (19001)

Context of Goal: FDA is striving to reduce the number of review levels for decision making within the Agency to no greater than four, which is consistent with the President's management initiatives and Departmental guidelines. The wording of this goal has therefore been revised so that the goal is linked to the department consolidation initiative. Reduction of review levels will allow for a more effective structure and a streamlined organization, as well as increase the span of control to some extent for managers across the Agency. There are, however, limits to span of control ratios at FDA. This is because FDA is a

knowledge-based organization, which utilizes complex scientific systems and oversees research activities. 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.
Performance: As of October 2002, the Center for Veterinary Medicine, the National Center for Toxicological Research, and the Office of the Commissioner have eliminated organizational components below the fourth management level. Additionally, in FY 2002, FDA has consolidated from seven Personnel Offices to one and FDA has completed the review for the Center for Devices & Radiological Health. The Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Food Safety and Applied Nutrition are scheduled to be completed by the end of FY 2003. ORA is scheduled for review during the first quarter 2004.
Data Sources: FDA Organizational charts, personnel databases, and functional matter experts.

2. Implement shared services concept and consolidate selected functions in the Agency. (19002)

Context of Goal: FDA is aligning itself with departmental guidelines for the consolidation of selected 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 selected 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. By the end of FY 2002, an assessment of administrative services was completed and preliminary recommendations for organizational structure were made. In FY 2003, detailed process design and organizational design work will be done to ensure the shared services organization is positioned to provide the highest level of service to customers in the most efficient way. Targeted date for "stand up" of the shared services organization is October 1, 2003 (FY 2004). The Shared Services Organization will be a customer-focused organization in which business units establish service priorities and services will be tailored to meet the individual needs of business units. Service level agreements will be drawn between administrative service providers and customers [business units]. Business units will be defined as the various FDA programs- e.g., Foods, Human Drugs, Animal Drugs and Feeds, etc. The shared service organization will be governed by a group which will include representatives of both providers and customers. In FY 2003, the governance infrastructure will be put into place to facilitate the migration from current organizational structure and service delivery methods to the shared services model of service provision. Performance will be monitored against 'best practices' in internal and external organizations. The shared services model will help FDA to focus on its 'core business', create satisfied customers and employees; leverage technology and

information; and more effectively manage costs. The 'shared services' initiative is considered as a complementary strategy to administrative consolidation. Together, the two strategies should lead to a more effective organization which is guided by unified policies, implements cost-effective processes and provides customer-responsive services.

- **FY 2004:** Refine cost structures and service level agreements under shared service organization.
- **FY 2003:** Consolidate the following administrative management functions:
  - Personnel
  - Procurement
  - Facilities
  - Grants
  - Information Technology
- **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

Performance: FDA completed an Agency-wide assessment of administrative services to prepare for implementation of the shared services initiative. 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 met its FY 2003 schedule to eliminate all targeted positions except the Principal Deputy Commissioner, as the Deputy Commissioner for International and Constituent Relations retired in September 2001. FDA is currently taking steps to consolidate certain administrative functions within the Agency by FY 2003.
Data Sources: FY 2001 FDA Workforce Restructuring Plan

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

Context of Goal: FDA has contracted for many of its commercial requirements and will continue to contract commercial work and identify in-house activities for competitive sourcing. In FY 2002, FDA studied the following commercial activities: graphic arts/visual information services, medical/scientific library services, web publishing, and a television studio in the Center for Devices and Radiological Health. These activities represent 5% of FDA's commercial FTEs on our 2001 FAIR Act Inventory. In FY 2003 FDA will study the following activities, representing an additional 10 percent of the agency's commercial FTEs: general accounting in the Office of Regulatory Affairs field components, biological technician and physical science technician services, and facilities/real property management services. We estimate that our FY 2004

target for competitive sourcing will be at least 10%. The total amount of positions studied will reach a total of 25% by the end of FY 2004.
Performance: FDA studied 4% or 57.7 commercial FTEs for outsourcing in FY 2002. FDA originally planned to study its web design and development activities, which included approximately 46 FTEs. However, due to the HHS and FDA IT consolidation, FDA decided to postpone a study of web design and development and instead, to directly convert the small amount of web publishing work that is not contracted out, approximately 3 FTEs. The agency expects to have approximately 36 contractible FTEs from the web design and development study. FDA also expects 57.8 contractible FTEs from our FY 2002 studies, instead of 76. FDA's FY 2003 studies will yield 167.4 contractible FTEs, which will result in achieving our 15% competitive sourcing goal by September 2003.
Data Sources: FDA Office of Management & Systems, 2001 FAIR Act InventoryIncrease the percentage of electronically purchased transactions.

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.
Performance: Ninety-three percent of eligible transactions were purchased electronically in FY 2002. FDA expects this figure to grow and also expects to exceed the departmental targets given to FDA. The Agency is conscientiously seeking to use the IMPAC Card instead of a purchase order for buying items under $2,500. By using the IMPAC Card, the Agency lowers the $90.00 overhead cost for each purchase. This then has led to the Agency exceeding its goal for FY 2002 as expected.
Data Sources: FDA Small Purchase System, statements from bank card company

5. Maintain a clean (or 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 not timely provided. Since then, FDA has managed to progressively perform at a higher level.
Performance: FY 2002 Performance is at 100 percent. Since FY 1997, the performance has steadily improved due to FDA taking many corrective actions, including establishing a branch organized in FY 2000 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 2001. 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 to develop and implement 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 Financial Business solutions will lead to improvements.
Data Sources: Fiscal Year 2001 FDA Chief Financial Officer's Annual Report.

6. Increase percentage of contract dollars allocated to performance based contracts. (19006)

Context of Goal: FDA is aligning itself with Departmental and OMB goals of awarding 20 percent of eligible contract dollars to firms using performance based contracts by FY 2002. This increase will lead to greater accountability of services provided by contractors, and increased efficiency. FDA exceeded the 20 percent target set by OMB in FY 2001 and set, more ambitious targets each subsequent year. It should also be noted that not all contract dollars will be eligible for this initiative.
Performance: Twenty-five percent of eligible contract dollars were awarded as performance based contracts during FY 2002, significantly exceeding the Department's goal. 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.
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.

7. Establish an Agency-wide Enterprise Architecture (EA). (19009)

Context of Goal: Clinger-Cohen, the President's Management Agenda, the Department's policy of "One HHS" and PDUFA III are the mandates driving the Agency towards the establishment of an EA. In addition, the EA is a major piece of the Agency's overall strategy in support of the CT program: it will provide the framework on which data can be standardized and integrated to enable real time access of information crucial to the CT effort.
Performance: For FY 02, $5 million has been allocated for the development of an Agency-wide Registration System. This will be accomplished through the development of an EA as a first step, with associated CT business processes receiving priority. A contract is expected to be awarded and work initiated in FY 02. For FY 03, it is expected that the EA will be completed for those CT processes, although the impact of the new Foods Registrations system that has been approved as part of the CT bill has not been determined.
Data Sources: EA Strategic Plan and Project Plan; progress reports to HHS, OMB and industry (PDUFA status reports)

8. Expand the Agency-wide IT security program to ensure all of Agency's IT assets that support the Agency's business processes are in compliance with the Government Information Security Reform Act (GISRA). (19010)

Context of Goal: GISRA has set requirements for Agency's to identify their key IT assets, assess them for security vulnerability and address any findings. Security is also part of the Department's overall IT Security program. As a result, the Agency is centralizing the security program to ensure security efforts are performed in a uniform and consistent manner, while at the same time leveraging efficiencies (bulk buys, Agency-wide contracts, etc.) that are only possible with Agency-wide scope.
Performance: In FY 01, the GISRA assessment identified vulnerabilities that were partly the result of inconsistent interpretation and application of security policies across the Agency. In FY 02, FDA assessed OC, NCTR and selected other critical components for GISRA compliance and resolved any access control issues. In FY 03, FDA is expected to assess 100% of the IT infrastructure and one third of the major systems for GISRA compliance and

provide any needed corrections.
Data Sources: Annual GISRA assessment and report

9. Implement Financial Enterprise Solutions, FDA's version of UFMS. (19017)

Context of Goal: FDA is complying with the department's goal to establish a unified financial management system. Specifically, the Department plans to utilize two accounting systems: one for the Center for Medicare and Medicaid Services (CMS), formerly the Health Care Financing Administration, and one serving the National Institute of Health (NIH), the Program Support Center (PSC) and its eight servicing OPDIVs, the Center for Disease Control and Prevention (CDC) and FDA. FDA will use the FY 2004 increase to complete the preparation to implement the general ledger and accounts payable systems. The goal of the UFMS project is to reduce costs, mitigate security risks, and provide timely and accurate information across DHHS. FDA will acquire and implement a new core financial management system as part of the UFMS project in FY 2005. Implementing a new financial system will provide qualitative and quantitative benefits to FDA because it will achieve improved business processes and provide more accurate and timely information to better support FDA's and DHHS' mission.
Performance: FDA has begun setting up the implementation team for Financial Enterprise Solutions, FDA's name for the Unified Financial Management system.
Data Sources: The sources are encompassed in the General Ledger & Federal Administrator, the Purchasing & Accounts Payable; and the Accounts Receivable. These sources are being prepared to transition to the Financial Business solutions system.

Strategic Goal Component 2:
Enhance the Agency's emergency preparedness and response capabilities in the event of a terrorist attack.

A. Strategic Goal Explanation

This strategic goal represents one of four key goals contained in FDA's strategic and action plans for Counterterrorism. The other three goals in the Agency's Counterterrorism Plan address: deterring, detecting, investigating and interdicting terrorist threats; assuring the availability of medical counter measures; and ensuring the safety of radiological products used in terrorist scenarios.

The emergency preparedness and response goal was singled out for discussion in this Agency-wide section of the Performance Plan because the subject matter has immediate relevance throughout all organizational components. Emergency preparedness, in particular requires a centralized

focus because a well-conceived and unified response to outside threats is crucial for success. FDA's emergency preparedness and response capability will help the Agency respond effectively to a wide range of terrorism-related emergencies. Key strategies necessary to achieve this goal include:

- **Preparing an Agency-wide emergency preparedness and response plan** which can serve as a general blueprint for action. The Agency Plan includes general protocols such as roles to be played by different agency and outside actors, criteria for escalating responses to terrorist crises, general procedures for accessing needed medical products, and approaches to securing human and physical assets. Specific emergency plans to respond to particular incidents can be patterned after the general Agency plan. (Performance Goal # 10) Within this Performance Plan additional performance goals have been formulated to develop emergency preparedness plans that respond to specific types of crises. See Goal # 15 in the Human Drugs Section; and Goal # 13 in the Medical Device and Radiological Health Section. Within individual program sections of the Performance Plan
- **Developing an emergency operations network** which links people and information necessary to make crucial command decisions in the event of a terrorist attack. The emergency operations network requires both the organizational and information infrastructures to work in an integrated fashion in order to be effective. (Performance Goal # 12)
- E**stablishing an emergency laboratory response network** that can quickly and accurately share analytical results of pathogen or hazard testing between federal and state laboratories. A critical component of this network is the electronic exchange network (eLEXNET), which will allow at least 79 federal and state laboratories to be contributing analytical data to the system by FY 2004. (Performance Goal # 13); and
- **Establishing continuity-of-operations plans** that will allow FDA to continue critical operations in the event of an attack on the Agency and its assets. These contingency plans will provide for continuity and dependability of operations as it relates to Agency leadership, essential program activities, protection of information and physical assets, and maintaining a capability to run the emergency operations system at an offsite location.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference

10. Expand federal/state/local involvement in FDA's eLEXNET system by having 79 laboratories participate in the system. (19003)	FY 04: Expand federal/state/local involvement in FDA's eLEXNET system by having 79 laboratories participate in the system. FY 03: 54 laboratories participating in eLEXNET FY 02: NA	FY 04: FY 03: FY 02: 51 laboratories participating in eLEXNET FY 01: 14 laboratories participating in eLEXNET	2 Outcome Goal
11. Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks. (19008)	FY 04: NA FY 03: Radiological Emergency Response Plan and the Chemical and Biological Emergency Response Plan will be reissued FY 02: Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks.	FY 04: FY 03: FY 02: Radiological Emergency Response Plan, issued March 2002 (draft 1), currently being redrafted based on comments received and exercises conducted. Chemical and Biological Emergency Response Plan, issued June 4, 2002 (draft 1), currently being redrafted based on comments received and bioterrorism exercises conducted in FY 02.	2

12. 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: NA	FY 03: NA FY 02: Developed and Implemented Agency Continuity of operations Plan; Participated with PSC to develop COOP. FY 01: NA	2
TOTAL FUNDING:* ($ 000)	FY 04: FY 03: FY 02: FY 01: FY 00:	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

* These goals are crosscutting goals with resources allocated across programs that are reflected as part of program resource totals.

C. Goal-By-Goal Presentation of Performance

10. Expand federal/state/local involvement in FDA's eLEXNET system by having 79 laboratories participate in the system. (19013)

Context of Goal: The electronic Laboratory Exchange Network (eLEXNET) is a seamless, integrated, secure network that allows multiple agencies (Federal,state and local health laboratories on a voluntary basis) engaged in food safety activities to compare, communicate, and coordinate findings of laboratory analyses. eLEXNET enables health officials to assess risks, analyze trends and provides the necessary infrastructure for an early-warning system that identifies potentially hazardous foods. The eLEXNET System plays a crucial role in the Nation's Food Safety laboratory system, and it is an integral component of the Nation's overall public health laboratory information system. That system encompasses CDC's Laboratory Response Network, and FDA's Food Emergency Response Network, which is a collaborative activity among FDA, CDC and FSIS.
FDA is developing eLEXNET as a key component of a total food laboratory response network that is intended, ultimately, to cover foods, drugs and biological products; and have the capability to test for the presence of biological, chemical, radiological and physical hazards. The larger network, which is patterned after CDC's laboratory response network, encompasses

several collateral functions that complement data exchange proficiency levels in sample analysis and testing.

The difference in the systems is that CDC collects human samples, while FDA collects product samples. FDA patterns its system after some of the principles used by CDC. These include:

- A workload management system which matches the flow of laboratory samples with the capacity of the laboratories that participate in the network;
- A protocol which provides for 'proficiency testing' of all samples that are included in the network;
- A system for ensuring the availability and quality of reagents used in laboratory analysis;
- A system for encouraging the development of new methods which are necessary to assess risks in anomalous or novel situations; and
- A rigorous training initiative to ensure that all analysts are at high

Performance:eLEXNET was released as a proof-of-concept system in FY 2001 to 14 laboratories (7 regional FDA, one regional USDA, and 6 state and local agriculture and public health laboratories). The system has expanded to include new laboratory partners in FY 2002, and by September 30, 2002, a total of 51 laboratories are actively submitting data to eLEXNET. The eLEXNET partnership will expand to include at least 54 laboratories submitting data to the system at the end of FY 2003. An additional 25 laboratories will be submitting data to the system by the end of FY 2004.
Data Sources: ORA will track the number of participating eLEXNET laboratories.

11. Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks.(19008)

Context of Goal: The Agency Emergency Preparedness Plan establishes an overall blueprint for FDA to follow in the event of a terrorist incident. The Plan is sufficiently generalized so that it can be tailored by individual Agency Programs to meet the needs of particular categories of events, including biological, chemical, physical or nuclear threats. 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.
Performance: This goal is new for FY 2004. The Radiological Emergency Response Plan, issued March 2002 (draft 1), is currently being redrafted based on comments received and exercises conducted. The Chemical and Biological

Emergency Response Plan, issued June 4, 2002 (draft 1), is currently being redrafted based on comments received and bioterrorism exercises conducted in FY 02. CFSAN contracted for a "Food and Cosmetics Chemical, Biological, and Radiological Threat Assessment," document which addresses the more specific issues of potential agents that may affect FDA products.
Data Sources: Office of Emergency Operations.

12. Assure continuity of FDA operations in case of an emergency.(19007)

Context of Goal: In light of the September 11, 2001 events, the Agency decided to develop a Continuity of Operations Plan (COOP) to assure the continuance of minimum essential functions across a wide range of potential emergencies. Executive Order 12656, Presidential Decision Directive 67 and Federal Preparedness Circular 65 reinforce this objective.
Performance: In FY 2002, FDA participated with PSC to develop a COOP Plan for the Parklawn Building. In addition, the FDA let a contract to develop a Continuity of Operations Plan for the Washington DC area offices (Phase I) and for FDA Regional and District Field Offices (Phase II). The COOP plans will be reviewed and enhanced regularly.
Data Sources: Office of Crisis Management, Security Operations, Policy and Planning

Strategic Goal Component 3:
Establish a system of global product safety and security that will assure the safety of FDA-regulated products regardless of their point of origin, pathway or final destination.

A. Strategic Goal Explanation

There is consensus that FDA can no longer just look at products as they cross the border but rather that we must hold the foreign manufacturer and importer responsible for the safety and efficacy of their products. To do this we must look at products from point of production, through shipment to the U.S., at the border, and through to the U.S. manufacturer and/or ultimate consumer. This expanded import life cycle is essential to successfully protecting domestic commerce from unsafe imported products. FDA is developing an Import Strategic Plan to reinvent the import process.

The reinvention process will focus on the extended life cycle of an import. While the Agency currently does some foreign inspections, engages in some education efforts, and participates in international agreements, our ability to ensure that production controls are in place for imported goods is limited. For the most part, FDA's current review of imported goods - the life cycle -- starts with the shipper and ends with the Customs broker or importer.

In order to protect the public from unsafe imports, the Agency must extend the life cycle. This means understanding what is happening with the product beginning with the raw materials, through the foreign manufacturers, carriers, and shippers, past the broker and importer, and all the way through to the distributor, consignee, domestic manufacturer (in the case of unfinished product), retail and to the ultimate consumer. The Agency must identify what data exist all along the extended life cycle of an imported product that signal the appearance of a processing problem and integrate those data for use in the entry review process.

The three goals below are designed to develop risk assessment and control strategies for imported products at FDA's traditional focal point entry across the border. These goals address the data integrity of the automated system that is used for initial screening of import entries and delves into various features of trade practices including the monitoring of goods refused in cooperation with the U.S. Customs Service.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
13. Perform 48,000 physical exams and conduct sample analyses on products with suspect histories. (19014 - this goal is repeated as number 11036 in the Foods Section)	FY 04: 48,000 exams FY 03: Increase exams by 100 % to 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 04: FY 03: FY 02: Hired 800 new investigators and analysts hired; 34,447 physical exams conducted. FY 01: 12,169	2
14. Perform at	FY 04: Perform	FY 04:	2

least 1,000 Filer Evaluations under new procedures. (19015)	at least 1,000 Filer Evaluations under new procedures. FY 03: NA FY 02: NA	FY 03: FY 02:	
15. Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported. (19016)	FY 04: Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported. FY 03: NA FY 02: NA	FY 04: FY 03: FY 02:	2
TOTAL FUNDING:[*] ($ 000)	FY 04: FY 03: FY 02: FY 01: FY 00:	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

[*] These goals are crosscutting goals with resources allocated across programs that are reflected as part of program resource totals.

C. Goal-By-Goal Presentation of Performance

13. Perform 48,000 physical exams and conduct sample analyses on products with suspect histories. (19014 - this goal is repeated as number 11036 in the Foods Section)

Context of Goal: In FY 2004 FDA will focus much of its resources on examination and follow-up on import shipments that pose the highest potential risks. Increases in the number of physical examinations will not continue to grow at the rate expected in FY 2002 and 2003. Given the continuing explosion in number of import shipments to this Country, it is not realistic to expect that FDA can keep up with the volume by simply expanding the number of physical examinations. Rather, a significant effort will be launched to develop the appropriate knowledge-based approaches that will give the Agency assurance that it is, in fact, addressing the most serious risks. Finding these risks is a great challenge considering that FDA-regulated imports have grown at 10 to 12% annual rate for several years, and may originate in any of more than 100

countries, many of which have regulatory systems in place which are much more primitive than that found in the U.S. The risk has now been exacerbated in light of security concerns raised by terrorism and counterfeiting incidents. During FY 2003 FDA will develop a more robust physical examination approach that merges the assessment of information integrity with the safety and security of the product. By FY 2004 FDA will have in place a new version of the import field exam. The new exam will routinely include: verification that the imported product is the same as that which was declared; assessment of security concerns related to labeling and source country; and traditional safety concerns. More importantly, these new exams will be conducted on import entries selected using a more rigorous risk assessment and management rubric. FDA will be developing during FY 2003 the criteria and, to the extend possible, the computer systems to be able to better identify, obtain, process, assimilate, and deliver data relating to an imported product's safety and security. This data will be delivered in a more meaningful and timely fashion to the primary decision makers in FDA's import process located at the borders and throughout the country monitoring imports electronically through OASIS. During FY 2003 FDA will pilot various features to develop a feasible implementation process, and to develop better time estimates so that appropriate resources can be matched with the revised approach. FDA will use a risk-based system to target suspect problem areas. Such areas may include:

- Filer Evaluation Field Audits;
- Pilot with filer evaluation, importer/trader inspections;
- Warehouse blitz programs;
- Transshipment-targeted field examinations;
- Sample collection and analysis for Counterterrorism;
- Implementation of program with Canada and Mexico to enhance advanced identification of transshipped cargo; and
- Expand in-bond entry evaluation including performing examinations of in-bond entries at port of arrival and port of entry or export.

During FY 2003 FDA will gather information about the number and characteristics of these potential targets so that by FY 2004 pilot programs can be identified with enough examination of each type so that practices can be revised again in subsequent years to reflect lessons learned. FDA anticipates that the measures that it uses to assess its success in monitoring the safety and security of imported products will continuously evolve as trade practices and information about risks change. During FY 2003 FDA will also decide on the appropriate methods including summary categories, if appropriate, that are best suited to track various components of this goal. Additional risk based candidates may be identified that will require further pilot studies in FY05 and later.

Performance: This goal was new for FY 2002 and FY 2003. The FY 2002 performance was 800 new investigators and analysts hired and 34,447 physical exams conducted. The FY 2001 baseline was 12,169 physical exams.

The FY 2002 goal targets 24,000 exams that target doubles to 48,000 in FY 2003. The FY 2004 goal remains at 48,000 because resources will be devoted to targeting and following through on suspect import entries rather than significantly expanding import coverage.
Data Sources: Field Data Systems

14. Perform at least 1,000 Filer Evaluations under new procedures. (19015)

Context of Goal: Food and Drug Administration (FDA) receives electronic import entry data for assessing the admissibility of regulated imported articles. The accuracy of these data directly relates to the level of confidence that American consumers can expect in the quality, safety and compliance of imported articles subject to FDA's jurisdiction. Entry data affects FDA's determination of the labeling, quality, safety, approval status and efficacy of FDA-regulated import articles.
FDA maintains an electronic interface with the United States Customs Service's (Customs) Automated Commercial System (ACS). After successfully completing an initial evaluation for participation in OASIS, filers may submit import data electronically to FDA through the Automated Broker Interface (ABI) and ACS. FDA uses an electronic entry screening system, Operational and Administrative System for Import Support (OASIS), to screen entry data transmitted by filers to perform various regulatory and service functions. Such screening may assess whether FDA import personnel should review an entry further. The FDA uses OASIS to determine whether an entry should be reviewed 'on screen,' further supported by entry documentation, physically inspected, sampled, or permitted to proceed into domestic commerce without further evaluation. FDA can use the data in the entry system to track an imported item that negatively affected the public health.
At a minimum, this updated procedure requires filers who fail an evaluation to implement an FDA-approved Corrective Action Plan (CAP) and to pass a tightened evaluation (more stringent criteria) before obtaining, maintaining or regaining the privilege of paperless filing. This protects public health by insuring quality improvement and reporting compliance for imported articles that FDA regulates. It also ensures FDA is notified when articles appear to be violative that have previously been offered for entry.
During FY 2003 ORA will continue to develop the policies and practices that will govern the implementation of a new version of the filer evaluation. The new filer evaluation will issue pilot testing assignments that are designed to refine practices and assess the amount of time that will be required to perform these evaluations. During this time FDA will develop a risk based stratification plan to determine the frequency of filer evaluations. During FY 2003 it is anticipated that FDA will develop, at minimum, an interim way to track filer evaluations with plans and a timeline to fully integrate the collection of data on this activity into field data systems.
Performance: This goal is new for FY 2004. There is no baseline data

because the Field data systems do not capture this activity in FY 2002. Filer evaluations will be substantially modified for FY 2004 to reflect increasing needs to assess data integrity.
Data Sources: Field Data Systems

15. Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported. (19016)

Context of Goal: In FY 2001 FDA refused about 18,000 products offered for import entry into the U.S. Because of safety and security concerns it is important for FDA to be sure that these goods do not slip into domestic commerce but are in fact sent out of the country. FDA monitors this activity in conjunction with Customs in a category of action described as follow up to refusals. If a product is refused admission, it must be destroyed or exported under Customs' supervision within 90 days of receiving the Notice of Refusal, or within such additional time as specified by Customs. FDA is responsible for the protection of the U.S. public regarding foods, drugs, devices, electronic products and cosmetics, and that responsibility exists until the violative article is either destroyed or exported. Although primary responsibility for supervising destruction or exportation rests with U.S. Customs, FDA monitors the disposition of refused shipments and maintains an open file until the product is exported is exported or destroyed. In cooperation with Customs, FDA will, at times, supervise destruction or examine products prior to export in order to ensure that the refused product is actually exported. In other cases FDA relies on notification from Customs that the refused product has been destroyed or exported. During FY 2003 will continue to develop the policies and practices that will govern the monitoring of the export of refused goods, issue pilot assignments that are designed to refine practices and assess the amount of time that will be required to perform these evaluations. During FY 2003 it is anticipated that FDA will develop, at minimum, an interim way to count these events with plans and a timeline to fully integrate the collection of data on the export of refused entries into field data systems.
Performance: This goal is new for FY 2004. There is no baseline data because the Field data systems do not capture this activity in FY 2002. As of May 2002 FDA estimates that it has performed 800 similar exams.
Data Sources: Field Data Systems

2.2 FOODS

2.1.1 Program Description, Context and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	413,208	412,097	393,256	287,504	279,704

The FDA's Foods Program is responsible for ensuring a safe, nutritious, wholesome, 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 safety 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.

Current 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; and,
- The dietary supplements industry has grown dramatically, as has consumption of dietary supplements.

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

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

- **Provide consumers quicker access to new food ingredients, 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, providing information for sound nutrition choices, and correcting problems that are identified.**

By striving toward these two goals, FDA will assure the safety and 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 Goal Components

Strategic Goal Component 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 FDA has proposed a mandatory premarket notification program for these foods.

The Food Program's key challenge in the premarket area is to expeditiously review 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 4-11034)
- 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 review and action on the safety evaluation of 75% of food and color additive petitions within 360 days of receipt. (11001)	FY 04: 75% FY 03: 65% FY 02: 60% FY 01: 50% FY 00: 40% FY 99: 30%	FY 04: FY 03: FY 02: 10/03 FY 01: 70% of 10 FY 00: 91% of 99 FY 99: 77% of 50	4
2. Respond to 95% of notifications for dietary supplements	FY 04: 95% FY 03: 95% FY 02: 95% FY 01: 90%	FY 04: FY 03: FY 02: 99% of 44	4

containing "new dietary ingredients" within 75 days. (11025)	FY 00: 90% FY 99: NA	FY 01: 100% of 22 FY 00: 100% of 25 FY 99: 100% of 23	
3. Complete processing of 80% of GRAS notifications within 180 days. (11003)	FY 04: NA FY 03: NA FY 02: NA FY 01: 80% 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 04: FY 03: FY 02: NA FY 01: roughly 80% of 27 FY 00: made progress toward finalizing GRAS rule FY 99: rule not completed, no measurement	4
4. Review 95% of premarket notifications for food contact substances within the statutory time limit (120 days). (11034)	FY 04: 95% FY 03: 95% FY 02: 95% FY 01: NA FY 00: NA	FY 04: FY 03: FY 02: 100% of 70 FY 01: 100% of 82 FY 00: 99% of 83	4
TOTAL FUNDING: ($ 000)	FY 04: 40,296 FY 03: 42,474 FY 02: 43,260 FY 01: 39,850 FY 00: 39,661	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

1. Complete review and action on the safety evaluation of 75% of food and color additive petitions within 360 days of receipt. (11001)

Context of Goal: In this goal, performance is defined in terms of a review of all parts of a petition. This review would be followed by issuance of a "not approvable" letter, or by publication of a response in the Federal Register, if appropriate.

This goal refers to completion of the safety evaluation of food and color additive petitions. This includes a review of the information in a filed petition, and one of two conclusions reached: either the petition does not support the requested action and a letter to that effect is transmitted to the petitioner with an explanation of why we reached the conclusion; or based on the review, we are prepared to recommend to the agency officials authorized to sign an order, that the use of the additive be approved (or denied), and communication of this information to the petitioner. It does not include the time to get the order and accompanying rationale for our decision reviewed, signed, and published in the Federal Register.

Almost uniquely among products FDA regulates, food and color additives are not permitted to be marketed by means of correspondence from the agency to the petitioner (except in the case of food additives that are food contact substances, see below). Rather, the statute provides that the agency must, using formal rulemaking, publish in the Federal Register an order laying out the conditions by which anyone (not just the petitioner) may use a food or color additive, or an order denying the request to use a food or color additive, with an explanation in each case of how we came to our conclusions. (Alternatively, a petitioner may choose to withdraw a petition. In that case, the Agency publishes a notice of the withdrawal in the Federal Register). The law also provides a variety of administrative remedies to those who object to FDA's order to permit, or deny, use of a food or color additive, these include stays and administrative hearings. (For example, in the case of a color additive order, any objection automatically stays the regulation). Although objections are not routine, when they occur, they necessitate further "action" on the part of the agency. However, we, and our stakeholders, have considered publication of an order in the Federal Register as "final action".

We have used the time to complete the evaluation of a petition as the goal because it is relatively unambiguous and measurable. It is also the part of the entire process that is most within the control of the organizations responsible for administering the food and color additive petition review process, and thus most amenable to improvement by those organizations. Publishing an order in the Federal Register is subject to factors outside the agency's control. (For example, the statute requires public notice of filing of food and color additive petitions; comments to such filing, which must be reviewed and possibly responded to, may be submitted at any time prior to publication.) Completion of the safety evaluation is also the step that is most analogous to final action in the case of the dietary supplement and food contact substance premarket review processes. Because stakeholders are most interested in publication of a final order, we recognize the need to make all involved parties accountable for reducing the total time to publication as much as possible.

The 360-day time frame used in this goal is not the same as 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 a report from a June 1995 House hearing and FDA recommended a change from the statutory time frame to '360 days of receipt' in a testimony before the House Committee on Government Reform and Oversight in 1996.
Subsequently, the Food and Drug Administration Modernization Act (FDAMA) established a notification process for food contact substances. The premarket notification program began to operate fully on January 18, 2000. 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 anticipated that performance on this goal could decline initially. Once the notification and the recent improvements to the petition review process are well established, FDA expects performance on this goal to increase substantially toward full performance in succeeding years.
Performance: In FY 2000, FDA exceeded its goal of completing the review of 40%, 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 than in previous years. Those that we do receive are for direct food additive uses of greater potential public health significance, which generally 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 conducted 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% of food and color additive petitions in 360 days for the 2003 receipt cohort is a fair and challenging level of performance. For the petition receipt cohort of FY 2001, completed the safety evaluation in less than 360 days for 7 out of 10 (70%) food and color additive petitions that do not qualify for expedited review. This meets our goal to complete 60% of these petitions within 360 days.
Data Sources: CFSAN's electronic workflow system

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

Context of Goal: FDA reviews premarket notifications for new dietary ingredients (NDI) of dietary supplements. Once the notification is received it is

reviewed for completeness and justification of safety. A letter is issued to the submitter acknowledging receipt of the notification and raising safety concerns if identified. This represents final action. This letter and notification are filed in Dockets Management Branch 90 days after receipt of the notification. This is the end of the process. The number of notifications the Agency has received in FY 2002 to date has more than tripled compared to what it received in FY 2001 (i.e., receipt of approximately 50 notifications for FY 2002 as of August 2002 versus receipt of 16 notifications in FY 2001). The complexity of the notifications also has increased in recent years. Nevertheless, the Agency will retain its review goal target of 95% for FY 2003 and FY 2004. Since the Agency does not know precisely what the workload will be in any given year, the 95% target is considered full performance the next two fiscal years. Additionally, in response to the additional regulatory responsibilities placed on FDA by the Dietary Supplement Health and Education Act of 1994 (DSHEA), FDA has also developed a Strategic Plan for implementing those responsibilities both in the premarket and postmarket areas. FDA's goal is to have a science-based regulatory program that will provide the Agency with the ability to successfully implement and carry out the regulatory responsibilities imposed by DSHEA within ten years, thereby providing consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products. The success of this strategy will, however, not only depend on adequate funding levels, but also on FDA's new and continued partnerships with other government agencies, academia, health professionals, industry, and consumers. FDA's FY 2004 OMB Budget Submission includes $2 million for implementation of the Agency's Dietary Supplement Strategic Plan.

Performance: FDA has completed 100% of its reviews of NDI notifications within the 75-day deadline from FY 1998 - FY 2001. 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. In FY 2002, the Agency reviewed 44 notifications for new dietary ingredients. All except one were reviewed within the 75-day statutory timeframe. Of the 44 notifications reviewed, 10 were filed without comment; 3 were filed with comments; and 31 were filed with objection (3 of the 31 were not dietary supplements and the remaining 28 notifications had one or more of the following deficiencies: did not meet minimum requirements of 21 CFR 190.6; did not provide an adequate basis that the new dietary ingredient was reasonably expected to be safe; or made disease claims for the new dietary ingredient, thereby representing if as a drug).

Data Sources: CFSAN's Correspondence Tracking System and manual tracking

3. Complete processing of 80% of GRAS notifications within 180 days. (11003)

Context of Goal: (Goal Dropped for FY 2002, 2003 and 2004). GRAS notification is a new program and the final rule creating a premarket notification process for independent GRAS determinations is planned for publication (The final rule on the GRAS Notification Program has been completed and is currently awaiting review and clearance from the Office of Chief Counsel (OCC). 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.
Performance: CFSAN responded to 59% of GRAS notices received in FY 2000 within 180 days. 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. In FY 2001, 21 of 27 (roughly 80%) GRAS notices received were completed in less than 180 days. The final rule on the GRAS Notice Program has been completed and is currently awaiting review and clearance from the Office of Chief Counsel (OCC).
Data Sources: CFSAN's electronic workflow system; Internal Office of Pre-Market Approval database.

4. Review 95% of premarket notifications for food contact substances within the statutory time limit (120 days). (11034)

Context of Goal: As provided in the Food and Drug Administration Modernization Act (FDAMA), the Agency was mandated to establish a premarket notification program for food contact substances as a vehicle to re-inventing the premarket review process for food and color additives. The Congress appropriated resources in FY 2000 to fully fund this Program, and the first notifications became effective in March 2000. The statute provides that a food contact substance notification shall become effective (i.e., the food contact substance may be lawfully marketed) 120 days after receipt unless the Agency objects that the use of the food contact substance has not been shown

to be safe. Thus, to ensure that unsafe food contact substances do not enter the marketplace, the program goal is to review all notifications within 120 days. "Final action" is used in the case of food contact substances because nothing more needs to be done before the substance can be legally marketed, unless we object, which is also a final action.
Performance: In FY 2000, the Agency completed review of 82 of 83 notifications for food contact substances within 120 days. In FY 2001, the Agency received 80 notifications and completed review of 82 notifications, all within 120 days of receipt. The number reviewed includes those that became effective or were withdrawn or placed in abeyance because of deficiency during the previous fiscal year. In FY 2002, the Agency completed review of all (70) premarket notifications for food contact substances in the receipt cohort of FY 2001 within 120 days.
Data Sources: CFSAN's electronic workflow system; Internal Office of Pre-Market Approval database.

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 the need to:

- Work 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;
- Encourage 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;

- Work with foreign countries exporting food and cosmetic products to the U.S. to ensure the implementation of comparable safety standards; and,
- Conduct consumer education and industry education aimed at disease prevention.
- Be prepared to develop new prevention control systems rapidly in response to the emergence of new public health concerns.

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 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.

FDA has requested increased funding in FY 2004 to initiate a grants program with the states under provisions of the recently passed Public Health Security and Bioterrorism Preparedness and Response Act of 2002. Grants to states are intended to prepare that part of the Nation's Food Safety System to better defend the food supply from terrorist threats and other challenges to public health and safety. The performance goal proposed to focus this initiative is outlined below.

Proposed Performance Goal: Enhance states' ability to protect the U.S. food supply from terrorist threats and other health and safety challenges by:

- Increasing surge capacity and sample testing capability in 8 state laboratories; and,
- Increasing the number of risk-based inspections conducted by states by 1,200 state inspections in FY 2004 for a total of 10,500.

Laboratory Analysis
Grants will be awarded to states to enhance their laboratory analysis capacity in order to respond to both terrorist threats and traditional food safety hazards. These labs would join the larger food laboratory response network and be coordinated with the overall public health laboratory information effort. The state labs would address all foods for biological, chemical and radiological issues. Each lab will be capable of doing all three, which makes this different from the long tem goal.

Grants would be targeted to an initial pool of labs in the following areas:

- Training - This would include overview of BT issues, sampling and shipment techniques, specific analytical methods and techniques, safety/environmental issues, etc;
- Proficiency samples - These samples would have to be designed, manufactured, and implemented to test the laboratories' ability to analyze food samples for these agents. They would be sent out quarterly to each of the Grant Labs;
- Reagents, expendables and equipment - As new methods are developed for these agents the labs will need the tools to run the samples;
- Facility maintenance - Due to the exotic nature of these agents considerable care must be taken to assure that the analysts are protected and the community around the test site is protected. This requires sound well-maintained facilities. This is particularly true for the BL-3 facilities, which may be required for some of the agents.
- Method extension - While there are plans to develop the actual methods at research organizations, considerable work will be done on both validation on a limited number of commodities and continual testing to expand the method to other commodities. This work can and should be performed by the labs who are responsible for the testing; and
- Laboratory accreditation and proficiency testing.

Inspections
Grants will also be used for examinations, inspections, investigations and related activities in several food areas. The number of agreements and funding will be increased each year beginning with FY04 to the maximum level in FY06. The grants, in the form of cooperative agreements will supplement the existing state contract program. This new initiative will allow the Agency to achieve a level of 10,500 state food manufacturing, processing, and wholesale inspections annually by 2004 and expand the number of states participating from 37 to the maximum number of states that would be interested in participating. The grants would also improve the equivalence of state programs with federal inspection programs, develop a consistent level of trained staff and achieve program uniformity through audits and oversight by FDA.

<u>Adverse Event Reporting</u>

Once food and cosmetic products are available to consumers, it is important to monitor and evaluate adverse events associated with the 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. 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 first 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; and,
- 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
5. Perform 48,000 physical exams and conduct sample analyses on products with suspect histories. (11036 - this goal is repeated as number 19014 in the Agency Wide section)	FY 04: 48,000 exams FY 03: Increase exams by 100 % to 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 04: FY 03: FY 02: Hired 800 new investigators and analysts hired; 34,447 physical exams conducted. FY 01: 12,169	2
6. Achieve adoption of the Food Code by at least one state agency in 43 states in the USA. (11010)	FY 04: 43 FY 03: 42 FY 02: 28 FY 01: 25 FY 00: 18 FY 99: 13	FY 04: FY 03: FY 02: 40 FY 01: 28 FY 00: 20 FY 99: 15	2 Outcome Gaol

7. Inspect 95% of estimated 7,000 high-risk domestic food establishments once every year. (11020)	FY 04: at least 95% once every year FY 03: at least 95% once every year FY 02: at least 95% once every year FY 01: at least 90% once every year FY 00: 90 -100% Once every one to two years	FY 04: FY 03: FY 02: 97% of 7000 FY 01: 78% of 6800 FY 00: 91% of 6250	2
8. 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 04: 8,000 + FY 03: 8,000 + FY 02: 8,000 + FY 01: 8,000 + FY 00: NA FY 99: NA	FY 04: FY 03: FY 02: 10,700 FY 01: 8,250 total (7,600 pesticide residues including 1,100 TDS; 650 dioxin including 250 TDS) 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.	2
TOTAL FUNDING: ($ 000)	FY 04: 372,912 FY 03: 369,623 FY 02: 349,996 FY 01: 247,654 FY 00: 240,043	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

5. Perform 48,000 physical exams and conduct sample analyses on products with suspect histories. (11036 - this goal is repeated as number 19014 in the Agency Wide section)

Context of Goal: In FY 2004 FDA will focus much of its resources on examination and follow-up on import shipments that pose the highest potential risks. Increases in the number of physical examinations will not continue to grow at the rate expected in FY 2002 and 2003. Given the continuing explosion in number of import shipments to this Country, it is not realistic to expect that FDA can keep up with the volume by simply expanding the number of physical examinations. Rather, a significant effort will be launched to develop the appropriate knowledge-based approaches that will give the Agency assurance that it is, in fact, addressing the most serious risks. Finding these risks is a great challenge considering that FDA-regulated imports have grown at 10 to 12% annual rate for several years, and may originate in any of more than 100 countries, many of which have regulatory systems in place which are much more primitive than that found in the U.S. The risk has now been exacerbated in light of security concerns raised by terrorism and counterfeiting incidents. During FY 2003 FDA will develop a more robust physical examination approach that merges the assessment of information integrity with the safety and security of the product. By FY 2004 FDA will have in place a new version of the import field exam. The new exam will routinely include: verification that the imported product is the same as that which was declared; assessment of security concerns related to labeling and source country; and traditional safety concerns. More importantly, these new exams will be conducted on import entries selected using a more rigorous risk assessment and management rubric. FDA will be developing during FY 2003 the criteria and, to the extend possible, the computer systems to be able to better identify, obtain, process, assimilate, and deliver data relating to an imported product's safety and security. This data will be delivered in a more meaninful and timely fashion to the primary decision makers in FDA's import process located at the borders and throughout the country monitoring imports electronically through OASIS. During FY 2003 FDA will pilot various features to develop a feasible implementation process, and to develop better time estimates so that appropriate resources can be matched with the revised approach. FDA will use a risk-based system to target suspect problem areas. Such areas may include:

- Filer Evaluation Field Audits;
- Pilot with filer evaluation, importer/trader inspections;
- Warehouse blitz programs;
- Transshipment-targeted field examinations;
- Sample collection and analysis for Counterterrorism;
- Implementation of program with Canada and Mexico to enhance advanced identification of transshipped cargo; and

- Expand in-bond entry evaluation including performing examinations of in-bond entries at port of arrival and port of entry or export.

During FY 2003 FDA will gather information about the number and characteristics of these potential targets so that by FY 2004 pilot programs can be identified with enough examination of each type so that practices can be revised again in subsequent years to reflect lessons learned. FDA anticipates that the measures that it uses to assess its success in monitoring the safety and security of imported products will continuously evolve as trade practices and information about risks change. During FY 2003 FDA will also decide on the appropriate methods including summary categories, if appropriate, that are best suited to track various components of this goal. Additional risk based candidates may be identified that will require further pilot studies in FY05 and later.
Performance: This goal was new for FY 2002 and FY 2003. The FY 2002 performance was 800 new investigators and analysts hired and 34,447 physical exams conducted. The FY 2001 baseline was 12,169 physical exams. The FY 2002 goal targets 24,000 exams that target doubles to 48,000 in FY 2003. The FY 2004 goal remains at 48,000 because resources will be devoted to targeting and following through on suspect import entries rather than significantly expanding import coverage.
Data Sources: Field Data Systems

6. Achieve adoption of the Food Code by at least one state agency in 43 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.
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.
The Food Code is a component of an even larger effort aimed at decreasing foodborne illness, the National Retail Food Regulatory Program Standards program. In FY 2004, FDA will assist state programs and provide oversight in implementing the Standards program, and complete the data compilation of the national baseline data collected by CDC during FY 2003. Additionally, FDA plans to enroll 60 new jurisdictions in the Standards and baseline program in

each year FY 2004 through FY 2009, while continuing to provide support and guidance to those 120 jurisdictions already enrolled. FDA will conduct audits of those enrolled in the Standards program in accordance with the Standards protocol.
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. In FY 2002, at least one state agency in 40 states adopted the Food Code.
Data Sources: Field Data Systems

7. Inspect 95% of estimated 7000 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. High-risk establishments are manufactures, packers/repackers, and warehouses processing products that include: modified atmosphere packaged products; acidified and low acid canned foods; seafood; custard filled bakery products; soft, semi-soft, soft-ripened cheese and cheese products; un-pasteurized juices; sprouts or processed leafy vegetables; fresh vegetables shredded for salads and processed root and tuber vegetables; sandwiches; prepared salads; infant formula; and medical foods.
During the course of FY 2002 additional high-risk products were identified that had not previously been included in the base FY 2002 high-risk inventory. These include establishments that manufacture a product that may contain a commonly allergenic substance (milk, eggs, fish, crustaceans, tree nuts, peanuts or soybeans), and dietary supplements that may contain bovine derived ingredients from BSE countries identified in the USDA regulation (9 CFR 94.18). Although the official FY 2003 establishment inventory will still be 7000 when we start, we expect that the inventory will increase as firms manufacturing products that contain allergenic substances and firms that manufacture dietary supplements that may contain bovine ingredients for BSE countries are confirmed.
A history of repeated incidence of a pathogen or a high level of a contaminant in a food product that results in acute or life threatening illness warrants consideration for high-risk designation. Until recently, risk assessments that characterize the hazard and associated foods have been based on historical information. More recently, formal risk assessments have been used. For example FDA conducted a formal risk assessment on the pathogen Listeria that resulted in a risk ranking of 21 food categories.

To date, no foods that have been identified as high-risk have been removed from the high-risk designation. However, in the future, foods may lose their designation as high-risk if it has been demonstrated that industry practices or technologies have eliminated or minimized the prior risk through a history of safe production. Industry practices can include the application of new technologies. Advances in science can also revise previous risk assumptions about the nature of the hazard in certain food types and may influence a food's risk characterization. Additionally, FoodNet, an active surveillance system administered by CDC, provides an annual update of foodborne illness in the U.S. This information affords a measurement of trends in foodborne illness due to exposure to pathogenic microorganisms and aids in food risk characterization.

As an added effort in the area of high-risk foods, FDA will determine the occurrence of the 5 CDC-identified foodborne illness risk factors and environmental risk factors in the inventory of the regulated Interstate Travel Conveyance facilities, in order to establish a reduction in foodborne illnesses over time. Interstate Travel Conveyance facilities serve 900 million meals and snacks annually. FDA's efforts will include the inspection of food and environmental facilities, such as water, wastewater and solid wastes in airline, train, bus and cruise ship airports, hubs, stations and port facilities. In FY 2004, FDA will develop a baseline data collection project, that will include developing forms, a statistical validity assessment, development of a sampling plan, conduct training, provide technical support, establish a pilot study and revise the baseline project as needed. Additionally, FDA will inspect 95 percent of the official establishment inventory (OEI) of the regulated Interstate Travel Conveyance facilities to collect the baseline data. These data collection activities would include the inspection of these high-risk facilities.

Performance: In FY 2000, the number of high-risk food inspections was approximately 5700 or 91% of the identified possible inventory of high-risk product/process domestic firms. In FY 2001, the Agency accomplished 78% of the identified possible 6800 inventory of high-risk product/process domestic firms. The reason FDA fell short of achieving this goal was because the Agency had to concentrate its resources and focus on an even greater threat of BSE that was breaking out in Europe at the time. In FY 2002, FDA conducted 6,784 domestic inspections of firms that produce "high risk" foods (through ORA and the states, under FDA auspices). This exceeded FDA's goal to annually inspect 95% (6,650) of the "high risk" domestic food establishments.

Data Sources: Field Data Systems

8. 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 (TDS). In conducting the Total Diet Study, FDA personnel purchase foods from retail outlets 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.
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).
In FY 2001, actual performances for pesticide residues and chemical

contaminants monitoring was 8,250 (7,600 for pesticide residues including 1,100 TDS and 650 dioxin including 250 TDS). This figure is slightly higher than the figure the Center previously reported as it contains a more accurate accounting of the total number of samples monitored under our regulatory monitoring program and our Total Diet Study program. Thus, FDA analyzed 7,600 samples for pesticide residues which includes 1,100 samples collected for the Total Diet Study. TDS analyzed for pesticide residues and other chemical contaminants in foods consumed by infants and children. The Total Diet Study is a major element of FDA's pesticide residue monitoring program. Some of the samples collected under the Total Diet Study have also been monitored for dioxins in the past couple of years and, possibly, for other chemical contaminants as well. Therefore, the samples collected for the TDS analyzed for pesticide residues and other chemical contaminants should be counted as "actual performances" under the "pesticides and environmental contaminants". The total number of samples analyzed for dioxins was 650 for a total actual performance of 8,250. 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. In FY 2002, FDA collected and analyzed 10,700 food samples to monitor for pesticides and environmental contaminants. This exceeded FDA's goal to collect and analyze 8,000 samples.
Data Sources: FACTS, CFSAN website

2.3 HUMAN DRUGS

2.3.1 Program Description, Context, and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	485,862	425,920	364,344	322,480	311,234

The Human Drugs Program promotes the public health by assuring that all prescription and over-the-counter drugs are safe and effective. The Center for Drug Evaluation and Research (CDER) evaluates all new drugs before they are sold, and serves as a consumer watchdog for the more than 10,000 drugs on the market to be sure they continue to meet the highest standards. CDER routinely monitors TV, radio, and print drug ads to ensure they are truthful and balanced. CDER also plays a critical role in providing health professionals and consumers information to use drugs appropriately and safely. Recent drug approvals represent important advances for children, women, elderly persons, and patients with heart disease and cancer, which are leading causes of death in the United States. To support this mission, the human drugs program focuses on three long-term strategic goals:

1. Protect and promote the health of Americans by providing access to important safe and effective drugs.
2. Enhance organizational performance in response to stakeholder needs with the highest degree of cost effectiveness and efficiency.
3. Prevent injury and death to the American public caused by adverse drug reactions, medication errors and product problems.

In addition to setting standards for safety and effectiveness testing, we also set standards for drug quality and manufacturing processes. We work closely with manufacturers to see where streamlining can cut red tape without compromising drug quality. As the pharmaceutical Industry has become increasingly global, we are involved in international negotiations with other nations to harmonize standards for drug quality and the data needed to approve a new drug. This harmonization will go a long way toward reducing the number of redundant tests manufacturers perform and help ensure drug quality for consumers at home and abroad.

We conduct and collaborate on focused laboratory research and testing. Research maintains and strengthens the scientific base of our regulatory policy-making and decision-making. We focus on drug quality, safety and

performance, improved technologies, new approaches to drug development and review, and regulatory standards and consistency.

2.3.2 Strategic Goals

Strategic Goal 1:
Protect and promote the health of Americans by providing access to important safe and effective drugs.

A. Strategic Goal Explanation

A drug company seeking to sell a drug in the United States must first test it. We monitor clinical research to ensure that people who volunteer for studies are protected and that the quality and integrity of scientific data are maintained. The company then sends us the evidence from these tests to prove the drug is safe and effective for its intended use. We assemble a team of physicians, statisticians, chemists, pharmacologists and other scientists to review the company's data and proposed use for the drug. If the drug is effective and we are convinced its health benefits outweigh its risks, we approve it for sale. By setting clear standards for the evidence we need to approve a drug, we help medical researchers bring new drugs to American consumers more rapidly. The average review time for new drugs covered under the Prescription Drug User Fee Act (PDUFA) has been reduced from more than 2.5 years to less than one year and patients with life-threatening illnesses are able to gain access to treatments sooner. We also review drugs that can be bought over-the-counter (OTC) (without a prescription) and generic versions of both over-the-counter and prescription drugs. CDER is also encouraging the development and expediting the review of medications for the prevention or treatment of injuries that could be caused by terrorists using biological, chemical, or nuclear agents.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Meet PDUFA III commitments for the review of original NDA submissions. (12001)	Standard NDAs within 10 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30% Standard NDAs within 12 months:	 FY 04: FY 03: FY 02: Final data available by 11/03. FY 01: 90% of 86 FY 00: 79% of 92 FY 99: 66% of 95 FY 04:	4

	FY 04: NA FY 03: NA FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90% Priority NDAs within 6 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	FY 03: FY 02: NA FY 01: 98% of 86 FY 00: 97% of 92 FY 99: 100% of 95 FY 04: FY 03: FY 02: Final data available by 7/03. FY 01: 100% of 10 FY 00: 97% of 29 FY 99: 100% of 31	
2. Increase the number of drugs that are adequately labeled for children. (12026)	FY 04: BPCA:Complete review and action on 85% of pediatric supplements in response to a Written Request (WR) within 6 months. Work with NIH to update Priority List of Drugs; issue 10-12 WRs for off-patent drugs; work with NIH to issue Requests for Proposals (RFPs) for contracts for the study of drugs (outlined in a WR) and publish 8-10 RFPs. Issue WRs for the study of on-patent drugs in the pediatric populations, make exclusivity determinations once final study reports are submitted, determine final pediatric label changes, and disseminate information. FY 03: BPCA:	FY 04: On-Patent Drugs: Pediatric Proposals Reviewed:Written Requests Issued:Amended WRs Issued:Exclusivity Determinations:Exclusivities Granted:Labels Changed: Off-Patent Drugs: WRs Issued:List Updated: FY 03: On-Patent Drugs: Pediatric Proposals Reviewed:Written Requests Issued:Amended WRs Issued:Exclusivity Determinations:Exclusivities Granted:Labels Changed: Off-Patent Drugs: WRs Issued:Priority List: to be published in January 2003. Peds Rule:	4

	Complete review and action on 80% of pediatric supplements in response to a WR within 6 months. Work with NIH to publish the initial Priority List of Drugs and work with NIH to update the list. Issue 6-8 WRs for off-patent drugs; work with NIH to issue RFPs for contracts for the study of drugs (outlined in a WR) and publish 5-7 RFPs. Issue WRs for the study of on-patent drugs in the pediatric population, make exclusivity determinations once final study reports are submitted, determine final pediatric label changes, and disseminate information. Pediatric Rule: Track all applications that would have triggered the pediatric rule, to include waivers, deferrals, and completed studies. FY 02: Exclusivity/BPCA:Work with NIH to develop, prioritize, and publish the initial list of off-patent drugs. Work with NIH to develop the Request for Proposal (RFP) process for contracts for study of off-patent drugs. Issue WRs for	FY 02: Exclusivity/BPCA: Pediatric Proposals Reviewed: 42Written Requests Issued: 54Amended WRs Issued: 48Exclusivity Determinations: 23Exclusivities Granted: 22Labels Changed: 18Suppl. Acted on 180 days: NAInfo Disseminated: 2 American Academe of Pediatrics (AAP) News articles published; 2 Pediatric Academic Societies (PAS) abstracts published; I journal article published; 1 Pediatric Advisory Subcommittee meeting held; 21 presentationsBPCA Off-Patent Drugs:WRs sent to NIH: 3WRs assessed and drafted: 4WRs issued to all approved application holders: 41Establishment of off-patent status of drugs: 284Coordination of the development, prioritization, and publishing of the priority list with NIH: 36 Pediatric Rule: Deferrals: 49Waivers: 65Completed Studies: 43 FY 01: Exclusivity:Pediatric Proposals reviewed: 81Written Requests Issued:	

	the study of on-patent drugs in the pediatric population, make exclusivity determinations once final study reports are submitted, determine final pediatric label changes and disseminate information. <u>Pediatric Rule:</u>Track all applications that would have triggered the pediatric rule, to include waivers, deferrals, and completed studies. FY 01: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule. FY 00: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	49Amended WRs Issued: 46Exclusivity Determinations: 19 Exclusivities Granted: 16Labels Changed: 10Info Disseminated: I Pediatric Advisory Subcommittee meeting heldPediatric Rule:Deferrals: 54Waivers: 78Completed Studies: 29 FY 00: <u>Exclusivity:</u> Pediatric Proposals reviewed: 39Written Requests Issued: 58Amended WRs Issued: 59Exclusivity Determinations: 19 Exclusivities Granted: 16Labels Changed: 7Info Disseminated: 1 Pediatric Advisory Subcommittee meeting held <u>Pediatric Rule:</u> Deferrals: 69Waivers: 79Completed Studies: 30 FY 99: <u>Exclusivity:</u> Pediatric Proposals reviewed: 155Written Requests Issued: 95Amended WRs Issued: 15Exclusivity Determinations: 9 Exclusivities Granted: 9Labels Changed: 4Info Disseminated: <u>Pediatric Rule:</u> Deferrals: 70Waivers: 79Completed Studies: 14	

	FY 99: Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.		
3. Complete review and action upon fileable original generic drug applications within 6 months after submission date. (12003)	FY 04: 90% FY 03: 80% FY 02: 65% FY 01: 50% FY 00: 45% FY 99: 60%	FY 04: FY 03: FY 02: 3/03 FY 01: 84% of 298 FY 00: 55.6% of 307 FY 99: 28% of 309	4
4. Increase the number of drugs adequately labeled available for OTC use. (12048)	FY 04: Complete review and action on 100% of Rx-to-OTC Switch applications within 10 months of receipt and make significant progress on completing 6 OTC monographs. FY 03: NA FY 02: NA	FY 04: FY 03: NA FY 02: NA	4
5. Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting onsite inspections and data audits annually. (12032)	FY 04: 685 or 90% of the field assignments made by 6/30/2004 FY 03: 685 or 90% of the field assignments made by 6/30/2003 FY 02: 780 FY 01: NA FY 00: NA FY 99: NA	FY 04: FY 03: FY 02: 635 inspections completed FY 01: 553 inspections completed FY 00: 697 inspections completed FY 99: 683 inspections	4

	Note: The number of inspections completed each year is dependent on the number of New Drug applications received.	completed	
6. Facilitate development and availability of medical countermeasures to limit the effects of the intentional use of biological, chemical, or radiologic/nuclear agents.(12045)	FY 04: Complete analysis of data from animal studies and incorporate information on pneumonic plague into drug product labeling; review and analyze data from animal studies conducted on inhalational anthrax; publish a revised guidance on potassium iodide for use in special populations. FY 03: Develop guidances for Industry on developing antiviral drugs; identify and begin to address labeling gaps in the therapeutic armamentarium; expedite the review of protocols for investigational new radioprotectant drugs; and facilitate human clinical trials. FY 02: NA	FY 04: FY 03: FY 02: NA	2, 4
7. Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax (post-exposure). (12033)	FY 04: NA FY 03: NA FY 02: Publish guidance for Industry on developing antimicrobial drugs for inhalational anthrax	FY 04: FY 03: FY 02: Announced the availability of a draft guidance for industry entitled "Inhalational Anthrax (Post-Exposure) -	2, 4

	(post-exposure).	Developing Antimicrobial Drugs."	
8. Facilitate the initiation of research in a non-human primate model of pneumonic plague. (12034)	FY 04: NA FY 03: NA FY 02: Facilitate the initiation of research in a non-human primate model of pneumonic plague.	FY 04: FY 03: FY 02: Facilitated the initiation of research through establishment of an Inter-Agency Agreement with NIAID/NIH and USAMRIID entitled "Non-Human Primate Studies of Antibiotic Efficacy for Treatment of Pneumonic Plague by Aerosolized Yersinia Pestis."	2, 4
9. 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 Agent, Autoinjectors (ATNAA). (12035)	FY 04: NA FY 03: NA FY 02: 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 applications (NDAs) to update current labling for Antidote Treatment Nerve Agent, Autoinjectors (ATNAA).	FY 04: FY 03: FY 02: Requested information from the American Academy of Pediatrics (AAP) in May 2002 regarding clinical data on atropine and pralidoxime to determine their use as therapies for nerve agent exposure in the pediatric population. On January 17, 2002, FDA approved nerve gas antidote ATNAA (atropine/pralidoxime) for the treatment of poisoning by susceptible organophosphorous nerve agents having anticholinesterase activity.	2, 4
10. Publish a final rule which allows the Agency to approve new drug and biological products for the treatment of chemical, biological,	FY 04: NA 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,	FY 04: FY 03: FY 02: The Final Rule on the "New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not	2, 4

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)	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.	Ethical or Feasible" was published by FDA in the Federal Register on May 31, 2002.	
TOTAL FUNDING: ($ 000)	FY 04: 358,080 FY 03: 310,104 FY 02: 273,258 FY 01: 257,984 FY 00: 233,425	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

1. Meet PDUFA III commitments for the review of original NDA submissions. (12001) **Context of Goal:**The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 reauthorizes the collection of user fees to enhance the review process of new human drugs and biological products and established fees for applications, establishments, and approved products. The PDUFA amendments of 2002 are effective for a five-year period with certain technical improvements. Specifically, Congress directed FDA to strengthen and improve the review and monitoring of drug safety, consider greater interaction between the Agency and sponsors during the review of drugs and biologics intended to treat serious diseases and life-threatening diseases, and develop principles for improving first-cycle reviews. A major objective of the human drugs program is to reduce the time required for FDA's review of all drugs. The first action is the first regulatory action the CDER takes (approvable, not approvable, or approval letter) at the end of the review of the original NDA submission (the first review cycle). So the first action times refer to the time it takes us to review and take an action on the original submission. This is different from total approval time which is the time it takes from the original receipt of the application until it is approved, which may take more than one review cycle. This includes the time we spend reviewing the application in each of the review cycles plus the time taken by the sponsor to respond to the issues raised in the approvable/not approvable letter(s) and resubmit the application for review. Applications for drugs similar to those already marketed are designated standard, while priority applications represent drugs offering significant advances over existing treatments. (Drugs for AIDS and cancer typically fall into the priority category.) FDA's timely performance of high-quality drug reviews in recent years reflects the importance of managerial

reforms and substantial additional resources provided under the Prescription Drug User Fee Act (PDUFA). Under PDUFA, the drug Industry pays user fees for new drug and biologics applications, establishment fees, and product fees. The fee revenues help the Agency hire additional scientists to perform reviews, bringing new drugs to the American consumer more rapidly. PDUFA III revenues will enable FDA to put the program on a sound financial footing, further enhance program efficiency, and improve efficiency for Industry innovators by providing sponsors earlier review, communication, and feedback on products in development. PDUFA III will also provide increased funds for risk management after new product approval.
Performance:CDER met all FY 2000 performance goals (see Table 1 below).

Table 1
Fiscal Year 2000 Cohort (closed out 10/31/01)

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%

In FY 2001, CDER took 186 actions on NDAs, 71 of which were approvals. Of the 71 NDA approvals, 15 were for NMEs. Of the 15 NMEs, five were drugs given a priority review (products offering a significant improvement over currently marketed drugs). CDER approved 18 priority applications (5 NMEs, 5 NDAs that were not NMEs, and 8 efficacy supplements).

CDER has exceeded all FY 2001 performance goals (see Table 2 below).

Table 2
Fiscal Year 2001 Receipt Cohort (closed out 9/30/02)

Submission Type	Number of Submissions Filed	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"

NDAs -- Priority	10	90% in 6 mo.	10	100%
NDAs -- Standard	86	90% in 12 mo (cum). 70% in 10 mo.	84 77	98% 90%

Several important new drugs were also approved by FDA in FY 2001 (see Table 3 below).

Table 3
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).
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

Drugs approved in FY 2001 under Subpart H (Accelerated Approval) regulations are listed below (see Table 4).

Table 4
NDAs Approved under Accelerated Approval in FY 2001

Drug	Approval Time/Subpart H Type[a]	Purpose	Approval Date
Gleevec	2.4	Treatment of patients with	5/10/01

(imatinib mesylate)	months/Surrogate	chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.	
Trizivir (abacavirSulfate, lamivudine, and zidovudine)	10.9 months/Surrogate	Used either alone or in combination with other antiretroviral agents for the treatment of HIV-1 infection.	11/14/00

[a] Under Subpart H, approval may be based on surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity ("Surrogate" in table) (21CFR 314.510), or a product may be approved with restrictions to assure safe use ("Restricted") (21 CFR 314.520).

FDA approved several important new drugs during the first eight months of FY 2002 (see Table 5 below).

Table 5
Significant NDAs Approved in FY 2002

Drug	Purpose
ARIXTRA™ (Fondaparinux Sodium) Injection	Reduces the risk of blood clots after orthopedic surgery for hip fracture, hip replacement, and knee replacement.
Eloxatin (Oxaliplatin)	Treatment of patients with colorectal cancer whose disease has recurred or become worse following initial therapy with a combination of irinotecan with bolus 5-FU and leucovorin. Eloxatin is to be used in combination with infusional 5-fluorouracil (5-FU) and leucovorin.
Entocort EC® (Budesonide)	Treatment of mild to moderate active Crohn's Disease involving certain sections of the small and large intestines.
Orfadin (Nitisinone)	Treatment for hereditary tyrosinemia type 1 (HT-1), a rarePediatric disease causing progressive liver failure and liverCancer in young children.

NuvaRing (Etonogestrel and EthinylEstradiol Vaginal Ring)	Vaginal contraceptive ring containing a combination of estrogen and progestin hormones released from a flexible polymer ring.
Zelnorm (Tegaserod Maleate)	Short-term treatment of women with irritable bowel syndrome (IBS) whose primary bowel symptom is constipation.

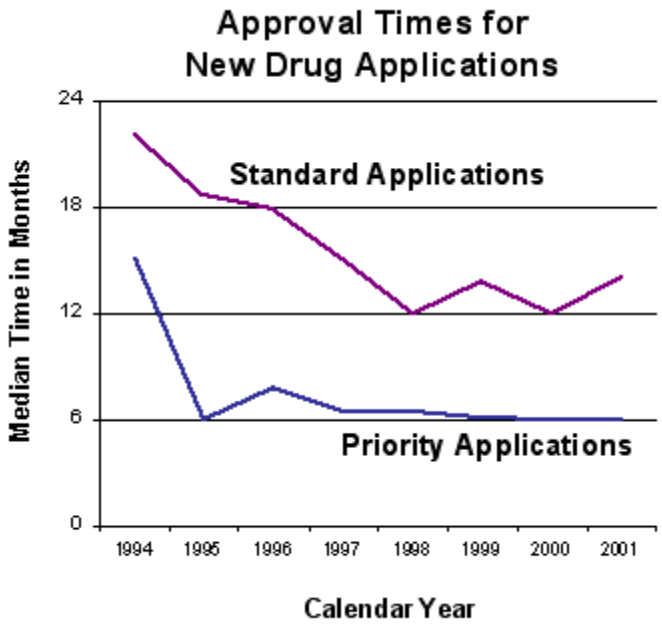
Drugs approved in the first eight months of FY 2002 under Subpart H (Accelerated Approval) regulations are listed below (see Table 6).

Table 6
NDAs Approved under Accelerated Approval in FY 2002

Drug	Approval Time/Subpart H Type[a]	Purpose	Approval Date
Viread (Tenofovir Disoproxil Fumarate)	5.9 months/ Surrogate	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.	10-26-01
Tracleer (Bosentan)	12.1 months/ Restricted	Treatment of pulmonary arterial hypertension.	11-20-01
Remodulin (Treprostinil Sodium)	19.1 months/ Surrogate	Provides for the use of Remodulin Injection 1.0, 2.5, 5.0, and 10.0 mg/ml for the treatment of pulmonary arterial hypertension.	5-21-02

[a] Under Subpart H, approval may be based on surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity ("Surrogate" in table) (21CFR 314.510), or a product may be approved with restrictions to assure safe use ("Restricted") (21 CFR 314.520).

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 has 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.



The following is the preliminary data for the FY 2002 receipt cohort as of November 30, 2002 (see Table 7). Final performance data will be available by November 30, 2003..

Table 7
Fiscal Year 2002 Receipt Cohort (as of 11/30/02)

Submission Type	Number of Submissions Filed	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
NDAs -- Priority	10	90% in 6 mo.	5	50%
NDAs -- Standard	89	90% in 10 mo.	36	40%

Data Sources: Review performance monitoring is being done in terms of cohorts, e.g., FY 2003 cohort includes applications received from October 1, 2002, through September 30, 2003. CDER uses the Center-wide Oracle Management Information System (COMIS) and 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.

2. Increase the number of drugs that are adequately labeled for children. (12026)

Context of Goal: In 1997, as part of the Food and Drug Administration Modernization Act (FDAMA), Congress enacted a law to provide marketing incentives to manufacturers who conduct studies in children. This law, which provides six months exclusivity in return for conducting pediatric studies requested by the FDA, is commonly known as the pediatric exclusivity provision. Pediatric provisions of the FDA Modernization Act of 1997 have had a profound impact on the study of drugs in children. Many of the studies reported to date have yielded new dosing and safety information. The recently enacted Best Pharmaceuticals for Children Act (BPCA) is expected to continue providing incentives for the effective development and labeling of information on how to properly use therapies in children. As a result of these initiatives, the number of ongoing pediatric clinical trials in the last 4 years has tripled and many companies have built and continue to build a pediatric research infrastructure that is similar to the one for adults which has been in place for decades.
As mandated by BPCA, pediatric supplements submitted in response to a Written Request (WR) issued by FDA should be reviewed and acted upon within 180 days (i.e., granted a priority review status). The workload associated with the implementation of the Act will be a growing resource challenge as substantial effort will be required in issuing WRs, reviewing the studies, and negotiating labeling changes within the 6-month timeframe. BPCA still allows sponsors of marketed drugs to obtain exclusivity if they conduct and submit pediatric studies that fairly respond to the terms outlined in the WR issued by FDA. WRs may be initiated by FDA or sponsors may submit a proposed pediatric study request (PPSR) to FDA. In response to the PPSR, FDA may issue a WR if they believe there is a public health benefit. In addition, BPCA amended the Public Health Service Act to establish a publicly funded contracting process for the studies of drugs that no longer have exclusivity or patent protection, but for which pediatric information is needed. FDA and NIH are collaborating to transform WRs into Requests for Proposals (RFPs) from NIH when firms do not respond to a WR to conduct clinical trials. All funds for these RFPs are controlled by NIH, along with the contracting process under these NIH-initiated RFPs. FDA's success in meeting this goal is dependent on NIH receiving adequate funding and then proceeding to publish RFPs.
Pediatric exclusivity has helped FDA uncover important new dosing and safety information that will help pediatricians and other prescribers use drugs to treat children more confidently. Additionally, we will enhance the surveillance of adverse events in children and coordinate the development of "off-patent" drugs for children with NIH. FDA also plans to negotiate labeling concerns with listed drug holders and further develop the science to address new pediatric issues.
Performance: Since 1998, FDA has reviewed 319 Proposed Pediatric Study Requests (PPSR), issued 259 Written Requests (WR) asking for over 606

studies to be conducted in the pediatric population, and has granted exclusivity to 67 out of the 76 products that have had an exclusivity determination. Forty-seven of the 76 products that have had an exclusivity determination now have approved labeling that incorporates information from the pediatric studies. Accurate dosing and safety information is now available for products labeled for use in allergies, diabetes mellitus, high blood pressure, pain, seizures, obsessive-compulsive disorder, HIV infection, atopic dermatitis, and many other conditions.

In response to the BPCA, the Agency has undertaken numerous collaborative activities with the Institute of Medicine (IOM), NIH and the American Academy of Pediatrics, including working with NICHD on the development of a Priority List of Drugs and a process for transforming WRs into RFPs. Four WRs for off-patent drugs have been assessed. Subsequently, two WRs were then issued to all identified NDA and ANDA holders of approved applications for these drugs. FDA worked with NIH in transforming the WRs into RFPs. In response, two FDA/NIH contract working groups have been established. Two implementation meetings for contracts have been held.

The fifth Pediatric Advisory Subcommittee meeting occurred on June 11, 2002. The Report to Congress mandated by FDAMA was sent to Congress on January 9, 2001. FDA developed an interactive pediatric web page to provide detailed information to the public regarding FDA's pediatric initiatives. In recognition of the need for clear ethical guidance in this pediatric arena and as mandated by the Children's Health Act of 2000, the Agency incorporated Subpart D of the DHHS regulations into FDA regulations *(Additional Safeguards for Children in Clinical Investigations of FDA-Regulated Products)* and published an interim final rule effective on April 30, 2001. The Agency defined and funded an inpatient pediatric database that is being 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.

Data Sources: Pediatric Exclusivity Database, Pediatric Page database, and CHCA inpatient database. The Pediatric Exclusivity Database tracks all data regarding pediatric exclusivity as mandated by FDAMA and reauthorized by BCPA. Specifically, this database tracks the number of WRs issued and the number of products for which pediatric studies have been submitted and for which exclusivity determinations have been made.

3. Complete review and action on fileable original generic drug applications within 6 months after submission date. (12003)

Context of Goal: Generic drugs are much appreciated for their cost-effectiveness. According to the Congressional Budget Office, they save consumers an estimated $8 billion to $10 billion a year compared with the price of trade-name products. 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. The basic requirements for approval of generic and

trade-name drugs are the same as new drug approvals, although the generic drug manufacturer does not need to repeat the safety and efficacy studies conducted by the developer of the original product. The approval time is measured from the date the application is received to the date a major action, either an approval or not approvable, is reached. In approving a generic drug, the FDA relies on its previous finding that the original drug is safe and effective. The generic version must have the same dosage form, safety, strength, route of administration, and conditions of use as the trade-name product. The generic drug's sponsor also must show that its active ingredient is absorbed at a rate and extent similar to the trade-name counterpart. This bioequivalence is critical for drawing the conclusion that both the original and generic drugs will produce similar therapeutic results. With the exception of language protected by patents or exclusivity, the labeling of the generic drug, including directions for use, must be virtually the same as that of the trade-name product. Both generic and trade-name drug companies are required to submit information to ensure that the approved products can be manufactured to FDA's specifications. Following approval, both generic and trade name firms must submit data to the FDA showing that their products continue to meet the Agency's specifications until the established expiration date. The FDA regularly assesses the quality of generic medications on the market and thoroughly researches and evaluates reports about their performance. Once a sponsor submits an abbreviated new drug application (ANDA) to the Agency, we have committed to acting on those submissions, e.g., issuing a complete response letter, within 6 months of the submission date.

Performance: In FY 1999, we set the FY 2001 target of 50 percent based on actual performance of 28 percent. FDA exceeded its goal for FY 2001 acting on 84 percent of original applications within 6 months after the submission date. The Office of Generics Drugs utilized increased funding levels to increase the efficiency of the review process thereby decreasing the average approval time. We have approved approximately 7,000 generic drugs for various treatments, including benign prostatic hyperplasia, various ovarian and breast cancers, and high blood pressure. The Office of Generic Drugs (OGD) continues to refine the review process to increase efficiency with the $1.2 million increase in FY 2001 as well as increases in past fiscal 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 issuance of a complete response letter is taken within the statutory time frame of six months. 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. We continue to refine the review process to increase efficiency. We are able to accept more electronic submissions to streamline the review process. The number of new staff hired in the last fiscal

year is now fully trained and are demonstrating high levels of productivity. We continue to examine every aspect of the review process to try to identify problem areas to be addressed. We also plan to revise the current system for amendment designation (major versus minor) to improve total review times.
CDER targeted a $2.5 million dollar increase in FY 2002 to improve the generic drug review process and educate various audiences in the safe and effective use of generic drugs as a substitute to their brand-name counterparts. Increased staff has provided the Office of Generic Drugs with scientific managers and experts, including a Director of Science, several chemistry reviewers and managers, a Medical Officer, and regulatory management officers. Furthermore, compliance and legal support to the Office of Generic Drugs was expanded. The increased staff were critical in reducing review times for ANDAs/generic drug applications and granting approval as quickly as possible. The percent of original ANDAs acted upon within 180-days exceed the Office's 2002 goal. This represents improvements in nearly every level and scientific discipline supporting the review of generic drug applications, culminating in a record number of approvals of ANDAs. The actual performance data for FY 2002 will not be available till 180 days after the close of FY 2002, approximately March 2003.
With the requested increases for FY 2003 and FY 2004, FDA plans to hire additional reviewers and other staff to accelerate the review and approval of Abbreviated New Drug Applications. In addition, we plan to improve the review of ANDAs without sacrificing product quality to allow the Agency to reach its goal of reviewing 80 percent of ANDAs in FY 2003 and 90 percent in FY 2004 within six months after submission. We also plan to hire additional inspectors to increase inspections of domestic and foreign firms associated with generic drug production, an activity critical to reducing total approval times; and, increase coverage of imported generic drugs to better monitor the quality of finished drug products and bulk drug substances from overseas. Additionally, the increase will also be used to conduct research that will allow us to address specific scientific questions regarding bioequivalence and chemistry of generic products. This research will be directed at evaluating ways to enable approval of generic drugs in areas that currently lack generic alternatives, such as inhalational or topical drug products.

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)
Tramadol Hydrochloride	Pain reliever
Lisinopril	Used to lower blood pressure, treat congestive heart failure, and improve the survival rate after a heart attack
Lovastatin	Reduce the amounts of LDL (bad) cholesterol and total cholesterol in a person's blood
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). CDER used a $1.2 million dollar increase in FY 2001 to fully annualize the positions added in FY 2000 and add several additional FTEs. 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.

Data Sources: 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.

4. Increase the number of drugs adequately labeled available for OTC use. (12048)

Context of Goal: Over-the-counter (OTC) drugs play an increasingly vital role in America's health care system. The trend to self-medication has increased greatly in recent years as health care costs have risen and consumers want to be empowered to treat minor ailments with safe and effective OTC drug products. However, safety, effectiveness, and proper labeling have not always been characteristic of OTC drug products in the United States. The Food and Drug Administration (FDA) has devoted extensive resources to the goal of having safe and effective OTC drug products in the United States, including a number of products formerly marketed by prescription. FDA's goal by 2010 is to complete its existing review of OTC drug products, to have considered a number of key foreign drugs for marketing in the United States, and to have considered a number of key potential "prescription (Rx)-to-OTC" switches that could result in further consumer empowerment in self-medication. FDA would like to be able to become more proactive in recommending Rx-to-OTC switch candidates and in identifying drugs with only foreign marketing experience as candidates for the U.S. OTC market. Accomplishing these goals will benefit both consumers and manufacturers of OTC drug products, as well as help to reduce health care costs. To do so will also require additional resources dedicated to the review of OTC drug products.

The OTC drug monographs are "recipes" for marketing OTC drug products without the need for FDA preclearance. The monographs list the allowed active ingredients and the dosage or concentration, the required labeling, and packaging and testing requirements if applicable. The monographs save manufacturers costs and reduce barriers to competition, as they allow both large and small companies to enter the market place with OTC drug products that have to meet the same, uniform criteria. Final monographs (agency final rules) need to be completed for a number of large product categories (e.g., external analgesics, internal analgesics, antimicrobials, oral health care products, laxatives). The process is very complex and requires extensive resources to fully address multiple issues for each product class. The agency's goal with increased resources is to complete the initial review of OTC monographs for 29 categories of drug products by 2010, thereby eliminating all unsafe and ineffective products from the OTC market. As more monographs are completed, this will reduce manufacturers' costs and increase generic competition of OTC drug products, as manufacturers will know exactly what is needed for a new OTC drug product to enter the market place.

With an estimated increase of $1 million, the agency will increase its staff dedicated to the OTC drug review. In addition, the Division of OTC Drug Products staff needs to devote resources to update the existing monographs as new situations arise, e.g., requests to add ingredients currently marketed OTC under new drug applications to the monographs (e.g., ibuprofen, clotrimazole).

Performance: The OTC drug review, to date, has been an evaluation of OTC drug products marketed only in the United States. Recognizing the importance of OTC drug products marketed in other countries and in response to manufacturers requests, FDA expanded the OTC drug review in 2002 to allow

OTC drug products without any U.S. marketing experience to become eligible for the review if they meet certain criteria. The Agency anticipates that a number of products will be submitted for consideration under the new drug application review process, and that eventual inclusion of these products into the OTC drug monographs will help reduce some health care costs, increase competition, and may introduce some new self-medication concepts into the United States. For example, loratadine may have been eligible for consideration under this process as it has been marketed OTC in other countries for some time. If this expansion of the review results in a large number of products being submitted for consideration, the agency will need additional OTC resources to both evaluate these products and complete the original review. Many drugs have been switched from prescription-to-OTC status under the OTC drug review (e.g., antihistamines, nasal decongestants, hydrocortisone for topical use). In recent years, most of the switches have occurred under new drug applications. In FY 2002 four new OTC drug products were approved and seven had approvable actions. FDA acted upon 100% of Rx-to-OTC applications within 10 months of receipt in FY 2002 and made significant progress on 5 OTC monographs (sunscreen, internal analgesic, healthcare antiseptics, laxative, and oral health care). The expansion of the OTC drug review to evaluate foreign OTC drugs is expected to increase switch requests in the near future. The OTC drug industry has stated in the past and continues to state that "Rx-to-OTC" switch has been the impetus for and is the future for growth of the self- medication movement. While CDER is hoping for a 50 percent increase in applications, we do not control the number of applications submitted. For this reason, we do not believe a specific number in this goal is appropriate. FDA recognizes that some of these switch requests involve issues of "OTCness" - determination that the drug is appropriate for OTC use and developing appropriate labeling and other information (such as was done for OTC stop smoking aid products) for safe and effective consumer use of these products without the intervention of a health care professional. Drug products to lower cholesterol are currently being considered, with multiple issues to be resolved. Some of these issues may require FDA research costs via consumer studies.

CDER must be a leader in developing research to better understand consumer behavior. Consumers often make errors in judgement either in selecting to use OTC products or not using OTC products correctly. These errors may lead to increased risk for adverse events for consumers or very little likelihood of benefit. The ability of consumers to appropriately use products marketed OTC is one of the more difficult hurdles for manufacturers to overcome. Many manufacturers are not willing to expend the resources needed to identify possible solutions to errors in consumer use and selection. Research needs to be directed toward understanding the factors that contribute to these consumer behaviors and identify mechanisms for influencing appropriate consumer use of products.

Data Sources and Issues: Review performance monitoring is being done in terms of cohorts, e.g., FY 2003 cohort includes applications received from

October 1, 2002, through September 30, 2003. CDER uses the Center-wide Oracle Management Information System (COMIS) and 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. Published monographs that establish acceptable ingredients, doses, formulations, and consumer labeling for OTC drugs.

5. Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting onsite inspections and data audits annually. (12032)

Context of Goal:FDA approves drug products only after the sponsors provide adequate and reliable information on which FDA can base its decision. 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 (IRB's), 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. Commercial sponsors (e.g., pharmaceutical companies) generally pay for the research studies reported to FDA. Such studies must comply with FDA regulations for informed consent, human subject protection, and the conduct of such studies (21 CFR 50, 56, 312). The Prescription Drug User Fee Act (PDUFA) mandates specific deadlines for review of sponsors' submissions. FDA shares information related to IRB inspections with the Department of Health and Human Services (DHHS) Office of Human Research Protection, which has oversight over federally funded research. DHHS ensures that such studies comply with 45 CFR 46, the "Common Rule."
Performance: PDUFA inspections of clinical investigator study sites are scheduled after a New Drug Application (NDA) has been submitted and, in general, the number of inspections conducted each year has been dependent on the number of NDAs received. The Agency completed 697 BIMO inspections in FY 2000, 553 in FY 2001 and 635 in FY 2002. In FY 2002, there was a reduction in the number of NDAs submitted and this reduced the number of completed inspections. In FY 2001, NDAs submitted to FDA decreased by 40% from the previous year. FDA plans to restore resources to inspections of non-clinical laboratory facilities and IRBs. In addition, FDA plans to conduct more inspections in the earlier stages of the drug development process, and for foreign studies, and those carried out in special populations (e.g.,

pediatrics, geriatrics). The original target of 780 is being revised to establish a new base line of inspection sites that are a result of decreasing NDA submissions in fiscal years 2001 and 2002. From 1997-2000, FDA received between 120-135 NDAs per year, and FDA diverted resources from inspections of non-clinical laboratory facilities and IRBs to inspections of clinical investigator study sites in order to accommodate this increase.
Data Sources: COMIS, Field Accomplishments and Compliance Tracking System (FACTS), and ACCESS databases are used to track assignments and results of inspections/data audits.

6. Facilitate development and availability of medical countermeasures to limit the effects of the intentional use of biological, chemical, or radiological/nuclear agents. (12045)

Context of Goal: The first therapy for those exposed to a biological, chemical, or radiological/nuclear agent is often a drug. FDA has been taking an aggressive and proactive approach to getting information on medical countermeasures into the labeling of already approved drugs. 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. For example, no drug is currently FDA-approved to mitigate the complications associated with vaccinia immunization. Human clinical trial data experience is needed to demonstrate safety and efficacy for specific treatments and to identify new therapeutic drug options.
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 Counterterrorism 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 Counterterrorism uses.
Performance: We have issued various guidance and regulations to help Industry develop drugs as medical countermeasures for biological, chemical, or radiological/nuclear agents.

- Federal Register Notice - "Prescription Drug Products; Doxycycline and Penicillin G Procaine Administration for Inhalation Anthrax (Post-Exposure) (10/19/01 - on display)
- Final Guidance - "Guidance on Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies" (12/10/01 - on display)
- Draft Guidance for Industry - "Inhalation Anthrax (Post-Exposure) Developing Antimicrobial Drugs" (03/15/02 - on display)
- Guidance for Industry - "KI in Radiation Emergencies -- Questions and Answers (04/22/02)

- Federal Register Final Rule - "New Drug and Biological Drug Products; Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible" (05/31/02 -- published) We are also working with other part of the Agency and government to facilitate development of medical countermeasures.
- In conjunction with CDC, developed a "streamlined IND" for the use of gentamicin to treat pneumonic plague.
- In conjunction with CDC, assessed the databases for the use of gentamicin for the treatment of inhalation plague and reviewed all known cases in this country since the 1950's.
- Worked with the CDC and the Defense Department to implement a shelf-life extension program for stockpiled drugs for civilian and military use.
- Coordinated within FDA and other agencies to halt the importation of unapproved Cipro.
- In an effort to have products in the National Pharmaceutical Stockpile (NPS) adequately labeled, the FDA is worked with CDC to identify products requiring an Investigational New Drug (IND) application. Together the FDA and CDC have developed the concept of a "Streamlined" IND, which meets the Agency regulatory requirements and allows access to the NPS armamentarium in the event of a terrorist event.

Data Sources and Issues: Published case reports of plague by the Center for Disease Control and Prevention, CDC National Pharmaceutical Stockpile (NPS) program, database from Department of Energy/REAC/TS (Oakridge), published guidances for Industry.

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

Context of Goal: This goal has been consolidated into goal #6 above for FY 04 and FY 03. 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.
Performance: Issued and posted the Draft Guidance for Industry: *Inhalational Anthrax (Post-Exposure) - Developing Antimicrobial Drugs* (dated March 18, 2002).
Data Sources: Published literature.

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

Context of Goal: This goal has been consolidated into goal #6 above for FY 04 and FY 03. 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.
Performance: The FDA has established an IAG with NIAID/NIH and USAMRIID entitled "Non-Human Primate Studies of Antibiotic Efficacy for Treatment of Pneumonic Plague Induced by Aerosolized Yersinia Pestis.
Data Sources: Published literature, interactions with USAMRIID and NIH as part of the FDA/NIH Antibiotic Working Group Interagency Agreement (IAG) with NIAID/NIH and USAMRIID.

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

Context of Goal: This goal has been consolidated into goal #5 above for FY 04 and FY 03. 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).
Performance: The FDA has contacted several of its review divisions to identify approved therapies and candidate therapies against nerve agents. A request for information from the American Academy of Pediatrics was made in May 2002 regarding clinical data on atropine and pralidoxime to determine their use as therapies for nerve agent exposure in the pediatric population. On January 17, 2002, FDA approved nerve gas antidote ATNAA (atropine/pralidoxime) for the treatment of poisoning by susceptible organophosphorous nerve agents having anticholinesterase activity. These two products are already approved separately, but this approval provides for one injection rather than two allowing for more efficiency and convenience on the battlefield. This product is a dual-chambered autoinjector intended for intramuscular administration. This product will initially only be used by the military, but there is some talk that it may be shared with first responders in the case of an emergency.
Data Sources: Published literature, data available from poison control centers, and from a survey of the American Academy of Pediatrics, COMIS, DFS.

10. 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: This goal has been consolidated in goal #6 above for FY 04 and FY 03. 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).
Performance: The Final Rule on the "New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficiency Studies Are Not Ethical or Feasible" was published by the FDA in the Federal Register on May 31, 2002.
Data Sources: Public comment on the Proposed Rule (October 5, 1999, 64 FR 53960).

Strategic Goal 2:
Enhance organizational performance in response to stakeholder needs with the highest degree of cost effectiveness and efficiency.

A. Strategic Goal Explanation

CDER¥s mission (to assure that safe and effective drugs are available to the American people) is primarily achieved through sound regulatory decision making. However, to ensure that drugs are available in a timely manner, our processes must be efficient. We must continually reevaluate our programs to make sure that they are meeting their goals and keeping pace with advances in technology.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
11. Improve the capability and efficiency of pharmaceutical development and manufacturing.(12052 - Formerly 12016)	FY 04: PAT - Present during 1 trade meeting and 3 conferences.Review comments to the draft guidance.PQRI - Continue with significant progress (defined as 50% toward completion for each project identified by PQRI).Implement eCTD guidance. FY 03: PAT - Present during 1 trade meeting	FY 04: FY 03:	8, 4

	and 2 conferences.Meet with 2 potential applicants.Prepare a draft guidance.PQRI - Move toward 25% of completion for each of the three projects. (Initiate draft blend uniformity guidance in response to PQRI comments and participate in 2 PQRI work groups to develop recommendations)Finalize eCTD guidance. FY 02: NA	FY 02: NA	
12. Create state-of-the-art information management systems and practices to move to a paperless environment(e-Government). (12051)	FY 04: 85% of original NDAs to contain some electronic portion;60% of original NDAs to be completely electronic;20% of supplemental applications to be completely electronic;20% of supplemental applications to contain some electronic portion FY 03: 80% of original NDAs to obtain some electronic portion;55% of original NDAs to be completely electronic;15% of supplemental applications to be completely electronic;15% of supplemental applications to contain some electronic portion FY 02: NA	FY 04: FY 03: FY 02: NA	8, 4 Efficiency
TOTAL FUNDING: ($ 000)	FY 04: 10,689 FY 03: 9,336 FY 02: NA FY 01: NA	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

	FY 00: NA	

C. Goal-By-Goal Presentation of Performance

11. Improve the capability and efficiency of pharmaceutical development and manufacturing. (12016)

Context of Goal: In conjunction with stakeholders from Industry and academia, FDA has started important initiatives to build a foundation of scientific data needed to modernize American drug manufacturing. Although Americans have the highest quality of drugs in the world, the processes used to produce some of them are outdated. An increasing trend of manufacturing-related problems, such as recalls, disruptions of manufacturing operations, and the loss of availability of essential drugs has affirmed CDER's role as a catalyst for this initiative. Implementation of modern technology into the manufacturing process will produce the same or higher quality standards while reducing the workload for Industry and for FDA and ensuring the highest quality drug products for American consumers. More than 40 years ago, Congress required that all drugs must be produced in accordance with current Good Manufacturing Practice (cGMP). This requirement was intended to address significant concerns about substandard drug manufacturing practices by applying quality assurance and control principles to drug manufacturing. As we approach the 25th anniversary of the last major revisions to the drug cGMP regulations, it is time to evaluate the currency of both the cGMP program and the pre-market review of chemistry and manufacturing issues. The initiative seeks to integrate quality systems and risk management approaches into the existing programs and encourages adoption of modern and innovative manufacturing technology. In addition, the initiative will use existing and emerging science and analysis to ensure that limited resources are best targeted to address important quality issues, especially those associated with predicted or identifiable health risks.
Performance: CDER has embarked on two important related activities: the Product Quality Research Institute (PQRI) and the Process Analytical Technology (PAT). PQRI is an effort between the FDA's Center for Drug Evaluation and Research (CDER), the pharmaceutical Industry and academia. PQRI is a foundation established under the auspices of the American Association of Pharmaceutical Scientists (AAPS). The purpose of PQRI is to conduct research on identified projects to establish better testing methods, standards, and controls for assessing product quality and manufacturing and management processes to look at risk/benefit of changing certain policies and requirements. This knowledge aids the Agency in developing consistent and reasonable requirements for product quality information in regulatory filings as a part of our risk management activities. 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. CDER is utilizing the Process Analytical Technology (PAT) Initiative to provide a science based regulatory framework. Industry has been hesitant to implement new technologies because of unknown factors that may arise under the regulatory environment in which it operates. CDER has formed a PAT subcommittee to the Advisory Committee for Pharmaceutical Science. A cadre of PAT specialists from the Office of Regulatory Affairs (ORA) and CDER has been established and trained.
In addition to the improvements of manufacturing development and new technologies, CDER has been very involved in promoting increased usage of electronic submissions. CDER plans to finalize guidance on Electronic Common Technical Document (eCTD), a standardized way of sending a CTD-based electronic submission from Industry to the regulatory authority, including foreign countries. CDER participates in the International Conference on Harmonisation (ICH), a collaboration of representatives from the US, the European Union (EU) and Japan. Implementation of eCTD will eliminate the need to repeat time-consuming and expensive technical tests that have already been performed in other countries participating in the ICH and will enable Industry to submit applications using a standard format.
Data Sources: Guidance documents. Relevant materials may be found on our website.

12. Create state-of-the-art information and knowledge management systems and practices to move to a paperless environment (12051)

Context of Goal: The use of current technology will allow CDER to receive and review regulatory submissions more efficiently. In order to move to a paperless environment in an efficient and cost effective manner, we must develop standards for submission.
Performance: CDER has been increasing its capability and capacity to receive and review electronic regulatory submissions. Currently, 75 percent of original NDAs received in CDER now include sections that conform to the electronic submission guidance. Only 15% of all NDA submissions are provided entirely in electronic format. In FY 2001, CDER received over 1000 electronic submissions, including full NDAs, supplemental NDAs, and amendments. Electronic submissions continue to provide a significant decrease in the average number of volumes per NDA submissions since the start of electronic submissions in 1997. We are in the process of developing the following regulations and guidance documents:

- Updating *Providing Regulatory Submissions in Electronic Format* - General Considerations with the participation of CBER, CDER, CDRH, CFSAN and CVM
- A joint CDER/CBER guidance, *Providing Regulatory Submissions in Electronic Format* - Annual Report for Approved NDAs.
- A guidance for electronic submissions of Drug Master Files.

- *Providing Regulatory Submissions in Electronic Format - Prescription Drug Advertising and Promotional Labeling* , which is being developed with CBER
- A proposed rule for changes to 21 CFR 201.56 and 201.57, *Requirements on Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format*
- A proposed rule is being developed to require electronic submissions of drug registration and listing information (DRLS). FDA is building upon the results of the pilot project and is working towards implementing a similar system on a larger scale in the near future. Implementation plans are being developed.

This past year CDER announced a pilot project involving the testing of the Patient Profile Viewer (PPV). The PPV is computer software being developed under a Cooperative Research and Development Agreement which allows a reviewer to display data collected from case report tabulations (CRTs) submitted in electronic format. This program is being developed to improve review efficiency, develop standards for submission of data, and eliminate the need for the submission of separate patient profiles by applicant of NDAs. CDER together with CBER is working on the development of an electronic Common Technical Document (eCTD) review tool for marketing applications. This tool is intended to utilize submissions in the eCTD format as specified by the technical working group in the International Conference on Harmonisation. This work will be the foundation for efforts on developing an electronic file management system for submission of other applications including the IND. CDER is also involved with the development and implementation of standards through a number of processes.

- CDER is a member of the FDA Data Council which serves as the agency focal point for coordination of standardized data elements and electronic data across all centers.
- CDER is participating in Health Level Seven, an ANSI accredited standards development organization for healthcare issues, for the development and implementation of standards.
- CDER is working on partnerships and leveraging opportunities to develop and implement study data standards to improve communication between organizations involved in regulated research.
- CDER has signed a Memorandum of Understanding with the National Library of Medicine to help with the establishment of medication reference terminology.

Data Sources: The Electronic Document Room

Strategic Goal 3:
Prevent unnecessary injury and death to the American public caused by adverse drug reactions, medication errors, and product problems.

A. Strategic Goal Explanation

The practical size of premarketing clinical trials means that we cannot learn everything about the safety of a drug before we approve it. Therefore, a degree of uncertainty always exists about the risks of drugs. This uncertainty requires our continued vigilance to collect and assess data during the postmarketing life of a drug. Once a drug is approved for sale in the United States, we monitor the use of marketed drugs for unexpected health risks. If new, unanticipated risks are detected after approval, we take steps to inform the public and change how a drug is used or even remove a drug from the market. We also monitor manufacturing changes to make sure they won't adversely effect the safety or efficacy of the medicine. We evaluate reports about suspected problems from manufacturers, health care professionals and consumers. Sometimes, manufacturers run into production problems that might endanger the health of patients who depend on a drug. We try to make sure that an adequate supply of drugs is always available. FDA also must be vigilant to protect Americans from injuries and deaths caused by unsafe, illegal, fraudulent, substandard or improperly used products. We monitor the quality of marketed drugs and their promotional materials through product testing and surveillance. As Americans are increasingly receiving the benefits of important new drugs before they are available to citizens of other countries, we must be especially vigilant in our surveillance to prevent fraudulent activities involved with the sale of approved and unapproved prescription drugs. In addition, we develop policies, guidance and standards for drug labeling, current good manufacturing practices, clinical and good laboratory practices and Industry practices to demonstrate the safety and effectiveness of drugs.

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. FDA has been partnering with others in DHHS to promote patient safety and prevent medical errors. FDA is taking the lead on a national adverse 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.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
13. Enhance postmarketing drug safety. (Formerly: Streamline adverse	FY 04: Increase the receipt of Periodic Safety Update Reports	FY 04:	5

drug event reporting system.) (12007)	(PSURs) electronically into CDER's electronic document room. (Receipt of the reports is voluntary).Publish final guidance to Industry on good risk assessment and risk management, and pharmacovigilance practices (PDUFA-3).Enhance AERS to support medication error capture and analysis.Submit majority of Adverse Drug Reaction (ADR) reports electronically. FY 03: Publish draft guidance to Industry on good risk assessment, risk management, and pharmacovigilance practices.Major reporting companies will be submitting all types of ADR reports electronically. Goal: 40% of all expedited ADR reports. FY 02: Continue AERS development. Accept electronic submissions from	FY 03: FY 02: AERS versions 3.0 (provides for MedDRA upgrade from v1.0 to v4.0); 3.1 (E2BM and DTD 2.1); and 4.0 (Oracle and Windows upgrade) were implemented. 291,422 ADR reports submitted. 20,560 ADR reports (7%) were submitted electronically, a 37% increase relative to FY01. Successful testing of electronic PSUR submissions completed. FY 01: AERS version 2.1 (Compliance) completed. AERS versions 2.2 (Electronic Submissions) and 2.3 (Data Entry)	

	companies and be current with MedDRA terminology versions. FY 01: Issue Proposed Rule on adverse event reporting requirements. Issue Guidance on electronic submission of adverse event reports. Grant waivers to companies wishing to submit adverse event reports electronically. Continue AERS development (post 2.0 functionality). Roll out of AERS Datamart to medical 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	both implemented. 15,000 ISRs submitted electronically. FY 00: Development and roll-out of AERS 2.0 was completed. Pilot program to increase participation in electronic expedited reporting is ongoing. FY 99: The AERS was successfully implemented and has been operational for nearly three years.	

	mandatory ADR reports.		
14. CDER will conduct laboratory research on projects identified as related to the mission of PQRI.(12016)	FY 04: NA FY 03: NA FY 02: Conduct laboratory research on at least 3 projects FY 01: Initiate laboratory research on at least 3 projects FY 00: 25% Goal metric changed for FY 01 and 02. See Context Section	FY 04: FY 03: FY 02: Conducted 3 laboratory research programs and performed the corresponding research in connection with the mission of PQRI; Oral Biopharmaceutics, Drug Product, and Drug Substance. FY 01: 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. 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	4

		bioequivalence.	
15. Inspect 55% of registered high-risk human drug manufacturers.(12020)	FY 04: 55% of an estimated 630 establishments in the high-risk category. FY 03: 55% of an estimated 630 establishments in the high-risk category. FY 02: Inspect 20% of registered human drug manufacturers, repackers, relabelers and medical gas repackers. FY 01: 26% FY 00: 22% FY 99: 22%	FY 04: FY 03: FY 02: 24% of 6407 FY 01: 19% of 6407 FY 00: 22% of 6407 FY 99: 26% of 6509	5
16. Give consumers and health professionals more easily understandable, accessible, timely, and accurate prescription and OTC drug information. (12027)	FY04: Initiate 3 new public education campaigns and continue work on 2 in progress. Implement the following electronic initiatives: Electronic Labeling Information Processing System (ELIPS), Medication Information Databases for new drug applications (MedID), web-based electronic drug registration	FY 04: FY 03: FY 02: NA FY 01: The OTC label education campaign was further developed and implemented and additional emerging consumer risk-management	5

	and listing database, DailyMed for new drug applications, and FDA/NLM public Ingredient Dictionary. FY 03: NA FY 02: NA FY 01: Give consumers and health professionals more easily 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.	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.	
17. 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	FY 04: NA 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	FY 04: FY 03: FY 02: Draft proposed rule is in development	2, 5

launch of the electronic database. (12042)	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 allow for complete and up-to-date data on all regulated drug products.		
18. Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax. (12043)	FY 04: NA FY 03: NA FY 02: Publish a Notice in the Federal Register on doxycycline and penicillin G procaine dosing recommendations for inhalational anthrax.	FY 04: FY 03: FY 02: The Notice, Prescription Drug Products: Doxycycline and Penicillin G Procaine Administration for Inhalational Anthrax (Post-Exposure) was published in the Federal Register on November 2, 2001.	2, 5
19. Issue guidance on the use of potassium iodide (KI) as a thyroid blocking agent in radiation emergencies. (12044)	FY 04: NA FY 03: NA FY 02: Issue guidance on the use of potassium iodide (KI) as a	FY 04: FY 03: FY 02: The Guidance: Potassium Iodide as a Thyroid	2, 5

	thyroid blocking agent in radiation emergencies.	Blocking Agent in Radiation Emergencies was published in November 2001. The Guidance for Industry: KI in Radiation Emergencies - Questions and Answers was published in April 2002.	
TOTAL FUNDING: ($ 000)	FY 04: FY 03: FY 02: FY 01: FY 00:	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

13. Enhance postmarketing drug safety. (Formerly: Streamline adverse drug event reporting system). (12007)

Context of Goal: CDER uses a number of postmarketing risk assessment approaches to ensure the continued safe use of drug products. Yet, approximately 1.3 million patients each year are injured from medical therapy with up to two thirds of these events due to medical management errors. Costs from these medical errors range from $37 to $50 billion annually. The Institute of Medicine estimates that as many as 100,000 Americans die annually as a result of preventable medical errors and the proliferation of new products may increase this number. In fiscal year 2002, FDA received 291,422 reports of suspected drug-related adverse events for entry into the Adverse Events Reporting System (AERS), of which 43% represented serious or unexpected events. 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. Reports of deviations from Good Manufacturing Practices that occur during the manufacturing, shipping, or storage of prescription or OTC drug products are sent to the FDA's Drug Quality Reporting System (DQRS). FDA receives medication error reports 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 adverse event and medication error reports to identify serious or potentially serious outcomes that

might be avoided by modifying the labeling or packaging or other means. AERS is an important risk assessment database essential for identifying and monitoring the incidence of adverse effects. 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. CDER is utilizing a $3 million increase in FY 2004 to support the design and implementation of improvements to the Adverse Events Reporting System (AERS) to enhance medication errors monitoring. Improved efficiencies in AERS will begin to address the challenges inherent in managing the risks and reducing preventable adverse events associated with medical product use by creating a seamless interaction between the FDA and consumers, health care personnel, and the regulated Industry.

CDER will also coordinate with Medical Device contractors to continue Implementation of drug products into Phase III of the Medical Device Surveillance Network (MeDSuN). MeDSuN is designed to train hospital personnel to accurately identify and report injuries and deaths associated with medical products. The MeDSuN model, currently designed to track and analyze adverse events due to medical devices, will be expanded to include drug products. Initial work included a feasibility and acceptability assessment of a small regional group of hospital pharmacists about incorporating MeDSuN into their reporting of adverse drug effects and medication errors. In FY 2003, follow-up activities will include additional focus group assessments and individual site visits. Subsequent research efforts will address the hospital's decision-making process to participate in MeDSuN and to integrate risk manager reporting on devices with the reporting of adverse drug events and medication errors by hospital pharmacists or other personnel. This is also described under the MeDSuN performance goal.

Performance: AERS has been operational for nearly five years. Note the following data:

Fiscal Year	Total # of Reports Submitted	# of Serious/Unexpected ADR reports (% of total)	# of ADR Reports Submitted Electronically (% of total)	% of Serious/Unexpected ADR Reports Submitted Electronically
1999	273,926	79,949 (29%)	0 (0%)	0%
2000	260,411	90,987 (35%)	537 (0.2%)	1%
2001	291,184	108,974 (37%)	13,240 (4.5%)	12%
2002	291,422	127,458 (44%)	20,560 (7%)	16%

In February 2001, AERS version 2.1 enhanced the compliance and Freedom of Information portions of AERS by making it more accessible to compliance staff and improving compliance-related search capabilities. In May 2001, AERS version 2.2 enhanced the ability of the system to accept electronic submissions. AERS version 2.3 was implemented in August of 2001. In FY 2002, AERS version 4.0, the Windows/Oracle upgrade, has been implemented. In addition, MedDRA coding version was upgraded to 4.0. AERS versions 3.0 (provides for MedDRA upgrade from v1.9 to v4.0); 3.1 (E2BM and DTD 2.1); and 4.0 (oracle and windows upgrade) were implemented on December 17, 2001; April 1, 2002; and September 23, 2002, respectively.CDER implemented an Electronic Submission Product Test Pilot for AERS in October 2000. This pilot is part of a step-level implementation program to provide a mechanism for companies to test and send electronic submissions of expedited reports via physical media or gateway directly into AERS. The pilot allows FDA to identify and resolve several process issues while regulatory and infrastructure changes are implemented. 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 pilot moved to a production phase in FY 2002. The number of ADR reports submitted electronically has increased each year. (See specific electronic submission data in the first paragraph.) The proposed rule on Adverse Drug Reporting (ADR) and guidance on electronic submissions is in the process of being finalized. In May 2001, a draft guidance for Industry, "Providing Regulatory Submissions in Electronic Format - Postmarketing Expedited Safety Reports" was released. On May 18, 2001, Postmarketing Expedited Safety Reports - 15-Day Alert Reports, was added to public Docket 92S-0251. This allowed for voluntary electronic reporting of 15-day (expedited) safety reports with no paper submissions required. In FY 2001, over 15,000 individual case safety reports were submitted electronically under the pilot program (see Figure 3 below).

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. Guidance document development is a goal included in PDUFA-3. The goal states that by the end of FY 2004, CDER and CBER will jointly develop final guidance documents that address good risk assessment, risk management, and pharmacovigilance practices. A pending proposed rule will include the replacement of periodic drug adverse experience reports (21 CFR 314.80) with Periodic Safety Update Reports (PSURs); currently, CDER encourages Industry to submit a waiver to allow submission of PSURs instead of periodic drug adverse experience reports. PSURs are in the format proposed by the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, Topic E2C. The PSUR summarizes the safety data received by a sponsor for an application from worldwide sources

for a specific timeframe. The number of PSURs received is dependent on the number of NDAs/ANDAs marketed.

Data Sources: AERS and DQRS.

14. CDER will conduct laboratory research on projects identified as related to the mission of PQRI. (12016)

Context of Goal: This goal has been consolidated into goal #11 above for FY 04 and FY 03. The Product Quality Research Institute (PQRI) is a prototype collaboration among FDA, academic, and Industry scientists to conduct research in the areas of pharmaceutical chemistry, biopharmaceutics. The purpose of this research on the three identified projects is to establish better testing methods, standards, and controls for assessing product quality and manufacturing and management processes to look at risk/benefit of changing certain policies and requirements. This knowledge aids the Agency in developing consistent and reasonable requirements for product quality information in regulatory filings as a part of our risk management activities. Leveraging scientific expertise in this way contributes to streamlining the drug development and approval processes for Industry and FDA while ensuring the highest level of product quality.
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. These programs are expected to contribute to developing/revising bioavailability/equivalence, SUPAC, and drug substance regulations for product quality. In FY 2002, FDA conducted 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 added to the Biopharmaceutics Classification System (BCS) database, performed in vitro permeability studies to support the review of BCS biowaiver requests, performed a third food effect clinical studies and continued to develop novel models of using in vitro methods to predict in vivo bioavailability and bioequivalence. The Drug Product program collected Near-IR spectra and then dissolution data of 240 tablets representing the 40 furosemide tablet formulations that were designed and manufactured in FY 2001. Using chemometric analysis, the feasibility of predicting product dissolution using a nondestructive test (Near-IR spectroscopy) was demonstrated. The Drug Product program also investigated regulatory applications of noninvasive imaging by Near-IR and conducted blend uniformity studies in final dosage form. The Drug Substance program initiated the API Test Study as an approach to rapidly detect counterfeit versus authentic drug substances. The study employed three fingerprint techniques: Near-IR, Raman and Ion Mobility. Four test sets (tropicamide, hydrocortisone, quinine, and tryptophan) were evaluated by each technique. The Drug Substance program also evaluated the regulatory acceptability of using Near-

IR to monitor drug substances for polymorphism and states of hydration. FDA met its goal for FY 2002. CDER will complete a review of at least one PQRI recommendation and participate in two PQRI work groups to develop additional recommendations. FDA will also cosponsor two scientific workshops to bring together our scientists with external experts. In FY 2004 CDER will continue with significant progress on the three identified project (defined as 50 percent toward completion for each project; completion is considering the recommendations, give them appropriate scientific vetting, and then changing, etc., our policies to incorporate the recommended change(s)).
Data Sources:

15. Inspect 55% of registered high-risk human drug manufacturers. (12020)

Context of Goal: FDA has changed the performance target for manufacturing inspections from 20 percent of all drug establishments to 55 percent of high risk establishments in support of a risk-based approach that focuses scarce inspectional resources on drug establishments where FDA intervention is likely to achieve the greatest public health impact. This approach will encourage more inspections at drug establishments where FDA can intervene to address or prevent manufacturing problems that would have the most significant adverse effect on drug safety and effectiveness. This goal measures performance for the inventory of registered domestic drug establishments which operate under high risk conditions. The categories are defined as follows:

- New registrants - Drug establishments registered over the past year for which no regulatory information about the firm is known. Inventory 100, 100 percent coverage, 100 inspections.
- Manufacturers of sterile drug products - The characteristics of products manufactured in this category are complex, unique and particularly vulnerable to contamination. Inventory 130, 50 percent coverage, 65 inspections
- Prescription drug manufacturers - Drug products that are used to treat, prevent or diagnose illnesses, which are more potent and susceptible to cross contamination and variability concerns. Inventory 400, 50 percent coverage, 200 inspections.

To accomplish this goal, inspections of new registrants may be carried out by FDA directly, or through State contracts or partnership agreements. Achievement of the goal relies on the willingness and ability of the States to contract with FDA to share in the workload. 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. With a working total inventory of 6000 registered/domestic-sited establishments, the 630 high risk establishments represent 11 percent of the total inventory of sites. For FY 2003

we are projecting a total inspection accomplishment of 1,275 inspections, the high risk establishments above plus the balance at other establishments from the inventory, for the assessment of compliance with the GMP requirement. This represents an overall rate of 21 percent against the biennial inspection requirement (50 percent rate).
Performance: There was no planned coverage percentage established in FY 2002. Target coverage percentages for 2003 is 55 percent of an estimated 630 establishments in the high risk inventory categories.
Data Sources: The inventory of high risk drug establishments is based on compliance status reports developed from the Field Information System and is augmented by a list of targeted establishments generated by the CDER, based on their judgement of those establishments that meet the high risk criteria defined above.

16. Give consumers and health professionals more easily understandable, accessible, timely, and accurate prescription and OTC drug information. (12027)

Context of Goal: (Dropped for FY 2002 and 2003) This goal was dropped for FY 2002 and 2003 because more specific and quantifiable milestones needed to be developed. The goal is being reinstated for FY 2004 with new, detailed targets. There is increasing 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. Information and outreach efforts will continue to concentrate on improving the safety of drug use. FDA is the recognized source for having the most up-to-date, accurate information. The Agency strives to conduct timely, relevant campaigns based on existing or emerging needs, issues, and events. Thus, the specific subjects of FY 2004 education campaigns will be determined as issues and events reveal themselves closer to FY 2004. Providing 'user-friendly', accurate information will increase patient safety by potentially reducing medication errors.
Performance: In FY 2001, the FDA met almost weekly with outside experts on difficult scientific and public health issues; responded to more than 52,000 individual requests for information. We also launched twice-yearly, week-long introductory workshops for our stakeholders; and received nearly 6.6 million visitors and about 111 million hits on our Internet information site. We launched a public education campaign on consumer-friendly brochure on how to play an active role to reduce risks and maximize benefits of using medications. We developed an outreach plan to eliminate deaths and injuries occurring when incorrect medical gas tanks are connected to oxygen lines in hospitals and nursing homes. 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.
FDA's Web site increasingly focused on consumer information, building

introductory pages on drug safety, bioterrorism drugs, and risk management. Examples of Consumer-oriented risk management information were posted on the web site in FY 2001. 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.
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. An initial step in synchronizing the Agency's consumer information campaigns with Web sites included Over-the-Counter labeling and food-drug interactions.
In cooperation with its leveraging partners, FDA continued to develop the Over-the-Counter Medicine Label Campaign in anticipation of full implementation by manufacturers in FY 2002. To address the growing problem of the emergence of drug-resistant bacteria and its effects on drug development and regulation, the Agency is developing approaches to provide education and information on the appropriate use of antibiotics to health care professionals and consumers. Details of these efforts and other resources are available on the Agency's web site.
Data Sources: Approval Letters and the Labeling Text or Final Printed Label (FPL) for new drugs; Consumer Drug Information Sheets for New Molecular Entities (NMEs); 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.

17. 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 drugs products, and follow this finalization with launch of the electronic database. (12042)

Context of Goal: Section 510 of the Federal Food Drug and Cosmetic Act requires all establishments engaged in the handling of pharmaceutical products to register and list their products with the Food and Drug Administration. Recently, Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Section 321 - Annual Registration of Foreign Manufacturers, electronic registration is required. CDER has been working to overhaul its legacy Drug Registration and Listing System data and processes, including revisions to the current regulations and mandatory electronic submission of DRLS data by the regulated Industry. This new automated system will provide timely, accurate information about the availability of drugs in an efficient process. 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. 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.
Performance: The current CDER proposal consists of continuing the Drug Listing and Registration paper based system, while concurrently developing the electronic e-DRLS system and moving toward publication of a proposed rule in FY 2003. The rapid development of the system over the next 6 to 12 months would be coordinated with the draft regulations as it works its way to final issuance. The electronic system would be implemented concurrent with the issuance of the final rule. FDA relies on complete and accurate establishment registration and product listing information to accomplish a number of its statutory and regulatory objectives. For example, FDA uses establishment registration and product listing information to: (1) Identify firms that manufacture a specific product or ingredient when that product or ingredient is in short supply or needed for a national emergency, for example, during a bioterrorism threat (for example, the drug listing database was used to identify sources of potassium iodide during the Three Mile Island incident); (2) Identify the locations of all establishment sites engaged in the manufacture, preparation, propagation, compounding, or processing of drugs or biologics; (3) Identify all the establishments involved in the processing of a drug or biologic from the original place of manufacture to the person who makes the final delivery or sale to the ultimate consumer or user; (4) Catalogue human and veterinary drugs and biological products in commercial distribution; (5) Administer FDA's postmarketing surveillance programs for human and veterinary drug products and licensed biological products; (6) Determine which products subject to section 505 of the act (21 U.S.C. 355) are being marketed without approved new drug applications; (7) Schedule and plan inspections of registered establishments as authorized under section 704 of the act (21 U.S.C. 374); and (8) Determine which marketed drug products are identical, related, or similar to drug products reviewed by the Drug Efficacy Study Implementation (DESI). The Agency also relies on registration and listing information to help determine which establishments and products are subject to user fees under the Prescription Drug User Fee Act of 1992 (Public Law 102-571), as amended by the Food and Drug Administration Modernization Act of 1997 (Modernization Act) (Public Law 105-115). In addition, the Agency uses registration and listing information to generate accurate estimates of registered establishments and marketed products that are affected by FDA rulemaking. These estimates help FDA assess the economic impact of its regulations on the regulated Industry, which the agency is required to do under the Regulatory Flexibility Act of 1980 (Public Law 96-354, as amended by Public Law 104-121), the Paperwork Reduction Act of 1995 (Public Law 104-13), and Executive Order 12866 (September 30, 1993). An electronic registration and listing system will enable FDA to use the latest technology to improve its current paper based registration and listing system, which would further its goal of protecting the public health. FDA also believes that the conversion to an electronic system will make the registration and listing

process more efficient for Industry and the agency.
Data Sources: Published literature; Drug Registration and Listing System (DRLS).

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

Context of Goal: This goal has been consolidated under goal #6 above for FY 04 and FY 03. 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.
Performance: The Notice, Prescription Drug Products; Doxycycline and Penicillin G Procaine Administration for Inhalational Anthrax (Post-Exposure) was published in the Federal Register on November 2, 2001
Data Sources: Published literature.

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

Context of Goal: This goal has been consolidated into goal #6 above for FY 04 and FY 03. 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.
Performance: The Guidance: *Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies* was published in November 2001. Additionally, the Guidance for Industry: *KI in Radiation Emergencies - Questions and Answers* was published in April 2002.
Data Sources: Published literature.

2.4 BIOLOGICS

2.4.1 Program Description, Context and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	169,791	199,699	177,842	147,230	140,717

The mission of the Biologics Program is to ensure the safety, purity, potency, and effectiveness of biological products (primarily vaccines and blood products) 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% 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 Component 1:
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).

FDA is in the process of establishing a comprehensive new system through the tissue action plan to regulate human cells, tissues, and cellular and tissue-based products. The goal of the new approach, published in the Federal Register on February 28, 1997, is to improve protection of the public health without imposing unnecessary restrictions on research and development, or on the availability of new products. This system is expected to lead to increasing

the safety of transplanted human cells, tissues, and cellular and tissue-based products, while encouraging the development of new products.

PDUFA Products: FDA worked with various stakeholders, including representatives from consumer, patient, health provider groups, and the pharmaceutical and biological prescription drug industries, to develop a reauthorization proposal for PDUFA that would build upon and enhance the success of the program. Title 5, Subtitle A, of the Public Health Security and Bioterrorism Preparedness and Response act of 2002 (Public Law #107-188) was enacted on June 12, 2002. The Act extends PDUFA through 2007.

The PDUFA authorized revenues from fees paid by the pharmaceutical industry to expedite review by the FDA of human drug applications, including biologics.

Fees that FDA collects 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 provides FDA with the resources necessary to sustain the larger application review staff. It also provides 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 goals were phased in over several years.

Non-PDUFA Products: The Biologics Program also reviews and approves license applications for products not covered by PDUFA. The mission of the Blood Program is to ensure that blood, blood products, biotechnology-derived hematologics, and devices associated with their manufacture and use, are safe, effective, and adequately labeled.

The blood supply is critical to the nation's health care system, and the United States has the safest blood supply in the world. Each year approximately 14

million blood units are drawn from volunteer donors for use in more than 3.5 million Americans. FDA vigorously continues to strengthen its efforts to protect the nation's blood supply and to minimize any risk to patients of acquiring the human immunodeficiency virus (HIV), hepatitis, Creutzfeldt-Jakob disease (CJD), and other blood-borne diseases.

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

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Complete review and action on 90% of standard original PDUFA NDA/PLA/BLA submissions within 10 months; and review and act on 90% of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt. (13001)	Standard Applications within 12 months: FY 04: NA FY 03: NA FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90% Standard Applications within 10 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30% Priority Applications within 6 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Standard Applications within 12 months: FY 04: FY 03: FY 02: FY 01: 100% of 5 FY 00: 100% of 10 FY 99: 100% of 5 Standard Applications within 10 months: FY 04: FY 03: FY 02: 09/03 FY 01: 100% of 5 FY 00: 100% of 10 FY 99: 100% of 5 Priority Applications	4

		within 6 months: FY 04: FY 03: FY 02: 04/03 FY 01: 100% of 3 FY 00: 100% of 4 FY 99: 100% of 1	
2. Complete review and action on 90% of standard PDUFA efficacy supplements within 10 months; and review and act on 90% of priority PDUFA efficacy supplements within 6 months of receipt. (13002)	Standard Applications within 12 months: FY 04: NA FY 03: NA FY 02: NA FY 01: 90% FY 00: 90% FY 99: 90% Standard Applications within 10 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30% Priority Applications within 6 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Standard Applications within 12 months: FY 04: FY 03: FY 02: FY 01: 100% of 14 FY 00: 100% of 11 FY 99: 100% of 8 Standard Applications within 10 months: FY 04: FY 03: FY 02: 09/03 FY 01: 100% of 14 FY 00: 100% of 11 FY 99: 100% of 8 Priority Applications within 6 months: FY 04: FY 03: FY 02: 05/03 FY 01: 100% of	4

		2 FY 00: 100% of 2 FY 99: 100% of 2	
3. Complete review and action 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. (13003)	Within 6 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90% Within 4 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 30%	Within 6 months: FY 04: FY 03: FY 02: 05/03 FY 01: 94% of 410 FY 00: 97% of 349 FY 99: 96% of 218 Within 4 months: FY 04: FY 03: FY 02: 03/03 FY 01: 95% of 186 FY 00: 92% of 241 FY 99: 93% of 259	4
4. Complete review and action on 90% of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90% of Class 2 resubmitted original PDUFA applications within 6 months of receipt. (13004)	Class 1 resubmissions within 2 months: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 70% FY 00: 50% FY 99: 50% Class 2 resubmissions within 6 months: FY 04: 90% FY 03: 90% FY 02: 90%	Class 1 resubmissions within 2 months: FY 04: FY 03: FY 02: 100% of 2 FY 01: 100% of 6 FY 00: 100% of 1 FY 99: 100% of 2 Class 2 resubmissions	4

	FY 01: 90% FY 00: 90% FY 99: 90%	within 6 months: FY 04: FY 03: FY 02: 05/03 FY 01: 100% of 10 FY 00: 100% of 8 FY 99: 100% of 12	
5. Complete review and action on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90% of PLA/BLA supplements within 12 months after submission date. (13005)	Complete Submissions: FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 85% FY 99: 60% Supplements: FY 04 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 90% FY 99: 90%	Complete Submissions: FY 04: FY 03: FY 02: 11/03 FY 01: 100% of 7 FY 00: 100% of 12 FY 99: 100% of 10 Supplements: FY 04: FY FY 02: 11/03 FY 01: 99% of 417 FY 00: 100% of 559 FY 99: 99% of 780	4
6. Facilitate the availability of safe and effective biological products to prevent, diagnose, and treat sicknesses or injuries associated with a terrorist attack. (13019)	FY 04: Issue guidance document regarding recommendations for deferral of blood donors who may have been exposed to smallpox. FY 03: Issue guidance	FY 04: FY 03:	2, 4

	document regarding recommendations for deferral of blood donors vaccinated for smallpox.Review and approve a supplement to the license application for use of a 1 to 5 dilution of Dryvax, the FDA licensed smallpox vaccine, to expand the total number of available smallpox vaccine doses. FY 02: NA	FY 02: NA	
TOTAL FUNDING: ($ 000)	FY 04: 134,427 FY 03: 160,550 FY 02: 140,731 FY 01: 114,849 FY 00: 111,968	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

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

The PDUFA application-review performance goals measure time to first action, not final action. The term "complete review and action on" is understood to mean the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval. The performance goals and this definition were developed in consultation with the industry and Congress and are contained in the Secretary's commitment letter 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. This definition enables to the Agency to approve only safe and effective products without having to issue not-approvable decisions on applications that are in some way not in condition for approval.

1. Complete review and action on 90% of standard original PDUFA NDA, PLA, and BLA submissions within 10 months; and review and act on 90% of priority original PDUFA NDA/PLA/BLA submissions within 6 months of receipt. (13001)
Context of Goal: The Prescription Drug User Fee Act authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. Standard original PLAs or BLAs, are license applications for biological products, not intended as therapies for serious or life-threatening diseases. A priority PLA/BLA is a license application for a therapy to treat serious or life-threatening diseases.
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 2002 data for standard applications within 12 months will be available after November 2003. The FY 2002 data for standard applications within 10 months will be available after September 2003.
Data Sources: CBER's Regulatory Management System

2. Complete review and action on 90% of standard PDUFA efficacy supplements within 10 months; and review and act on 90% of priority PDUFA efficacy supplements within 6 months of receipt. (13002)
Context of Goal: The PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A supplement is a change to an approved licensed product. An efficacy supplement provides information to FDA to modify the "approved effectiveness" in the labeling of a product such as a new indication, and normally includes clinical data.
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 2002 data for standard applications within 12 months will be available after November 2003. The FY 2002 data for standard applications within 10 months will be available after September 2003
Data Sources: CBER's Regulatory Management System

3. Complete review and action 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. (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.
Performance: CBER has met or exceeded these performance goals since 1994. These applications are tracked by year of receipt, which is the cohort year.
Data Sources:CBER's Regulatory Management System

4. Complete review and action on 90% of Class 1 resubmitted original PDUFA applications within 2 months; and review and act on 90% of Class 2 resubmitted original PDUFA applications within 6 months of receipt. (13004)
Context of Goal: PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A resubmitted original application is a complete response to an action letter addressing all identified application deficiencies. Class 1 resubmitted applications are applications resubmitted after a complete response letter that include one or more of the following items: final printed labeling; draft labeling; safety updates; stability updates; commitments to perform Phase IV (postmarketing) studies; assay validation data; final release testing; a minor re-analysis of data; other minor clarifying information; or other specific information requested by the Agency. Class 2 resubmissions include any other items.
Performance: These applications are tracked by year of receipt, which is the cohort year. FDA's FY 2002 performance for review of Class 1 resubmissions within 2 months was 100%.
Data Sources: CBER's Regulatory Management System

5. Complete review and action on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90% of PLA/BLA supplements within 12 months after submission date. (13005)
Context of Goal: Blood bank and source plasma applications are not covered by PDUFA. The non-PDUFA review resources in CBER are not protected from cuts as the PDUFA resources are by the PDUFA legislation. CBER's non-PDUFA review resources have been cut in recent years to meet unfunded pay raises, increased current service costs, and other budget actions.
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 2002 data for review of complete submissions and for major supplements will be

available after November 2003.
Data Sources: CBER's Regulatory Management System

6. Facilitate the availability of safe and effective biological products to prevent, diagnose, and treat sicknesses or injuries associated with a terrorist attack. (13019)
Context of Goal: An essential element of the Counterterrorism initiative includes the expeditious development and licensing of biological 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.
Guidance documents assist the Center staff and regulated industry in identifying issues and areas where more specific direction can be outlined and thus contribute to expediting the review process. Issues that need to be explored with respect to the safety and availability of blood and blood products include viral testing and removal in blood, blood products, and plasma derivatives in the event that exposed individuals donate prior to detection; and, the impact on the safety of the blood supply from donations by individuals vaccinated with live vaccines. Identifying areas in the regulatory process where more specific direction regarding requirements is needed facilitates the review process.
Performance: New goal/not available
Data Sources: CBER's Regulatory Management System and the Regulations and Policy Staff

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 goal 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
7. Meet the biennial inspection statutory requirement by inspecting 50% of the approximately 2,700 registered blood banks, source plasma operations and biologics manufacturing establishments to reduce the risk of product contamination. (13012)	FY 04: 50% of approximately 2,700 establishments FY 03: 50% of approximately 2,700 establishments FY 02: 50% FY 01: 50% FY 00: 50% FY 99: 50%	FY 04: FY 03: FY 02: 52% of 2,730 FY 01: 57% of 2,756 FY 00: 57% of 2,756 FY 99: 64% of 2,790	5
TOTAL FUNDING: ($ 000)	FY 04: 35,364 FY 03: 39,149 FY 02: 37,111 FY 01: 32,381 FY 00: 28,749	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

7. **Meet the biennial inspection statutory requirement by inspecting 50% of the approximately 2,700 registered blood banks, source plasma operations and biologics manufacturing establishments to reduce the risk of product contamination.** (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. The inspections are conducted to ensure compliance with Current Good Manufacturing Practices (CGMPs), and ensure the purity of the biological products. There are currently 2,693 establishments in the Biologics Program inventory covered under this statute. The establishments include high-risk establishments such as blood collection facilities, plasma fractionator establishments and vaccine manufacturing establishments. There are 1,665 additional establishments in the Biologics Program inventory not covered under this statute.
   Performance: In FY 2002, FDA inspected 52% of the establishments in the Official Establishment Inventory, exceeding the goal of 50%. The drop in inspection coverage from 64% in FY 1999 to 52% in FY 2002 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.
   Data Sources: Program-Oriented Data System, Official Establishment Inventory.

2.5 ANIMAL DRUGS AND FEEDS

2.5.1 Program Description, Context and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	89,974*	88,972	85,643	64,070	49,593

*Includes proposed user fees.

As a consumer protection organization, the mission of the Animal Drugs and Feeds Program is to foster public and animal health by approving safe and effective products for animals and by enforcing applicable provisions of the Federal Food, Drug, and Cosmetic Act and other authorities. Two strategic goals support the mission of the program:

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 FDA 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 the Animal Drugs and Feeds Program to address problems or safety issues before they become a threat to public health. The Animal Drugs and Feeds Program accomplishes these goals by working with partners in industry, academia, consumers, and other government agencies on: review of animal drugs, compliance and related actions, post-approval monitoring, animal feed safety, inspections, and collection and analysis of samples. The Animal Drugs and Feeds Program approach to achieving the strategic goals and a summary of the key performance goals are explained later in this document.

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 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 harmful drug residue when they reach the consumer. Also, the availability of safe and effective drugs ensures companion and service animals live healthier and longer lives.

The Animal Drugs and Feeds Program, working with industry sponsors, promotes the availability and diversity of animal drugs and feeds by being involved throughout the new animal drug development process. The Agency is committed to improving the review time for new animal drug applications, as well as continuing work to decrease the backlog of pending overdue submissions (Performance Goals 3 and 4). 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 5). To ensure that FDA has the science capability and intellectual capital necessary to assess data and make regulatory decisions, the framework for a staff college has been developed (Performance Goal 6).

These premarket performance goals help the Agency take the specific steps needed to achieve this strategic goal and therein: assure safer human food produced from animals; reduce the cost and time associated with animal drug development; and, improve quality of life for segments of our population because companion and service 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 04: NA FY 03: NA FY 02: 80% FY 01: 80% FY 00: 73%	FY 04: FY 03: FY 02: 85% FY 01: 80% FY 00: 75%	4
2. Complete review and action on 90% of all new animal drug	FY 04: NA FY 03: Complete review & action on 90% of all new animal drug	FY 04: FY 03:	4

applications and supplements received in FY 03 within 275 days; and Complete review and action on 90% of all investigational new animal drug submissions received in FY 03 within 325 days. (14017)	applications and supplements received in FY 03 within 275 days and complete review & action on 90% of all investigational new animal drug submissions received in FY 03 within 325 days. FY 02: Complete review and action on 50% of NADAs/ANADAs within 180 days of receipt. FY 01: 75% FY 00: 73%	FY 02: 67%1932 of 2895 % completed on-time FY 01: 47%961 of 2044 % completed on-time FY 00: 84%1539 of 1841 % completed on-time	
3. Reduce pending overdue Animal Drug submissions by 25%. (14019)	FY 04: 25% FY 03: 15% FY 02: 15%	FY 04: FY 03: FY 02: 64%	4
4. Complete review and action on 90% of NADAs & reactivations of such applications within 295 days; complete review and action on 90% of investigational animal drug study submissions within 320 days; and complete review and	NADAs & reactivations of such applications; FY 04: within 295 days. FY 03: NA Y 02: NA FY 01: FY 00: Investigational animal drug study submissions. FY 04: within 320 days: FY 03: NA FY 02: NA FY 01:	FY 04: FY 03: FY 02: 3/03 FY 01: w/in 776 days FY 00: w/in 588 days FY 04: FY 03: FY 02: 3/03 FY 01: w/in 625 days FY 00: w/in	4

action on 90% of investigational animal drug submissions consisting of protocols, without substantial data, within 125 days. The benefits of the user fee program are provided under the goal presentation. FY 00-01 performance is provided as "baseline" information.(This goal is contingent upon the combined budget authority and user fees.) (14020)	FY 00: Investigational animal drug submissions consisting of protocols without substantial data; FY 04: within 125 days: FY 03: NA FY 02: NA FY 01: FY 00:	498 days FY 04: FY 03: FY 02: 3/03 FY 01: w/in 199 days FY 00: w/in 179 days	
5. Continue electronic submission enhancements. (14002)	FY 04: Continue to expand electronic submissions process & development of Corporate Document Management System. FY 03: Receive & act on protocols forms electronically. FY 02: Pilot and validate the procedure for receiving protocol submissions electronically.	FY 04: FY 03: FY 02: Electronic submission of protocols from industry pilot successfully validated. FY 01: Changed focus of protocol submission to hard media	4, EfficiencyGoal

	FY 01: Initiate the development of a method for receiving protocol submission electronically FY 00: Completed an additional 4 phases - Notices of Slaughter;Notices of Animal Final Disposition;Meeting Agendas;USDA Slaughter Reports FY 99: Complete 1 phase - Notices of Claimed Investigational Exemptions (NCIE).	(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. FY 00: Wrote guidance on 4 phases. Developed technology for logging/routing of electronic submissions. FY 99: 1 phase completed (NCIE).	

6. Continue development, expansion and integration of the Staff College. (14018)	FY04: Continue integration of LMS system w/Center and Agency infrastructure; continue to expand content of in-house programs. FY 03: Expand content of in-house programs. Research and develop components and integration of competency-based learning management system (LMS) with Center and 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 04: FY 03: FY 02: Completed plan and design of Phase I. FY 01: Initiated the development of a Staff College (Phase I).	
TOTAL FUNDING: ($ 000)	FY 04: 34,525 FY 03: 30,120 FY 02: 29,186 FY 01: 26,751 FY 00: 21,117	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

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: (Goal dropped in FY 03.) 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 Animal Drug Availability Act (ADAA) 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.
Performance: Presubmission conference tracking was established in FY 00. The goal was met in FY 00, FY 01 and FY 02. This goal is dropped in FY 03 since the performance appears to be stable, and therefore, no longer provides a useful measurement for Center management.
Data Sources: Submission Tracking and Reporting System (STARS).

2. Complete review and action on 90% of all new animal drug applications and supplements received in FY 03 within 275 days and complete review and action on 90% of all investigational new animal drug submissions received in FY 03 within 325 days. (14017)
Context of Goal: In FY 03, CVM changed this performance goal to a new measure that is 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 submissions. FDA is taking steps to move closer to statutory requirements in future years. Additionally, these steps are contingent on the combined budget authority and user fees. When a new animal drug application is submitted, CVM evaluates the information contained or referenced in the application. A determination is made whether the application is approved or not approved. The sponsor receives a letter informing them either of the approval or describing the deficiencies in the application.
The "days to review" refers to the time it takes to review and take an action on the original submission, or if needed, on subsequent recycles. This is different from total approval time which is the time it takes from the original receipt of the application until it is finally approved, which may take more than one review cycle. This includes the time we spend reviewing the application in each of the review cycles plus the time taken by the sponsor to respond to the issues raised in the not approved letter(s) and resubmit the application for review.
Performance: The performance reporting for FY 00 through FY 02 pertains to the review and action on NADAs and ANADAs within 180 days of receipt. CVM exceeded the FY 00 target with a performance rate of 84%.
CVM found it necessary to shift focus in its performance regarding animal drug application review in FY 2000. The Office of New Animal Drug Evaluation (ONADE) needed to reduce the backlog of overdue submissions. This required working on the oldest, already overdue submissions. 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 submissions, CVM's on time

completion rate for NADAs and ANADAs was adversely affected in FY 01 with 47% of NADAs and ANADAs reviewed on time.
The goal for FY 02 was revised to complete review and action 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. In FY 02, the Animal Drugs and Feeds Program achieved 67% performance for this goal.
Data Sources: Submission Tracking and Reporting System (STARS).

3. Reduce pending overdue Animal Drug submissions by 25%. (14019)
Context of Goal: During FY 2000, the Animal Drugs and Feeds Program conducted an evaluation of performance in the new animal drug review process and determined that priorities needed to shift in order to eliminate the growing backlog in pending new animal drug submissions. This goal was created to facilitate that process and to provide the needed emphasis on this strategic goal of making more animal drugs available. The Animal Drugs and Feeds program will reduce the backlog of pending overdue animal drug submissions by 15% in both FY 02 and FY 03. The target is increased to 25% in FY 04.
Performance: In FY 02, the Animal Drugs and Feeds Program reduced its backlog of pending overdue submissions 64%.
Data Sources: Submission Tracking and Reporting System (STARS).

4. Complete review and action on 90% of NADAs & reactivations of such applications within 295 days; complete review and action on 90% of investigational animal drug study submissions within 320 days; and complete review and action on 90% investigational animal drug submissions consisting of protocols, without substantial data, within 125 days. (14020)
Context of Goal: Established for FY 04, this performance measure is consistent with goals industry has agreed to for user fees. These goals reflect a representative portion of the user fee goals. The benefits provided by the proposed user fee program include: an increase in the reduction rate of the backlog; shorter review times; a more meaningful measure for industry; a more predictable and stable review process; and, an overall reduction in drug development time. (This goal is contingent upon the combined budget authority and user fees.)
When a new animal drug application is submitted, CVM evaluates the information contained or referenced in the application. A determination is made whether the application is approved or not approved. The sponsor receives a letter informing them either of the approval or describing the deficiencies in the application.
The "days to review" refers to the time it takes to review and take an action on the original submission, or if needed, on subsequent recycles. This is different from total approval time which is the time it takes from the original receipt of the application until it is finally approved, which may take more than one review

cycle. This includes the time we spend reviewing the application in each of the review cycles plus the time taken by the sponsor to respond to the issues raised in the not approved letter(s) and resubmit the application for review.
Performance: As mentioned above, for the first time the Animal Drugs and Feeds Program will initiate a user fee program. The user fee program, proposed to start in FY 04, reflects the implementation of a five (5) year plan to improve the performance for animal drug review. A "baseline" reference to performance of the representative user fee goals reflects the effort to eliminate the backlog in pending overdue new animal drug submissions
The following are is the review time in "number of days" for fiscal years 2000 and 2001

NADAs & reactivations of such applications: FY 2000 - 588, FY2001 - 776
Investigational animal drug study submissions: FY 2000 - 498, FY2001 - 625
Investigational animal drug submissions consisting of protocols without substantial data: FY2000 - 179 , FY2001 - 199
Data Sources: Submission Tracking and Reporting System (STARS).

5. Continue electronic submission enhancements. (14002)
Context of Goal: Better-automated information systems, including those supporting electronic submission of applications by sponsors, are being developed to facilitate and expedite the review process. The Animal Drugs and Feeds Program has successfully completed several electronic submission processes for use by the animal industry. Our intention is to move toward a paperless office as rapidly as possible.
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 e-mail to submit electronic information expanded from 13 to 15 sponsors. 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.

In July, 2001, the Center 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 (down from a maximum 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 Animal Drugs and Feeds Program has 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 in October 2002. CVM will participate in the Agency guidance and acceptance of submission to the Agency of Manufacturing Stability data in extensible markup language (XML) format. The Center participated in an Agency Panel at the Drug Information Association Meetings in February 2002.
In FY 02, the draft guidance document and protocol submission were completed. The implementation plan for the pilot and validation of receipt of protocols was drafted. Recruitment of pilot partners began and modification of programming to support receipt of protocols through the Center's Electronic Submission System (ESS) email.
Additional phases of electronic submissions will be initiated in FY 03 in support of this goal. In FY 04, CVM will continue to expand the electronic submission process and development of the Corporate Document Management System.
Data Sources: CVM's priority project tracking system.

6. Continue development, expansion and integration of the Staff College. (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 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.
Performance:
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.
- 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. Reviewed 130 candidates.
- 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.

The goal to plan and design Phase I of the Staff College was completed:

- Developed and implemented a CVM Competency Model through the automated Knowledge Center (KC). The KC is a Learning Management System (LMS) that has and will continue to help reduce administrative costs associated with managing and tracking training and development for the Center. This allows Staff College personnel to devote more time towards development of substantive programs that are responsive to the needs of the Center. The KC also creates and automates an Individual Development Plan (IDP) process for every employee to ensure that both the organizational and individual employee training and developmental needs are addressed.
- Built state-of-the-art training facilities to accommodate distance learning initiatives as well as other traditional learning venues.
- Continuing development of several in-house scientific/reviewer training programs.

Data Sources: CVM's priority project tracking system.

Strategic Goal 2:
Reduce the risks associated with marketed animal products.

A. Strategic Goal Explanation

Once animal drugs are on the market, the Animal Drugs and Feeds Program continues managing public health risks through post-market surveillance activities such as inspections, monitoring, and research. The Animal Drugs and Feeds Program strategies for assuring safety compliance and scientific monitoring are made possible through partnerships with industry and the states. Surveillance of marketed products and industry is accomplished through review of drug experience reports and compliance programs. This involves inspections, sample collections and analysis, investigations, and other

activities (Performance Goal 7). Regulatory actions are taken as needed to control violative goods and firms.

The Animal Drugs and Feeds 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 human food products derived from animals are safe, and ensure quality health care of animals.

The National Antimicrobial Resistance Monitoring System (NARMS) tells FDA when foodborne bacteria that causes disease in humans begins to develop resistance to antimicrobials used in food animals. NARMS (Performance Goal 8), 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.

A 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. The Animal Drugs and Feeds Program plans to conduct 100% inspections of all known renderers and feed mills processing products containing prohibited material in order to maintain compliance with the BSE feed regulation (Performance Goal 9).

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
7. Maintain biennial inspection coverage by inspecting 50% of 1,440 registered animal drug and feed establishments.	FY 04: 50% FY 03: 50% FY 02: 50% FY 01: 50% FY 00: 27% FY 99: 27%	FY 04: FY 03: FY 02: 56% of 1440 FY 01: 37% of 1460 FY 00: 39% of 1460 FY 99: 25% of	5

(14009)		1418	
8. Enhance the transparency of the NARMS program to stakeholders, the public, and other interested parties by increased reporting and communicating of NARMS results and program information. (14005)	FY 04: Post NARMS standard laboratory methods on the Internet to provide easy access by other laboratories conducting antimicrobial resistance research & background information for persons reviewing the NARMS results. Present NARMS susceptibility testing results at Scientific meetings via poster or oral presentations. Publish Annual Reports of NARMS animal, human and retail meat data. Post NARMS publication references on the NARMS website. FY 03: Present NARMS susceptibility testing results at Scientific meetings via poster or oral presentations. Publish Annual	FY 04: FY 03: CY 02: 3/03 CY 01: Total 8,899 Salmonella isolates - 1,671 (human); 6,795 (veterinary); 433 (retail meat) 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)	5

	Reports of NARMS animal, human and retail meat data. Post NARMS publication references on the website. 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)		
9. Conduct targeted BSE inspections of 100% of all known renderers and feed mills processing products containing prohibited material. (14006)	FY 04: 100% FY 03: 100% FY 02: 100%	FY 04: FY 03: FY 02: 100% of 1,305	5
TOTAL FUNDING: ($ 000)	FY 04: 55,449 FY 03: 58,852 FY 02: 56,457 FY 01: 37,319	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

	FY 00: 28,476	

C. Goal-By-Goal Presentation of Performance

7. Maintain biennial inspection coverage by inspecting 50% of 1,440 registered animal drug and feed establishments. (14009)

Context of Goal: FDA exercises considerable discretion regarding the frequency and comprehensiveness of inspections. The Animal Drugs and Feeds Program has a statutory obligation to inspect all regulated animal drug and medicated feed establishments once every two years. 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.
Performance: : FY 99 = 25%; FY 00 = 39%; FY 01 = 37%; FY 02 = 56%. 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.
The goal was not met in FY 2001. The program did accomplish 37% biennial inspection coverage of registered animal drug and feed establishments. Due to the increase in reported cases of BSE in Europe, in FY 2001 FDA concentrated its efforts on performing BSE inspections in the U.S. This intense inspection effort was intended to prevent an outbreak of BSE in the U.S by completing 100% inspection of all firms. In FY 02, FDA inspected 56% of the 1,440 registered animal drug and feed establishments.
Data Sources: Field Accomplishment Compliance Tracking System (FACTS) [formerly known as the Program Oriented Data System (PODS)], Official Establishment Inventory.

8. Enhance the transparency of the NARMS program to stakeholders, the public, and other interested parties by increased reporting and communicating of NARMS results and program information. (14005)

Context of Goal: NARMS is a major national surveillance effort 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. NARMS is adding to our knowledge of drug susceptibility and is helping ensure the continued effectiveness of human and veterinary drugs.
One of the NARMS program goals has always been to provide timely information on antibiotic resistance to physicians and veterinarians to allow them to make informed decisions on treatment options for their patients. For example, a multi-drug resistant variant of Salmonella Newport emerged in humans and animals and was detected in the NARMS data. The participating NARMS agencies alerted the human and veterinary medical communities to this emergence so that they were aware and could take appropriate actions in treating infections with this organism.
Performance: In CY 99 = collected 8,510 animal and 1,706 human isolates; CY 00 = collected 9,000 animal and 2,000 human isolates. CY 01 = collected 6,795 animal, 1,671 human and 433 retail meat isolates. Although, NARMS testing was expanded in CY 01 (retail meats sampling added), fewer veterinary isolates were available for study. Salmonella sampling was not a part of the 2001 USDA/APHIS National Animal Health Monitoring System (NAHMS) program; therefore, isolates were not received from that program for NARMS antimicrobial susceptibility testing in 2001. CY 02 performance is expected by March 2003. CVM revised the goal for FY 03. Previously, the goal reflected dependence on factors beyond FDA's control such as the number of humans contracting a foodborne disease as well as the sampling issue mentioned above. The goal has been revised to reflect how CVM will use NARMS data to communicate with the public on antibiotic resistance.
Data Sources: National Antimicrobial Resistance Monitoring System.

9. Conduct targeted BSE inspections of 100% of all known renderers and feed mills processing products containing prohibited material. (14006)

Context of Goal: FDA 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) feed regulations. Using an inventory of all known renderers and feed mills processing products containing prohibited material, 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. The current inventory number for all known renders and feed mills processing products containing prohibited materials is 600.
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 approach in its efforts to realize 100% compliance with the 1997 feed rule-education, a strong and visible inspection presence, and enforcement action. More than 17,000 inspections have been done since 1997 at over 10,000 firms including renderers, feed mills, and protein blenders. Due to the increase in reported cases of BSE in Europe, in FY 2001 FDA concentrated its efforts on performing BSE inspections in the U.S. This intense inspection effort was intended to prevent an outbreak of BSE in the U.S by completing 100% inspection of all firms. This goal was revised based on evaluation of BSE inspection data, the BSE crisis in Europe, and to reflect a more accurate view of FDA efforts. FY 02 performance was 100%.
In FY 03, the goal is revised to reflect FDA's focus on inspection of firms which process products containing prohibited material.
Data Sources: FDA Field Data Systems.

2.6 MEDICAL DEVICES & RADIOLOGICAL HEALTH

2.6.1 Program Description, Context and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	216,729	220,6052	193,657	177,565	170,257

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, Counterterrorism 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 regulate an ever-changing, rapidly growing industry. The number of domestic and international device firms has increased from 9,061 in FY 1997 to 13,701 in FY 2001 and projected to increase to well over 15,000 in FY 2004. The medical device industry of the 21st century is developing increasing numbers of more complex devices based on 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. All three of the preceding factors add to projected increases in device review times. FDA is also responsible for regulating 10,000 mammography facilities under the MQSA and over 4,000 radiological health firms under RCHSA plus the responsibly for oversight of 15,000 active clinical investigators. FDA uses risk management to maximize the impact of our limited resources. FDA's premarket functions support the Department's Prevention initiative, and the postmarket functions support the Department's initiative Re-aligning the Possibilities of 21st Century Health Care. Many devices used by the elderly directly relate to the Department's priorities for patient diagnostic care. CDRH regulates diabetes diagnostics.

CDRH has established two program goals to accomplish its mission for the future.

1. **To promote the public health by assuring devices are safe and effective before they go to market.**
2. **To protect the public health by keeping marketed products safe.**

To achieve its mission, CDRH has developed four key strategies to more effectively promote and protect the public health in a dynamic 21st Century environment:

- Total Product Life Cycle (TPLC) -- Efficiently focus regulatory resources, in the least burdensome way, through the total life cycle of a product - from concept development to active marketing or modification. Apply TPLC with stakeholders
- Magnet for Excellence -- Attract and retain a diverse workforce to serve the public health;
- Meaningful Metrics -- Measure and communicate our impact on the public health;
- Knowledge Management - Bring the right knowledge at the right time to relevant decisions.

The scorecard below illustrates several areas within the Medical Device and Radiological Health Program that are not working as well as they should because of major infrastructure gaps in areas such as training, international harmonization, and information systems. The Center is working toward improving performance in these areas by implementing its strategies.

Program Area	Working Well	Working But Facing Challenges	Not Working Well
Device Review		X	
Regulatory Science		X	
Device Inspection			X
Device Post-MarketSurveillance			X
Mammography	X		
Radiation Safety			X

2.6.2 Strategic Goals

Strategic Goal 1:
To promote the public health by assuring devices are safe and effective before they go to market.

A. Strategic Goal Explanation

Medical Devices marketed in the United States are subject to rigorous premarket review by FDA. Prior to marketing a device, manufacturers must seek FDA clearance or safety and effectiveness approval of their products using FDA's device review processes. Medical devices vary widely in complexity and their degree of risk or benefits, and do not all need the same degree of regulation. The FD&C Act places all medical devices into one of three regulatory classes based on the level of control needed to provide reasonable assurance of safety and effectiveness. Definitions of device applications are at the end of this section.

The FY 2004 President Budget requests a $5 million investment in device review: $1 million in appropriated funds to sustain device review performance and $4 million in new user fees to significantly improve device review performance. This funding package would provide significant improvements in review performance of about 25 percent to 50 percent in most areas over the next few years. FDA needs this investment to promote the public health by keeping marketed products safe. Resource increases will enable the Agency to maintain high levels of performance in light of environmental factors such as the following:

- Recent Improvements In Device Review Time Have Mortgaged The Future: Recent improvements in review time have been achieved by diverting significant resources from other FDA programs, and comprehensive reengineering of device review. These tools can't achieve similar future results. CDRH is operating legacy systems to scan and track applications, and lacks the IT infrastructure to move toward electronic reviews.

- FDA's Ability to Accommodate Increasingly Complex Workloads is Diminished FDA is challenged in meeting its statutory review requirements because device technology is increasingly complex, but its science infrastructure needed to keep reviewers current has eroded. Approximately 25 percent of PMA applications are for breakthrough technologies that present novel questions and issues that go beyond the current experience and training of FDA review staff. In addition, more than 25 percent of PMAs come from mostly small, first time submitters, with extra needs for outreach and interaction. In addition, FDA reviewers require ongoing training to enhance their capabilities to judge these new, complex technologies.

The table below summarizes key performance goals for FY 2004. These goals are derived from the Secretary's Letter to Congress ("Goals Letter") that accompanies the Medical Device User Fee and Modernization Act of 2002.

Performance goals in the Goals Letter take two forms: cycle goals and decision goals. Cycle goals identify the number of days for FDA to take an action on an application within any one cycle. For example, "First action - major deficiency letter to issue within 150 days" is a cycle goal. Decision goals identify the number of days for FDA to perform a complete review and issue a decision letter. Decision letters include: approval, approvable, approvable pending GMP inspection, not approvable and denial. Decision goals are more stringent than cycle goals because only the issuance of a letter reflecting complete review decision is counted as a success; the issuance of interim letters, such as major deficiency letters (for PMAs) or additional information letters (for 510(k)s), do not count as a success.

Neither of these goals are final action goals. Final action goals would count the time it takes FDA to reach an approval or a denial decision. These types of goals are not appropriate and have not been incorporated in this Performance Plan. FDA review time is largely dependent on the quality of the incoming submission, both with respect to the quality of the data provided and in ability of that data to support reasonable safety and effectiveness of the product. For those applications currently received that are of poor quality, CDRH attempts to work with applicants, often over multiple review cycles, to obtain the needed information such that safe and effective products can be brought to market. If final action goals were put in place, this type of interaction, which usually benefits smaller companies and first-time submitters, would be greatly reduced, resulting in a greater number of denials. Further, the goals presented in the Goals Letter are those that were discussed and agreed to by FDA and industry representatives in the development of MDUFMA. To alter those goals would be an abrogation of that agreement.

Although the goals below are derived from the Goals Letter associated with MDUFMA, baseline data for these categories will not be available until late in FY 2003 or in some cases, FY 2004. As our tracking systems are refined to capture data in these selected categories, the table will be populated with current performance data. It is important to note that each of these categories represents a challenge to the Center (between 10 and 25 percent improvement) based on best estimates of current performance.

FDA Performance Goals Derived From the Medical Device User Fee and Modernization Act of 2002

		Performance Level (by FY) (- indicates no quantitative goal)

Activity [1]	Review Time	2003	2004	2005	2005	2007
PMAs, Premarket Reports, Panel-Track Supplements						
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable, denial) [2]	320 days	X	X	X	80%	90%
First action - "major deficiency" letter	150 days	X	X	75%	80%	90%
First action - all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	180 days	X	X	75%	80%	90%
Expedited PMAs: These goals apply when FDA has granted expedited status; the applicant has attended a pre-filing meeting; manufacturing facilities are ready for inspection; and the PMA is substantively complete.						
First action - all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	300 days	X	X	70%	80%	90%
First action - all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	120 days	X	X	70%	80%	90%
First action - all other first actions (approval, approvable, approvable pending GMP inspection, not approvable, or denial)	170 days	X	X	70%	80%	90%
180-day Supplements						
FDA decision	180 days	X	X	80%	85%	90%

(approval, approvable, approvable pending GMP inspection, not approvable, denial)						
First action - "not approvable" letter	120 days	X	X	80%	85%	90%
501(k)s						
FDA decision (SE/NSE)	90 days	X	X	70%	75%	80%
First action - "additional information" letterr	75days	X	X	70%	80%	90%

[1] The following definitions apply:
PMA an application for approval of a device submitted under section 515(c) of the Public Health Service Act; or a product development protocol described in section 515(f).

Premarket report
a report submitted under section 515(c)(2).

Panel-Track Supplement
a supplement to an approved premarket application or premarket report under section 515 that requests a significant change in design or performance of the device, or a new indication for use of the device, and for which clinical data are generally necessary to provide a reasonable assurance of safety and effectiveness.

180-day Supplement
a supplement to an approved premarket application or premarket report under section 515 that is not a panel-track supplement and requests a significant change in components, materials, design, specification, software, color additives, or labeling.

[2]**For PMAs and PMA supplements:** "FDA decision" also includes withdrawal, conversion and other final administrative actions not resulting in approval or denial. For 510(k)s, "FDA decision" also includes final administrative actions that do not result in a substantially equivalent/not substantially equivalent decision, because the application was withdrawn, deleted due to lack of response, a duplicate, a transitional device, not regulated by CDRH, a general purpose article, exempted by regulation or other miscellaneous action.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Complete Review and Action on 90% of Premarket Approval Application of an estimated 80 (PMA) first actions within 180 days. /1 (15001)	FY 04: 90% FY 03: 90% FY 02: 90% FY 01: 90% FY 00: 85% FY 99: 65%	FY 04: FY 03: FY 02: 97% of 33 FY 01: 97% of 70 FY 00: 96% of 67 FY 99: 74% of 43	3
2. Complete Review and Action on 95% of an estimated 725 PMA supplement final actions within 180 days. /1 (15009)	FY 04: 95% FY 03: 95% FY 02: 90% FY 01 90% FY 00: 85%	FY 04: FY 03: FY 02: 95% of 498 FY 01: 98.4% of 641 FY 00: 98.7% of 545	3
3. Complete Review and Action on 95% of an estimated 4,500 510(k) (Premarket Notification) first actions within 90 days. /1 (15002)	FY 04: 95% FY 03: 95% FY 02: 95% FY 01: 95% FY 00: NA	FY 04: FY 03: FY 02: 100% of 4322 FY 01: 100% of 4248 FY 00: 100% of 4202	3
4. Expedite review for 100% of an estimated 5 Bioterrorism Diagnostic Medical Device Applications. (15028)	FY 04: 100% FY 03: 100% FY 02: NA FY 01: NA	FY 04: FY 03: FY 02: 1 approval FY 01: NA	4
5. Complete 95% of PMA	FY 04: 95% FY 03: 95%	FY 04: FY 03:	3

"Determination" meetings within 30 days. (15024)	FY 02: 95% FY 01: 95% FY 00: 95%	FY 02: 100% of 1 FY 01: 100% of 3 FY 00: 100% of 3	
6. Recognize 20 new or enhanced standards to use in application review. (15003)	FY 04: Recognize 20 new or enhanced standards to use in application review. FY 03: Recognize 20 new or enhanced standards to use in application review. FY 02: Recognize 20 new or enhanced standards to be used in application review. FY 01: Recognize 20 additional application review standards FY 00: Review 50Standards for continued applicability and 50 standards for recognition FY 99: Recognize over 415 standards for	FY 04: FY 03: FY 02: 657 Standardsrecognized FY 01: 597 Standards recognized FY 00: 567 Standards recognized FY 99: 450 StandardsRecognized	3

	use in application review		
7. Conduct 295 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.) (15025)	FY 04: 295 FY 03: 295 FY 02: 290 FY 01: 250	FY 04: FY 03: FY 02: 360 FY 01: 238 FY 00: 249	3
TOTAL FUNDING: ($ 000)	FY 04: $ 92,115 FY 03: $ 77,891 FY 02: $ 77,766 FY 01: $ 74,164 FY 00: $ 64,698	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

NOTES:
PMA first actions include: approval, approvable, approvable pending GMP inspection, not approvable, denial or "major deficiency letter.
PMA Supplement final actions include: approval, approvable, approvable pending GMP inspection, not approvable, or denial.
510(k) first actions include: SE, NSE, or "additional information" letter.
/1 Efficiency goals used as interim tracking while MDUFDA baseline data is collected. These goals are for review of submitted packages and may not result in a final decision by the FDA.

C. Goal-By-Goal Presentation of Performance

1. Complete Review and Action on 90 percent of Premarket Approval Application of an estimated 80 (PMA) first actions within 180 days. (15001)
Context of Goal: Complete review and action constitutes the comprehensive review of the application package initially received by FDA and FDA's response back to the product sponsor. 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. FDA anticipates significant complexity of PMAs. For example, many new devices will incorporate computer technology as part of the diagnostic capability of the device itself and continuing improvements in image technology will require more sophisticated review skills. In addition, 40 percent of PMA are breakthrough technologies and approximately 25 percent are from first-time submitters. These factors add time to the normal review process.
Performance: In FY 2001, FDA performance was 97 percent for the applications received in FY 2001. The performance strategy has been to redirect resources from low-risk to high-risk devices. However, in FY 2002, the Center's direct review effort was reduced by 20 FTEs and the projected performance goal for FY 2003 has been reduced from 95 percent to 90 percent. FY 2004 was projected based on being able to maintain the FY 2003 performance, the FDA will only be able to meet a 90 percent FY 2004 performance goal. If the user fee proposed increase is approved FA will be able to improve the performance listed in this document in the future. 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.
Data Sources: Center for Devices and Radiological Health (CDRH) Premarket Tracking System and Receipt Cohorts.

2. Complete Review and Action on 95 percent of Premarket Approval Application of an estimated 725 (PMA) supplement final actions within 180 days. (15009)
Note: workload will continue to increase in FY 2004 due to advances in technology.
Context of Goal: Complete review and action constitutes the comprehensive review of the application package initially received by FDA and FDA's response back to the product sponsor. 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 641 PMA supplements chose real-time reviews, mostly by teleconference.
Performance: FY 2002 performance was 94 percent for the applications received in FY 2002.
Data Sources: CDRH Premarket Tracking System and Receipt Cohorts.

3. Complete Review and Action on 95 percent of an estimated 4,500 510(k) (Premarket Notification) first actions within 90 days. (15002)
Context of Goal: Complete review and action constitutes the comprehensive review of the application package initially received by FDA and FDA's response back to the product sponsor. This is an FY 1999 goal, dropped in FY 2000, and picked back up for FY 2001, FY 2002, 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. Pressures to improve review time will increase in FY 2004 for two reasons: 1) rapid advances in device technology are expected to continue. Past history shows that the 510(k) average review time has increased 38.5 percent from FY 1994 to FY 2001. 2), FDA has exempted Class I lower risk devices from 510(k) review in order to streamline the review process. Because more complex Class II and Class III applications will constitute the future 510(k) workload it will also contribute to longer average review times, and a lower percentage reviewed within 90 days.
Performance: FY 2002, performance is 100 percent. This performance has resulted, in part, from FDA utilizing innovative ways to improve review efficiency. The two efforts listed under the heading of "Third Party Reviews" below are illustrative of FDA device review improvements. FDA encourages firms to use these regulatory options.
Data Sources: CDRH Premarket Tracking System and Receipt Cohorts.

- **3. 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/.
- 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 an estimated 5 Bioterrorism Diagnostic Medical Device Applications. (15028)
Context of Goal: 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 was a new performance goal for FY 2003. Work will continue in FY 2004.
Performance: This is a new goal for FY 2003 and therefore, has no performance history.
Data Sources: CDRH Premarket Tracking System and Receipt Cohorts.

5. Complete 95 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.
Performance: FY 2002, performance was 100 percent.
Data Sources: CDRH Premarket Tracking System and Receipt Cohorts.

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.
Performance: FDA recognized 60 standards in FY2002, 30 standards in FY 2001 and 117 standards in FY 2000 for a cumulative total of 657 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.
Data Sources: Standard status document reports.

7. Conduct 295 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.). (15025)
Context of Goal: In FY 2004, FDA plans to conduct 295 BIMO Inspections, the same number as in FY 2003. 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.
Performance: This goal is a new reporting commitment in FY 2002, and FDA met this goal by conducting 360 inspections. In FY 2001, 238 BIMO inspections were conducted. FDA did not achieve its performance goal of 250 device bioresearch inspections because the program did not receive its full appropriation request in FY2001 reduced the number of Field staff available to do device bioresearch inspections.
Data Sources: CDRH Field Data Systems.

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 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 (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. However, FDA is facing challenges of eroding infrastructure that support the device review program.

Program Goal 2:
To protect the public health by keeping marketed products safe.

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 bio-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 grow to well 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 conducts inspections to protect the public from unsafe or ineffective medical devices or radiological products, and to verify medical device firms follow Good Manufacturing Practices (GMP). Inspections of devices fall into three categories: 1) Routine Surveillance; 2) Targeted Inspections: for approval to market high risk devices, adverse reaction incidents, or recalls; 3) Compliance Inspections: to collect evidence for enforcement. (Performance Goals 7 - 10)

Medical devices and electronic products are increasingly complex, and industry is growing domestically and internationally. Inspection coverage has decreased and domestic violation rates have increased. In FY 2002, FDA requested an appropriated funding increase for domestic inspections and additive user fees for foreign inspections and imports, but these increases did not enable FDA to meet statutory inspection requirements.

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.

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

FDA is responsible for addressing radiation safety for both medical and consumer products. For example, FDA issued a public health notification to emphasize the importance of correct radiation doses during computed tomography (CT) procedures. The overexposure of children or small adults during 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 we estimate 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. Radiation-induced skin burns are an example of a resurgence of an old radiation issue. Reports in the MDR database and medical literature show these injuries result from the use of fluoroscopy in conjunction with interventional procedures. FDA is also responsible for regulating an expanding inventory of overseas facilities, which contribute roughly 335 million foreign made products.

FDA will prioritize 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 Product 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 adjusted the performance goal downward from 125 facilities to 80 facilities. CDRH had to delay recruitment efforts this year to address various policy issues within the Agency, and to make major software changes to respond to new information technology security demands. FDA projects a MeDSuN network of 180 facilities in FY 2003, and will use increased resources in FY 2004 to expand the network of hospitals and nursing homes to 240 facilities. (Performance Goal 12)

CDRH and its MeDSuN contractors will coordinate with CDER to continue implementation of drug MeDSuN. MeDSuN is designed to train hospital personnel to accurately identify and report injuries and deaths associated with medical products. The MeDSuN model, currently designed to track and analyze adverse events due to medical devices, will be expanded to include drug products. Initial work included a feasibility and acceptability assessment of a small regional group of hospital pharmacists about incorporating MeDSuN and to integrate risk manager reporting on devices with the reporting of adverse drug events and medication errors by hospital pharmacists or other personnel. This is also described in the Drugs performance plan.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
8. Utilize Risk	FY 04: 20%	FY 04:	3

management to target inspection coverage for Class II and Class III domestic medical device manufacturers at 20% of estimated 5,300. (15005.01)	FY 03: 20% FY 02: 20% FY 01: 17% FY 00: 22% FY 99: 26%	FY 03: FY 02: 20% of 5,300 FY 01: 20% of 4,980 FY 00: 13% of 5,462 FY 99: 30% of 2,930	
9. Maintain inspection and product testing coverage of Radiological Health industry at 10% of an estimated 2000 electronic products. (15027)	FY 04: 10% FY 03: 10% FY 02: NA FY 01: NA	FY 04: FY 03: FY 02: 5% of 2,000 FY 01: 10% of 2,000 FY 00: 10% of 2,000	3
10. Utilize Risk management to target inspection coverage for Class II and Class III foreign medical device manufacturers at 9% of estimated 2,500. (15005.02)	FY 04: 9% FY 03: 9% FY 02: 9% FY 01: 9% FY 00: 9% FY 99: NA	FY 04: FY 03: FY 02: 8% of 2,500 FY 01: 11% of 2,418 FY 00: 11% of 2,370 FY 99: 10% of 2,080	3
11. Ensure at least 97% of an estimated 8749 domestic mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems. (15007)	FY 04: 97% FY 03: 97% FY 02: 97% FY 01: 97% FY 00: 97% FY 99: 97%	FY 04: FY 03: FY 02: 97% of 9008, with less than 3% (serious) problems. FY 01: 97% of 9262; but with 3.4% with Level I (serious) problems. FY 00: 97% of 9443FY 99: 97% of 9583	3

12. Expand implementation of the MeDSuN System to a network of 240 facilities. (15012)	FY 04: Build a MeDSun hospital network of 240 facilities. FY 03: Build a MeDSun hospital network of 180 facilities. FY 02: Implement MeDSuN by recruiting a total of 80 facilities for the network FY 01: Recruit a total of 75 hospitals to report adverse medical device events FY 00: Develop MeDSuN based on approximately 25 user facilities FY 99: Implement Pilot	FY 04: FY 03: FY 02:FDA recruited, trained and have functioned 80 facilities for the network FY 01: FDA began feasibility testing with 25 hospitals and worked on software changes needed for website health data security. FY 00: Developed MeDSuN Phase II Pilot based on approximately 25 user facilities. FY 99: PilotCompleted	3
13. Implement Emergency Counterterrorism Preparedness and Response Plan for radiation. (15029)	FY 04: Implement Emergency Counterterrorism Preparedness and Response Plan for radiation. FY 03: Implement Emergency Counterterrorism Preparedness	FY 04: FY 03: FY 02: Developed Emergency Counterterrorism Preparedness and Response Plan for	4

	and Response Plan for radiation. FY 02: Develop Emergency Counterterrorism Preparedness and Response Plan for radiation.	radiation.	
14. Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places. (15030)	FY 04: Continue to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places. FY 03: Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places. FY 02: NA FY 01: NA	FY 04: FY 03: FY 02: NA FY 01: NA	4
TOTAL FUNDING: ($ 000)	FY 04: $124,614 FY 03: $128,749 FY 02: $115,891 FY 01: $103,401 FY 00: $105,559	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

8. Utilize Risk management to target inspection coverage for Class II and Class III domestic medical device manufacturers at 20 percent of estimated 5,300. (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. The inventory of Class II and III medical device firms is estimated at 5,304. In FY 2002, the Center has developed an estimated inventory of 1,009 High/Significant Risk devices based largely on the Center's established critical device list. These high/significant risk devices (e.g., Cardiovascular Heart Valves) have been targeted for inspections in FY 2004. Reuse inspections have been incorporated into the domestic high/significant risk inventory. FDA plans to conduct 100 reuse hospital inspections in FY 2004, 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. By FY 2003, 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.
Performance: In FY 2002, FDA met its performance target by inspecting 1062, or 20 percent, of approximately 5.300 domestic high risk Class II and Class III medical device 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 firms.
Data Sources: CDRH Field Data Systems.

9. Maintain inspection coverage and product testing coverage of the Radiological Health industry at 10 percent of an estimated 2,000 electronic products. (15027)
Context of Goal: 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. 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 5,000 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.
Performance: This is a new goal for FY 2003. In FY 2002, FDA estimates there were approximately 2,000 active radiological health firms FDA is responsible for regulating domestically and internationally. In FY 2002, CDRH was able to check the compliance status for about 5 percent of these firms, by reviewing inspection reports and product testing reports submitted by manufacturers. FDA initiated activities to prioritize and leverage its radiation protection efforts with state governments, professional societies, and other federal agencies. This compliance status was estimated by CDRH's Office of Compliance by reviewing inspection reports from FDA and State inspectors and product testing reports submitted by industry.
Data Sources: CDRH Radiological Health Data Systems.

10. Utilize Risk management to target inspection coverage for Class II and Class III foreign medical device manufacturers at 9 percent of an estimated 2,500 firms. (15005.02)
Context of Goal: The foreign higher risk Class II and III inventory is expected to continue to increase. As workload increases, inspection coverage is expected to be 9 percent in each of FY 2002, FY 2003 and FY 2004. 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 will be maintain foreign inspections or successfully implement the MRA with. 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.
Performance: FDA met its FY 2002 performance goal of inspecting 8 percent of registered foreign Class II and Class III Medical Device manufacturers. In FY 2002, FDA foreign inspection rate was 8 percent and 209 inspections were conducted compared to 266 inspections conducted in FY 2001. FDA did not

reach the 9% coverage goal since international climate post '9/11/01' adversely impacted foreign travel. The compliance program is focused on the improvement of enforcement actions by redirecting current resources to high?risk devices such as implants.
Data Sources: CDRH Field Data Systems.

11. 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 improve the quality of mammography in the United States. In the Mammography Quality Standards Reauthorization Act (MQSRA) 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 was implemented in 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 89 percent of inspections. Inspectors performed science-based inspections to determine the radiation dose, to assess image quality, and to empirically evaluate the quality of the facility's film processing. MQSA requires FDA to collect fees from facilities to cover the cost of their annual facility inspections. FDA also employed an extensive outreach program to inform mammography facilities and the public about MQSA requirements. These included a quarterly newsletter for facilities, an internet website, collaboration with NIH to provide a list of MQSA-certified facilities, a consumer brochure, meetings with consumer groups, and interactive teleconferencing for facilities.
Performance: During FY 2002, FDA ensured that 97 percent of mammography facilities met inspection standards and with less than 3 percent with Level 1 (serious) problems. This was the fourth consecutive year of achieving this high standard. Inspection data continue to show facilities' compliance with the national standards and with the quality for 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.
Data Sources: CVM's priority project tracking system.

12. Expand implementation of the MeDSuN System to a network of 240 facilities. (15012)
Context of Goal: FDAMA gives FDA the option to replace universal user facility reporting with the Medical Product 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

mis-use. 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. Data collection began in March 2002 and continues to date, along with recruitment of participating centers. By the end of 2003 we will have recruited 180 facilities. For 2004, with increased funding, FDA will be able to expand the enrollment of 240 facilities. FDA will recruit new facilities to expand the network and to replace those that choose to leave. Additionally, FDA plans to use the cohort of 240 facilities to pilot the effectiveness of various incentives, to pilot use of the MeDSuN facilities as a laboratory to obtain specific medical product information, and to pilot various types of feedback intended to encourage reporting by the facilities.
Performance: In FY 2002, FDA recruited, trained and had functioning 80 facilities for the network. In FY 2001, FDA did not meet the goal of recruiting 75 hospitals because most of the effort was focused on resolving internal policy issues and addressing information technology security requirements. During the past year, FDA extended software development to accommodate Internet-based reporting system (interactive web-based form and database), and took steps to ensure that reporters had internet access to secure servers. FDA did recruit 25 hospital facilities.
Data Sources: CDRH Adverse Events Reports.

13. Implement Emergency Counterterrorism Preparedness and Response Plan for radiation. (15029)
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 Counterterrorism funds, CDRH will update the radiation emergency response plan to include Counterterrorism events. In FY 2004, CDRH will initiate contracts with Federal, State, and independent 3rd party laboratories to conduct safe use requirements and to conduct risk assessment. CDRH will also continue emergency preparedness activities in the area of radiation safety. Specifically, CDRH continues to monitor, evaluate and follow-up on the public health needs of new medical devices or their use in Counterterrorism preparedness and response and regulate them appropriately. CDRH is working with other Federal and State agencies to address mail decontamination issues and CDRH has participated in developing the new standard for X-Ray screening. Additionally, the center is in the process of classifying diagnostic test kits used to detect biological agents based on FDA's Microbiology Devices panel recommendations. The Center is also expanding technical assistance to industry and the DOD to expedite, review, and expand outreach to civilian emergency medical professionals and provide more information about new devices in their field.

Performance: This was a new goal for FY 2003 and therefore, has no performance history. In FY2002, FDA Developed Emergency Counterterrorism Preparedness and Response Plan for radiation.
Data Sources: CDRH's radiation emergency preparedness response plan.

14. Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places. (15030)
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 Counterterrorism resources. FDA will work with the other stakeholders to maximize benefit of FDA's limited resources in this area.
Performance: This is a new goal for FY 2003 and therefore, has no performance history.
Data Sources: CDRH standard setting documents.

2.7 NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

2.7.1 Program Description, Context, and Summary of Performance

	FY 2004 Request	FY 2003 Current Estimate	FY 2002 Actual Obligations	FY 2001 Actual	FY 2000 Actual
Total $000	40,151	40,688	39,259	36,248	36,522

The National Center for Toxicological Research (NCTR) conducts FDA mission-critical, peer-reviewed research that is targeted to develop a 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 risk and anticipate new product technology in support of FDA's commitment to bring this technology to the market rapidly.
- Understand mechanisms of toxicity and design better risk assessment/management techniques and methods for use in premarket review and product health surveillance.

The NCTR provides the Agency with a risk focused 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 meet the Agency's risk management and communication 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 ORA. NCTR's strategic research goals support FDA's mission to bring safe and efficacious products to the market rapidly and to reduce the risks of regulated products. NCTR's strategic goals are to:

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 risk to enhance the efficiency and effectiveness of pre-market product reviews or post market safety.**
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 those already 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 risk associated with FDA-regulated 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 risk 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.

Scientists are developing and using new technologies and tests to better understand chemical toxicity and strengthen the extrapolation from animal models to humans. America's quest for good health, in addition to increasing evidence of adverse drug/chemical reactions in humans, point to a need to identify and protect susceptible sub-populations 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 carcinogenic and mutagenic risk 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 sub-populations, particularly as they relate to individual susceptibility (Performance Goal 2).

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
1. Introduce the knowledge of new genetic systems and computer-assisted toxicology (toxicoinformatics) into the risk management process. (16001)	FY 04: Use toxicoinformatics, combining information technology with toxicity data, to assess human risk for one regulated product (proof of concept) 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 predictive 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 04: FY 03: FY 02: A series of investigations in neonatal mice were conducted to examine genotoxic consequences of AIDS drugs. 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	4

	FY 00: Evaluate a new biological assay to measure genetic changes and validate two existing models that predict human genetic damage. FY 99: Develop better Biological assays to measure genetic changes and predict human genetic damage	measurements; utilized AHH 1 human lympho-blastoid system to evaluate risk to human genome. FY 99: The Big Blue Rat and NCTR Tk+/- in vivo bioassays were developed and two cell lines were used to predict human genetic damage.	
2. Develop, with other organizations, gene chip and gene array technology. (16002) (16002)	FY 04: Develop a method for using a rat and human gene chip to obtain an enzyme profile for each species. 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 04: FY 03: FY 02: Scientists used microarray gene expression analysis to identify a number of genes altered in rodents given dichloroacetic acid.Established a fully automated microarray printing process to screen known rodent and human genes. FY 01: Risk chip	4

	FY 01: Develop "risk 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 susceptible sub-populations. FY 99: Complete biochemical and epidemiological studies to define the basis of susceptibility of humans to the toxicity of regulated products	used to screen population resulted in initiation of negotiations to extend the use of biomarkers and other sub-populations 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.	
TOTAL FUNDING: ($ 000)	FY 04: 18,871 FY 03: 19,123 FY 02: 18,451	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS	

	FY 01: 23,271 FY 00: 17,1601	Strategic Plan

C. Goal-By-Goal Presentation of Performance

1. Introduce the knowledge of new genetic systems and computer-assisted toxicology (toxicoinformatics) into the risk management process. (16001)

Context of Goal: Rapid identification of risk is important to the public health mission of the Agency. It is critical that NCTR scientists, in collaboration with Agency reviewers and inspectors, understand and accurately interpret scientific data dealing with risk 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 and/or microbial biomarkers will be the measure of applicability to the regulatory process.
Performance: Collaboratively with other FDA centers, NCTR researchers will determine if animal data required for pre-market approval of drugs and other products can adequately predict possible 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, which studies the chemical basis of genetic damage, is shown to detect most, if not all, of the mutational events leading to human cancer. Initial experiments indicated that zidovudine, but not lamivudine, is mutagenic, and that lamivudine does not alter the responses induced by zidovudine. During FY 2002 these studies were expanded to include other AIDS drugs (stavudine, didanosine, zalcitabine, and nevirapine). 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.
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.

2. Develop, with other organizations, gene chip and gene array technology. (16002)

Context of Goal: The importance of gene chip technology is that it allows researchers to screen large numbers of samples, either rodent or human, simultaneously for different types of genes. 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 adverse effects, such as 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 universities and industry.

Performance: Research focus is on developing and printing a complete rat and human gene chip that will be used to establish a genetic profile for each species. Increasing evidence of adverse drug and chemical reactions in sub-populations of humans (specific classifications such as race, gender, geographic location, common disease), point to a need to identify and protect groups of people at higher risk from exposure to specific drugs, contaminated food, or other FDA-regulated products. NCTR scientists in collaboration with scientists at the University of Arkansas for Medical Sciences (UAMS) have established a fully automated microarray printing process to screen known rodent and human genes. 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. NCTR scientists collaborated with Environmental Protection Agency (EPA) scientists and successfully used microarray gene expression analysis to identify a number of genes altered in rodents given dichloroacetic acid, a known rodent carcinogen, in their drinking water. They identified specific genes that are involved in cell growth, tissue modeling, normal cell death, cancer progression, and foreign chemical metabolism. This study demonstrates the potential utility of the new DNA microarray technology in evaluating the mechanisms by which chemicals exert their toxicity.

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.

Strategic Goal 2:
Develop computer-based systems (knowledge base) that predict human risk to enhance the efficiency and effectiveness of premarket product reviews or postmarket safety.

A. Strategic Goal Explanation

To meet the challenges of rapidly changing technology, the Agency needs unique computer-based predictive systems to aid in assessing human risk and to improve the safety of regulated products. FDA reviewers and investigators face an ever-increasing quantity and complexity of data in new drug, import and product applications. Clearly, tools that provide quick access to relevant scientific information and a capability for predicting risk can expedite important decisions.

An integrated information technology knowledge base that puts relevant scientific knowledge in the hands of an inspector or reviewer can have an immediate effect on assessing and managing human risk.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
3. Develop computer-based models and infrastructure to predict the health risk of biologically active products (16003)	FY 04: Expand current technologies to include risk assessment for two biologically active products of interest to the FDA. 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	FY 04: FY 03: FY 02: Developed an integrated Toxicoinformatic System that includes a central data archive, mirrored public databases, and analysis functions. FY 01: Predictive model for androgen receptors was developed and assessment of 204 chemicals completed. FY 00: The estrogenicity of 150 chemicals was assessed using an estradiol receptor-binding assay validating the predictive model. Two	4

	compounds. FY 99: Demonstrate a model toxicity knowledge base to support and expedite product review	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).	
TOTAL FUNDING: ($ 000)	FY 04: 372,912 FY 03: 369,623 FY 02: 349,996 FY 01: 247,654 FY 00: 240,043	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

3. Develop computer-based models and infrastructure to predict the health risk of biologically active products (16003)

Context of Goal: Using a scientifically based endocrine disruptor knowledge base (EDKB), FDA-regulated drugs, food additives, and food packaging have been shown to contain estrogenic activity. This raised the level of concern regarding adverse effects on human development/reproduction and contributions of these compounds to high incidences of cancer and/or risk of other diseases. Following the success achieved with the EDKB, NCTR scientists will identify and predict, using knowledge bases, whether the increased exposure to naturally occurring and other synthetic products can adversely impact public health.
Performance: The development of the knowledge base for assessing risk associated with other regulated products continues. NCTR developed an integrated Toxicoinformatic System that includes a central data archive, mirrored public databases, and analysis functions. The central data archives

contain a set of relations databases, each storing experiment information. These databases are continually being updated and enhanced with new linkages and additional experimental data. These databases have been used to assess compounds for NCTR, CFSAN, CDER and EPA.
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.

Strategic Goal 2:
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 regarding human risk. 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 and/or human clinical trails.

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. Research into how microorganisms may be used by bioterrorists continues to be of interest to scientists at the Center. Techniques are being developed to rapidly characterize both native and engineered biological organisms; to identify explosives in enclosed containers and to explore the risk associated with low dose exposure to neurotoxins in seafood.

B. Summary of Performance Goals

Performance Goals	Targets	Actual Performance	Reference
4. Study the risk associated with how a FDA regulated compound or product interacts with the human body. (16004)	FY 04: Evaluate the risk of thimerosal, a vaccine preservative, to human health FY 03: Continue toxicological 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 04: FY 03: FY 02: Studies were conducted on the herb-drug interactions of the supplement St. John's Wort, garlic oil, Panax ginseng, and Ginkgo biloba. 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	4

		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.	
5. Develop risk assessment methods and build biological dose-response models in support of the Food Safety Initiative. (16007)	FY 04: Under the Food Safety Initiative, establish a nutrition program in collaboration with other centers to address the risk associated with obesity in children, nutrition in pregnant women and poor nutrition in sub-populations; and initiate analysis on samples requiring high levels of containment in an accredited biosafety level 3 (BL-3) facility FY 03: Identify and characterize the role antibiotic resistance plays in emerging	FY 04: FY 03: FY 02: Researchers published approximately 50 publications and made approximately 20 presentations relating to food safety. FY 01: Performed	2

	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 strains of bacteria. FY 01: Provide model to replicate bacterial survival in the stomach. FY 00: Develop methods of predicting, more quickly and accurately, the risk associated with such foodborne pathogens as Salmonella spp., Shigella spp., and Campylobacter spp. FY 99: Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants	pre-validation studies that examine the effect of low-level antibiotic residues on 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 risk in	FY 04: Apply neural imaging to identify and quantify neurotoxicity in	FY04:	2

a bioterrorism environment(16012)	exposed populations; and upgrade NCTR's animal quarantine facility to conduct animal research requiring BL3 containment in order to evaluate the effect of bioterrorism agents contaminating the food supply. 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 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	FY03: FY 02: Scientists are working on streamlining this methodology for use on meat as well as seafood.Equipment was purchased and calibrated.An outside firm assessed the NCTR facility for laboratory architecture and requirements; and, a floor plan was developed. One computational scientist, three chemists and two microbiologists were hired. FY 01: Application/extension of Fresh TagÆ technologies for detection of nitrogen-based explosives began. FY 00: Goal not meet due to lack of funding	

	Computational Science, Chemistry and Microbiology. FY01: Begin developing solid-phase colorimetric bacterial detection system. FY 00: Begin developing solid-phase colorimetric bacterial detection system.		
7. Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of risk. (16013)	FY 04: Compile scientific knowledge and expertise in new technologies to determine risk and develop appropriate regulatory authority. 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 04: FY 03: FY 02: NCTR scientists published a journal article exhibiting their development of a quantitative structure-activity relationships (QSAR) approach that can be used to screen thousands of chemicals and determine the likelihood that they would be estrogenic. FY 01: Three concept papers were submitted and approved: 1) design and analysis of gene array expression data; 2) develop-ment of glass-slide	5

		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 04: 16,462 FY 03: 16,682 FY 02: 16,096 FY 01: 14,863 FY 00: 14,980 FY 99: 13,172	Numbers in the Reference column corresponds to the relevant strategic goal in the HHS Strategic Plan	

C. Goal-By-Goal Presentation of Performance

4. Study the risk associated with how a FDA regulated compound or product interacts with the human body. (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 only on 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.

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 relevant to human risk. Major efforts are continuing in the area of phototoxicity with emphasis on the potential interaction between ultraviolet (UV) light and substances found in dietary supplements, such as aloe vera and ephedra. Besides using aloe vera as a topical ointment, oral products are now on the market for ingestion. Studies that were conducted on the herb-drug interactions of the supplement St. John's Wort, garlic oil, Panax ginseng, and Ginkgo biloba have shown measurable induction of the activity of cytochromes that may be used to predict herb-drug interactions in the public. The task of determining human risk of these products rests with the FDA.

Data Sources: Evidence that mechanistic data are used in the regulatory process; NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board.

5. Develop risk assessment methods and build biological dose-response models in support of the Food Safety Initiative. (16007)

Context of Goal: The Agency is mandated by law to assure that 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 for imported foods and/or microbial contamination. With the FY 2004 increase, NCTR will be bringing the BSL-3 laboratory online by initiating samples analysis to evaluate the effect of possible contamination agents.
Performance: Researchers at the NCTR and the Center for Veterinary Medicine (CVM) are continuing to perform studies on bacterial identification techniques both in the food supply and in microbial contamination. This research includes the elucidation of the mechanisms of resistance to antimicrobial agents among bacteria from poultry and vegetables.
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.

6. Catalogue biomarkers and develop standards to establish risk in a bioterrorism environment. (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. 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. This research is conducted in collaboration with the Centers for Disease Control (CDC), the Department of Defense (DoD), Naval Research Labs, the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) and the Center for Food Safety and Applied Nutrition (CFSAN). NCTR will upgrade the Center's BSL-3 animal quarantine facility to evaluate the effects of possible bioterrorism agents.
Performance: 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) to detect explosives in airline cargo. Studies are being conducted to compare and contrast several new mass spectrometry techniques to more rapidly evaluate microbial risk.
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.

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

Context of Goal: Staying abreast of new technologies in science is important for the Agency to protect public health. This 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.
Performance: NCTR scientists are developing a new research focus area in these technologies and applying them to fundamental risk assessment questions. The quantitative structure-activity relationship (QSAR) was developed and validated against experimental data. This QSAR approach was then applied to three environmental data sets identified by EPA, and to a list of chemicals of concern identified by CFSAN and CDER. The QSAR screen provided a list of priority chemicals for further experimental evaluation and/or regulatory decision-making.
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.

Appendix A: *FDA's Plan is aligned with HHS Strategic Goals*

FDA's strategic goals are an integral part of HHS' one department philosophy. All of FDA's initiatives are aligned with HHS-wide strategies. The table below indicates this alignment.

HHS Strategic Goals	FDA Strategic Goals				
	Risk Management	**A Strong FDA**	**Counterterrorism**	**Adverse Events and Medical Errors**	**Consumer Information**
1. PREVENTING DISEASE AND ILLNESS					**X**
2. PROTECTING OUR HOMELAND	**X**		**X**		
3. CLOSING THE GAPS IN HEALTH CARE					
4. IMPROVING HEALTH SCIENCE	**X**				
5. REALIZING THE POSSIBILITIES OF 21ST CENTURY HEALTH CARE				**X**	
6. WORKING TOWARD INDEPENDENCE					
7. LEAVING NO CHILD BEHIND					

8. IMPROVING DEPARTMENT MANAGEMENT		**X**			

Appendix B: FDA PROGRESS MEASURING LONG TERM OUTCOME GOALS

This Appendix contains a status report on FDA's progress in developing and measuring long term, quantifiable outcome goals that will improve the health and well-being of the American Public. . The Agency is exploring approaches for developing a measurement capability, and strategies for achieving outcome success in four areas of FDA responsibility:

1. Medical Product Safety
2. Foodborne Illness Reduction
3. Counter Terrorism
4. Managing the Risk Associated with BSE (Bovine Spongiform Encephalopathy)

In each of these areas, FDA is attempting to strengthen its outcome measurement and achievement capability through the following efforts:

Examining the linkage between FDA program efforts and ultimate health and safety outcomes; and evaluating possible performance indicators for these end outcomes which may be relevant for FDA.

Exploration of intermediate outcome measures which may serve as good leading indicators of ultimate health outcomes. Many of these intermediate measures are more proximate to FDA efforts and therefore may be more within the influence of Agency actions. The Chart below outlines the broad linkages between FDA efforts and outcomes at different stages:

FDA Links to Outcomes				
FDA Activities	**Outputs**	**Initial Outcomes**	**Intermediate Outcomes**	**End Outcomes**
Application Reviews	**Approval Decisions**	**Product Availability**	**Informed Product Use**	**Improved Health Outcomes:** • **Mortality** • **Morbidity** • **Health**
Inspections	**Enforcement actions**	**Safe, affordable, products**	**Access by target populations**	
Surveillance reports	**Educational efforts**	**Industry compliance**	**Consumer confidence**	

Research efforts	**Product standards**	**Consumer, health prof. awareness of risk information**		

Identification of data sources that will serve as valid and reliable sources of information on the selected intermediate and end outcome measures. In some cases these data sources have been identified; in many other cases the search for such sources is still underway.

Formulation of data strategies to make databases more accessible and useable for FDA. In some cases data sources are in place, but are not collecting information in categories that would be relevant for FDA. To illustrate, representatives of the Agency's Food Safety and Nutrition Program are working with CDC to augment their foodborne illness morbidity and mortality information so that it is collected for products that FDA regulates. In other cases, data must be purchased from outside sources; and in still other instances, such as adverse event reporting systems, the databases have to be constructed This takes time and considerable investment of resources.

Analysis and evaluation, as appropriate, to strengthen our understanding of the relationship between FDA program efforts and both intermediate and end health outcomes. An effort will also be made to identify studies that have already been completed, and which may contribute to our understanding of these relationships.

A discussion of progress in outcome measurement and achievement follows for each of the areas identified above:

1. MEDICAL PRODUCT SAFETY

FDA will work to establish relationships between availability of new medical products as a result of Agency product approvals, widespread use of these products to treat disease, and reduced incidence of the disease. To illustrate: Following approval of a new molecular entity (NME) intended to improve survival following a stroke, the Agency would monitor its use in the patient population suffering from strokes. Usage data might be tracked through data sources that track the number of drug prescriptions written. Once the utilization of the NME in the stroke population was determined, then the effect on mortality in the population treated could be investigated in various ways, including: 1) extrapolating to the affected population the results of existing studies that have examined relationships between use of stroke products and stroke mortality/morbidity rates; 2) original in-house analysis of use-disease data through such techniques as statistical inference and mathematical

modeling; 3) funding outside researchers to conduct studies that examine quantitative and qualitative studies of the health status of patient groups. The Agency can use internal and external data sources to track an indicator. External data sources, such as data tapes from Center for Medicare and Medicaid Services within the Department of Health and Human Services (CMS), could link the products the federal government is funding with a defined set of patients. Information from IMS, a company that collects market data, might be useful to verify an increase in the number of prescriptions while National Center for Health Statistics could provide longitudinal data to track changed health status.

FDA will also explore the use of post-market information to determine the safety of products on the market as well as the use of these products. Both product safety and safe use of products are intermediate outcome indicators that could be partial predictors of positive health outcomes. One measure of product safety would be the number of product recalls. Examination of recall data should lead to reasons for product failures - e.g., failure of prosthetic hips - and to subsequent correction of these problems through Agency and/or industry actions. FDA's adverse event and medical error databases will serve as increasingly rich sources of information to determine significant problems associated with product use, and enable the Agency to isolate reasons for these problems so that appropriate intervention strategies can be designed. These monitoring systems will require time in order to establish a baseline to identify and reduce the number of negative health outcomes from adverse events.

2. FOODBORNE ILLNESS

Consuming foods is an event that touches every American life daily. To maintain public health requires a nutritious, wholesome and safe food supply. The impact of eating contaminated food can be so widespread that it remains a high priority for public health officials to reduce foodborne disease. Through scientific investigation and assembling of characteristics for certain foodborne outbreaks, public health officials have developed many databases and networks to respond in such an event. It is appropriate, therefore, to use such health outcomes data, contaminant surveillance data, firm/facility compliance data, and other survey data to measure the broad success of food safety programs. Many infections and intoxications are often caused by foodborne microbial pathogens, and trends in their occurrence are especially relevant to assess the effectiveness of food safety programs. The Agency is exploring the long-term outcome goal to reduce the rate of infections and mortality caused by key foodborne pathogens tabulated by Center for Disease Control (CDC).

Exploring intermediate outcome measures is the first step toward realizing the long-term goal. Some of these measures would focus on preventing contaminated food from reaching the consumer. For example, FDA's Center for

Food Safety and Applied Nutrition (CFSAN) could measure food handling or food processing practices that are known to contaminate food and then determine changes in practices after introduction of new FDA regulations or programs that are likely to affect these practices. As another example, CFSAN could sample foods for pathogen contamination by various factors such as food type, seasonality and geographic location that are associated with specific illnesses. Targeted sampling could be done before and after FDA program activities that are expected to prevent or reduce food contamination. The number of import examinations that target the most suspicious products and the number of domestic inspections aimed at high-risk food establishments could be another measure to keep contaminated products from consumers. As a partner with states, military installations and tribal nations, the Agency encourages adoption of the Food Code. Other measures could be aimed at increasing the capabilities and capacity of State and Federal laboratories, by actions such as increasing the number of laboratories in the National Laboratory Response Network, which analyzes and identifies the causes of foodborne illnesses.

Current data sources allow the Agency to use valid and reliable information in developing, implementing and monitoring its science-based regulatory programs. For instance, the Foodborne Diseases Active Surveillance Network (FoodNet) is the principle foodborne disease component of CDC's Emerging Infections Program (EIP). FDA, in collaboration with CDC, nine states, (California, Colorado, Connecticut, Georgia, New York, Maryland, Minnesota, Oregon and Tennessee), and the U.S. Department of Agriculture (USDA) is part of FoodNet. This effort consists of active surveillance for several foodborne diseases and related epidemiologic studies designed to help public health officials better understand the epidemiology of foodborne diseases in the United States. Foodborne diseases included in FoodNet are infections caused by bacteria such as *Salmonella*, *Shigella*, *Camppylobacter*, *Escherichia coli*, *Listeria monocytogenes*, *Yersinia enterocolitica*, and *Vibrio* and parasites such as Cryptosporidia and Cyclospora Other data sources at CDC, including foodborne disease outbreak surveillance data, also provide important public health outcome indicators.

A key CFSAN effort is to formulate strategies for working with CDC to facilitate collection of foodborne illnesses by categories relating to FDA-regulated foods using FoodNet. This effort is designed to link FDA-regulated products with foodborne pathogens that are having a severe impact on the American public's health. Also key to our efforts is data collection from industry, academia and private sources. For example, FDA recently worked with the Joint Institute for Food Safety and Applied Nutrition and National Food Processors Association to obtain information related to the foodborne pathogen *Listeria monocytogenes* in ready-to-eat foods. Information has been collected on consumer behaviors and understanding about food handling, processing and pathogens. Additional strategies on research, inspections, surveillance,

standards and education will be designed in coordination with key federal agencies (e.g., CDC, FSIS), tribal nations, state governments, academia and our stakeholders. For example, FDA has developed and implemented prevention strategies for seafood, juice, fresh fruits and vegetables, and sprouts. Epidemiological data combined with intermediate data, such as pathogen counts and production and handling variables, can measure the effectiveness of these programs.

The Foods Program will continue to analyze and evaluate information from all sources, conduct and participate in research, surveillance and education and coordinate initiatives with our partners to address those factors in our purview that could lead to lower incidences of foodborne pathogens. Our efforts are focused on tying FDA programs in selected areas with compliance and tracking the results via public health outcome databases. For example, for *Vibrio* which appears in shellfish, FDA is working with the National Seafood Sanitation Program to educate fisherman about the risk factors that could lead to their products becoming infected and harming consumers. Since Vibrio is tracked by FoodNet and by the Gulf coast *Vibrio* Surveillance Program, the agency might be able to determine the success of this effort. Similarly, the Agency developed the Egg Safety Action Plan with egg producer associations to control *Salmonella* contamination on whole shell eggs. The results might be seen in outbreaks that are recorded in FoodNet and Salmonella Enteritis outbreak surveillance by CDC. For Norwalk-like viruses that appear in food contaminated from retail workers and contamination of molluskan shellfish, the Agency could develop a surveillance system to track the future incidences.

The Foods program will continue to develop a list of priority research needs annually. The Agency is mindful that as a leader in food safety, communicating these needs to other agencies, academic, industry partners and our stakeholders is critical to achieving its health outcomes.

3. COUNTER TERRORISM

The Agency is exploring the feasibility of establishing long term outcome goals that will demonstrate FDA's contribution to the Nation's preparedness to minimize the effect of potential terrorist threats. Two measures, in particular, are being examined: ensuring safe and effective medical counter measures; and developing a National laboratory capacity to test for terrorist agents in food products.

Medical Counter Measures - One intermediate measure being investigated is the ability to assure that FDA regulated products in the National Pharmaceutical Stockpile (NPS) will be approved as safe and effective, and will be appropriately labeled to treat the medical consequences of biological, chemical, or radiation attacks. The Agency is also examining measures that would be able to track the proportion of these products that might have to be

deployed while they are still in experimental or investigational status. The aim would be to minimize the number of these agents that are experimental and have not been approved as safe and effective.

FDA is examining several strategies and indices for increasing the supply of critical drugs, biologicals and devices that would be useful medical countermeasures. Also being considered are strategies for increasing efficient and timely access to products in the National Pharmaceutical Stockpile. The Agency's commitment to this effort reflects a philosophical change from passive observer to active participant, where FDA works proactively to develop medical products and offers incentives for market behavior.

Other related strategies include:

- Removing regulatory roadblocks that impede the development and approval of medical countermeasures - e.g. increase the use of the regulation that allows animal tests as the sole evidence of efficacy for drug and biologic approval;
- Ensuring, where appropriate, that counter terrorism indications are approved for all products.
- Fostering the development of products that can be used as medical countermeasures through various incentive programs - particularly where commercialization opportunities are not otherwise obvious;
- Exploring expansion of current grant programs to encourage firms to produce the necessary data for drug approval or labeling changes.
- A key overarching strategy is to communicate effectively with constituents in the counterterrorism community. Specifically, outreach to health professionals, health organizations, and other federal agencies to educate and enlist their resources will be formalized. To illustrate: FDA will coordinate post-event data collection with federal agencies (e.g., Center for Disease Control and Department of Defense) and state and local authorities to ensure they are aware of the type of information required by Subpart H and I approvals. Health professionals and patients will be encouraged to provide clinical follow-up data to federal agencies when marketed medical countermeasures are prescribed for other than labeled indications (off-label use, i.e., cidofovir for vaccinia complications).

To support the overall outcome measurement effort, there are numerous data sources the Agency could explore to support approval of products and assure they are labeled to address the consequences of a terrorist attacks. First is the varied literature on drug use that is aimed at medical professionals. A second source is unpublished data from companies, other government agencies, academia and foreign governments reflecting experience with counter terrorism products of interest. Finally, certain offices within FDA may have historical data from numerous sources that could be reviewed for support of product approvals.

National laboratory capacity - FDA is considering the development of intermediate outcome measures that will gauge the capacity of the Nation to rapidly and accurately test for the presence of terrorist-introduced hazardous agents into the U.S. food supply. Ideally, there should be some level of laboratory analysis capacity in every state with the capability to conduct biological and/or chemical and/or radiological testing of foods. Laboratories with these capabilities should be located in those geographic areas with high concentrations of domestic food processors and food imports.

State laboratory capacity will be part of The Food Emergency Response Network (FERN), which consists of both state and FDA laboratories that are committed to analyzing food samples in case of a biological and/or chemical and/or radiological terrorist event. This effort is a component of Center for Disease Control's (CDC) much larger Laboratory Response Network (LRN), a network of state/government public health laboratories developed to provide normal and surge capacity for samples resulting from a public health emergency caused by a select agent. The LRN focuses on clinical testing, whereas the FERN focuses on food testing.

The FERN will be based on a number of characteristics. The Federal government, or an organization contracted by the government, will conduct research to develop rapid methods of analysis of food samples. Laboratories will be strategically located across the country using criteria such as concentration of food imports and domestic food processors. In the event of a catastrophe, the system is designed to handle sudden surges in samples for analysis. As envisioned, this means that a laboratory is capable of analyzing sudden increases in volume of samples or for multiple agents. To support this infrastructure, a national data sharing system, eLEXNET, is intended to provide a mechanism by which multiple government agencies have the ability to rapidly share food safety data.

Further, a baseline of state laboratory capabilities to identify gaps and develop strategies to fill these gaps in normal and surge capability would be established. Capability data could be secured through a survey instrument or physical exam of the state laboratories.

Several measures are being considered to evaluate the quality and quantity of national laboratory capacity.

First, laboratories joining the FERN, could be documented, tracked, and measured through proficiency testing. Proficiency testing is a training technique to test the laboratory's ability to analyze and identify an unknown contaminant in a food sample. **(Measure #1)**

Second, the availability of equipment necessary to conduct certain tests could be monitored. For example, each chemical or radiological lab might be

expected to include: the presence of liquid chromatograph-mass spectrometers, gas chromatograph-mass spectrometers, fourier transform infra-red spectrometers, ion chromatographs, and inductively coupled plasma mass spectrometer. **(Measure #2)**

Third, a minimum number of courses that must be taken by laboratory personnel would be established. These will include handling chemical, radiological, and biological contamination. (This may have to be further broken down to training of each of the potentially identified microorganisms, e.g. B. anthracis, etc.) Training will also include instruction on the operation of key instruments and using FDA procedures to detect contaminants. Training records will be maintained by Office of Regulatory Affairs' (ORA's) Division of Human Resource Development, which is responsible for training programs for FDA and state officials. **(Measure #3)**

4. BSE (Bovine Spongiform Encephalopathy)

FDA is exploring outcome measures that would gauge the readiness of the industry to prevent the spread of the disease and minimize any potential impact on the U.S. economy.

The Harvard BSE (Bovine Spongiform Encephalopathy) Risk Assessment indicated that if a case of BSE were detected in the United States, a high compliance rate with the FDA feed rule would prevent the spread of the disease and would in fact lead to its elimination over several years.

Consistent with this conclusion FDA will continue to inspect 100% of all known renderers and feed mills processing products containing prohibited material annually; and ensure that at a minimum 92% of firms are in compliance with the feed rule through inspection and enforcement actions. The Agency will also continue to explore intermediate outcome measures that link our program efforts [rule making, inspectional effort] to assurance that beef continues to be protected from BSE hazards; and consumer confidence in these products remains high.

Appendix C: *Disposition of FY 2003 Performance Goals*

Goal ID	Original Goal Statement as stated in FY 03 Congressional Justification	Disposition	Revised FY 2003 Targets	Explanation
FOODS				
11001	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.	Revised	Complete review and action on the safety evaluation of 65% of food and color additive petitions within 360 days of receipt.	FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ"
11010	Achieve adoption of the Food Code by at least one state agency in 33 states in the USA.	Unchanged		
11020	Inspect 95 percent of high-risk domestic food	Unchanged		

	establishments once every year.			
11025	Respond to 95 percent of notifications for dietary supplements containing "new dietary ingredients" within 75 days.	Unchanged		
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		
11034	Review 95 percent of premarket notifications for food contact substances in the receipt cohort of FY 2002 within the statutory time limit (120 days).	Unchanged		
11035	Publish a final rule to require premarket notification for bioengineered foods.	Dropped		This goal has been dropped because developing the final rule will require further intensive analysis focused at

				least in part on the question of statutory authority as well as elaborating the process, and the decision criteria and endpoints of such a program. These new challenges make this goal unrealistic for the coming fiscal year.
11036	Increase the number of physical exams by 100% to 48,000 exams and conduct sample analyses on products with suspect histories.	Unchanged		This goal statement and target are unchanged, however this goal has been repeated in the Agency-wide Program Section that focuses on Global Product Safety and Security to reflect the Agency's coordinated response to terrorist threats.
11037	Enhance productivity at the 45 additional ports through focused training.	Dropped		This goal has been dropped because it is not specific enough. It is being replaced

				with more specific and effective measures starting in FY 04 in the Agency-wide Program Section that focuses on Global Product Safety and Security.
Human 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.	Revised	Meet PDUFA III commitments for the review of original NDA submissions. Standard NDAs within 10 months- FY 03: 90%. Priority NDAs within 6 months- FY 03: 90%.	The goal has been revised to incorporate PDUFA III.
12003	Review and act upon fileable original generic drug applications within 6 months after submission date.	Revised	Complete review and action on fileable original generic drug applications within 6 months after submission date.	FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete

				review and action onÖ"
12007	Streamline adverse drug event reporting system.	Unchanged		
12016	CDER will conduct laboratory research on at least three projects identified as related to the mission of PQRI	Unchanged		
12020	Inspect registered human drug manufacturers, repackers, relabelers and medical gas repackers.	Revised	Inspect 55% of registered high-risk human drug manufacturers.	The revised goal supports a risk-based approach by encouraging inspections at drug establishments that address or prevent manufacturing problems that would have the most significant adverse effect on drug safety and effectiveness.
12026	Implement, evaluate, track and report on the clinical trials FDA is requesting under FDAMA or requiring under the Pediatric Rule.	Revised	Increase the number of drugs that are adequately labeled for children.	The revised goal clearly indicates FDA's intent on the behalf of the pediatric population.

12032	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.	Revised	Protect human research subjects who participate in drug studies and assess the quality of data from these studies by conducting onsite inspections and data audits annually	Decreasing NDA submissions in FY 2001 and 2002 has necessitated the need to establish new baselines. The number of inspections is dependent on submissions and will fluctuate accordingly.
12036	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.	Dropped		Replaced by new counter terrorism goal below #12045.
12037	Develop guidance for Industry on developing antiviral drugs	Dropped		Replaced by new counter terrorism goal below #12045.

	for the mitigation of complications associated with vaccinia immunization.			
12038	Facilitate human clinical trials in pneumonic plague for antimicrobial drugs that are not yet labeled for this treatment indication.	Dropped		Replaced by new counter terrorism goal below #12045.
12039	Develop guidance for Industry on developing antiviral drugs for the treatment of smallpox.	Dropped		Replaced by new counter terrorism goal below #12045.
12041	Expedite the review of protocols for investigational new radioprotectant drugs (including heavy metal chelators) for use in the event of a radiation emergency.	Dropped		Replaced by new counter terrorism goal below #12045.
12042	Finalize rulemaking to establish a web-based electronic drug registration and listing database to allow for complete and up-to-date data	Dropped		Combined with re-added goal #12027 below.

	on all regulated drug products, and follow this finalization with launch of the electronic database.			
12027		Re-added	Give consumers and health professionals more easily understandable, accessible, timely, and accurate prescription and OTC drug information.	Was in the performance plan in FY 01, was dropped, re-added, and combined with goal #12042.
12045		New	Facilitate development and availability of medical countermeasures to limit the effects of the intentional use of biological, chemical, or radiologic/nuclear agents.	New counter terrorism goal with specific milestones to replace previous counteterrorism goals.
12051		New	Create state-of-the-art information management systems and practices to move to a paperless environment (e-Government).	The use of current technology will allow CDER to receive and review regulatory submissions more efficiently. Standards for submission must be developed in order to move to a paperless

				environment in an efficient and cost effective manner. This goal also falls under the President's Management Agenda of e-government.
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	Revised		FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ"
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	Revised		FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each

	within 6 months of receipt.			program's unique terminology. These goals now include the statement "complete review and action onÖ"
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.	Revised		FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ"
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 receipt.	Revised		FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique

				terminology. These goals now include the statement "complete review and action onÖ"
13005	Review and act on 90% of complete blood bank and source plasma PLA/BLA submissions, and 90% of PLA/BLA supplements within 12 months after submission date.	Revised		FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ"
13012	Meet the biennial inspection statutory requirement by inspecting 50% of registered blood banks, source plasma operations and biologics manufacturing establishments.	Unchanged		
13013	Expedite review of product specific lot	Dropped		Replaced by new counter terrorism goal

	release and extension of dating submissions for the Anthrax Vaccine Absorbed (AVA).			below #13019 that has more specific milestones.
13014	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.	Dropped		Replaced by new counter terrorism goal below #13019 that has more specific milestones.
13015	Facilitate expedited development and review of new vaccines for protection and/or treatment against bioterrorism related threat diseases (e.g., smallpox and anthrax vaccines).	Dropped		Replaced by new counter terrorism goal below #13019 that has more specific milestones.
13016	Facilitate expedited development and review of new gamma globulins for protection	Dropped		Replaced by new counter terrorism goal below #13019 that has more specific milestones.

	and/or treatment against bioterrorism related threat diseases.			
13017	Evaluate the need for guidance documents to assist in the development of products such as immunoglobulins and select vaccines.	Dropped		Replaced by new counter terrorism goal below #13019 that has more specific milestones.
13019		New	Facilitate the availability of safe and effective biological products to prevent, diagnose, and treat sicknesses or injuries associated with a terrorist attack.	New counter terrorism goal with specific milestones to replace previous counteterrorism goals
Animal Drugs and Feeds				
14002	Continue to pilot and validate procedures to receive protocol submissions electronically. FY 03 Target: Receive protocols and ADE active form.	Revised	Continue electronic submission enhancements.FY 03 Target: Receive and act on protocols forms electronically.	Revised to reflect a more direct goal. Also, since the Adverse Drug Event (ADE) active form is a postmarket function, it was deleted from this premarket performance plan goal/target.

14005	CY 03 Goal/Target: Maintain isolate testing rate for Salmonella in the National Antimicrobial Resistance Monitoring System (NARMS) at 12,000.	Revised	FY 03 Goal: Enhance the transparency of the NARMS program to stakeholders, the public, and other interested parties by increased reporting and communicating of NARMS results and program information.FY 03 Target: Present NARMS susceptibility testing results at Scientific meetings via poster or oral presentations. Publish Annual Reports of NARMS animal, human and retail meat data. Post NARMS publication references on the website.	This change was presented during the OMB PART Assessment. Previously, the goal reflected dependence on factors beyond FDA's control such as the number of humans contracting a foodborne disease and a change in the type of isolate samples collected by USDA. The goal was revised to reflect how the Animal Drugs and Feeds Program will use NARMS data to communicate with the public on antibiotic resistance.
14006	Conduct targeted BSE inspections of 100% of all known renderers and feed mills handling prohibited material.	Revised	Conduct targeted BSE inspections of 100% of all known renderers and feed mills processing products containing prohibited material.	This change is to better define the inventory of firms being inspected. The definition now indicates inspections of known renderers and feed mills processing

				products containing prohibited materials, not just handling products containing prohibited materials.
14007	Maintain the level of requested pre-submission conferences conducted with industry sponsors at 80%	Dropped		This goal was dropped because the performance is stable, and therefore, no longer provides a useful measurement for Center management.
14009	Maintain biennial inspection coverage by inspecting 50% of registered animal drug and feed establishments.	Unchanged		
14017	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.	Revised	Complete review and action on 90% of all new animal drug applications and supplements received in FY 03 within 275 days and review and act on 90% of all investigational new animal drug submissions received in FY 03 within 325 days.	FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology.

				These goals now include the statement "complete review and action onÖ".
14018	Begin to design and implement a Staff College. 03 Expansion of content and developmental components & integration w/Center & Agency IT infrastructure.	Revised	Continue development, expansion and integration of the Staff College.FY 03 Target: Expand content of in-house programs. Research and develop components and integration of competency-based learning management system (LMS) with Center and Agency IT infrastructure.	Revision provides better detail.
14019	Reduce pending overdue Animal Drug applications by 15%.	Revised	Reduce pending overdue Animal Drug submissions by 15%.	Clarifying language.
Medical Devices				
15001	Review and Complete 95% of Premarket Approval Application (PMA) first actions within 180 days.	Revised	Complete review and action on 90% of Premarket Approval Application of an estimated 80 (PMA) first actions within 180 days.	FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated

				with each program's unique terminology. These goals now include the statement "complete review and action onÖ".Dropped to 90% because of the increase of the workload. Added workload information.
15002	Review and complete 95% of 510(k) (Premarket Notification) first actions within 90 days.	Revised	Complete review and action on 95% of an estimated 4,500 510(k) (Premarket Notification) first actions within 90 days.	FDA has changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ".Dropped to 90% because of the increase of the workload. Added

				workload information.
15003	Recognize 20 new or enhanced standards to use in application review.	Unchanged		
15005.01	Provide inspection coverage for Class II and Class Ill domestic medical device manufacturers at 20%.	Revised	Utilize Risk management to target inspection coverage for Class II and Class Ill domestic medical device manufacturers at 20% of estimated 5,300.	Revised by using risk management to target Class II and Class III Ill domestic medical device manufacturers. Added workload information.
15005.02	Provide inspection coverage for Class II and Class Ill foreign medical device manufacturers at 9% for FY 2003.	Revised	Utilize Risk management to target inspection coverage for Class II and Class Ill foreign medical device manufacturers at 9% of estimated 2,500.	Revised by using risk management to target Class II and Class III Ill domestic medical device manufacturers. Added workload information.
15007	Ensure at least 97% of mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems.	Revised	Ensure at least 97% of an estimated 8749 domestic mammography facilities meet inspection standards, with less than 3% with Level I (serious) problems.	Added workload information.
15009	Review and	Revised	Complete review	FDA has

	complete 95% of PMA supplement final actions within 180 days.		and action on 95% of an estimated 725 PMA supplement final actions within 180 days	changed all its major premarket goals to be consistent agency-wide, and decrease the potential for confusion that is associated with each program's unique terminology. These goals now include the statement "complete review and action onÖ".Also added workload information
15012	Implement the MeDSuN System by expanding the network to 180 facilities.	Unchanged		
15024	Complete 95% of PMA "Determination" meetings within 30 days.	Unchanged		
15025	Conduct 290 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Revised	Conduct 295 BIMO inspections with an emphasis on vulnerable populations (e.g., mentally impaired, pediatric, etc.)	Target increased.

15027	Provide inspection and product testing coverage of Radiological Health industry at 10%	Revised	Maintain inspection and product testing coverage of Radiological Health industry at 10% of an estimated 2000 electronic products.	Revised to maintain inspection to reflect more specific performance target in the goal statement.
15028	Expedite review for 100% of Bioterrorism Diagnostic Medical Device Applications.	Revised	Expedite review for 100% of an estimated 5 Bioterrorism Diagnostic Medical Device Applications.	Added workload information
15029	Implement Emergency Counter Terrorism Preparedness and Response Plan for radiation.	Unchanged		
15030	Begin to develop radiation standards for the safety of novel or new technology used to scan people in airports and other places.	Unchanged		
NCTR				
16001	Introduce the knowledge of new genetic systems and computer-assisted toxicology	Revised	Introduce the knowledge of new genetic systems and computer-assisted toxicology (toxicoinformatics)	To enhance FDA's risk management process.

	(bioinformatics) into the application review process.		into the risk management process.	
16002	Develop, with other organizations, gene chip and gene array technology.	Unchanged		
16003	Develop computer-based models and infrastructure to predict the health impact of increased exposure to estrogens and anti-estrogen compounds.	Revised	Develop computer-based models and infrastructure to predict the health risk of biologically active products	To broaden FDA's ability to evaluate risks associated with regulated products.
16004	Study FDA-regulated compounds to relate the mechanism(s) by which a chemical causes toxicity.	Revised	Study the risk associated with how a FDA regulated compound or product interacts with the human body.	To broaden FDA's ability to evaluate risks associated with regulated products.
16007	Develop methods and build biological dose-response models to replicate bacterial survival in the stomach.	Revised	Develop risk assessment methods and build biological dose-response models in support of the Food Safety Initiative.	To broaden FDA's risk assessment methods to ensure a safe food supply.
16012	Catalogue biomarkers and develop standards to establish safety	Revised	Catalogue biomarkers and develop standards to establish risk in a	Focus research efforts to support FDA's counter-terrorism

	and effectiveness of imaging devices for potential use in the diagnosis of toxicity.		bioterrorism environment	efforts.
16013	Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of toxicity.	Revised	Use new technologies (bioinformatics, imaging, proteomics, and metabonomics) for diagnosis of risk.	To broaden FDA's ability to evaluate risks associated with regulated products.
Agency Wide				
19001	Increase supervisory ratio to increase the span of control among management personnel.	Reduce the number of review levels in the Agency to help streamline operations. Develop and implement a plan to delayer CBER, CFSAN and ORA; Transfer Legislative and Public Affairs function to DHHS	Revised	The attempt was made to incorporate language from the Booze Allen study and bring the goal more in sync with the consolidation idea.
19002	Consolidate administrative functions in the agency.	Revised	Implement 'shared services' concept and consolidate selected functions in the agency.	The attempt was made to incorporate language from the Booze Allen study and

			Personnel, Finance, Budget, Procurement, Grants, Information Technology, Legislative & Public Affairs. Begin implementation of shared services concept in accordance with the BAH Administrative Consolidation Study.	bring the goal more in sync with the consolidation idea.
19003	Increase the percentage of Commercial FTE that will be reviewed for outsourcing.	Unchanged		
19004	Increase the percentage of electronically purchased transactions.*	Unchanged		
19005	Maintain a clean (or unqualified) audit opinion with no material weakness.	Unchanged		
19006	Increase percentage of contract dollars to performance based contracts from 30 percent.	Unchanged		
19007	Assure continuity of FDA operations	Dropped		Goal is essentially completed and

	in case of an emergency.			only requires maintenance.
19010		New	Expand the Agency-wide IT security program to ensure all of Agency's IT assets that support the Agency's business processes are in compliance with the Government Information Security Reform Act (GISRA). Assess OC, NCTR and selected other critical components for GISRA compliance, and resolve any access control issues.	Goal was included to bring the agency into compliance with the GISRA and to generally protect information and prevent waste, fraud, and abuse.
19017		New	Begin implementation of a new financial system. Financial Business Solutions at FDA.	To bring the agency into compliance with HHS's new financial system
19015		New	Perform at least 1,000 Filer Evaluations under new procedures.	The combination of new hires and a shift to a more risk based approach to ensuring public education and safety has allowed FDA to

				add this goal.
19016		New	Conduct 2,000 examinations of FDA refused entries as they are delivered for exportation to ensure that the articles refused by FDA are being exported.	The combination of new hires and a shift to a more risk based approach to ensuring public education and safety has allowed FDA to add this goal to move one step closer to ensuring that refused articles are being exported.
19013		New	Expand federal/state/local involvement in FDA's eLEXNET system by having 79 laboratories participate in the system. 54 laboratories participating in eLEXNET in 2003.	New technologies have allowed FDA to apply a more effective risk-based approach to ensuring the safety of foods and working with other agencies.
19008		New	Enhance the Agency Emergency Preparedness Plan to establish protocols for responding to terrorist attacks.	FDA has added this goal to help better prepare the agency and it's individual programs to respond more efficiently to emergencies.
19014		Revised	Perform 48,000 physical exams	Copied from Foods section

			and conduct sample analyses on products with suspect histories. Increase exams by 100 % to 48,000 exams	to the agency wide. Previously goal # 11036

Appendix D: *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.

Appendix E: *Verification and Validation*

Agency Wide

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.

Foods

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.

Drugs

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.

Biologics

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) was developed 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 and 606.171) 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 deviations and unexpected events, and to respond appropriately to reported biological product deviations 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. The final rule was published on November 7, 2000. On August 10, 2001, FDA published two draft guidance documents: (1) "Draft Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments," and, (2) "Draft Guidance for Industry: Biological Prodcut Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components." The comment period for the guidance documents ended November 13, 2001.

In FY 2001, the Agency received 25,367 biologics product deviation reports. FDA estimates that over 27,000 biologic product deviation reports would be received under the proposed regulation. In June 2001, FDA implemented an electronic reporting system to permit the electronic submission of biologic product deviation reports. This will allow the Agency to receive electronic submission of reports; and to process, analyze and evaluate more than 27,000 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.

Animal Drugs and Feeds

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; checks are in place to ensure that the person who enters the data does not audit the data.

CVM works with data from other governmental agencies such as CDC and USDA. To ensure that our federal partners address our data needs, we have established Interagency Agreements, memorandums of understanding, and memorandums of need with other agencies. To accomplish our Food Safety Initiative goal (Performance Goal 8 - 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 residue reported to FDA by USDA's Food Safety and Inspection Service (FSIS). FSIS develops an annual statistical residue sampling plan with input from FDA. However, the majority of violations reported to FDA for investigative follow-up, result from samples from suspect animals. FSIS recently modified sampling criteria, which resulted in an increased number of suspect animals being tested and an increase in violative samples being reported to FDA. Under the new Hazard Analysis Critical Control Point (HACCP) plan, the requirements for how slaughter plants choose samples for testing has also changed substantially so it is extremely hard to judge how many residue reports will be sent to FDA for follow-up investigation.

Medical Devices and Radiological Health

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.

NCTR

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.

Appendix F: *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

End of Performance Plan