FOODS

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$435,517,000**	**$438,721,000**	**$449,687,000**	**+$10,966,000**
Center	*$152,260,000*	*$153,568,000*	*$148,363,000*	*-$5,205,000*
FTE	*884*	*881*	*817*	*-64*
Field	*$283,257,000*	*$285,153,000*	*$301,324,000*	*+$16,171,000*
FTE	*2,059*	*1,962*	*1,940*	*-22*
Budget Authority	**$435,517,000**	**$438,721,000**	**$449,687,000**	**+$10,966,000**
Center	*$152,260,000*	*$153,568,000*	*$148,363,000*	*-$5,205,000*
FTE	*884*	*881*	*817*	*-64*
Field	*$283,257,000*	*$285,153,000*	*$301,324,000*	*+$16,171,000*
FTE	*2,059*	*1,962*	*1,940*	*-22*
Pandemic Preparedness	*--*	*--*	*$8,348,000*	*+$8,348,000*
FTE			*15*	*+15*
Food Defense	*$142,379,000*	*$149,865,000*	*$168,253,000*	*+$18,388,000*
FTE	*732*	*743*	*747*	*+4*
Cost of Living				*+$6,877,000*
Strategic Redeployment			*-$22,647,000*	*-$22,647,000*
FTE			*-105*	*-105*
Budget Authority FTE	**2,943**	**2,843**	**2,757**	***-86***

[1/] *Includes a one percent rescission*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$406,824,000	$406,824,000	--	3,167
2004 Actual	$407,052,000	$407,052,000	--	3,082
2005 Actual	$435,517,000	$435,517,000	--	2,943
2006 Enacted	$438,721,000	$438,721,000	--	2,843
2007 Estimate	$449,687,000	$449,687,000	--	2,757

Statement of the Budget Request

The Foods Program request is $449,687,000 to perform the following:

- Ensure that the food supply is safe, nutritious, wholesome, and honestly and otherwise properly labeled and that cosmetics are safe and honestly and otherwise properly labeled.

- Safeguard the U.S. public by defending the food system against terrorist attacks, major disasters, and other emergencies.

- Identify food-related health hazards.
- Support Homeland Security Presidential Directive/HSPD-9, "Defense of the United States Agriculture and Food."
- Take corrective action to reduce human exposure to food related health hazards and the possibility of food-related illnesses and injuries.
- Take timely and appropriate action on new food ingredients before they go on the market to ensure their safety.
- Continue applied research programs that provide the necessary basis for regulatory decisions for protecting public health.
- Educate and train consumers and industry on food safety and food security.
- Set standards and develop regulations for the food industry.
- Conduct investigational, inspectional and laboratory functions to ensure that FDA- regulated products comply with the laws and regulations that FDA is charged with enforcing.
- Respond rapidly to emergencies, and redirecting field efforts, as necessary, to respond to unforeseen events.
- Manage and conduct criminal investigations of matters within the Agency's jurisdiction, including advising and assisting the Commissioner and other key officials on legislation and policy involving criminal justice matters.
- Monitor clinical research and conduct inspections of FDA-regulated products before they are marketed to ensure that manufactured products will be safe.
- Perform field examinations of imported products to determine whether import entries comply with FDA regulations.

Program Description

The Foods Program regulates all food except meat, poultry, and liquid, frozen and dried eggs, which are regulated by the USDA. The Center for Food Safety and Applied Nutrition (CFSAN), in conjunction with ORA, promotes and protects public health by ensuring that the food supply is safe, sanitary, wholesome, and honestly and otherwise properly labeled, and that cosmetic products are safe and properly labeled. Current trends in the food industry promise better nutrition, greater economies and wider choices for the U.S. consumer than ever before. We face many challenges to ensuring food safety and food defense, including:

- The volume and diversity of imported foods has risen dramatically over the last few decades, with foods once considered exotic now found throughout the U.S.

- The global food supply means that foods we consume are being produced by a much larger number of source countries.
- The biotechnology explosion has opened new frontiers in plant derived foods using biotechnology, with many containing genetic characteristics that resist pests. Other foods with additional traits, such as higher nutrient content or improved flavor, are expected soon.
- The dietary supplements industry and the consumption of these products have grown dramatically.

Each of these present food safety regulatory and food security/defense challenges for FDA. The Agency's job is to give consumers the confidence to enjoy the benefits of these expanded food choices.

Scope of Responsibility

CFSAN, along with ORA, regulates $417 billion worth of domestic food, $49 billion in imported foods, and $59 billion (including $4 billion imported) in cosmetics sold across state lines. FDA's regulatory responsibility takes place from a products' point of U.S. entry or processing to its point of sale, with approximately 210,000 food establishments (or 420,000 if foreign establishments that must register with FDA to export food to the U.S. are included) and 1,500 cosmetic firms.

The Foods program's primary responsibilities include regulatory and research programs to address health risks associated with foodborne chemical and biological contamination. Activities include:

- Current good manufacturing practice compliance; seafood Hazard Analysis and Critical Control Point (HACCP), and juice HACCP regulations.
- Good agricultural practices.
- Safety of food ingredients and packaging (including ionizing radiation) and color additives.
- Safety of foods and ingredients developed through biotechnology.
- Regulations and activities dealing with the proper labeling of foods (e.g., ingredients, nutrition health claims) and cosmetics.
- Regulations and policy on the safety of dietary supplements, infant formulas, and medical foods; food industry postmarket surveillance and compliance.
- Consumer education and industry outreach; cooperative programs with state and local governments; and regulatory and research programs to address the safety of cosmetic products.

The Foods program is also responsible for development and implementation of the food defense provisions outlined in the Bioterrorism Act of 2002 (BT Act) and implementing Homeland Security Presidential Directive-9 (HSPD-9) to safeguard the food supply. Because a growing proportion of the U.S. food supply is imported, we also work with international organizations

and occasionally directly with foreign governments to ensure their understanding of U.S. requirements and to harmonize international food standards.

Through risk-based domestic and foreign inspections of food establishments conducted by ORA, we are able to assess industry compliance with current Good Manufacturing Practice (cGMP) and HACCP requirements for a myriad of products. In particular, ORA inspects thousands of domestic firms identified as high-risk food establishments consisting of manufacturers and packers/repackers processing products. These products 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.

In addition to overseeing regulated products on a surveillance or "for cause" basis, ORA responds to emergencies and investigates incidents of product tampering and natural or intentional disasters that may affect FDA-regulated goods. In instances of criminal activity, the regular field force is complemented by the Office of Criminal Investigations (OCI).

Performance Analysis

During FY 2005, which was the latest performance period, the Foods program successfully achieved or exceeded 7 out of 9 targets for its FY 2005 performance goals. Of those not achieved, one target is expected to be met when data becomes available later in FY 2006. Another showed improvement over the FY 2004 actual data and narrowly missed the target because changes in one state's legislation did not take place in time to adopt the Food Code within fiscal year 2005. For more information about these performance goals and results, please see the Performance Detail section.

The American public fully expects its food --including any substances added to food--to be safe, regardless of who consumes the food, the quantity consumed, or the period of time over which it is consumed. The requirement that chemical substances used as food additives be shown to be safe before they can be introduced into the food supply is a critical link in the food safety chain. Under the FD&C Act, FDA must review and approve food and color additives for safety before food manufacturers and distributors may market them. To initiate this review, sponsors are required to submit a petition that includes appropriate test data to demonstrate the safety of the substance for its intended use. Performance is defined in terms of a review of all parts of a petition within 360 days of receipt. In addition, the FDA Modernization Act (FDAMA) established a notification program for food additives that are food contact substances (e.g., packaging materials). Under the provisions of this notification, a food contact substance may be marketed 120 days after notification unless the agency objects. As part of the FY 2007 strategic redeployment of resources to fund higher priority FDA programs (e.g., food defense and pandemic influenza), this program will be discontinued. The Agency also has a notification program for substances that are Generally Regarded as Safe (GRAS). In addition, the Agency consults with developers of foods derived from bioengineered plants to ensure that any safety and regulatory questions are resolved prior to marketing. Finally, the Agency reviews notifications for dietary supplements containing "new ingredients" within 75 days as well as

infant formula notifications within 90 days. CFSAN's key challenge in the premarket area is to expeditiously review new food products without jeopardizing public safety.

Performance Highlight:

FY 2007 Goal Target	FY 2004 Results	Context
Complete review and action on the safety evaluation of 50% of direct and indirect food and color additive petitions which includes petitions for food contact substances within 360 days of receipt.	FDA has met the targets for this performance goal consistently since FY 1999.	This goal refers to completion of the safety evaluation of food and color additive petitions which includes those for food contact substances. 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.

Statement of Budget Request

This request for Budget Authority supports various activities that contribute to the accomplishment of program outputs and performance goals, and presents FDA's justification of base resources and selected FY 2005 accomplishments by strategic goal.

Program Resource Changes

Budget Authority

Pandemic Preparedness: +$8,348,000 and 15 FTE

The National Strategy for Pandemic Influenza, issued by President Bush November 1, 2005, guides our nation's preparedness and response to an influenza pandemic, with the intent of (1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. The Strategy charges the U.S. Department of Health & Human Services with leading the federal pandemic preparedness.

FDA will focus resources on those foods that require surveillance and testing to ensure that the virus is not present or, if present, to ensure that the food can be properly treated to ensure safety. Specifically, FDA will:

- Develop/validate detection methods in foods of concern (shell eggs, soups containing poultry, bird game meats).
- Conduct inactivation/intervention studies of bird flu virus during processing of foods of concern.
- Coordinate with USDA on sampling and testing poultry products at import inspection stations and poultry processing plants for traces of antiviral residues.
- Issue Custom Alerts to prevent the illegal importation of antivirals into the U.S.
- Develop, integrate and execute FDA animal and food response plans and quarantine activities, in coordination with USDA and CDC.
- Equip field labs and support technology transfer and training of field scientists to ensure adequate capacity to respond to outbreaks of avian influenza.
- Improve FDA's capacity to conduct domestic and import surveillance and respond to reports of food or foodborne illness associated with viruses.
- Support national pandemic influenza surveillance integration efforts with a comprehensive system to detect highly pathogenic strains of avian influenza.
- Provide technical assistance to industry and conduct public education on the potential risks of foodborne avian influenza and measures to prevent illness.

Food Defense: + $18,388,000 and 4 FTE

FDA's food defense program supports Homeland Security Presidential Directive (HSPD-9) on safeguarding the American Public by defending America's food supply against terrorist attacks post-September 11, 2001. HSPD-9 lays out a framework for augmenting the nation's food safety protections and establishing a partnership among the various organizations responsible for protecting the nation's food supply.

CFSAN will use the additional funds to continue lab preparedness efforts and for necessary short term research projects. Many of the projects undertaken are derived from direct interaction with industry following vulnerability assessments. The results of these projects can be communicated directly to industry. These efforts will result in a better understanding of which interventions work, and which do not, for certain agents in specific foods.

Further joint food defense and food safety assignments will enhance and facilitate the integration of food defense with food safety. In these assignments, samples that are obtained as part of routine food safety programs will also be tested in a variety of labs for a range of select agents that are of most concern. The foods chosen for these assignments are generally ones that we have most concern about based on vulnerability assessments.

The Field will use the additional resources for the following activities.

- Expand the FERN system to include 16 State laboratories, provide grants and technical support to these laboratories and build analytic surge capacity to respond to a terrorist attack.

- Manage, through the National Program Office, FERN's ability to respond for a terrorist attack on (or threat to) the food supply or other food-related emergency by creating capability in FERN laboratories through training and proficiency testing.

- Continue Field support for food defense operations, including targeting potentially high-risk imported foods through Prior Notice Import Security Reviews based on intelligence, FDA inspection reports, discrepancies in prior notice reporting and sample collection and analysis.

Cost of Living +$6,877,000

FDA's request for inflationary pay costs is essential to accomplishing our public health mission. Payroll costs account for more than sixty-percent of the FDA budget, and the Agency is not able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Foods portion of this increase is $6,877,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Foods Reductions -$22,647,000 and -105 FTE

To fund FY 2007 priority initiatives such as such as food defense and pandemic influenza, FDA re-deployed resources from base programs. To accomplish this strategic redeployment and fund new, high priority initiatives, CFSAN reductions include: Research, Cosmetics, Dietary Supplements, Proficiency Testing, Outreach and Standard Setting, Regulatory Support, Premarket Food and Color Additives, and Food Contact Substances Notification. The Field – Foods reductions include lower levels of effort in these activities: analysis of low-risk domestic and import samples (FDA will continue to analyze high risk samples, including those flagged by the Prior Notice Center), research related to laboratory analytical methods, compliance and recall functions and management, supervisory, and coordination personnel at multiple locations.

Proposed Fees (Reclassified as Mandatory - Non-Add)

Reinspection User Fee (Mandatory): $5,215,000 and 44 FTE (Non-Add)

The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an amount sufficient to fully fund reinspections. The Foods program component of this user fee is $5,215,000 and 44 FTE.

Food and Animal Feed Export Certification User Fee: $3,473,000 and 23 FTE (Non-Add)

The Administration is proposing legislation authorizing FDA to collect user fees for issuing food and animal feed export certificates. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $3.5 million in revenue, an amount sufficient to fully fund the export certificate program. Private sector exporters would bear the cost of the

program, but would reap its benefits through the Agency's enhanced ability to facilitate exports of their products. The Foods program component of this user fee is $3,473,000 and 23 FTE.

Justification of Base

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Healthier Americans

The single most important factor in ensuring that citizens lead long, healthy lives and minimize the likelihood of chronic disease is the availability and effective use of science-based nutrition information. This will help consumers make wise choices about the foods they consume. This year the agency published two final regulations that will provide consumers with better label information and foster the development of healthier food products for American consumers. First, the trans fat labeling rule requires the amount of trans fat to be declared on the Nutrition Facts panel directly below the saturated fat line. The level of trans fatty acids in the diet affects risk of coronary heart disease. This rule was published in 2003 and became effective January 1, 2006 for all food under FDA jurisdiction. FDA estimates that 3 years after the January 1, 2006 effective date, trans fat labeling can lead to the prevention of 600 to 1,200 cases of coronary heart disease and 240-480 deaths each year, saving $900 million to $1.8 billion per year in medical costs, lost productivity, and pain and suffering.

Second, the term "healthy" is a very strong nutrient content claim. It specifies strict nutrient levels for fat, saturated fat, cholesterol, sodium and beneficial nutrients. The "healthy" final rule modifies the sodium levels in foods permitted to bear the term "healthy". Such foods include individual foods, meal products like burrito meals, and main dish products like chicken pot pie. These sodium limits are lower than for similar conventional foods, but not so low that manufacturers would be discouraged from developing and marketing products that have healthy levels of a variety of nutrients.

Research Development and Evaluation Activities

CFSAN's research, development, and evaluation activities are an integral part of the programs needed to achieve this strategic goal. Activities under this goal include ensuring food safety and food defense, and enhancing the ability for consumers to make sound nutrition choices. This research is necessary to ensure the health and well being of the American public and to identify and eliminate foodborne hazards, both naturally occurring and intentionally introduced into the food chain. The research is typically not conducted by industry or other research agencies. It provides the basis for nutrition labeling regulations and guidance, identification of foodborne pathogens, toxins and select agents, and the development of mitigation and prevention strategies. The research provides the scientific basis for regulating the food-producing and processing industries to ensure a safe and nutritious food supply from farm-to-table. Applied research activities include efforts to:

- Develop, with available resources, analytical methods for measuring specific nutrients or dietary ingredients that are potential safety concerns (e.g., toxic or carcinogenic components of botanicals).
- Develop analytical methods for measuring food components that are the subject of proposed regulations (e.g., soy isoflavones and *trans* fatty acids) to establish and maintain the

credibility of information on the food label.

- Evaluate and/or validate test kits for food allergen contamination. This is necessary in order to systematically assess key characteristics of proteins (e.g., thermal stability, acid digestion resistance) that may be associated with potential food allergenicity and to establish and maintain the credibility of information on the food label.
- Continue, at a reduced level, research on botanical ingredients in dietary supplements (acquisition, validation, and characterization of authentic botanical reference materials), as part of the 10-year Dietary Supplement Strategic Plan. This will be done through a cooperative agreement between FDA and the University of Mississippi's National Center for Natural Products Research.
- Conduct research in support of the 2010 Dietary Guidelines for Americans, such as:
    - Developing a scientifically valid definition for "nutrient density" for use on the food label and determining what criteria are necessary for foods to meet this definition.
    - Conducting studies to determine the barriers to complying with the guidelines for children, low-income populations, and various ethnic groups to change their eating behaviors and identifying various mechanisms to motivate individuals to change.
    - Developing and testing both individual-based and population-based interventions designed to implement the guidelines
    - Conducting consumer research to evaluate food safety messages and corresponding changes in behavior.
- Continue the development of a Food Source Identification and Tracking System. This is a stand-alone computer modeling tool for projecting the probabilities and distribution of human morbidity/mortality outcomes and economic effect, associated with foodborne hazards. It is intended to aid in developing strategies to respond quickly and efficiently to crises and emergencies involving the food supply.
- Develop enhanced sampling and detection methods for surveillance for priority chemical, microbiological, and radiological agents in vulnerable foods, including field deployable and in-line sensor-based screening, analytical, and investigational (forensic) technologies;
- Develop multiple-analyte surveillance methods that allow the simultaneous, real-time evaluation of foods for several hundred toxic chemicals of food safety and/or food defense concern.
- Develop bioinformatic techniques that provide enhanced use of genomic, proteomic, and metabolomic information to allow more effective food safety, food defense, and nutrition regulatory decisions by considering the diversity of humans, foods, and food processing technologies.

Nutrition

- *Calories Count:* Continue, through CFSAN's Obesity Working Group (OWG), to confront the obesity epidemic in the U.S. and help consumers lead healthier lives through better nutrition by outlining and implementing an action plan to combat obesity.

- *Labeling/Health Claims:* Continue to develop better information for consumers about the health consequences of their diet. Also, continue to devote resources to finalize and implement programs focusing on the guidance and procedures for qualified health claims in the labeling of conventional human food and human dietary supplements.
- *Keystone Dialogue:* Draft a final report for FDA review. In June 2004, FDA contracted with the Keystone Center to convene a national forum/dialogue with stakeholders, including public and private decision makers, to explore and work toward agreement on concrete steps that can be taken to address obesity in the context of away-from-home foods. FDA is represented on Keystone's planning group for the dialogue sessions and these completed sessions are the basis for the final report.

Food Safety

- *Food Code:* The Food Code model assists food control jurisdictions at all levels of government. The model provides them with a scientifically sound technical and legal basis for regulating the retail and food service segment of the industry. FDA will continue to update the Food Code. FDA will also increase risk management strategies and communication to government, industry and consumers for ensuring the safety of the nation's food supply. This will be accomplished by quantifying actual performance of the percentage of the total US population that will live in States that have adopted the Food Code. The Food Code is a component of an even larger effort aimed at decreasing foodborne illness, the National Retail Food Regulatory Program Standards program. Through this program, FDA will continue to:
    - Assist state programs and provide oversight in implementing the standards program.
    - Continue to provide support and guidance to jurisdictions already enrolled.
    - continue support of conducting audits of those enrolled in the standards program.

- *Surveillance Systems:* CFSAN will continue to evaluate the CDC foodborne disease outbreak surveillance system data to identify and analyze outbreaks associated with FDA-regulated products. Areas of focus will include the number of outbreaks, cause agents, morbidity and mortality, seasonality, geographic location, site of food preparation, contributing factors and whether the product is domestic or imported. CFSAN will also help sustain enhancements to the strategic data systems for surveillance and inspection activities of the food supply that help FDA inspectors focus on and analyze products suspected to have microbiological and chemical contamination.

Food Safety for Moms-to-Be

FDA launched a new comprehensive food safety education program focusing on prevention of foodborne illness for pregnant women. Six million American women become pregnant each year and 10,000 give birth each day. This program highlights foodborne illness risks that pregnant women and their fetuses are particularly vulnerable to, such as Listeria monocytogenes, methylmercury, and the Toxoplasma parasite. FDA created an educator's toolkit, including a fact-filled Educator's Resource Guide and an award-winning video featuring the Discovery Channel's Dr. Andrea Pennington, for healthcare professionals to use when talking with women about pregnancy and foodborne illness. The agency produced and distributed about 60,000 free kits to organizations such as the American College of Nurse Midwives, American Academy of Medicinal Administration, Association of Women's Health, Obstetric, and Neonatal Nurses, National Women's, Infants', and Children's Association, USDA Cooperative Extension Service locations, and many others. FDA continues to offer kits in two languages, English and Spanish, upon request. FDA is also promoting a website (http://www.cfsan.fda.gov/pregnancy.html) to women and healthcare professionals, so they can get information directly.

- *FoodNet/PulseNet:* CFSAN will continue to participate in national surveillance and emergency response programs, such as the Foodborne Disease Active Surveillance Network (FoodNet) and PulseNet. FoodNet, a collaborative project with the CDC and USDA, conducts active surveillance for foodborne diseases and related epidemiology studies; PulseNet is a national network of public health laboratories that performs DNA "fingerprinting" on bacteria that may be foodborne.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Research Development and Evaluation Activities

The Foods program's research, development, and evaluation activities support this strategic goal with work performed in food safety and defense, food nutrition, and cosmetic product safety. The effective and timely evaluation and subsequent scientific review of new technologies for enhanced food and cosmetic safety, as well as innovative products for enhanced nutritional well-being, are critical for the United States to maintain its leadership role in the increasingly global trade of food. This research provides the scientific basis for identifying and recommending the adoption of innovative technologies that reduce public health concerns related to foodborne pathogens, toxins, and select agents. The research provides the scientific basis for regulating the food producing and processing industries to ensure a safe and nutritious food supply from farm-to-table. With available funding, the foods program will:

- Develop risk assessments, risk assessment techniques, and critical scientific data needed to ensure that international food safety standards developed through intergovernmental organizations are based on sound science.
- Develop innovative "in shell" pasteurization techniques that lead to the development of new egg products that eliminate the risk of egg-associated *Salmonella* Enteritidis infections.

Food Safety

- *Premarket Program:* The American public fully expects its food --including any substances added to food--to be safe, regardless of who consumes the food, the quantity consumed, or the period of time over which it is consumed. The requirement that chemical substances used as food additives be shown to be safe before they can be introduced into the food supply is a critical link in the food safety chain. Base resources will continue to be devoted to the following premarket activities.

    - Continue, at a reduced capacity, to review the safety of food and color additives before they are marketed by food manufacturers and distributors.

    - Continue the review of notifications for substances that are Generally Regarded as Safe (GRAS).

    - Provide, through the Food Additives Regulatory Management (FARM) system, information management tools for food additive petition reviewers. These tools will maximize productivity and expedite the petition review process and subsequent safety decisions. This system also helps FDA perform associated activities such as responding to and managing FOIA requests and correspondence. All paper and electronic documents are converted to standard formats and stored in an electronic document management system. Each reviewer is able to retrieve documents at their desks using a combination of attribute and full-text search capabilities supported by a thesaurus maintaining nomenclature control.

- *Bioengineered Foods:* Continue to consult with developers of foods derived from bioengineered plants to ensure that any safety and regulatory questions are resolved prior to marketing. Activities involve labeling, consultations with industry and the issuance of guidance to developers of these foods.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Research Development and Evaluation Activities

CFSAN's research, development, and evaluation activities in food defense and safety, food nutrition, and the safety of cosmetic products support the strategic goal. The food defense research priorities are based on determining the food/agent combinations of highest concern. Mission critical knowledge gaps are filled by translational research focused on anticipating, preventing, detecting, responding to, and recovering from terrorist assaults on the food supply. Food defense and safety research provides the basis for identifying and countering foodborne pathogens, toxins, and select agents. The research also provides the scientific basis for regulating the food producing and processing industries to ensure a safe and nutritious food supply from farm-to-table. CFSAN's food safety and food defense research approach is threefold, involving an intramural program, an extramural program, and consortia with industry and/or academia.

- *Food Safety Research – the program will use available funds for:*
  - Delineating microbial pathogen risks associated with foods by: examining emergence in the food supply, adaptation to the barriers that are traditionally used to keep food safe, and rapid detection; characterizing the survival, growth, and inactivation of the pathogens.
  - "Fingerprinting" pathogens in food; studying unique intervention technologies to prevent contamination; and arraying all this information, using risk assessment techniques, to inform risk managers. This research is the critical underpinning of regulatory policy.
  - Conducting studies of how heat, ultraviolet light, irradiation, and high pressure processing can improve the safety of cheese, sprouts, juice, and eggs. These studies provide industry with information on how these technologies may be used to prevent pathogen contamination and allow FDA to develop scientifically sound guidance for small businesses.
  - Enhancing foodborne virus (including avian flu) research, surveillance and response capability, and programs covering shell eggs, seafood, game meats, and other potentially at-risk foods.
  - Providing the scientific tools to identify foodborne viruses in foods and technologies to remove or reduce their public health impact.
  - Conducting outreach and education to inform industry and consumers of potential risks and steps to prevent virus contamination, and, as part of FDA's food safety surveys, assessing the success of consumer understanding of these risks.
  - Conducting studies to provide criteria for prevention, reduction, or elimination of safety hazards affecting seafoods within the unique HACCP requirements regulating this program and/or the cooperative National Shellfish Sanitation Program with industry.

- *Food Defense Research Program* activities include*:*
  - Determining the behavior of microbiological, chemical, radiological, and biologically-derived toxic agents in priority vulnerable foods during the stages of production, distribution, marketing, and preparation to develop more effective intervention technologies and conduct better vulnerability assessments.
  - Enhancing information on the susceptibility of the population to microbiological, chemical, radiological, and biologically-derived toxic agents in priority vulnerable foods to identify "at risk" populations and conduct better vulnerability assessments.
  - Identifying, developing, and validating new techniques for "shielding" priority vulnerable foods and their application to the development of new prevention and/or security technologies.
  - Developing effective methods for ensuring that critical food production and manufacturing infrastructure can be rapidly and effectively decontaminated in event of a terrorist attack;

- Communicating foods defense research deliverables to Federal, state, and local entities and with industry, as appropriate, to further protect the food supply from deliberate attack.

- *Cosmetic Safety and Color Certification Research Program* activities will include, to a limited extent:
  - Acquiring scientific information and developing analytical procedures to support regulatory policy and actions for cosmetic products, including methods development for contaminants, the development of methods for measuring skin absorption and metabolism, and investigating the photoactivity of cosmetics and colors.
  - Developing new methods for improving the efficiency of sample analysis and confirmatory analysis in color additive certification and on the synthesis of standards used in these analytical procedures.

Food Defense

Base resources will help strengthen FDA's capability to identify, prepare for, and respond to potential terrorist threats and incidents. Base funds will support to following efforts:

- Continue the evaluation of the public health consequences (risk) of product-agent-activity combinations associated with tampering and/or terrorist activity.

- Continue to identify and document the types of preventative measures that companies can take to minimize the risk that food or cosmetics under their control. Resources will also enable CFSAN to continue to work with industry to ensure that the appropriate preventative measures are implemented.

- Continue efforts to develop and validate new methods for use in surveillance and monitoring of potential threats. New microbiological, chemical, and radiological methods must be developed, validated, and used to detect, enumerate and identify potential non-traditional agents that may threaten the food supply. A particular emphasis is the need to develop biosensors and other technologies to permit continuous monitoring of foods both during production and at import entry sites.

- Continue efforts to improve the safety of food through prevention technologies. FDA studies food prevention technologies to improve the safety of food and establish guidelines and or performance standards for industry. Information is needed about new technologies and / or technology enhancements that can increase food safety and protect against potential exposure to non-traditional pathogens, toxins and chemicals during possible high threat situations. For example, critical information is needed to determine if prevention strategies such as changing pasteurization times and temperatures could be used to safeguard foods and beverages while maintaining the quality that the consumer expects.
- Continue work involving Agent Characteristics. Essential to improving FDA's ability to detect, quantify and control foodborne pathogens, toxins and chemicals that threaten the food supply is performing additional assessments. These are assessments of the abilities of non-

traditional microbial pathogens to survive and grow in foods during processing and storage, or the stability and activity of chemical agents while present in foods, and the potential for their inactivation during food processing.

- Continue Dose Response Relationships/ Threat Assessments. Essential to accurately estimate the threat posed by such exposures is an understanding of the dosage amounts needed to inflict human disease or produce adverse reactions, where exposure occurs through consumption of different food matrices.. In turn, knowledge of dose response helps determine methods development performance parameters (e.g., sensitivity, ruggedness, statistical confidence) that assure safety and security of the food supply.

- Continue the development of scientific methods to support the critical infrastructure. This includes:
    - Articulation of interim methods.
    - Development and delivery of training modules.
    - Establishment and integration of laboratory communication systems and protocols.
    - Integration with agency crisis management procedures.
    - Establishment of methods validation systems.
    - Enhancement of the preparedness of CFSAN laboratories that are part of FERN and/or CDC's Laboratory Response Network.

- Continue the laboratory accreditation program. This program covers all center foods facilities for harmonizing practices in food laboratories. The program better ensures acceptance of FDA laboratory results throughout the world (this will include enhanced data quality systems and support for instrument validation).

- Continue diagnostic tests to produce tools needed for field and import examinations to determine if a product has been tampered with or tainted.

- Maintain the number and capabilities of state health and agriculture laboratories, and current laboratories connected to the electronic Laboratory Exchange Network (eLEXNET). Doing so allows the labs to exchange data on select biological agents (possibly including anthrax, botulinum toxin, brucellosis and other potential infectious diseases) and food pathogens. This is the first Internet-based food safety system that will link state and local organizations with Federal partners to respond more quickly to outbreaks.

- Maintain preventative standards, education campaigns and research to improve food safety and security through rapid tests of detection.

- Continue streamlining techniques to rapidly detect and assess bacterial strains of bioterrorist agents (pathogens/chemicals).

- Continue to assist in developing irradiation techniques and methods to kill anthrax spores in the mail by coordinating efforts with industry, which already uses irradiation to sanitize poultry, ground beef, spices, and medical equipment.

- CFSAN will enhance coordination of food defense and counter-terrorism issues with Federal, state, and local governments and other organizations through full participation in the White House Interagency Food Working Group and sub-groups.

Vulnerability Assessments

FDA built its food security programs on the foundation of food safety infrastructure and developed processes to assess the vulnerability of different categories of food. Through these risk assessments, FDA has ranked the most serious risks of intentional food contamination during its production and distribution. Since September 11, 2001, FDA has conducted many vulnerability assessments for those food products under our regulatory jurisdiction. The agency carried out its own initial analysis of the likelihood of an attack on the food supply taking place, and the severity of its public health impact. The agency's findings were subsequently validated by two respected scientific institutions -- the Institute of Food Technologists and the Battelle Memorial Institute.

FDA continues to refine the tools used to conduct vulnerability assessments – Operational Risk Management (ORM) and CARVER + Shock. Working in partnership with the food industry, vulnerability assessments have been completed for bottled water, fluid dairy products, juice products, and infant formulas. Evaluations involving other foods are in process. Results of these assessments will be used to develop technology interventions and countermeasures, identify research needs, and provide more guidance to the private sector. Industry uses the results of these assessments to better protect their food production processes and products from intentional contamination.

FDA has joined with FBI, USDA and DHS to engage industry and states in conducting these assessments through the Strategic Partnership Program-Agroterrorism (SPPA). This effort focuses on enhancing local law enforcement and food safety officials' lines of communication and improving preparedness and response capabilities based on knowledge of food production vulnerabilities. To date, under the SPAA, FDA has completed two assessments - 1) a yogurt production assessment in Minnesota and 2) a grain export elevator assessment in Louisiana. Assessments are planned for New Jersey, New Hampshire, Florida, Nebraska, Iowa and California in 2006.

Food Defense – Field Activities

- Continue to implement regulations under the Bioterrorism (BT) Act, such as detaining suspect food when the agency has credible evidence or information that it presents a threat to humans or animals.

- Strengthen relationships with State partners through the FERN, a national laboratory network that enables FDA to test thousands of food samples within a matter of days if there is a food terrorism event, or a foodborne illness outbreak.

- Fund FERN state Cooperative Agreements for increased laboratory surge capacity and the National Surveillance Sampling Program to build the capacity to effectively monitor the food supply.

- Conduct training and proficiency testing of FERN laboratories to assure that these laboratories can achieve consistent testing results.

- Expand the use of eLEXNET which collects lab analytical data on chemical, microbiological, and other contaminants and links federal, state, and other laboratories. This data capture and exchange system provides the necessary infrastructure for an early-warning system that identifies potentially hazardous foods and enables health officials to assess risks and analyze trends.

- Develop effective prevention strategies to "shield" the food supply from terrorist threats, including the capacity for rapid, coordinated responses to a food borne terrorist attack.

- Intensify the review of products offered for import into the U.S. for safety and security issues.

- Expand field laboratory and contract activities to evaluate and develop existing and potential laboratory and field test kits for product contaminants.

- Provide training, equipment, facilities, and information technology support to field staff to work on counter terrorism initiatives with a focus on imports.

- *FDA Unified Registration and Listing System (FURLS):* FURLS supports the requirements of the BT Act of 2002 as it relates to Food Facility Registration, Drug Facility Registration and Listing, and Prior Notice of Food Shipments into the U. S. FDA began this effort by identifying opportunities for unification between the FDA Drug Facility Registration and Listing requirements with those of the Food Facility Registration Requirements.

- Continue to develop the Food Registration and Prior Notice systems that became operational in the first quarter of FY 2004.

- Collaborate with Customs and Border Patrol. This will include:
    - Monitoring the importation of regulated products and follow-up on the status of products refused entry.
    - Evaluating the accuracy of information import filers provide to the FDA automated entry review system regarding regulated products offered for entry into domestic commerce.

- Continuing to conduct food import exams of food products offered for import into the country.

- Expand import surveillance at international mail facilities and courier hubs.

Food Safety

- *Bovine Spongiform Encephalopathy (BSE):* BSE is a deadly chronic, degenerative disorder affecting the central nervous system. BSE and Chronic Wasting Disease (CWD) both belong to a group of fatal progressive degenerative neurological diseases, including those that affect humans such as Creutzfeldt-Jakob disease (CJD). Regulated products that can contain these substances are ruminant protein-containing cosmetic products that are packaged and ready for sale, and bovine-derived materials intended for human consumption as either finished dietary supplement products, or for use as ingredients in dietary supplements. Base funding will enable FDA to:

    - Continue to identify, at a reduced level of effort, food and cosmetic products containing brain, spinal cord, and other specific risk materials, including the origin of the animal and country, and infectious agents in foods.
    - Continue to conduct research on decontamination or deactivation procedures.

- *Natural Disaster Food Safety Response:* Natural disasters, such as Hurricane Katrina, pose many food safety related issues. FDA plays a critical role in food safety response and recovery efforts. Base funding will enable FDA to continue to:

    - Provide assistance to state and local governments to address food safety issues.
    - Provide information to consumers to aid in evaluation of stored food and water they have in their homes in light of power outages and contaminated water supplies.
    - Continue to ensure food imported and/or donated food from other countries as part of relief efforts is safe and does not pose unreasonable risks to human safety.
    - Provide assistance in decontamination efforts for food processing and food service facilities during clean up and recovery.
    - Provide assistance in adapting good agricultural practices for foods grown in disaster areas.

- *Chemical Contaminants, Pesticides and other Hazards*
    - Pesticides Monitoring: Continue, at a reduced level, to collect and analyze food samples for pesticide residues not only to ensure that the U.S. food supply is safe, but also to reduce dietary exposure.

- FDA's Dioxin Strategy: FDA will continue, at a reduced level, implementation of its dioxin strategy including monitoring, methods development, and identification of opportunities to reduce exposure.

- Perchlorate Analytical Method: FDA developed an accurate and sensitive method to determine the level of perchlorate in selected fruits and vegetables and also in bottled water and milk using ion chromatography-tandem mass spectrometry. FDA will continue, at a reduced level, to use of this method for the detection of perchlorate.

- *International Codex-Related Activities:* **C**ontinue, at a reduced level, its public health involvement in the work of the Codex Alimentarius Commission (Codex). FDA's scientific expertise has been crucial to the development of critical scientifically sound international food safety standards that are used by countries importing food into the United States, by US companies exporting to other countries, and are also used by the World Trade Organization to resolve trade disputes.

- *Food CGMP Modernization:* Complete the Agency's review of the draft report on Current Good Manufacturing Practices (CGMP) modernization and develop a proposed rulemaking in relation to food CGMP modernization. FDA last revised the CGMP regulation for food in 1986. Since 1986, there has been a significant change in both the food industry and in our understanding of foodborne disease. Among the many changes that have taken place, ready-to-eat foods and fresh produce constitute a larger share of the American diet than was the case 18 years ago. These foods are commonly consumed without further cooking by the consumer and have been implicated in foodborne disease outbreaks.

- *Listeria and Methylmercury:* Continue to provide education and outreach activities to target audiences in the effort to train health educators to teach food safety to pregnant women and women who may become pregnant about the risks of methylmercury in seafood and *Listeria monocytogenes* in refrigerated food.

- *Seafood Safety:* Continue to work to encourage the post-harvest treatment of Gulf Coast oysters and to monitor progress toward the ISSC illness reduction goals. FDA will not be able to continue to provide funds to the ISSC to promote educational and research activities related to shellfish safety.

- *Seafood and Juice Hazard Analysis and Critical Control Points (HACCP) Programs:* Continue to evaluate the programs' performance, with an emphasis on identifying factors that inhibit improvements in compliance rates, in order to assess whether the program is accomplishing its objectives and to identify where and how the program needs to be re-directed. The HACCP system focuses on identifying and preventing hazards that could cause food borne illnesses rather than relying on spot-checks of manufacturing processes of finished products to ensure safety.

- *Produce Safety:* Foodborne illness outbreaks attributed to fresh produce have increased in the last ten years. There are a number of possible explanations, including (1) an increase in the consumption of fresh produce, (2) improved detection of outbreaks and increased

awareness of fresh produce as a vehicle for foodborne illness, (3) increased complexity and reach of distribution systems, and (4) increased numbers of consumers at high risk of foodborne disease (e.g., the elderly and persons with compromised immune systems). FDA will continue to devote base resources to its produce safety programs in order to contribute to the reduction in the number of illnesses associated with these products.

Egg Safety

CDC estimates that there are approximately 118,000 illnesses per year caused by consumption of Salmonella Enteritidis (SE) in contaminated eggs. These illnesses can be very serious, especially to the very young, the elderly, and persons with weakened immune systems. If an individual eats an egg that is contaminated with SE and that has not been fully cooked, he or she may suffer mild to severe gastrointestinal illness, short term or chronic arthritis, or death.

Working with state egg quality assurance officials, industry and consumer groups, FDA has published a proposed rule to require egg safety measures to prevent the contamination of shell eggs with SE during egg production. FDA expects to publish a final rule in 2006. Implementation of the provisions in the final rule will reduce SE prevalence in eggs.

It is estimated that implementation of the final rule will reduce the number of SE illnesses by 33,500 and be a major factor in realizing the public health goals of a 50% reduction in all salmonella illnesses and a 50% reduction in SE outbreaks by 2010. FDA will continue to devote base resources to its egg safety program in order to contribute to the reduction in the number of these illnesses.

- *Dietary Supplements*: The dietary supplement industry is one of the world's fastest growing with over 1,500 establishments claiming to manufacture dietary supplements and sales of $17 billion in 2000. Between 1994 and 2000, consumer spending on dietary supplements nearly doubled, with over 158 million consumers, and sales growing more than 10 percent per year. Nearly 20 million consumers use dietary supplements in conjunction with prescription products. Although this rapid growth in a time of constrained resources represent a significant challenge, FDA has published a dietary supplement strategy that sets clear program goals.

- *CGMPs:* Continue towards finalization of this activity. The Dietary Supplement Health and Education Act (DSHEA) provided FDA with express statutory authority to prescribe CGMP requirements for dietary supplements. On March 13, 2003, FDA published proposed CGMPs for manufacturing, packing, labeling or holding dietary supplements. The proposed CGMP requirements are intended to ensure that manufacturing practices will prevent the production of adulterated dietary supplements. The proposed CGMP rule includes provisions on the manufacturing, packaging, labeling, testing, quality control, releasing for distribution and holding of dietary supplements. Public comments have been reviewed and a draft final rule has been drafted and is currently being reviewed by OMB for clearance.

- *Ephedra:* Dietary supplements containing ephedrine alkaloids are adulterated because they present an unreasonable risk of illness or injury and may not be sold in the U.S. Base resources will continue to be devoted to:

- Taking strong enforcement action against continuing efforts to illegally sell these products in the U.S. or illegally export existing stock.
- Evaluating safety concerns related to dietary supplements containing other sympathomimetics, such as Citrus aurantium.
- Working with FTC, DEA, and other partners to protect the American public.

- *New Dietary Ingredients*: Continue to respond to premarket notifications for new dietary ingredients within the statutory time frame of 75 days.

- *Food Allergens:* Continue to provide more information on food labels so that allergic consumers can make safe food choices. On August 2, 2004, President Bush signed into law the "Food Allergen Labeling and Consumer Protection Act" (Public Law 108-282). The law is consistent with FDA's initiatives to empower consumers to make healthy dietary choices. It is also consistent with the Healthy People 2010 goal of reducing the number of deaths due to anaphylaxis caused by food allergens. FALCPA amends the Federal Food, Drug, and Cosmetic Act to require that the eight "major food allergens" be declared on the labels of food products labeled on or after January 1, 2006. The eight major allergens identified by FALCPA are milk, egg, fish, crustacean shellfish, tree nuts, wheat, peanuts, and soybeans. These foods account for 90% of food allergic reactions.

- *Cosmetics: C*ontinue to devote base resources, at a significantly reduced level, to ensure the safety of cosmetics. The FD&C Act prohibits the marketing of adulterated or misbranded cosmetics in interstate commerce. Violations of the Act involving product composition--whether they result from ingredients, contaminants, processing, packaging, or shipping and handling--cause cosmetics to be adulterated and subject to regulatory action.

Foods Field Activities

Import Entry Evaluations, Investigations, and Laboratory Analyses

Since the emergence of the "global marketplace" imported foods have grown increasingly important to the U.S. food supply. At the current rate of increase, FDA estimates that by FY 2007 the number of imported food lines will have nearly quadrupled since 1999. This rapid growth combined with the security concerns raised by terrorism and counterfeiting incidents has increased the need to electronically and physically assess the status of imported products. FDA electronically screens imports through OASIS, which is an automated system for processing and making admissibility determinations for FDA regulated products that are offered for import. Filers transmit information electronically which is then checked against automated screening criteria set by the Division of Import Operations & Policy. These criteria assign either "FDA Review" or "May Proceed" status to an entry. If a product is assigned FDA review status, then a field exam, which is a physical examination of the product to determine whether the product is in compliance with FDA requirements, may be performed. FDA's electronic screening of imports will be enhanced by the completion of the Mission Accomplishment and Regulatory Compliance System (MARCS). Field activities include the following efforts.

- Review more than 19 million import lines for admissibility into domestic commerce by the end of FY 2007.
- Focus analysis of OASIS import line data to expand use of information on manufacturer, supplier, source country, and past violations to make enhanced admissibility decisions.
- Continue to perform laboratory analysis on products offered for import into the United States.
- Continue to conduct inspections of foreign establishments as part of the Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Devices and Radiological Health programs.
- Perform periodic filer evaluations in which the import data submitted electronically to OASIS is compared against the paper documents accompanying the imported product to ensure that the data being provided to FDA is accurate.

Domestic Inspections and Laboratory Analyses

Inspections and surveillance are the primary means of assuring the safety of marketed products. Consumers rely on the FDA to prevent dangerous and unreliable products from entering commerce. Field efforts include the following activities:

- Identify the food source and contaminant of food borne illness outbreaks ranging from chemical and microbiological to physical hazards.
- Develop laboratory analytical methods to permit the analyses of products for chemical and microbiological hazards.
- Continue to analyze food samples for pesticides and environmental contaminants at a reduced rate.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

CFSAN Adverse Events Reporting System (CAERS)

Prior to June 2003, several systems existed to monitor adverse events: the Adverse Reaction Monitoring System for food and color additives, the Cosmetics Adverse Reaction Monitoring Database for cosmetic products and the Special Nutritional Adverse Event Monitoring System (SN/AEMS) for dietary supplements, infant formulas, and medical foods. These systems are now combined into the CAERS database, with which CFSAN staff now track, evaluate, and monitor adverse events and consumer complaints received about regulated food products. CFSAN will continue these activities, but at a reduced rate in FY 2007. CAERS is a useful tool for identifying new and emerging food and cosmetic public health problems.

Besides mining food and cosmetic adverse event data for patterns, trends and signals, CAERS provides a database search engine capable of responding to a large variety of stakeholder inquiries, and is capable of generating yearly reports that describe the voluntary food and cosmetic adverse event reports received from consumers.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Bioterrorism Rule Outreach

- Conducted nine domestic meetings to discuss the final Recordkeeping regulation implementing Section 306 (Maintenance and inspection of Records) of the Bioterrorism Act of 2002. The final rule was published in the *Federal Register* on December 9, 2004. The purpose of these meetings was to provide information on the rule to the public and to provide the public an opportunity to ask questions of clarification.

Egg Safety – In-lid Labeling

- Published in the *Federal Register* a proposed rule entitled: *"Food Labeling: Safe Handling Statements: Labeling of Shell Eggs."* This notice proposes to amend the Agency's food labeling regulations to permit the egg industry to place the safe handling statement for shell eggs on the inside lid of egg cartons if the statement "Keep Refrigerated" appears on the principal display panel or information panel.

2005 Food Code

- Completed the 2005 FDA Retail Food Code, a model that assists food control jurisdictions at all levels of government by providing them with a scientifically sound technical and legal basis for regulating the retail and food service segment of the industry (restaurants and grocery stores and institutions such as nursing homes). Local, state, tribal, and federal regulators use the *FDA Food Code* as a model to develop or update their own food safety rules and to be consistent with national food regulatory policy.

Safe Handling of Produce

- Launched a consumer education campaign on the safe handling of produce. A new brochure has been completed and circulated to specific risk groups as well a general distribution.

Listeria Education Program

- Carried out a multicultural food safety initiative educational program for pregnant women through Hispanic media and community-based public health specialists in high density Spanish-speaking areas on the risk of *Listeria monocytogenes* in cheese.

Establish FDA's Obesity Working Group (OWG 2)

- Established the Obesity Working Group 2 to carryout the short-term and long-term recommendations for dealing with the Nation's obesity problem set forth by OWG 1 in FY 2004. A detailed matrix of the status of the OWG 1 Report recommendations has been maintained and updated.

Consumer Knowledge of *Trans* fats, Saturated fats and Omega-3 fats

- Collected, compiled and analyzed baseline data begun in FY 2004 for these fats and acids. The 2004 Health and Diet Survey Supplement surveyed consumer awareness of fatty acids (saturated, *trans*, and omega-3) and their knowledge of the link between fatty acid consumption and risk for coronary heart disease.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Salmonella in Sprouts

- Evaluated a testing protocol for the recovery of *Salmonella* in sprout seeds. This work has now been completed and this improvement has been recommended for use as a pre-enrichment method to use with a *Salmonella* culture method to isolate *Salmonella* from alfalfa seed.

Dioxin Analysis Results/Exposure Estimates

- Published on the CFSAN Web site "FDA Analysis of Food and Feed for Dioxin-like Compounds (DLC)." This analysis was completed as part of specific goals for FDA's Dioxin Monitoring Program to obtain baseline data for DLC levels in food and animal feed ingredients susceptible to DLC contamination and to determine opportunities for DLC reduction by identifying contamination sources that can be eliminated or significantly reduced.

Peanut Protein Test Kits

- Initiated an Association of Official Analytical Chemist (AOAC) interlab study for immunochemical peanut protein test kits. CFSAN is working closely with AOAC International to evaluate validation study test results conducted by the European Standards Organization (CEN) test kits for the detection of peanuts in food products.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Food Facility Registration Final Rule

- Published in the *Federal Register* a final rule entitled: Registration of Food Facilities Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002.

Establishment and Maintenance of Records Final Rule

- Published in the *Federal Register* a final regulation entitled: "Establishment and Maintenance of Records Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002." The final regulation requires the establishment and maintenance of records by persons who manufacture, process, pack, transport, distribute, receive, hold, or import food in the United States.

Establishment and Maintenance of Records Small Entity Compliance Guide

- Published a Small Entity Compliance Guide as a booklet entitled: "*What You Need to Know About Establishment and Maintenance of Records.*" This booklet informs domestic persons in the U.S. who manufacture, process, pack, transport, distribute, receive, hold or import food for humans or animals, and foreign persons who transport food in the U.S., about a final regulation that establishes requirements regarding the establishment and maintenance of records.

Administrative Detention Guidance to Industry

- Published guidance entitled: "*What You Need to Know About Administrative Detention of Foods.*" This guidance informs food manufacturers, processors, packers, transporters, importers and exporters about expedited procedures for perishable foods, as well as procedures describing how FDA will detain an article of food and the process for appealing a detention order.

Furan Action Plan

- Issued an Action Plan for Furan in Food. The action plan outlines FDA's accomplishments, goals, and planned activities on the finding of furan in food, and it will guide FDA's activities on the issue of furan over the next several years. Some animal data suggest that high levels of furan exposure might have a carginogenic effect in humans, but its true effect on humans at low levels is not known.

Furan in Food

- Published on the CFSAN Web site expanded exploratory data on furan in food. FDA is now posting furan data that were collected through November 18, 2004. Data are presented in chronological order with data collected between June 10, 2004 and November 18, 2004. FDA is presenting these data to inform the public of FDA's progress and to help stimulate research into the formation of furan in food. The results reflect furan levels detected in samples of individual food products.

NACMCF Report on Ready-to-Eat Foods

- Published a report advising on the necessary scientific parameters for establishing safety-based use-by-date labels for refrigerated ready-to-eat foods to help reduce the incidence of foodborne listeriosis. A copy of the Report can be viewed at: http://www.fsis/usda.gov/ophs/nacmcf/2004/NACMCF. House Report 108-193 of the Agriculture Rural Development, Food and Drug Administration and Related Agencies 2005 Appropriations Language directed FDA to provide the Appropriations Committee a copy of the report by the National Advisory Committee on Microbiological Criteria for Foods (NACMCF).

Acrylamide in Food

- Published on the CFSAN Website expanded exploratory data on acrylamide in food. This is part of FDA's continued efforts to investigate how acrylamide is formed in food, seek to identify ways to reduce acrylamide levels, and study the human health risk of consuming acrylamide in food. Acrylamide can cause cancer in laboratory animals at high doses, but it is not clear if it causes cancer at much lower levels in food.

Seafood HACCP

- Completed an evaluation of program performance through the sixth year, with an emphasis on identifying factors that may be inhibiting improvements in compliance rates. Based on FDA's historical compliance classification system, approximately 91% of firms were in compliance through the sixth year of the Seafood HACCP Program. This is a significant increase over the 85% compliance rate of 2001.

Foods cGMPs

- Published a report entitled: "Food cGMP Modernization – A Focus On Food Safety." The report summarizes the comments, both written and oral, that were offered to the Agency in response to its *Federal Register* notices and during three public meetings. The report addresses the major opportunities for modernization of the food cGMPs as suggested by the respondents.

Guidance on Enforcement Discretion for Ozonation of Juice

- Issued guidance for industry entitled "Recommendations to Processors of Apple Juice or Cider on the Use of Ozone for Pathogen Reduction Purposes." This guidance addresses the use of ozone to treat apple juice to meet the pathogen reduction requirements of 21 CFR Part 120 "Hazard Analysis and Critical Control Point (HACCP) Systems" (the juice HACCP regulation) and 21 CFR 101.17(g) "Juices that have not been specifically processed to prevent, reduce, or eliminate the presence of pathogens" (the juice labeling regulation). The guidance notes that FDA is currently unaware of any validated treatments for juice using ozone.

Final Rule for Arsenic in Bottled Water

- Published in the *Federal Register* a final regulation for arsenic levels in bottled water. The final regulation requires manufacturers to monitor their finished bottled water products for arsenic at least once each year and to monitor their source water for arsenic as often as necessary, but at least once every year.

Final Generic "Channels of Trade" Guidance

- Published in the *Federal Register* guidance for industry entitled "Channels of Trade Policy for Commodities with Residues of Pesticide Chemicals for which Tolerances have been Revoked, Suspended, or Modified by the Environmental Protection Agency Pursuant to Dietary Risk Considerations." This guidance presents FDA's general policy for implementing the channels of trade provision in the Federal Food, Drug, and Cosmetic Act, as amended by the Food Quality Protection Act of 1996, for food containing residues of pesticide chemicals, for which tolerances have been revoked, suspended, or modified pursuant to dietary risk considerations.

BSE

- Published several amendments to a July 2004, interim final rule on bovine spongiform encephalopathy (BSE) entitled "Use of Materials Derived From Cattle in Human Food and Cosmetics

- Amended the interim final rule to allow use of the small intestine in human food and cosmetics, provided that the distal ileum has been removed. The amendments also clarify that milk and milk products, hides and hide-derived products, and tallow derivatives are not prohibited for use in human food and cosmetics.

"Healthy"

- Published in the *Federal Register* an amendment to the regulations concerning the maximum sodium levels permitted for foods that bear the implied nutrient content claim ``healthy." The Agency is retaining the currently effective, less restrictive, ``first-tier" sodium level requirements for all food categories, including individual foods (480 milligrams (mg)) and meals and main dishes (600 mg), and is dropping the ``second-tier" (more restrictive) sodium level requirements for all food categories.
- Determined that requiring the more restrictive sodium levels would likely inhibit the development of new ``healthy" food products and risk substantially eliminating existing ``healthy" products from the marketplace. After reviewing the comments and evaluating the data from various sources, FDA has become convinced that retaining the higher first-tier sodium level requirements for all food products bearing the term ``healthy" will encourage the manufacture of a greater number of products that are consistent with dietary guidelines for a variety of nutrients.
- Revised the regulatory text of the ``healthy" regulation to clarify the scope and meaning of the regulation and to reformat the nutrient content requirements for ``healthy" into a more readable set of tables, consistent with the Presidential Memorandum instructing that regulations be written in plain language.

Dietary Supplements: Strategy for the Further Implementation and Enforcement of the Dietary Supplement Health and Education Act of 1994 (DSHEA)

- Published in the *Federal Register* (69 FR 64957) the strategy for the further implementation of DSHEA. The strategy sets forth a series of specific, integrated research and regulatory measures, including guidance, regulations, and science-based compliance and enforcement mechanisms. By implementing these measures, CFSAN hopes to improve the transparency, predictability, and consistency of both its scientific evaluations of dietary supplement products and ingredient safety, and of its regulatory actions to protect consumers against unsafe dietary supplements and dietary supplements making unauthorized, false or misleading claims. CFSAN expects that this improved transparency will help engage stakeholders in developing further measures to implement DSHEA.

Dietary Supplement Labeling Guide

- Published on the CFSAN Web site guidance for industry entitled: "A Dietary Supplement Labeling Guide." This guide was prepared to help assure that dietary supplements sold in the U.S. are properly labeled. This guide applies to dietary supplements produced domestically as well as those produced in foreign countries.

Alpha Hydroxy Acids Guidance

- Published in the *Federal Register* a guidance document entitled: "Guidance for Industry: Labeling for Topically Applied Cosmetic Products Containing Alpha Hydroxy Acids as Ingredients." This guidance recommends content for a labeling statement for cosmetic products containing alpha hydroxy acids (AHAs) as ingredients.

Report to Congress – Perchlorate Survey

- Completed report and submitted to Congress. Senate Report 108-340 of the Agriculture Rural Development, Food and Drug Administration and Related Agencies 2005 Appropriations Language directed FDA to report on the findings of the CFSAN perchlorate surveys of food and bottled water.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

FALCPA Implementation

- Held approximately 20 meetings about FALCPA with groups representing consumers, state and local regulators, and various food industries.

Field Program Selected Accomplishments

The FDA promotes and protects the public health by ensuring that the food supply is safe, sanitary, wholesome and honestly and properly labeled; and, that cosmetic products are safe and properly labeled. The Field supports the Foods program through a variety of activities. Examples of accomplishments and activities appear below organized by strategic goal.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Food Emergency Response Network (FERN)

- Currently, there are 123 laboratories representing 50 States and Puerto Rico that have satisfactorily completed the FERN Laboratory Qualification Checklist.
- Awarded eight cooperative agreements to state laboratories to support additional capacity for food analysis related to chemical terrorism and to enhance state, local, and tribal food safety and security efforts
- Participated in two FDA surveillance assignments, the Food Security Surveillance Assignment and the Interstate Travel Program Water Assignment.

- Issued six proficiency test samples including one joint proficiency test sample with CDC/LRN for microbiology laboratory testing of *Bacillus anthracis*; three chemistry proficiency test samples; and, two radiological proficiency test samples.
- Conducted five FERN training courses.

Food Security Surveillance Assignment

- Collaboration with forty-four states and the Commonwealth of Puerto Rico conducted a Food Security Surveillance Assignment (FSSA) for six weeks. The primary goals of the FSSA were to deter intentional contamination of the food supply through heightened and targeted preventive activities at various points in the food distribution chain and to exercise the systems and networks for responding to a food related emergency during a period of increased food security risk.

Mobile Laboratories

- Took possession of two completed mobile laboratories in April 2005: one for microbiological sample analysis; and, the second for chemical sample analysis.
- Trained 30 FDA laboratory personnel have been in the mobile laboratory platform.
- Ran a test deployment of the mobile laboratories at NCTR to demonstrate that analysts were able to set up the laboratories on a location site and run sample analyses using only the mobile laboratory facilities.

State Contracts, Grants and Partnership Programs

- Awarded contracts with state and local governments to perform food safety, domestic seafood HACCP, and juice HACCP inspections. ORA also implemented electronic State Access to FACTS (eSAF) in 15 state food programs and conducted the associated training for FDA and state personnel. Audits were completed of all state food inspectors working under contract. Pilot tested an audit program for contracts with New York State.
- Awarded Cooperative Agreement grants for Food Safety projects in 34 states; and, awarded new grants for Health Fraud prevention projects in 11states. ORA also provided Conference Grants to six National Conferences, i.e., the Association of Food and Drug Officials to provide for State and local agency personnel to attend national meetings.
- Maintained and continued to develop new partnerships (e.g., seafood HACCP inspections) that have contributed to the exchange of inspection and sampling data and have facilitated the receipt of training and distribution of equipment to the states.

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Ephedra-Containing Dietary Supplements

- Identified more than thirty internet and retail firms selling banned ephedra products
- Conducted investigations to identify physical locations and other information for regulatory action to uphold the ban on ephedra containing products.

Foods
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actual	FY 2006 Estimate	FY 2007 Estimate
FOOD & COLOR ADDITIVE PETITIONS*			
Petitions Filed	7	12	25**
Petitions Reviewed **	14	12	10**

* Beginning in FY 2007, this program will include petitions for food contact substances. We expect the number of petitions received to increase in subsequent years to at least 60-90 incoming petitions, because of the elimination of the food contact substance notification program..
**Number reviewed includes those approved, withdrawn, or placed in abeyance because of deficiencies during the FY.

PREMARKET NOTIFICATIONS FOR FOOD CONTACT SUBSTANCES			
Notifications Received	88	110	0
Notifications Reviewed *	73	110**	0

* Number reviewed includes those that became effective or were withdrawn.
** FDAMA established a notification program for food additives that are food contact substances (e.g. packaging materials). The number of "notifications reviewed" appears to be the same, in some instances, because under the provisions of this notification, a food contact substance may be marketed 120 days after notification unless the agency objects. Due to strategic re-deployment, beginning in FY 2007, this program will be eliminated and will result in the statutorily mandated safety review for food contact substances having to be submitted through the rulemaking process for food and color additives.

INFANT FORMULA NOTIFICATIONS			
Notifications Received *	21	30	35
Notifications Reviewed **	21	30	35
FDA Review Time	90 Days	90 Days	90 Days

* Number of submissions received in current FY include some received late in the FY.
** Number of submissions reviewed includes some submissions that were received in the previous FY.

NEW DIETARY INGREDIENT NOTIFICATIONS ***			
Submissions Received [a]	66	75	83
Submissions Reviewed [b]	68	75	83
FDA Review Time	75 Days	75 Days	75 Days

*** A single notification may address one or more new dietary ingredients. For example, FDA as received at least 15 notifications that pertain to 2 up to 16 new dietary ingredients in a single notification
[a] Number of submissions received in current FY includes some received late in the FY that will be completed in the next FY when the due date occurs.
[b] Number of submissions reviewed in the current FY includes some submissions that were received in the previous FY when the due date occurred in the current FY.

FIELD FOODS PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	**FY 2005 Actual**	**FY2006 Estimate**	**FY2007 Estimate**
Domestic Food Safety Program Inspections	4,573	3,400	3,400
Imported and Domestic Cheese Program Inspections	477	400	400
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	481	400	400
Domestic Fish & Fishery Products (HACCP) Inspections	2,467	2,480	2,480
Import (Seafood Program Including HACCP) Inspections	500	500	500
Juice HACCP Inspection Program (HACCP)	490	375	375
Interstate Travel Sanitation (ITS) Inspections	1,510	1,700	1,700
State Contract Food Safety (Non HACCP) Inspections	6,992	8,130	8,130
State Contract Domestic Seafood HACCP Inspections	953	1,135	1,135
State Contract Juice HAACP	47	35	35
State Partnership Inspections	1,284	1,300	1,300
Total Above FDA and State Contract Inspections	**19,774**	**19,855**	**19,855**
Total Domestic Reinspections (Non-add)	**523**	**523**	**523**
State Contract and Grant Foods Funding	$6,825,000	$7,100,000	$6,940,000
Number of FERN State Laboratories	8	10	16
Annual FERN State Cooperative Agreements/Operations	$12,270,000	$7,037,000	$12,236,000
Total State & Annual FERN Funding	**$19,095,000**	**$14,137,000**	**$19,176,000**
Domestic Field Exams/Tests	3,528	5,000	5,000
Domestic Laboratory Samples Analyzed	15,390	11,425	9,425
All Foreign Inspections	129	200	100
Total Foreign Reinspections (Non-add)	**15**	**15**	**15**
Import Field Exams/Tests	84,997	75,000	71,000
Import Laboratory Samples Analyzed	25,549	31,600	29,600
Import Physical Exam Subtotal	110,546	106,600	100,600
Import Line Decisions	8,672,168	10,059,715	11,669,269
Percent of Import Lines Physically Examined	1.27%	1.06%	0.86%
Prior Notice Security Import Reviews (Bioterrorism Act mandate)	86,187	45,000	60,000

HUMAN DRUGS

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$482,134,000**	**$517,557,000**	**$534,961,000**	**+$17,404,000**
Center	*396,036,000,2,*	*$431,705,000*	*$448,961,000*	**+$17,256,000**
FTE	*220*	*2,360*	*2,382*	**+22**
Field	*$86,098,000*	*$85,852,000*	*$86,000,000*	**+$148,000**
FTE	*698*	*664*	*659*	**(5)**
Program Level FTE	**2,918**	**3,024**	**3,041**	**17**
Budget Authority	**$291,484,000**	**$297,716,000**	**$305,003,000**	**+$7,287,000**
Center	*$210,481,000*	*$217,797,000*	*$225,209,000*	*$7,412,000*
Field	*$81,003,000*	*$79,919,000*	*$79,794,000*	*-$125,000*
Critical Path		*$750,000*	*$6,690,000*	*+$5,940,000*
Drug Safety	*$26,900,000*	*$36,531,000*	*$40,095,000*	*+$3,564,000*
Cost of Living			*$4,874,000*	*+4,874,000*
Strategic Redeployment			*($7,091,000)*	*($7,091,000)*
FTE			*(20)*	*(20)*
Budget Authority FTE	**1,837**	**1,914**	**1,906**	**(8)**
User Fees	**$190,650,000**	**$219,841,000**	**$229,958,000**	**+$10,117,000**
Center PDUFA	*$185,555,000*	*$213,908,000*	*$223,752,000*	*+$9,844,000*
Field PDUFA	*$5,095,000*	*$5,933,000*	*$6,206,000*	*+$273,000*
User Fee FTE	**1,081**	**1,110**	**1,135**	**+25**

[1/] *Includes a one percent rescission.*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$403,848,000	$274,073,000	$129,775,000	2,696
2004 Actual	$396,491,000	$229,372,000	$167,119,000	2,190
2005 Actual	$482,134,000	$291,484,000	$190,650,000	2,918
2006 Enacted	$517,557,000	$297,716,000	$219,841,000	3,024
2007 Estimate	$534,961,000	$305,003,000	$229,958,000	3,041

Statement Of Budget Request

The Human Drugs Program is requesting $534,961,000 in program level resources for accomplishing its mission activities including:

- Ensuring that prescription, generic, and Over-the-Counter (OTC) drug products are adequately available to the public and are safe and effective.

- Monitoring the use of marketed drug products for unexpected health risks.
- Monitoring and enforcing the quality of marketed drug products.

Program Description

The Human Drugs Program is responsible for ensuring that America's supply of brand name, over the counter, and generic drugs is adequately available, safe and effective, and of the highest quality. The process for approving drug products begins with the companies who must first test their products. CDER monitors their clinical research to ensure that people who volunteer for studies are protected and that the quality and integrity of scientific data are maintained. CDER assembles a team of physicians, statisticians, chemists, pharmacologists, and other scientists to review the company's data and proposed use of the drug. If the drug is deemed effective and if health benefits outweigh its risks, the drug is approved for sale. CDER does not actually test the drug when the Center reviews the company's data. By setting clear standards for the evidence FDA needs to approve a drug, the Agency helps medical researchers bring new drugs to American consumers more rapidly.

Once a drug is approved for sale in the United States, FDA continues to monitor the use of marketed drugs for unexpected health risks. If new, unanticipated risks are detected after approval, steps are taken to inform the public and change how a drug is used or, if necessary, even remove a drug from the market. CDER also monitors product manufacturing changes to make sure that changes to the way drug products are made do not adversely affect the safety or efficacy of the medicine. CDER evaluates 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. CDER tries to make sure that an adequate supply of drugs is always available.

In addition to setting standards for safety and effectiveness testing, CDER also sets standards for drug quality and manufacturing processes. FDA works closely with manufacturers to see where streamlining can cut red tape without compromising drug quality. As the pharmaceutical industry has become increasingly global, CDER is 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 do and help ensure drug quality for consumers at home and abroad.

Accurate and complete information are vital to the safe use of drugs. Drug companies have historically promoted their products directly to physicians. More and more frequently now, they are advertising directly to consumers. While the FTC regulates advertising of over-the-counter drugs, CDER oversees the advertising of prescription drugs.

FDA conducts and collaborates on focused laboratory research and testing. Research maintains and strengthens the scientific base of CDER's regulatory policy-making and decision-making. Most recently, and consistent with the Agency's Critical Path Initiative, FDA is focusing on new ways to review drug quality, safety, and performance; evaluate improved technologies; validate new approaches to drug development and review; and develop regulatory standards and consistency.

The field component, the Office of Regulatory Affairs (ORA), supports the Human Drugs Program by conducting risk-based domestic and foreign premarket and postmarket inspections of drug manufacturers to assess their compliance with Good Manufacturing Practices (GMPs). Besides overseeing regulated products on a surveillance or "for cause" basis, ORA staff also respond to emergencies and investigate incidents of product tampering and terrorist events or natural disasters. To complement the regular field force, the Office of Criminal Investigations investigates instances of criminal activity in FDA regulated industries.

Performance Analysis

During the latest performance period (FY 2005), the Human Drugs program successfully met seven of its center performance measures; expects to meet the other three when the data is reported; and met its one field performance goal. CDER expects to successfully achieve the target for its Generic Drugs performance goal when data becomes available. For more information about these performance goals and results, please see the Performance Detail section.

Performance Highlight:

FY 2007 Goal Target	FY 2004 Results	Context
Decrease the average FDA time to approval or tentative approval for the fastest 25% of original generic drugs applications by 0.5 months.	FDA exceeded its goal for FY 2004 by acting on 91 percent of 563 original applications.	Generic drugs are much appreciated for their cost-effectiveness. 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. Prior to approval, generic drug sponsors are required to demonstrate bioequivalence to the innovator drug product by showing that the active ingredient in their product is absorbed at a rate and extent similar to the innovator counterpart. 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.

Program Resource Changes

Budget Authority:

Drug Safety: + $3,564,000 and +6 FTE

FDA requests an increase of $3,960,000 to improve drug safety through modernizing and expanding the existing drug safety system. To improve drug safety, we will create an enhanced Adverse Events Reporting System and collaborate with the Centers for Medicare and Medicaid Services. These activities will enable FDA to more efficiently and effectively track adverse events, analyze and interpret findings, take appropriate regulatory action and transmit critical drug safety information to health care practitioners and consumers. This initiative will contribute to the Secretary's goal to reduce the number of preventable injuries and deaths among Americans. The Human Drugs Program component of this request is $3,564,000 and 6 FTE.

Critical Path to Personalized Medicine: +$5,940,000 and +6 FTE (CDER)

Under the FDA Modernization Act (P.L. 105-115), Congress expanded FDA's mission to include the promotion of public health through review of clinical research and collaborations with partners in government, academia, and industry. Coupled with these regulatory changes, the funding of basic biomedical research has doubled in the last few years. Yet, the number of applications submitted to FDA for review has decreased.

Because the agency sees product development failures industry-wide, FDA, consistent with its public health mission, is in a unique position to identify priority hurdles to medical product development and the means to overcome them. By facilitating communication between industry and the agency and providing guidance for modernizing the medical product development process (the Critical Path), FDA can overcome the bottlenecks to drug development and ensure that more people have access to the products they need.

FDA can also assist medical product development by advancing new techniques that will identify product characteristics that make a drug, biological product or device safe and effective for particular individuals. This will allow Americans to benefit from an era of personalized medicine.

The amount requested for this initiative is $5,940,000 and 6 FTE.

Cost of Living: +$4,874,000

FDA's request for inflationary pay costs is essential to accomplishing our public health mission. Payroll costs account for more than sixty-percent of the FDA budget, and the Agency is not able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Human Drugs portion of this increase is $4,874,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Human Drugs Reductions: -$7,091,000 and -20 FTE

To fund FY 2007 priority initiatives such as Drug Safety and the Critical Path to Personalized Medicine, FDA re-deployed resources from base programs. To accomplish this strategic redeployment and fund new, high priority initiatives, Human Drugs reductions include: generic drugs research contracts, animal care contract services, research/lab scientists, laboratory upkeep, and communications, staff for FOI requests, management services, and information processing modernization for the generic drugs program.

User Fee:

Prescription Drug User Fee Act: +$10,117,000 and 25 FTE
PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These fees expand the resources available for the process of reviewing human drug applications. Fee resources pay for the salaries of scientists and other professionals who review drug applications, and for information management, space costs, acquisition of fixtures, furniture, equipment and other materials necessary to conduct drug product reviews and to ensure that safe and effective drug products reach the American public more quickly.

In 2002, the Bioterrorism Act included PDUFA III, which reauthorized FDA to collect user fees to enhance the review process of new human drugs and biological products. PDUFA III also reauthorized fees for applications, establishments and approved products. The reauthorization directs FDA to strengthen and improve the review and monitoring of drug safety, consider greater interaction with 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. The increases will contribute to meeting these directives.

In FY 2007, FDA will work with Congress on the reauthorization of the Prescription Drug User Fee Act. This increase of $10,117,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Proposed Fees (Reclassified as Mandatory - Non-Add)

Reinspection User Fee (Mandatory): $2,009,000 and 16 FTE (Non-Add)
The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an amount sufficient to fully fund reinspections. The Human Drugs program component of this user fee is $2,009,000 and 16 FTE.

Justification of Base

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

The practical size of pre-marketing clinical trials means that CDER cannot learn everything about the safety of a drug before approval. Therefore, a degree of uncertainty always exists about the risks of drugs. This uncertainty requires CDER's continued vigilance to collect and assess data during the post-marketing life of a drug. Once a drug is approved for sale, CDER monitors the use of marketed drugs for unexpected health risks. If new, unanticipated risks are detected after approval, steps are taken to inform the public and change how a drug is used or even remove a drug from the market. CDER also monitors manufacturing changes to make sure

they won't adversely affect the safety or efficacy of the medicine. CDER evaluates reports about suspected problems from manufacturers, health care professionals and consumers, and tries 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, and substandard or improperly used products. Among the key functions performed by the Program are:

- Monitoring the quality of marketed drugs and their promotional materials through product testing and surveillance.
- Developing 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.
- Conducting investigations of reported errors to collect information program managers need to assess the error, and develop error reduction strategies with manufacturers and the medical community.
- Reviewing adverse event and complaint files at manufacturers during inspections for compliance with FDA reporting regulations and to conduct follow up inspections on adverse event reports when information from the manufacturer is needed to evaluate the risks involved.
- Operating the MedWatch Program, which permits health care professionals to voluntarily report observed or suspected defects and quality problems associated with marketed drug products.
- Working with interested governmental agencies and private organizations to coordinate collection of adverse event data.
- Monitoring promotion of drug and biologic products to assure the American public that information provided presents a fair balance of risks and benefits and is not false or misleading.
- Identifying health hazards associated with the manufacturing, labeling, and packaging of pharmaceuticals and biologics; removing unsafe and ineffective products from the marketplace.
- Coordinating with Medical Device contractors to continue implementation of drug products into MeDSuN, which is designed to train hospital personnel to accurately identify and report injuries and deaths associated with medical products.
- Providing training for field staff to improve the information gathered through investigation of consumer complaints and reports of medical errors.

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. To supplement CDER's adverse event data, FDA is working to establish contracts for safety monitoring data links that include data on product exposure and extensive patient information.

CDER is developing access to external databases with other government agencies, states, academia, and independent health organizations such as hospitals, to enhance FDA's ability to monitor the public health impact of FDA regulated products.

Enhanced Communication

FDA is committed to enhancing CDER's communication methods to prevent any harm to the American public that may occur due to the lack of accurate and timely information about a drug product. FDA's human drug program is engaged in a variety of activities designed to better enable consumers to make informed decisions weighing benefits and risks of FDA-regulated products, and is developing education campaigns to disseminate consumer friendly information on drug products to promote the safety and quality of drug products. Key activities include:

- Continuing a Generic Drug Education Program aimed at both consumers and healthcare professionals to inform them about the safety, effectiveness and quality of generic drug products.
- Developing timely press releases that warn the public about potential hazards associated with purchasing particular products from stores or over the Internet. For example, the Agency issued several press releases that advised the public not to purchase products promoted as alternatives to illicit street drugs (street drug alternatives) and not to purchase products with special safety considerations, such as Accutane, over the Internet.

Human Subject Protection

FDA takes its role of protecting human subjects involved in clinical trials very seriously, evidenced by its conscientious daily performance of the following:

- Verification of the quality and integrity of data submitted to us to assure patient safety.
- Protection of human research subjects who participate in drug studies and assess the quality of data from these studies by conducting annual onsite inspections and data audits.
- Performance of on-site inspections of clinical trial study sites, institutional review boards, sponsors, study monitors, and contract research organizations.
- Conducting of inspections to increase oversight of high-risk IND applications and convene conferences of investigators who are the most experienced professionals in the field discuss appropriate monitoring practices.

Compliance Oversight of Marketed Prescription Drugs

FDA continues to protect the public health by assuring that marketed prescription drugs comply with the new drug approval and labeling requirements of the Federal Food, Drug and Cosmetic Act. This helps ensure that drug products available to the consuming public are safe and effective and labeled correctly to assure their proper use. Major functions include:

- Review and support of litigation for recommended regulatory and legal actions, in both civil and criminal proceedings.

- Responding to requests for information from both internal and external stakeholders on new drug and labeling compliance issues.
- Preparing assignments to FDA field offices for inspections and investigations, and coordinating case development and compliance actions with regard to new drug and labeling violations.

Internet Drug Sales

At present, there are an exploding number of new web sites marketing FDA regulated products to the American consumer and medical professionals. Due to resource limitations, FDA currently conducts only limited levels of web-based oversight, of which the key components are:

- Monitoring potentially fraudulent Internet sites to identify targets for investigation and sampling of products.
- Conducting undercover purchases of prescription drugs from Internet sites suspected of engaging in illicit drug sales, distribution, and/or marketing.
- Providing oversight of mail and courier packages entering from foreign sources.
- Using a risk-based assessment protocol, prioritize and take enforcement action against firms that are illegally marketing products over the Internet. Actions include warning letters, untitled letters, seizures and injunctions.

Research, Development, and Evaluation (RD&E) Activities

CDER research activities associated with patient safety include:

- Analyzing specific immune deficiencies in animal models of bioterrorism-related radiation injury to clarify clinical problems that might be treated by therapeutic proteins.
- Studying broadly-acting stimulators of the immune system in animal models to assess protective effects against various infectious agents that could be used in bioterrorist attacks.
- Developing new assays for anthrax toxin that more closely models toxin activity in humans than current mouse cell assays, and provide biomarkers for assessing anthrax toxin effects in vivo.
- Clarifying normal function of novel proteins proposed as targets for cancer therapy, in order to predict adverse effects due to inhibition of these proteins in normal cells.
- Studying novel cytokines to suggest new potential therapeutic strategies in autoimmune diseases for which current therapies have a poor risk/benefit profile.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

The Human Drugs Program within FDA is responsible for ensuring the safety and effectiveness of drug and therapeutic biologic products.

New Drug Review

FDA reviews and evaluates New Drug Applications (NDAs) to determine whether or not a new drug is both safe and effective. Drugs for diseases such as cancer and AIDS are given priority status and evaluated through an accelerated approval process. Major activities associated with the process include:

- Administering FDA's accelerated drug approval program to help make promising products for serious or life threatening diseases available earlier in the development process.
- Reviewing and evaluating biological therapeutic products, including establishing standards, conducting mission related research, participating in inspections, developing policy and procedures, and evaluating trial results and reports of adverse events.

Over-the-Counter Drugs

FDA is committed to providing consumers with safe, effective, and affordable drugs. Increasing the number of safe and effective over-the-counter (OTC) drugs that are available to consumers is consistent with this goal. Major functions of the program include:

- Reviewing OTC drugs to ensure their safety and effectiveness and assists consumers on how to best use OTC products by providing clear, easy-to-read drug information.
- Funding consumer behavior research to identify and manage the risks associated with the use of OTC drugs.

Generic Drugs

FDA continues to support an active generic drugs program to complete review and action on Abbreviated New Drug Applications (ANDAs). As a result, there are continuing efforts to expand the availability of high-quality generic drug products to the public and providing consumers with information on their safety and effectiveness. Generic drugs save consumers billions of dollars each year. Accordingly, FDA is committed to bringing as many safe and effective generic drugs to market as possible by addressing 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 inhalation or topical drug products. Key functions of the program include:

- Assuring generic product conformance to manufacturing standards equal to the standards of the brand name pharmaceuticals.
- Increasing efficiency and improving generic drug review times by evaluating ways to improve communications with industry.

FDA Approves First Pediatric Generic AIDS Drug for U.S. Marketing

September 2005: FDA announced approval for marketing several generic versions of drugs that treat HIV, the virus that causes AIDS. Previously, the products had been only tentatively approved and were not available in the United States because patent or market exclusivity blocked their approval. With the expiration of those patents, the following products today have receive full marketing authorization for the United States: (1) zidovudine (zye-DOE-vue-deen) tablets manufactured by Ranbaxy Laboratories Limited of Guragon, India; (2) zidovudine tablets and oral solution manufactured by Aurobindo Pharma LTD. Hyderabad, India; and (3) zidovudine tablets manufactured by Roxane Laboratories of Columbus, Ohio, U.S.A. These are the first generic versions of the already-approved Retrovir brand manufactured by GlaxoSmithKline to be approved for marketing in the U.S. FDA previously determined as part of a tentative approval action that these products meet all U.S. manufacturing quality and clinical safety and efficacy standards.

"These approvals will now allow those infected with HIV more access to these life-saving drugs within our country. Some of these products have been available for purchase outside the U.S. as tentatively approved products under the President's Emergency Plan for Aids Relief," said Health and Human Services Secretary Mike Leavitt. "Generic products help reduce costs to patients and for the first time this antiretroviral drug will be available as a generic pediatric dosage form."

President's Emergency Plan for AIDS Relief (PEPFAR)

FDA plays a key role in the President's Emergency Plan for AIDS Relief (PEPFAR). In May 2004, in direct support of PEPFAR, Secretary Thompson announced that the FDA would implement a new, expedited review process to ensure that the US could provide safe, effective drugs to developing countries. PEPFAR's major activities are:

- Providing medical and scientific expertise necessary to fulfill the President's commitment to ensure the quality of HIV/AIDS drugs purchased by the US for developing countries.
- Performing outreach to pharmaceutical firms – including many foreign firms who are unfamiliar with FDA's regulatory processes.
- Conducting its traditional drug product review activities for both new products and for generic forms of existing drug products to ensure product safety and effectiveness.
- Developing a program to conduct pre-approval inspections and pre-operational visits.

Protecting America's Children

CDER is responsible for fulfilling the requirements of recent legislation and for making significant progress in protecting children who need prescription or OTC drug products. Due to the inadequacy of pediatric use information found in the majority of prescription medications in the U.S., Congress enacted several legislative initiatives to promote drug development for children. 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, was reauthorized in January 2002 under the Best Pharmaceuticals for Children Act (BPCA).

As a result of these initiatives, the number of ongoing pediatric clinical trials in the last 5 years has increased dramatically. The BPCA also established a publicly funded contracting process for studies of drugs that no longer have exclusivity or patent protection for which pediatric studies are needed. Finally, on December 3, 2003, Congress enacted the Pediatric Research Equity Act (PREA) which provides FDA the authority to require pediatric studies for certain new and already marketed drug and biological products.

Research for Treatments of Orphan Diseases

Office of Orphan Products Development (OOPD) has been dedicated to promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions since it was created in 1982. Major activities include:

- Interacting with the medical and research communities, professional organizations, academia, and the pharmaceutical industry, as well as rare disease groups.
- Administering the major provisions of the Orphan Drug Act (ODA) which provide incentives for sponsors to develop products for rare diseases
- Administering the Orphan Drug Grants Program which provides funding for clinical research in rare diseases.

Research, Development, and Evaluation Activities

Research CDER performs ensures that FDA has sufficient expertise to develop regulatory standards and risk assessment criteria to reach sound, science-based public health decisions. Important components of the research include:

- Clarifying mechanisms of cell death induced by cancer drugs in order to enable better bioassays to serve as markers for safety and efficacy of novel cancer drugs.
- Characterizing differences between antibodies produced in vivo versus those produced by novel synthetic technologies to help assess potential adverse effects of synthetically derived therapeutic antibodies.
- Identifying biomarkers of cancer development and progression to facilitate diagnosis and monitoring of treatment efficacy.
- Investigating novel ways to synthesize short pieces of DNA with proposed indications in treating and diagnosing diseases.

Planning for Emergencies and Protecting Americans from Terrorism through Medical Countermeasures

Increased funding over the last five years has strengthened CDER's capability to identify, prepare for, and respond to biological, chemical, and radiological/nuclear threats and incidents.

FDA is engaged in many efforts to promote the development of medical countermeasures, among which are:

- Encouraging early and frequent interactions with sponsors, whether they are developing a novel compound or a new indication for a previously approved product
- Expanding the availability of safe and effective medical countermeasures for special populations (e.g., pregnant or lactating women, infants, elderly) through contracts that fund pharmacokinetic and safety studies of antibiotics likely to be used to prevent or treat illness following a terrorist attack.
- Assuring processes are in place if unapproved product is required in response to an event.
- Collaborating with other agencies on the development of INDs to allow access to investigational medical countermeasures.
- Conducting GMP inspections of drug manufacturing sites whose products are stockpiled as part of the government's counterterrorism efforts.
- Assuring regulated drug and therapeutic biological products are not used as vehicles of terrorism.
- Participating in committees to facilitate development of medical countermeasures and to provide recommendations on acquisition of products.
- Interacting frequently with the Strategic National Stockpile to support the development, availability, maintenance, and deployment of stockpiles of medical countermeasures.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Ensuring that the highest possible quality products are marketed is a large part of FDA's mission of protecting the public's health. The Agency ensures product quality by facilitating effective and efficient scientific assessment of relevant pharmaceutical and biotechnology information in regulatory submissions. The Agency facilitates those scientific and technological innovations that improve understanding of product performance, quality and efficiency of development, manufacturing, and quality assurance processes. Ensuring quality of products involves recognizing the level of scientific knowledge supporting product applications, process validation, and process capability. In accomplishment of this strategic goal, CDER performs the following:

- Applies a risk-based regulatory scrutiny that relates to the level of scientific understanding of how formulation and manufacturing process factors affect product performance and relates to the capability of process control strategies to prevent or mitigate risk of poor product performance.
- Evaluates and analyzes inspection findings for trends in deficiencies by focusing on product quality standards and manufacturers' compliance with GMP regulations.

- Develops, deploys, and maintains risk-based compliance inspection models for prioritizing GMP inspections by risks to product quality.
- Performs targeted drug quality surveillance studies to detect emerging threats to drug quality and develop baselines for risk-based drug quality monitoring by creating data resources and maintaining access to industry data resources for efficient and accurate assessments of drug products marketed and drugs consumed.
- Conducts criminal investigations of reported product tampering, counterfeit products, and other fraudulent criminal activities involving regulated drug products.
- Performs laboratory validation of analytical methods submitted to support pre-market product applications.
- Verifies the reliability and accuracy of NDA data collected by regulated industry in animal and human studies, and evaluates approaches that may be used to facilitate the introduction of modern process analytical technologies and pharmaceutical engineering principles.

Federal Authorities Cease Sale and Distribution of Counterfeit Lipitor

August 2005 FDA and the United States Attorney for the Western District of Missouri, Kansas City, Missouri, today announced the indictments of 11 individuals, a drug repacker, and two wholesale distributors in cases related to the sale of Lipitor, a popular cholesterol reducing drug.

The indictment alleges numerous charges including conspiracy to sell counterfeit, illegally imported and misbranded drugs as well as conspiracy to sell stolen drugs. The conspiracy involved the manufacture of counterfeit Lipitor at a clandestine facility in Central America, the purchase of genuine Lipitor intended for distribution in South America, and the illegal importation into the United States of both products.

Managing Quality by Industry Self-Compliance

FDA operates a comprehensive program to guide, assist, and manage industry self-compliance with manufacturing quality objectives of the Federal Food, Drug and Cosmetic Act. In support of the program, CDER organizes FDA experience and expertise into published guidance on how industry may meet requirements for manufacturing quality on focused areas of technology and procedures. CDER also provides input on industry-generated voluntary standards and guidance documents to assure broad consensus for effective compliance.

Over the last few years, FDA has conducted a major effort to bring a 21st Century focus to the regulation of pharmaceutical manufacturing and product quality by providing high quality, cost-effective oversight of industry manufacturing, processing and distribution. FDA focuses on product quality standards and compliance by manufacturers with the GMP regulations to ensure that the highest possible quality products are marketed. CDER ensures the latest technological advances are encouraged, including application of the requirements of Part 11 regulations. Further CDER efforts include:

- Providing inspection assessments of conformance with current good manufacturing practice requirements for self correction and improvement of operations.
- Assisting Industry in voluntary recalls of products from the market and in the investigation, evaluation, and corrections of the conditions and practices which led to the recalls.
- Certifying conformance with current good manufacturing practice by the Industry for use in facilitating export of US pharmaceutical production to countries with limited regulatory systems.
- Consulting with industry and coordinating of FDA program activities to alleviate drug shortages in the US market.

Compliance Oversight of Marketed OTC Drugs

Enforcement of the OTC Drug Review regulations is tantamount to maintaining the integrity of the NDA process. Those members of the regulated industry who market their OTC drugs in compliance with applicable monographs expect FDA to eliminate unfair competition from those who ignore monograph requirements. Further, NDA holders for OTC drugs expect their investments to be protected by vigorous FDA enforcement against those who flaunt these NDA requirements. This type of enforcement helps provide the consuming public with the assurance that they are buying safe and effective OTC drugs.

Pharmacy Compounding

FDA believes that a significant number of licensed pharmacies are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is outside the bounds of traditional pharmacy practice. For example, some pharmacies make large quantities of unapproved drug products in advance of receiving a valid prescription for them, or copy commercially available drug products when there is no medical need for a compounded product. Furthermore, some pharmacies have been found to compound drugs that are contaminated or that are dangerously subpotent or superpotent in a manner that can threaten public health. In such situations, FDA may need to take enforcement action in accordance with the Act to protect the public health. FDA continues to work with state regulatory authorities, providing support as needed for their regulation of pharmacy compounders.

Import Compliance

FDA has worked with the Agency field import district offices and the U.S. Customs and Border Protection (CBP) to develop categories of drug products targeted for "blitz" operations scheduled at different major mail import centers. These "blitz" operations are held cooperatively with CBP to identify the type and origin of drug products being offered for import into the U.S. through the mail, with emphasis placed on counterfeit, misbranded, adulterated, and restricted distribution drug products. CDER also responds to inquiries concerning import and export regulations and enforcement policy from the regulated industry, consumers, consultants, and health care professionals. Other inquiries come from field import offices concerning importation of unapproved and investigational drug products, and drugs being imported in advance of application submission and final approval.

Research, Development, and Evaluation (RD&E) Activities

CDER's research efforts associated with manufacturing quality include:

- Studying the biology of prions (agents of "Mad Cow Disease") to facilitate development of detection procedures for prions in human- and animal-derived material used in manufacturing biological agents.
- Clarifying the mechanisms by which antibodies to interferons and cytokines can impact the safety and efficacy of these products.
- Studying factors inducing some patients to mount immune responses against therapeutic proteins, responses that terminate effectiveness of these proteins and threaten patient safety.
- Studying the mechanism of action of therapeutic enzymes and cytokines to alert reviewers to potential adverse effects and facilitate improved potency assays.
- Investigating a biochemical pathway of internal cell signaling in lymphocytes to facilitate novel therapies targeting lymphocytes in autoimmune and malignant diseases.
- Developing model systems to study interactions between drugs with anti-inflammatory effects (e.g. statins) and therapeutic proteins that modulate the immune system.
- Developing new tests and novel breast cancer cell lines for analyzing cell proliferation and potential for metastasis, to facilitate bioassays of proposed cancer therapeutics.
- Studying cytokines that are secreted by HIV-infected cells and that act on HIV-infected cells, in order to facilitate development of surrogate markers to monitor therapeutic and adverse effects of new AIDS therapeutics.
- Develop new strategies for downstream manufacturing processes to ensure the safety of biotechnology products from adventitious virus contamination.

Field Operations

ORA's field actions to ensure the safety and quality of the nation's drug supply include:

- *Operation Safeguard Pharmaceutical*: In a joint operation with Customs and Border Protection, FDA conducted blitzes of several international mail facilities across the country. The blitzes revealed substantial numbers of shipments of unapproved drugs, and provided useful information for future targeting efforts.
- *Operation Bait and Switch:* FDA conducted a multi-district operation to detect import parcels which were shipped via postal service from a country other than Canada, and which contained pharmaceutical products labeled or identified as coming from a Canadian pharmacy. FDA found that such products sourced from 39 different countries. ORA drug laboratories analyzed 487 samples and found 28 products that were counterfeit (not consistent with authentic product) and one significantly sub potent sample. In addition, label reviews found some products labeled entirely in a foreign language. Operation Bait and Switch confirmed that U.S. consumers have no assurance of quality when purchasing medications from sources outside the normal distribution channels in the U.S.

- *State Partnership Program:* The Agency and the States maintained and continued to develop new partnerships (e.g., compressed medical gas and drug GMP inspections) that have contributed to the exchange of inspection and sampling data and have facilitated the receipt of training and distribution of equipment to the states.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Strong and sound science means Human Drug Program scientists stay on the cutting edge of new technologies. CDER's mission depends more than ever on a solid cadre of experienced physicians, toxicologists, chemists, statisticians, mathematicians, project managers and other highly qualified and dedicated professionals.

Information Technology

FDA is working to apply information technology by developing and managing systems that provide staff with the technical tools to manage the review process and to provide the means to evaluate post-marking drug safety.

- Developing Automated Drug Information Management System (ADIMS) as a fully electronic information management system to receive, evaluate, and disseminate information about investigational and marketing submissions for human drugs and therapeutic biologics.
- Addressing, within ADIMS, its electronic document receipt and validation processes and efforts to develop scientific tools that aid submission evaluation, such as tools to review structured clinical data, labeling data, and drug ingredients.
- Leveraging the wealth of data in its Adverse Event Reporting System to assist medical officers involved in the review process by providing a data mining tool to identify trends in adverse event data.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Risk management is at the core of CDER's mission. Almost everything the center does in the review and approval of Human Drugs relates to weighing the benefits of a product to its risks. CDER's FY 2005 accomplishments include new, generic, and OTC drugs as well as accomplishments of managing the risks of drugs in the pediatric population.

As the Agency Strategic Plan explains, "efficient risk management" requires using the best scientific data, developing quality standards, and using efficient systems and practices that provide clear and consistent decisions and communications for the American public and regulated industry. Accomplishments toward objectives and strategies of the Agency Strategic Plan are included here as well.

Significant NDAs Approved in FY 2005

- *Tarceva* (erlotinib) - For the treatment of locally advanced or metastatic Non Small-Cell Lung Cancer (NSCLC) after failure of at least one prior chemotherapy regimen. Approval was based on improved overall survival.
- *Macugen* (pegaptanib sodium injection) - For the treatment of neovascular (wet) age-related macular degeneration. Macugen was shown to slow vision loss in patients. It is an alternative to traditional laser treatment and one of the first treatments to target the underlying biology of the disease. This product was given Fast Track Status.
- *Baraclude* (entecavir) - For the treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. Baraclude slows the progression of chronic hepatitis B by interfering with viral replication. The virus can cause lifelong infection, liver scarring, liver cancer, liver failure, and death.
- *Increlex* (mecasermin [rDNA origin]) - For the long-term treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone. This is drug treats an Orphan indication.
- *Kepivance* (palifermin) - To decrease the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving high doses of chemotherapy and radiation followed by stem cell rescue. Mucositis is an inflammation of the mucous membranes (lining of the mouth) that can be caused by chemotherapy and radiation. Palifermin works by stimulating the growth and reproduction of the cells that line the mouth, speeding up the healing process.
- *Velcade* (bortezomib) - Received regular approval for the treatment of multiple myeloma patients who have received at least one prior therapy. Velcade was originally approved under the accelerated approval program in May 2003; approval was based on a decrease in the size of tumors. Regular approval means that the FDA has determined that Velcade has demonstrated clinical benefit showing a survival benefit. At the time of original approval, Velcade was the first of a new class of anticancer agents called proteasome inhibitors.
- *BiDil* (hydralazine/isosorbide dinitrate) - For the treatment of heart failure in self-identified black patients. BiDil is the combination of two older drugs, neither approved for heart failure. Approval was based on a trial conducted in over 1,000 self-identified black patients based on results from previous trials which showed no benefit in the general population but suggested a benefit in black patients. Hydralazine is an anti-hypertensive agent; isosorbide dinitrate is an anti-anginal agent.

NDAs Approved under Accelerated Approval in FY 2005

- *Clolar* (clofarbine) - For the treatment of pediatric patients 1 to 21 years old with relapsed or refractory acute lymphoblastic leukemia (ALL) after at least two prior regimens or is unresponsive to other treatments. ALL is responsible for 80 percent of all acute childhood leukemias. This drug is for an Orphan indication.

- *Aptivus* (tipranivir) - In combination with ritonavir, for the antiretroviral treatment of HIV-1 infected adult patients with evidence of viral replication, who had already used many HIV medicines, and had a type of virus resistant to currently available HIV therapy. This new combination therapy provides a new treatment option for patients with limited options. This is the only second drug approved for patients with advanced HIV disease.

Generic Drug Review

OGD continues to approve greater numbers of generic products thus helping to lower drug costs for millions of Americans. The following are significant generic drugs approved in FY 2005 that will contribute to the goal and assure greater access to affordable health care:

- *Levofloxacin* - A broad spectrum fluoroquinolone antibiotic used to treat conditions such as sinusitis, community-acquired pneumonia, and urinary tract infections.
- *Fentanyl Transdermal System* - The "patch" provides continuous systemic delivery of this potent opioid analgesic for 72 hours and is useful for patients with severe chronic pain, such as cancer sufferers.
- *Azithromycin* - This is an azalide antibiotic used to treat a number of infections including Disseminated Mycobacterium avium complex disease in persons with advanced HIV infection.
- *Fexofenadine* - As a histamine antagonist, it is used to treat seasonal allergic rhinitis and is used by large numbers of the population.
- *Zidovudine* - This is a pyrimidine nucleoside analogue that is active against the human immunodeficiency virus used in combination with other antiretroviral agents for the treatment of HIV infection. It is also used for the prevention of maternal-fetal HIV transmission.
- *Ramipril* - An angiotensin converting enzyme (ACE) inhibitor used to treat hypertension and certain patients at risk of myocardial infarction and stroke.

The Office has demonstrated full support for the President's Emergency Plan for AIDS Relief (PEPFAR). CDER has approved or tentatively approved 12 applications for a number of products. More firms have expressed interest in submitting applications and have provided OGD with their projections for future applications. CDER views the applications as priority for review and provides extensive guidance to the firms, who are often from the developing countries that will use the products.

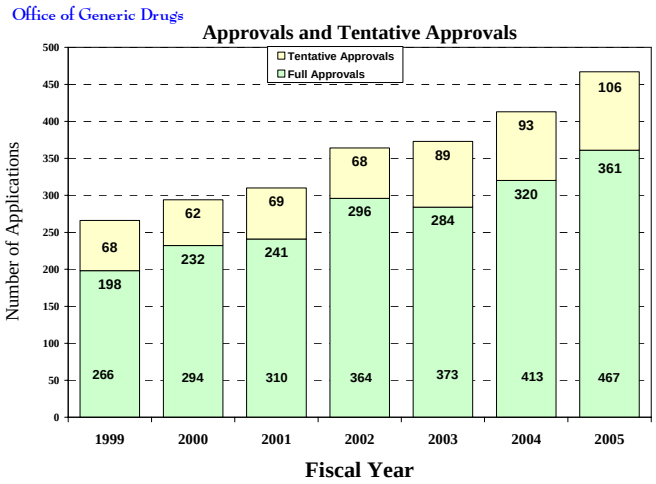


Figure 1 ANDA Approvals

As seen in Figures 1, there were 467 abbreviated new drug applications (ANDAs) approved or tentatively approved in FY 2005, an increase of 13percent. There was a median approval time of 16.3 months seen this year.

There was a staggering 36percent increase in receipts in FY 2005 as shown in Figure 2. This increase is in addition to the 24 percent increase in receipts from FY 2002 to FY 2003 and an additional 25 percent increase from FY 2003 to FY 2004. With the continuing high numbers of submissions, mechanisms are needed to increase efficiency. An emphasis over FY 2005 is working to streamline the review process. The third division of chemistry is nearly complete and is functioning effectively. The chemistry and bioequivalence review divisions are relying more on the project manager staff to triage supplements and information requests so that only those that require particular scientific expertise are put into the reviewers' queue. Groups of applications for single products are reviewed by a dedicated team in order to capitalize on the knowledge gained about the product.

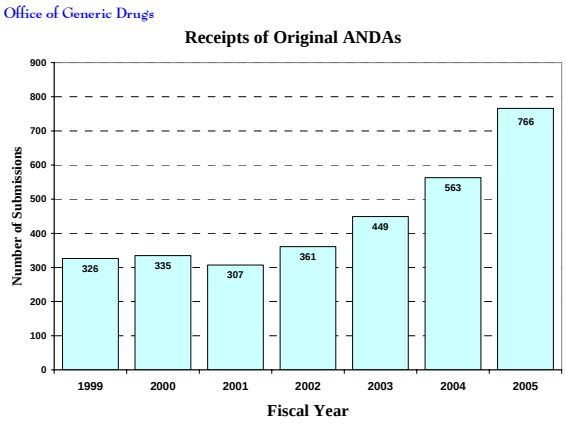


Figure 2 ANDA Receipts

OGD has developed a question based review (QbR) for its CMC evaluation that is focused on critical pharmaceutical quality attributes. The goal is to transform the CMC review into a modern, science and risk-based pharmaceutical quality assessment under the FDA's cGMPs for the 21st Century Quality and PAT initiatives. With the move to the QbR, there is more emphasis on moving towards the common technical document (CTD) format for generic drug submissions since the QbR is more closely aligned with that format. Firms are also encouraged to move to the electronic format of the CTD.

Finally, to address the advent of electronic prescribing, electronic health records, and interest in the computerized distribution of up-to-date medication information FDA adopted Structured Product Labeling (SPL). By selecting this format, FDA hopes to provide labeling that is both human and machine readable, faster to disseminate, and improves patient risk management. It will also allow easier review when changes are made and greater accessibility by prescribers and consumers through the National Library of Medicine.

OTC Drug Products

In FY 2005, the OTC staff approved a total of 2 NDAs (Reviewed 6). Significant approvals included:

- Loperamide Soft Gel Capsules (1 and 2 mg)

Highlights for other significant accomplishments include:

- Approved three new efficacy supplements for new product uses;
- Acted on 112 supplement submissions regarding changes to manufacturing procedures;
- Acted on 28 labeling supplement submissions regarding changes to product labeling;
- Conducted 52 meetings with drug companies;
- Published 11 Federal Register notices for OTC monographs;
- Responded to 9 health hazard evaluations;
- Answered 8 citizen petitions;
- Completed 7 time and extent applications; and
- Published 2 guidance documents.
- Significant new Federal Register Publications regarding OTC products included: publishing six proposed rules,1 final rule and 3 notices of eligibility.

Pediatric Drug Studies

- Reviewed 388 Proposed Pediatric Study Requests (PPSRs), issued 307 Written Requests (WRs) for on-patent drugs that asked for over 714 studies to be conducted in the pediatric population, and granted pediatric exclusivity for 114 out of 125 drugs that have had pediatric exclusivity determinations. Ninety-eight of these 125 drugs had labeling incorporating information from pediatric studies approved.
- Determined pediatric exclusivity for 14 drugs, 13 of which were granted pediatric exclusivity.
- Approved 16 labels for drugs responsive to WRs.
- Continued collaboration with NIH as a result of the Best Pharmaceuticals for Children Act (BPCA). Further, FDA continues its implementation of section 3 of the BPCA (the study of drugs with no marketed protection in the pediatric population) and issued four Written Requests for drugs on NIH's annual list.
- Collaborated on 2 Pediatric Advisory Committee meetings that presented post-pediatric exclusivity adverse events reports on 14 drugs.
- Disseminated to the public 21 medical and clinical pharmacology reviews for supplements submitted in response to Written Requests.

Responding to Emergencies and Protecting Americans from Terrorism

CDER plays a key role in countering terrorism in the U.S., especially in preparing the country to have medical countermeasures readily available in the event of any chemical, biological, or radiological or nuclear attack. In FY 2005, FDA approved several products for indications related to counter-terrorism:

- *Radiation Threats:* ThyroShield™ (potassium iodide oral solution) was approved as a thyroid blocking agent for use in radiation emergencies. This oral solution is appropriate for use in children or in adults who cannot swallow tablets. In February 2005, CDER assisted HHS in a BioShield procurement of ThyroShield™ for the Strategic National Stockpile (SNS). Tentatively approved were CIS-US's Ca-DTPA (Kelacal) and Zn-DTPA (Kelazin).and Degussa's Manoplex (insoluble Prussian blue)
- *Biological Threats:* Levaquin (levofloxacin) was approved for an additional indication of post-exposure prophylaxis of inhalational anthrax. Cipro (ciprofloxacin) tablets, IV solution, and oral suspension received approval for revised labeling for the Indications and Usage, Adverse Reactions, and Inhalational Anthrax-Additional Information sections of the package insert. These changes were based on information obtained from the Centers for Disease Control and Prevention during the 2001 anthrax attacks. FDA also released Bayer from its Subpart H commitment to report data from confirmatory anthrax studies. Four generic ciprofloxacin applications were also approved during FY05.

In FY2005, FDA also performed the following counterterrorism tasks:

- Collaborated with NIH/NIAID to establish the animal model requirements necessary for development of medical countermeasures against nuclear/radiological threat agents and on the development of a non-human primate natural history model for inhalational anthrax disease.
- Published the draft Guidance: "Internal Radioactive Contamination-Development of Decorporation Agents."
- Coordinated emergency response activities, including non-CT incidents and natural disasters. For eample, CDER assisted in response issues related to Hurricanes Katrina, Rita, and Wilma by coordinating web postings on the safety of medications potentially damaged by flooding or high temperature.
- Coordinated 25 urgent requests from the FDA Emergency Operations Center since March of 2005, addressing issues such as product quality, counterfeit products, mislabeled products, recalled products, product shortages, product theft / diversion, and severe adverse events.
- Prepared for pandemic influenza and avian flu by participating in intercenter and interagency working groups and developing the Center’s response plan to pandemic flu.
- Participated in TOPOFF 3 (Top Officials), a full-scale inter-departmental emergency response exercise intended to test the national preparedness to simultaneous terrorist attacks using multiple threat agents.
- Published the draft Emergency Use Authorization Guidance in July 2005.

Information Technology

CDER accomplished several significant advances in applying information technology solutions to drug review processes:

- Implemented the Electronic Labeling Information Processing System (ELIPS) was. This system standardizes drug labels to improve patient safety by ensuring that medication information is readily available to health care providers, patients, and the public, in its most up-to-date form.
- Implemented FDA Review, a product that provides greater eCTD submission processing and reviewer tools. The implementation of this new product allows the FDA to process high volumes of eCTD submissions and allows the reviewer to see the cumulative lifecycle of a marketing application submitted in eCTD format.

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Patient and Consumer Protection

- Approved a strengthened distribution program for isotretinoin, called iPLEDGE, aimed at preventing use of the drug during pregnancy.

- In FY 2005 approximately 50 percent of expedited individual safety reports were submitted electronically CDER estimates the cost of receiving a report is cut from $34 per paper report to $20 per report for those submitted electronically. Approximately 30 percent of expedited individual safety reports were submitted electronically in FY 2004, an increase from approximately 20 percent the previous year.

Drug Safety

- Initiated a contract with the Institute of Medicine (IOM) to study the effectiveness of the United States drug safety system with emphasis on the post-market phase, and assess what additional steps could be taken to learn more about the side effects of drugs as they are actually used. The committee will examine FDA's role within the health care delivery system and recommend measures to enhance the confidence of Americans in the safety and effectiveness of their drugs.
- Conducted and completed a national search to fill the currently vacant position of Director of the Office of Drug Safety, which is responsible for overseeing the post-marketing safety program for all drugs.
- FDA issued three guidances:
    - "Premarketing Risk Assessment," which describes additional safety testing, monitoring, and interventions that may be helpful in selected circumstances and address pre-market risk assessment;
    - "Development and Use of Risk Minimization Action Plans," which outlines the development, implementation, and evaluation of risk minimization action plans (called RiskMAPs); and
    - "Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment," which illustrates good pharmacovigilance practices and assessment of reported adverse events.

- Announced on May 10, 2005 the availability of draft guidance for industry entitled, "FDA's Drug Watch for Emerging Drug Safety Information." This document provides guidance about how FDA intends to develop and disseminate important emerging drug safety information concerning marketed drug products to healthcare professionals and patients.

Reforms Will Improve Oversight and Openness at FDA

February 2005: HHS Secretary Mike Leavitt shared an emboldened vision for the FDA that included a new culture of openness, improved oversight and enhanced independence. In keeping with this vision, the FDA will create a new independent Drug Safety Oversight Board to oversee the management of drug safety issues, and will provide emerging information to doctors and patients about the risks and benefits of medicines.

"The public has spoken and they want more oversight and openness," Secretary Leavitt said during a meeting with FDA employees at the Parklawn Headquarters in Rockville, Md. "They want to know what we know, what we do with the information, and why we do it. We will address their concerns by cultivating openness and enhanced independence."

Drug Safety Oversight Board

- Created an independent Drug Safety Oversight Board (DSB)to oversee the management of important drug safety issues within the Center for Drug Evaluation and Research (CDER). The DSB comprises members from FDA and medical experts from other HHS agencies and government departments (e.g., Department of Veterans Affairs) who will be appointed by the FDA Commissioner. The board consults with other medical experts and representatives of patient and consumer groups.

Better Communication to Consumers and other Stakeholders

- Revised and expanded its presentation of consumer and patient education resources on the CDER web site. This effort included adding or updating drug-specific information and regrouping educational materials more effectively for primary use by two targeted audiences: consumers and health care intermediaries.
- Designed a new Patient Information Sheet that provides more information than the older-format Consumer Information Sheets and also places more emphasis on taking drugs safely.
- Review the Consumer Information Sheets already on the web site and updated the information in the form of Patient Information Sheets.
- Redesigned CDER Internet home page to draw attention to drug safety information. We also created a new page, the "Index to Drug-Specific Information," to help users locate Information Sheets and Drug Information pages. The site also provides a link to Drugs@FDA, a searchable database of all FDA drugs and therapeutic biologics, and includes links to consumer and patient information materials, as well as approved labeling.
- Updated many topical pages, such as the Influenza page (http://www.fda.gov/cder/drug/antivirals/influenza/default.htm),

- Added a number of pages to provide needed hurricane recovery information promptly (http://www.fda.gov/cder/emergency/default.htm), such as the safe use of insulin when it can not be refrigerated. .

Public Service Campaigns

- Developed a partnership with the United Health Foundation that produced a joint public service announcement (shown below) that appeared in a number of national magazines, including Parade, People, Better Homes and Gardens, Family Circle, Woman's Day, Ladies Home Journal, Ebony, Good Housekeeping, and Reader's Digest. The Foundation spent about 14 million dollars to run these ads.

- Completed and disseminated radio, television and/or print public service announcements about buying drugs online; the safe use of OTC pain relievers*; Know Your Child's Weight; Safe use of Prescription Pain Relievers*; clinical trails; aging, medicines and alcohol; and antibiotic resistance (English and Spanish.)
- Created the *Generics* and *Aging, Medicines & Alcohol* radio spots which garnered a total almost 63,000 plays reported by 233 AM and FM stations across the country. This equates to a little more than 526 hours of airtime worth an estimated $3.2 million.
- Signed ten co-sponsorship agreements with healthcare organizations. These organizations combine to reach more than 240 million consumers with information about the safe and effective use of drug products.
- Completed and disseminated six brochures: *Buying Prescription Medicine Online, Kids Aren't Just Small Adults (Spanish-language version), Medicines in My House*, antibiotic resistance; generic drugs (English and Spanish plain-language versions

As a result of meeting and collaborating with various health-related businesses and educational organizations, FDA-developed materials were disseminated throughout the world. Below are a few examples:

- The New York State Patient Safety Center reprinted and promoted FDA's OTC pain reliever products. Nearly 5,000 retailers, hospitals, poison control centers, and county offices received copies. In addition, New York's Dept of Health announced to NY ENTs, pediatricians and family physicians the release of FDA's *Kids Aren't Just Small Adults* brochure.

- Provided print PSAs to the Director of Pharmacy of the U.S. Army Europe Regional Medical Command in Germany. The materials were disseminated to U.S. Army personnel and families in Germany, Belgium, and Italy. This involved 29 clinics and three medical centers.
- Developed with the Consumer Healthcare Products Association a news release promoting the *"My Medicines Guide."* The release generated 188 newspaper articles in 23 different states with a readership of more than 4.5 million people.

Field Operations

ORA protected consumers from many sources of unsafe drugs, including:

- *Internet Storefront Drugs:* FDA obtained a preliminary injunction against one storefront operation facilitating the Internet sale and importation of unapproved prescription drugs from Canada. FDA also coordinated regulatory activities with state regulatory bodies and national regulatory organizations against internet and storefront operations that import unapproved prescription drugs.

- *Pharmakon Labs:* On July 27, 2005, FDA announced a permanent injunction shutting down operations at Pharmakon Labs of Florida. The company manufactured and distributed cough and cold liquids, tablets and caplets. Following inspections by FDA, it was determined that drug products sold by Pharmakon Labs, Inc., did not meet current good manufacturing practice (CGMP) standards and other legal requirements.

- *Genendo Pharmaceutical N.V:* On August 22, 2005, U.S. District Judge James F. Holderman entered an order of permanent injunction against Genendo Pharmaceutical N.V.; a drug importer located in Curacao, Netherlands, Antilles. The Order held that Genendo violated the Federal Food, Drug, and Cosmetic Act when it imported name-brand drugs that were labeled in foreign languages and manufactured and/or packaged in facilities not identified in FDA-approved new drug applications (NDAs).

FDA Strategic Goal: Improving Product Quality, Safety, And Availability Through Better Manufacturing And Product Oversight

Inspection and Enforcement Initiatives

Program staff played a key role in a major agency-wide initiative on "Pharmaceutical Current Good Manufacturing Practices (cGMPs) for the 21st Century: A Risk Based Approach," a two-year program that applies to pharmaceuticals, including biological human drugs and veterinary drugs. FDA issued its final report on the cGMP initiative (http://www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm). The report discusses:

- The Agency's completed assessment of the current good manufacturing practice regulations, current practices and the new tools in manufacturing science that will enable a progression to controls based on quality systems and risk management.
- Specific steps the Agency has taken and will take to develop and implement quality systems management and a risk-based product quality regulatory system.

FDA also took many other steps to enhance the consistency and coordination of its drug quality regulatory programs. These accomplishments include:

- Piloting a risk-based computer model for prioritizing cGMP inspections for domestic manufacturing sites, in order to further a systematic risk-based approach to inspectional oversight of pharmaceutical manufacturing.
- Training and certifying a Pharmaceutical Inspectorate, a select cadre of field inspectors who will specialize in pharmaceutical pre-approval and cGMP inspections.
- Issuing a final guidance on aseptic processing used in the manufacturing of sterile drugs, thereby encouraging the adoption of modern science and technology and risk-based approaches.
- Actively collaborating internationally on pharmaceutical manufacturing issues, in order to move towards implementation of an internationally harmonized plan for a pharmaceutical quality system based on an integrated approach to risk management and science.

FDA also took many other compliance and enforcement steps to protect the American public, including:

- Providing regulatory support to the work of the Strategic National Stockpile (SNS) which is charged with delivering critical medical assets to the sites of national emergencies. Agency support for the SNS included reviewing the labeling and approval status of stockpile drugs;.ing a risk-based selection process to choose establishments for inspections to assess compliance with regulatory requirements for adverse drug safety event reporting.,
- Increasing industry awareness of post-marketing adverse event reporting requirements through an industry education program and development of a public website.

Human Drugs
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actual	FY2006 Estimate	FY 2007 Estimate
NEW DRUG REVIEW			
Priority New Drug Application (NDA/BLA) Reviews	41	30	30
Standard NDA/BLA Reviews	141	165	165
Priority NDA/BLAs Approved	27	16	16
Standard NDA/BLAs Approved	82	72	72
Time from Receipt to Approval (mo.s)(mean)-Priority NDA/BLAs	10.1	(8.5)	(8.5)
Time from Receipt to Approval (mo.s)(mean)-Standard NDA/BLAs	20.6	(18.0)	(18.0)
Time from Receipt to Approval (mo.s)(median)-Priority NDA/BLAs	6.0	(6.0)	(6.0)
Time from Receipt to Approval (mo.s)(median)-Standard NDA/BLAs	12.9	(13.5)	(13.5)
NDA Supplemental Reviews (NDAs only)	2,793	3,300	3,300
INDs (Active) (Drugs and Biologics—Commercial+Research)	13106	13,000	13,000
Clinical Pharmacology/BioPharmaceutic Reviews	1,875	1,600	1,600
BIOLOGIC THERAPEUTICS REVIEW			
Total Original License Application (PLA/ELA/BLA) Reviews	3	7	7
PLA/BLA Approvals	3	5	5
License Supplement (PLA/ELA/BLA) Reviews	318	220	220
Commercial IND/IDE Receipts (Biologics Only)	68	80	80
IND/IDE Amendments Receipts (Biologics Only)	9,772	8,800	8,800
GENERIC DRUG REVIEW			
Abbreviated New Drug Application (ANDA) Actions	1496	1,553	1612
ANDA Approval Actions (both Tentative and Full Approvals)	467	450	470
Average Review Time from ANDA Receipt to Approval (median in months)	16.3	16.9	17.5
ANDA Supplemental Actions (Labeling and Manufacturing)	4,566	5,406	5,610
OVER-THE-COUNTER DRUG REVIEW			
OTC Monographs Under Development	17	25	20

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actual	FY2006 Estimate	FY 2007 Estimate
OTC Final Monographs Published	8	5	5
BEST PHARMACEUTICALS FOR CHILDREN ACT			
Approved Labels with New Pediatric Information	16	22	22
PATIENT SAFETY			
Adverse Reactions Reports	462,284	508,512	559,364
Percentage of Adverse Drug Reaction Reports Submitted Electronically (% of total)	29%	36%	40%
Percentage of Serious/Unexpected Adverse Drug Reaction Reports Submitted Electronically	51%	66%	75%
Drug Quality Reporting System Report	2,933	3,400	3,500

DRUGS FIELD PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate
Pre-Approval Inspections (NDA)	149	130	130
Pre-Approval Inspections (ANDA)	81	135	135
Bioresearch Monitoring Program Inspections	562	520	520
Drug Processing (GMP) Program Inspections	1,365	1,500	1,440
Compressed Medical Gas Manufacturers Inspections	125	155	150
Adverse Drug Events Project Inspections	106	135	135
OTC Monograph Project Inspections and	11		
Health Fraud Project Inspections [1]	53	45	45
State Partnership Inspections: Compressed Medical Gas Manufacturers Inspections	85	110	110
State Partnership Inspections: GMP Inspections	57	50	50
Total FDA and State Partnership Inspections	**2,594**	**2,780**	**2,715**
Total Domestic Reinspections (Non-add)	**220**	**220**	**220**
Domestic Laboratory Samples Analyzed	1,446	1,735	1,600
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Foreign Pre-Approval Inspections (NDA)	163	180	180
Foreign Pre-Approval Inspections (ANDA)	77	60	60
Foreign Bioresearch Monitoring Program Inspections	85	65	65
Foreign Drug Processing (GMP) Program Inspections	217	195	195
Foreign Adverse Drug Events Project Inspections	10	25	25
Total Foreign FDA Inspections	**552**	**525**	**525**
Total Foreign Reinspections (Non-add)	**17**	**17**	**17**
Import Field Exams/Tests	4,288	4,400	4,400
Import Laboratory Samples Analyzed	1,045	355	300
Import Physical Exam Subtotal	4,850	4,850	4,700
Import Lines	264,559	317,471	380,965
Percent of Import Lines Physically Examined	1.83%	1.53%	1.23%

Note:

1. The OTC Monograph and Health Fraud Inspections will no longer be planned separately in FY 2006.

Office of Orphan Products Development

	FY 2005 Actual	FY 2006 Estimate [1/]	FY 2007 Estimate	Increase or Decrease
Program Level [2/]	$16,959,000	$17,378,000	$17,378,000	0
Grants [3/]	$14,277,000	$14,696,000	$14,696,000	0
Program Administration [4/]	$2,682,000	$2,682,000	$2,682,000	0

1/Includes a 1 percent rescission.
2/The Office of Orphan Products Development is shown for illustrative purposes and is not contained as a separate line item in the All Purpose Tables.
3/The Grants piece is part of the aggregate amount of budget authority contained in the CDER budget line item of the All Purpose Tables.
4/The Program Administration piece is part of the aggregate amount of budget authority contained in the Other Activities budget line item of the All Purpose Tables.

Historical Funding

Fiscal Year	Program Level
2002 Actuals	$13,364,000
2003 Actuals	$16,002,000
2004 Actuals	$15,895,400
2005 Actuals	$16,959,000
2006 Estimate	$17,378,000
2007 Estimate	$17,378,000

Does not include GSA Rent or Other Rent and Rent Related Activities.

Statement Of Budget Request

The Office of Orphan Products Development (OOPD) is requesting $17,378,000 in program level resources for accomplishing the four functional activities of its mission:

- Review and designate qualified drugs and biologics as Orphan Products;
- Review and designate qualified medical devices as a Humanitarian Use Devices;
- Award and administer grants for clinical research studies of promising new orphan drugs, biologics, medical devices and medical foods for rare diseases and conditions; and,
- Outreach to advance the development of orphan products; includes determining whether a request for formal research protocol assistance (research on a treatment for a rare disease) qualifies for consideration.

Program Description

The Orphan Drug Act (ODA) (P.L. 97-414) amended the Federal Food, Drug, and Cosmetic Act, as of January 4, 1983, and established that the Federal government would provide incentives to assist and encourage the identification, development, and availability of orphan drugs. Under the ODA, the law guarantees the developer of an orphan product seven years market exclusivity for a specific indication following the approval of the product by FDA.

Orphan drugs, as defined by the ODA, are drugs for the safe and effective treatment of rare diseases/disorders affecting fewer than 200,000 people in the U.S., or affecting more than 200,000 persons but not expecting to recover development and marketing costs. There are an estimated 6,000 rare diseases that affect more than 25 million people in the U.S.; between 85 and 90 percent of which are serious or life-threatening. Orphan drugs provide important breakthroughs for patients who would otherwise be left lacking therapy. One example is the approval of Fabryzme for the treatment of Fabry's disease, which is a rare life-threatening genetic disease. Another is approval of Orfadin for the treatment of Tyrosinemia, a fatal metabolic disease affecting children.

In 1982, FDA created the Office of Orphan Products Development, which continues to assist the private sector in producing orphan products (drugs, biologics, medical devices, and medical foods) necessary to treat a patient population that otherwise would be considered too small for profitable research, development, and marketing.

Rationale for Budget Request

This request for budget authority supports activities contributing to the accomplishment of program outputs. The request further presents FDA's justification of base resources for FY 2007 and selected FY 2005 accomplishments by strategic goals.

Justification of Base

The Office of Orphan Product Development program is responsible for promoting and advancing the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. The OOPD administers an orphan product designation process, provides research study design assistance to sponsors of orphan products, encourages well controlled clinical studies, and manages clinical research grants program. The OOPD supports FDA's strategic goals by improving the efficiency of translating new discoveries into safe, effective and accessible treatments for patients.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Grants

Orphan product grants are a proven method of successfully fostering and encouraging the development of new safe and effective medical products for rare diseases/conditions in a timely manner with a very modest investment.

Number of New Orphan Product Grants Awarded by Fiscal Year				
2003	2004	2005	2006*	2007*
15	15	15	16	16

* estimated

The table above shows only new grants funded. Grants generally are funded for three years. Typically there are 45 to 60 ongoing grant-funded projects at any one time. So a major portion of the appropriated funds for a given year go towards continued funding of prior approved grants. The rapid increase in the cost of individual clinical trials in recent years has precluded an increase in the number of new grants.

The major grant management activities include:

- Review of solicited grant applications by OOPD staff to ensure program requirements are met.
- Coordinate and convene peer review panels to provide technical review of grant proposals to ensure the best scientific proposals are funded.
- Select grant applications for funding.
- Monitor the grant-funded products to satisfy regulatory and program requirements.

Program Administration

Besides managing the Orphan Grants Program, the OOPD manages an orphan drug designation process, a Humanitarian Use Device designation process, and provides research study design assistance to sponsors of orphan products. The major activities include:

- Review and designation of orphan drug and humanitarian use device[1] designations;

[1] A Humanitarian Use Device (HUD) designation from OOPD is required for a device prior to applying for a Humanitarian Device Exemption (HDE) from CDRH. An HDE for a specific device allows the sponsor to bring the device to market for a very small patient population (less than 4,000 patients per year in the U.S.) after demonstrating the safety and probable benefit of the device.

- Serve as an intermediary between sponsors and FDA medical product review divisions in the drug development process to help resolve outstanding problems, discrepancies, or misunderstandings that often complicate review division/sponsor relationships;
- Provide expertise in clinical trial design and outcome review.

The anticipated workload for the orphan designation requests is expected to continue to increase as noted by the trend in the table below.

Orphan Drug Requests, Designations, and Market Approvals by Fiscal Year					
Activity	**2003**	**2004**	**2005**	**2006***	**2007***
Designation Requests	154	160	187	200	210
Designations	93	102	109	115	120
Market Approvals	15	13	15	15	17

* estimated

HUD Requests and Designations by Fiscal Year					
Activity	**2003**	**2004**	**2005**	**2006***	**2007***
Designation Requests	25	25	13	25	25
Designations	6	6	5	10	10

* estimated

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

OOPD assists patients and advocacy groups on issues addressing rare diseases and orphan products.

- OOPD staff members are trusted sources of expertise in the patient community, which is why OOPD pays special attention to patient support and advocacy groups.
- OOPD staff members respond to many invitations to attend meetings and conferences to speak about the FDA process, Orphan Products Program, and the science of developing a therapeutic product for rare diseases/conditions.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

OOPD continuously strives to improve the efficiency and effectiveness of its IT infrastructure systems used to support it operations and in turn review grant and designation applications in a shorter amount of time. Current ongoing initiatives include:

- Efforts to modernize the transmission of applications and other review information through full electronic submissions and paperless reviews for quicker designation and grant application reviews.

- Improvements to the OOPD database system for more efficient and effective retrieval of information and other internal management practices.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

OOPD continues to encourage the development of therapies for rare diseases by administering the Orphan Drug Act and other programs that provide incentives to companies willing to develop drugs, biologics, medical devices, and medical foods for rare diseases.

Program Administration

- *Orphan Drug Designations:* Of the 1,539 orphan designations issued by OOPD, as of December 30, 2005, 282 have resulted in marketing approval with orphan exclusivity. Since the Orphan Drug Act passed in 1983, more products are now available to treat a potential patient population of more than 14 million Americans. In contrast to this current pace of designating orphan drugs to treat rare diseases, and subsequent market approval, the decade prior to 1983 saw fewer than 10 such products come to market.

  The number of Orphan Product designation applications continues to increase dramatically. In FY 2005, there were 187 applications, a record number, representing a 40 percent increase over the average (133/year) of the prior four years. These include potential treatments for many kinds of cancers, Crohn's Disease, cystic fibrosis, and tuberculosis. In FY 2005, 109 drugs were designated and 15 orphan designated drugs were approved for marketing. These numbers are expected to increase in future years as more new drugs are developed that are targeted at specific genetic disorders.

List of FY 2005 Orphan Product Approvals

Sponsor	Generic Name	Trade Name	Indication
Serono Laboratories, Inc.	Recombinant human luteinizing hormone	Luveris	For use in association with recombinant human follicle stimulating hormone for the treatment of women with chronic anovulation due to hypogonadotropic hypogonadism.
Medicis Pharmaceutical Corp.	benzoate/phenylacetate	Ammonul	Treatment of acute hyperammonemia and associated encephalopathy in patients with deficiencies in enzymes of the urea cycle.
Schering-Plough	temozolomide	Temodar	Treatment of malignant glioma

Research Institute			
Genzyme Corporation	clofarabine	Clolar	Treatment of acute lymphoblastic leukemia
DynPort Vaccine Company LLC	Vaccinia Immune Globulin (Human) Intravenous		Treatment of severe complications from the smallpox vaccine
Mutual Pharmaceutical Company, Inc.	Quinine Sulfate		Treatment of Malaria
CoTherix, Inc.	Iloprost inhalation solution	Ventavis	Treatment of pulmonary arterial hypertension
Tercica, Inc.	Mecasermin	Increlex	Treatment of growth hormone insensitivity syndrome
BioMarin Pharmaceutical, Inc.	N-acetylgalactosamine-4-sulfatase, recombinant human	Galsulfase	Treatment of mucopolysaccharidosis Type VI (Maroteaux-Lamy syndrome)
Bausch & Lomb Pharmaceutical Company, Inc.	Fluocinoline	Retisert	Treatment uveitis involving the posterior segment of the eye
Boehringer Ingelheim Pharmaceuticals, Inc.	Mexloxicam	Mobic	Treatment of juvenile rheumatoid arthritis
Millennium	Bortezomib	Velcade	Treatment of multiple myeloma with prior therapy
DynPort Vaccine Company, Inc.	Vaccinia Immune Gobulin (Human) Intravenous		Treatment of severe complications from the smallpox vaccine
Novo Nordisk, Inc.	Coagulation factor VIIa (recombinant)	NovoSeven	Treatment of bleeding episodes in patients with congenital factor VII deficiency
Novo Nordisk, Inc.	Coagulation factor VIIa (recombinant)	NovoSeven	Prevention of bleeding episodes in patients with hemophilia A or B, with or without inhibitors
Novo Nordisk, Inc.	Coagulation factor VIIa (recombinant)	NovoSeven	Prevention of bleeding episodes in patients with congenital factor VII deficiency

- Updated regulations for designating orphan products were drafted in order to produce more consistent, understandable, and predictable outcomes, which benefits sponsor companies who invest in developing these products.

- *Humanitarian Use Device (HUD) Designations:* Since the HUD regulations took effect in October 1996, OOPD has received 163 applications and designated 109 devices. Of the 109 designated devices, 39 have been approved for an Humanitarian Device Exemption. In FY 2005, 13 HUD applications were received and 6 of these have been designated, including a monitor for phenylalanine in the blood.

- *Outreach:* In FY 2005 OOPD continued its outreach activities to increase the feasibility and level of sponsor interest in orphan products development. For example, in FY 2005 presentations were made at the:
    - University of Salerno (Italy) on the development of drugs for rare diseases emphasizing in enzyme replacement therapy as a result of the U.S. Orphan Drug Act.
    - University of California, Irvine (UCI), to discuss development of orphan products through a joint venture between the Octane Group and UCI.

    OOPD staff members also met with representatives of the European Union, Japanese government, and Australian government and their rare disease groups regarding their orphan product programs.

- *Facilitation:* OOPD acts as a facilitator for small companies in their dealings with various FDA centers. For example, in FY 2005 a presentation was made to MannKind Corporation and other small biotech firms who are interested in developing orphan products.

<u>Grants</u>

OOPD supported new and continuing extramural research projects that test the safety and efficacy of promising new drugs, devices, and medical foods for rare diseases and conditions through human clinical trials. OOPD conducted site visits to grantees to ensure extramural funded studies, which involve human subjects, are consistent with grant agreement terms and minimize FDA's exposure to risk of violations in human subject protection requirements. A peer review process was used to select the highest quality scientific research projects.

- The $14.696 million appropriated in FY 2006, an increase of $419,000 over FY 2005, for research will be used to fund 11 to 14 new grants and maintain approximately 60 ongoing grant-funded clinical study projects. The number of grants awarded has been decreasing year-by-year as a result of continued increases in the cost of clinical trials.
- In FY 2005, there were 89 grant applications received. Although the number of grants awarded is slowly declining, the number of applications to be reviewed and scored has steadily increased since 2000.
- Since its inception, 40 orphan products have been approved using data obtained from OOPD grants. Most recent was an expandable rib prosthesis for previously fatal thoracic insufficiency syndrome in children.
- Another benefit from the OOPD grant funded studies has been the hundreds of publications in peer-review journals that has come about that have changed the state of medical care for Americans with rare diseases/conditions.

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

OOPD partnered with other HHS organizations and national and international non-governmental organizations to increase awareness and create similar orphan product development programs in other countries. For example, presentations were made at the:

- Israel Medical Association Conference to discuss orphan product legislation in Israel.
- First International Conference on Rare Diseases and Orphan Drugs in Stockholm.
- Tenth Asian European Workshop on Inborn Errors of Metabolism in Egypt.

OOPD increased patient and provider awareness of available orphan products. For example, presentations were made at the:

- Annual Meeting of the Society of Inherited Metabolic Disorders.
- International Federation of Associations of Pharmaceutical Physicians on the topic: Orphan Drugs: Current Issues and Activities.
- Annual Meeting of the National Organization for Rare Diseases.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

In FY 2005, OOPD made improvements to the OOPD database, which is used to effectively and efficiently review applications for orphan and humanitarian device designations, grant applications, and funded grants. Improvements included:

- Linking Business Objects software for easy data mining.
- Improving compatibility with the IMPAC II grants management system managed by the National Institutes of Health.

OOPD is also working on the Critical Path Initiative and FDA's contractor, C-Path, to enhance the methodology using orphan drugs programs as a prototype for faster drug development without compromising safety and efficacy.

BIOLOGICS PROGRAM

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Total Program Level	**$170,684,000**	**$195,492,000**	**$210,000,000**	**14,508,000**
Center	*$143,030,000*	*$165,177,000*	*$177,934,000*	12,757,000
FTE	*818*	*876*	*898*	22
Field	*$27,654,000*	*$30,315,000*	*$32,066,000*	1,751,000
FTE	*223*	*227*	*235*	8
Total Program Level FTE	**1,041**	**1,110**	**1,167**	**57**
Budget Authority	**$123,109,00**	**$139,016,000**	**$150,582,000**	**11,566,000**
Pandemic Preparedness	*$4,735,000*	*$24,793,000*	*$39,713,000*	*$14,920,000*
FTE			*159*	*56*
Tissues			*$2,475,000*	*$2,475,000*
FTE			*18*	*18*
Cost of Living			*$1,937,000*	*1,937,000*
Strategic Redeployment			*($7,766,000)*	*($7,766,000)*
FTE			*(30)*	*(30)*
Budget Authority FTE	**768**	**836**	**880**	**44**
User Fees:	**$47,575,000**	**$56,476,000**	**$59,418,000**	**2,942,000**
PDUFA	*$42,218,000*	*$47,675,000*	*$49,869,000*	2,194,000
FTE	*250*	*242*	*252*	10
MDUFMA	*$5,357,000*	*$8,801,000*	*$9,549,000*	748,000
FTE	*23*	*32*	*35*	3
User Fee FTE	**273**	**274**	**287**	**13**

[1/] *Includes a one percent rescission.*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
2003 Actual	$193,436,000	$145,318,000	$48,118,000	1,229
2004 Actual	$148,391,000	$103,537,000	$44,854,000	1,064
2005 Actual	$170,684,000	$123,109,00	$47,575,000	1,041
2006 Enacted	$195,492,000	$139,016,000	$56,476,000	1,110
2007 Estimate	$210,000,000	$150,582,000	$59,418,000	1,167

Statement of Budget Request

The Biologics Program is requesting $210,000,000 for its mission activities including:

- To ensure the safety, efficacy, potency and purity of biological products including vaccines, cells, tissues, gene therapies, and related drugs and devices intended for use in the prevention, diagnosis and treatment of human diseases, conditions or injuries;

- To ensure the safety of the Nation's supply of blood and blood products;

- To evaluate the safety and effectiveness of biological products before marketing, and monitor the pre-clinical and clinical testing of new biological products;

- To license biological products and manufacturing establishments, including plasmapheresis centers, blood banks, and vaccine and biologic product manufacturers; and,

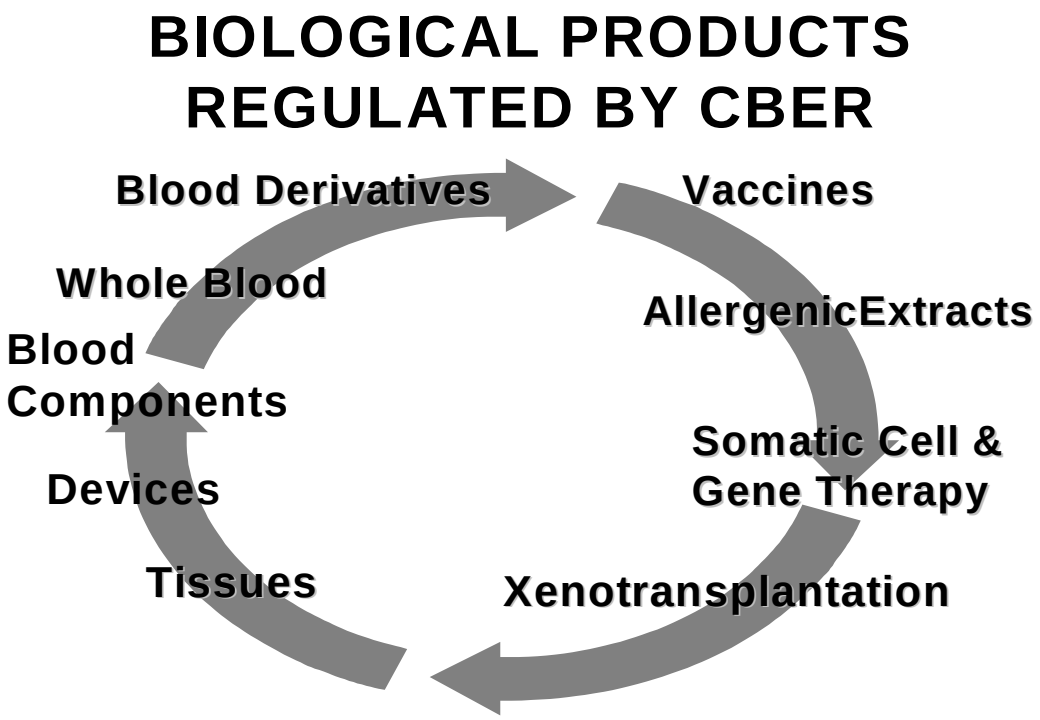
- To conduct regulatory research to establish product standards and develop improved testing methods.

Program Description

The Biologics Program is responsible for addressing regulatory challenges related to ensuring the safety and efficacy of a wide range of biologic products including: blood and blood products, human tissue, cell and gene therapies, vaccines, and allergenic products. The products regulated by the Center for Biologics Evaluation and Research (CBER) touch the lives of people everyday. Some examples include: over 14 million units of blood and blood components transfused yearly in the U.S.; more than 235 million vaccinations administered; and greater than one million human tissues transplanted last year. In addition, there were over 800 active human trials studying experimental cell and gene therapies, vaccines, and blood products for serious diseases such as HIV, cancer, diabetes and heart disease.

The Office of Regulatory Affairs (ORA) Field staff supports CBER by conducting premarket activities such as: bioresearch monitoring of clinical research, preapproval inspections and laboratory method validations needed for application decisions, and inspecting manufacturing facilities to ensure their ability to manufacture the product to the specifications stated in the application. ORA also conducts risk-based domestic and foreign postmarket inspections of medical products to assess their compliance with Good Manufacturing Practice requirements.

In addition to overseeing regulated products on a surveillance or “for cause” basis, ORA staff also respond to emergencies and investigate incidents of product tampering, terrorist events and natural disasters. To complement the regular field force, the Office of Criminal Investigations investigates instances of criminal activity in FDA regulated industries. In FY 2006, ORA will expend an estimated $30,315,000 in support of the Biologics Program.



Performance Analysis

During the latest completed performance period, (FY 2004), the Biologics Program successfully achieved all seven performance targets. So far, the Biologics program successfully achieved the only FY 05 target that has data available. The Biologics program expects to meet the other six targets when data becomes available later in FY 2006. For more information about these performance goals and results, please see the Performance Detail section.

The performance targets for implementing the Prescription Drug User Fee Act (PDUFA III) are very high. To sustain these ambitious targets, adequate funding must be assured.

Performance Highlight:

FY 2007 Goal Target	FY 2004 Results	Context
Review and act upon 90% of standard original PDUFA NDA/BLA submissions within 10 months; and review and act on 90% of priority original PDUFA NDA/BLA submissions within 6 months of receipt.	Since 1994, FDA has met or exceeded the performance goals of completing review and action on 90% of standard original PDUFA NDA/BLA submissions within 10 months; and reviewing and acting on 90% of priority original PDUFA NDA/BLA submissions within 6 months of receipt	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

Program Resource Changes

Budget Authority

Pandemic Preparedness (Influenza) + $ 14,920,000 and + 56 FTE
FDA plays a unique and vital role in the Nation's preparedness for an influenza pandemic. We facilitate the development and availability of safe and effective vaccines in the event of an outbreak of an influenza pandemic.

FDA is requesting resources for an enhanced and sustained preparedness effort to:

- Facilitate rapid development, evaluation and availability of new influenza vaccines to prepare for a pandemic, including using new technologies such as cell culture and recombinant production, as well as antigen sparing approaches.
- Provide extensive outreach and training in manufacturing quality. Conduct timely and efficient inspections of manufacturing facilities to assure product quality and prevent problems that threaten safety or availability of products essential to respond to the pandemic threat. Assure that vaccines meet manufacturing and testing specifications and build sufficient surge capacity for such evaluation.
- Monitor the safety and effectiveness of vaccines administered to patients using improved information technology systems, electronic reporting mechanisms and analytic tools to identify vaccine safety signals.
- Through reverse genetics and other emerging technologies, prepare a library of pandemic influenza virus high growth reassortants (seed strains) and needed reagents for rapid response and manufacturing when a pandemic strikes.
- Assure that all strains and reagents used for manufacturing are high quality, safe and suitable for high-yield, large-scale manufacturing.
- Promote international regulatory cooperation, harmonization and information sharing in vaccine evaluation and safety activities.

Human Tissues Safety: + $ 2,475,000 + 18 FTE
FDA is implementing a new, risk-based approach to assure the safety of the human cells, tissues, and cellular and tissue-based products (HCT/Ps) used for human tissue transplants. This initiative will allow FDA to address issues related to safety and effectiveness of a rapidly growing industry.

The FDA has finalized three new rules that give the Agency more authority and oversight over a broader range of tissues and the establishments that process them. The rules also expand on the communicable diseases that are checked for, and they strengthen procedural and recordkeeping requirements for facilities that handle tissues. The three rules concern registration and listing, donor eligibility, and good tissue practices related to HCT/Ps. The Agency has tailored the regulations to the degree of risk posed by each product.

This initiative will fund monitoring and follow-up of adverse events and deviation reports, inspections of HCT/P establishments, guidance for the tissue industry and outreach activities. The human tissue safety initiative is funded at $2.5 million. This request includes $1.237

million, 8 FTE for the Center for Biologics Evaluation and Research and $1.238 million, 10 FTE for the Field portion supporting CBER.

Cost of Living-Pay: + $1,937,000
FDA's request for pay inflationary costs is essential to accomplishing its public health mission. Payroll costs account for over sixty-percent of our total budget, and the Agency is no longer able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Biologics portion of this increase is $1,937,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Biologics Reductions -$7,766,000 and -30 FTE
To fund FY 2007 priority initiatives such as Pandemic Preparedness and the Human Tissues Initiative, FDA re-deployed resources from base programs. To accomplish this strategic redeployment and fund new, high priority initiatives, CBER reductions include: guidance development, early interactions with sponsors, non-emergency communications and outreach, activities related to blood and to cell and gene therapy products, and certain related post-market, safety, research and international harmonization activities.

User Fees

Prescription Drug User Fee Act: +$2,194,000 and +10 FTE
PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These fees expand the resources available for the process of reviewing human drug applications including reviewers, information management, space costs, acquisition of fixtures, furniture, equipment and other necessary materials so that safe and effective drug products reach the American public more quickly. In 2002, the Bioterrorism Act included reauthorization 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 (PDUFA III). The reauthorization directs FDA to strengthen and improve the review and monitoring of drug safety; consider greater interaction with 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. The increases will contribute to meeting these mandated directives. In FY 2007 FDA will work with Congress on the reauthorization of the Prescription Drug User Fee Act. This increase of $2,194,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Medical Devices User Fee and Modernization Act: +$748,000 and + 3 FTE
The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amends the Federal Food, Drug, and Cosmetic Act to provide FDA important new responsibilities, resources, and challenges. MDUFMA was signed into law October 26, 2002 and was amended by the Medical Device User Fee Stabilization Act of 2005. MDUFMA has three particularly significant provisions. These provisions allow for the collection of user fees for

premarket applications, allow establishment inspections to be conducted by third parties and place new regulatory requirements on reprocessed single use devices. The revenues from these fees, and the appropriated trigger amounts will allow FDA to pursue a set of ambitious performance goals that will provide patients earlier access to safe and effective technology, and will provide more interactive and rapid review to the medical device industry. In FY 2007 FDA will work with Congress on the reauthorization of the Medical Device User Fee and Modernization Act. This increase of $748,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Proposed User Fees (Reclassified as Mandatory): (Non-Add)

Reinspection User Fee (Mandatory): + $410,000 and + 3 FTE (Non-Add)
The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an estimated amount sufficient to fund the FY 2007 reinspections. The Field – Office of Regulatory Affairs component of this user fee is $410,000 and 3 FTE.

Justification of Base

Protecting and promoting the public health in the 21st Century is a great responsibility. Mastering it requires meeting some unprecedented challenges: attracting and retaining the most talented scientists; utilizing dynamic and responsive regulation to reduce risks; promoting quick access to needed new medical technologies that are safe and effective; assuring the continuing safety and availability of regulated products; helping consumers get true and useful information about the products they use; and facilitating quick responses to the challenges of bioterrorism as well as emerging infectious diseases. The Biologics Program will continue to play both a facilitating and a leadership role in meeting these challenges, including seeking input from and having effective collaboration with our partners.

The Biologics Program also is responsible for addressing regulatory challenges related to ensuring the safety and efficacy of biological products. Meeting these challenges successfully will require knowledge and utilization of scientific advances in areas such as proteomics, genomics and gene therapies, xenotransplantation, new vaccine technologies and delivery methods, and novel cellular and tissue therapies. In these and other areas, CBER research, often in collaboration with others, helps to identify opportunities to advance new and emerging technologies, and provide needed standards, assays and models to better measure and assure product safety, efficacy and consistency. These contributions move innovative products more rapidly along what has been termed the “critical path” to availability for patients who can benefit from them, consistent with FDA’s Critical Path Research Initiative (http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.pdf).

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

FDA enables consumers to make smarter decisions by getting them better information to weigh the benefits and risks of FDA-regulated products.

Communications with Stakeholders and Consumers

In order to carry out our mission, FDA regularly consults with experts in science, medicine, and public health, and collaborates with healthcare providers, consumers, and industry. Furthermore, FDA is enhancing communication methods to mitigate the risks due to the lack of accurate and timely information to the public about a biologic product. In pursuit of this objective FDA:

- Collaborates with scientists to support regulatory decisions by assessing risks associated with regulated products; sets standards that minimize risk and tests products against those standards; improves the usefulness and precision of risk assessment methods; and develops methods to increase the accuracy of sample analysis and detection of biological substances.

- Provides information on research projects and scientific articles emphasizing the importance of our regulatory research as mission critical work underpinning regulatory decisions.

- Provides access to new guidance documents, safety information and the opportunity to discuss important issues with Agency experts at numerous trade associations, scientific, and community meetings.

- Maintains outreach with industry and provides training as required by FDAMA and the Small Business Regulatory Enforcement Fairness Act.

FDA seeks continuous improvements in patient and consumer safety by reducing risks associated with FDA-regulated products. FDA's work on medical errors and SARS are examples of efforts in this area.

Medical Errors

The prevalence of avoidable health complications involving the use of FDA-regulated products presents a challenge for the Biologics Program. Our central public health role is to help ensure that biologic products are safe and effective. Therefore, we must ensure that quality standards are adhered to by the various biological product establishments by:

- Conducting product safety biomedical research in areas such as new cells used to produce drugs and biologics; rapid advances in technology and the evolving HIV pandemic necessitate the need to use new types of cell substrates and to develop new assays and assess the reliability of current assays used to monitor product safety.

- Developing new, specific and sensitive techniques and assays to validate and detect a greater variety of known potentially infectious viruses.

- Enhancing vaccine and biologic safety surveillance through implementation of ongoing programs of cutting edge technology; including increasing use of healthcare databases.

- Maintaining the system of post-market surveillance and risk assessment program to identify adverse events that did not appear during the product development process by collecting, evaluating and acting on information of Adverse Event Reports (AERS) associated with marketed products.

- Sustaining reporting systems to collect biological product deviation events that occur during manufacturing processes or storage of biological products.

- Establishing contracts for safety monitoring data links that include product exposure and extensive patient information To enhance FDA's ability to monitor public health impact, the Agency is developing access to external databases with other government agencies, states, academia and independent health organizations such as hospitals.

Counterterrorism

The Agency's strategic goal to "Protect America from Terrorism" focuses on preparation and response to a terrorist attack on the U.S. population. FDA plays a crucial role in protecting the public health by ensuring the availability of safe and effective medical countermeasures for mitigating the public health consequences of a bioterror event.

The Biologics Program is responsible for regulating the development and licensure of new biological products including vaccines, blood products including antisera for diseases such as botulism and anthrax, human tissues, cells and gene therapies. By working closely with industry and government agencies, FDA helps to assure an adequate supply of these products, which include immunization against anthrax, smallpox and other bio-threats that might be used by terrorists as well as products to treat burn, blast and trauma injuries. FDA also collaborates closely with other federal agencies to develop protocols, conduct animal studies, and define reference databases on treatment and alternative therapies for infectious diseases caused by the intentional use of biological agents. FDA also monitors adverse events to identify patterns of significant reactions to these new vaccines. Finally, support has been increased for the protection of regulated products from contamination and tampering to ensure availability of products. More specifically, the Biologics Program works to:

- Ensure the safety and efficacy of biological products, including vaccines, blood and blood products, and diagnostic countermeasures to support the development, maintenance and deployment of stockpiles of medical countermeasures.

- Help ensure that sufficient quantities of medical products are available; and implement post-event follow-up and data collection for these products, some of which are investigational.

- Conduct and support active applied research programs directed toward optimizing the availability of safe and effective new products for the treatment, prevention or cure of diseases in humans.

- Evaluate the types of non-clinical data that may be acceptable for product licensure if pre-licensure clinical studies are not feasible or ethical.

- Evaluate over 100 active investigational new drug applications on products under development for use either to mitigate or prevent the pathological effects of terrorism-related pathogens in humans.

- Participate in activities to facilitate the availability of the currently approved vaccine for anthrax; and continue counterterrorism activities associated with the development of new smallpox and anthrax vaccines; vaccines for plague, tularemia, and Venezuelan Equine Encephalitis, as well as other encephalitis-causing viruses.

- Monitor production of biologics from the early stages all the way through post marketing with lot release testing to ensure the individual lots continue to meet safety, purity, potency and efficacy requirements.

Science Based Review

CBER's Critical Path research program ensures efficient evaluation of the safety, efficacy and manufacturability of complex biological products that are aimed at prevention or treatment of life-threatening diseases.

CBER science based evaluation aimed at ensuring safety and efficacy of complex biological products for the public encompasses:

- Development, evaluation and application of formal risk assessments and methods to develop risk reduction strategies for licensed products, e.g., protecting the blood supply from TSE (Mad Cow Disease) and from vaccine-associated adverse events.

- Continuing evaluation of vaccine safety after licensure by identifying and studying adverse events in patients receiving these products in the clinical setting, e.g., rotavirus and intestinal disease, pneumococcal vaccine allergic responses, influenza vaccine/meningitis vaccine and neurological diseases.

- Development and evaluation of tests to better predict the protective response to biodefense vaccines, e.g., smallpox, botulism, anthrax.

- Development and evaluation of biomarkers for product efficacy and to support personalized medicine, e.g., better targeting of vaccines, and blood products for hemophilia.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Base resources will be used to conduct science-based risk management in all Agency regulatory activities so that the Agency's resources can provide the most health promotion and protection at the least cost to the public. These activities include the efforts discussed below.

Gene Therapy

One of the most exciting and highly publicized areas in biomedical research today is human gene therapy – the replacement of a person's faulty genetic material with normal genetic material to treat or cure a disease or abnormal medical condition. Over time and with proper oversight, this may become an effective weapon in modern medicine's arsenal to help fight diseases such as cancer, diabetes, high blood pressure, heart disease and other genetic disorders.

Since FY 2000, FDA has received over 489 requests from medical researchers and manufacturers to study gene therapy and to develop gene therapy products. Presently, FDA is overseeing approximately 249 active investigational new drug gene therapy studies.

Human Cells, Tissues and Cellular and Tissue Based Products

The term "human cells, tissues, and cellular and tissue-based products (HCT/P's)" covers many products transplanted for medical uses, such as skin replacement following severe burns, tendons and ligaments to repair injuries, bone replacement, and corneas to restore eyesight. In this rapidly growing industry, the number of musculoskeletal tissue transplants increased from approximately 350,000 in 1990 to over 1 million conducted annually. Over the past decade advancing technology and improved techniques have expanded the therapeutic uses of tissue-based products.

FDA seeks to accomplish three primary goals with respect to human tissues while not discouraging the development of new products: (1) to prevent the spread of communicable diseases; (2) to ensure that safety and efficacy are demonstrated for cellular and tissue-based products that are also drug, biological, and medical device products; and, (3) to help enhance public confidence in these products so that, where appropriate, they can fulfill their great potential for improving and saving lives.

Pandemic Influenza

Preparation for the next pandemic of influenza requires action in the inter-pandemic period, including the production of vaccines, which is unique among vaccine products in that the viruses are changed on a frequent basis and the time available for making and distributing each year's new vaccine is fixed at 6 to 8 months. CBER scientists:

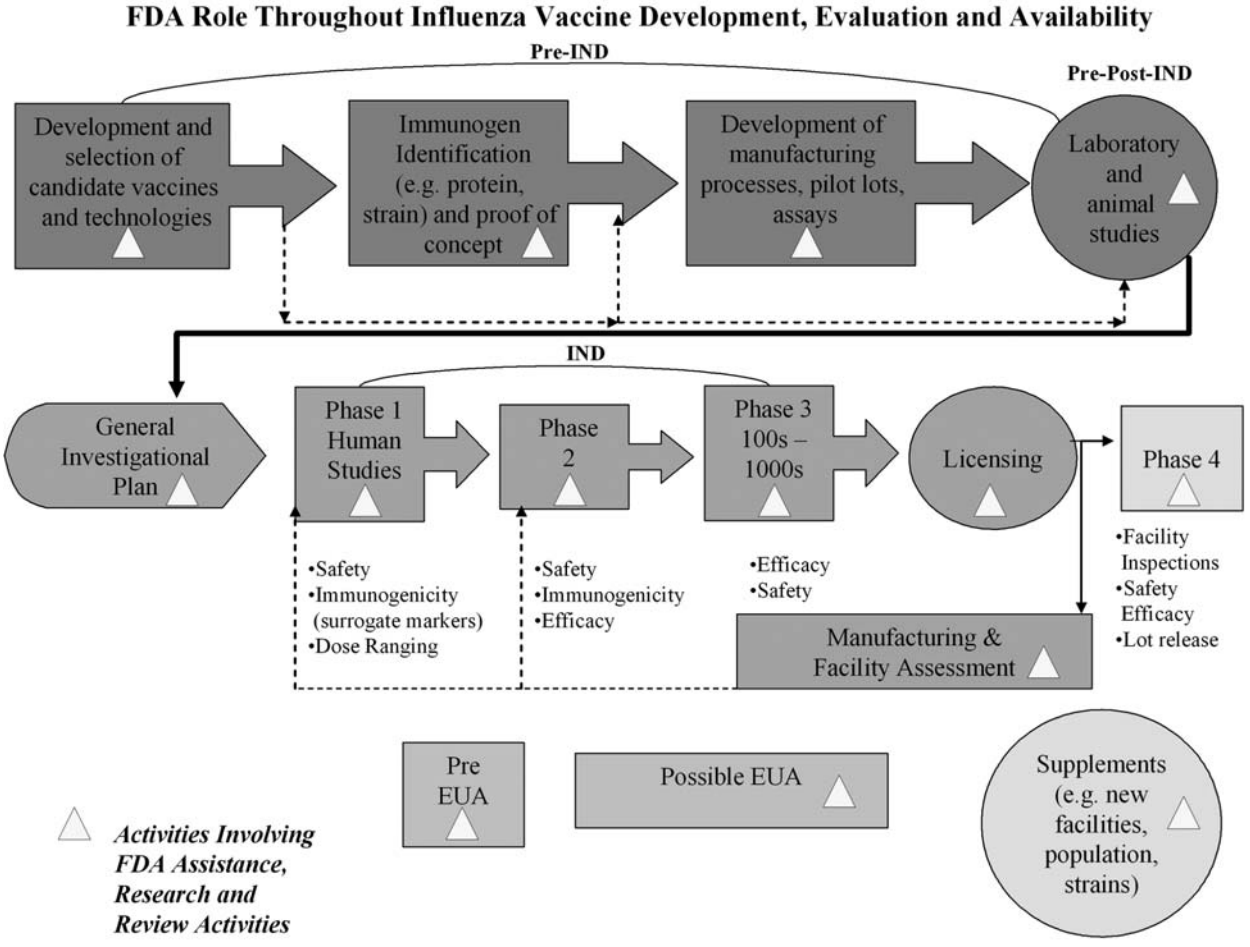
- Actively advise national and international public health groups such as WHO, CDC, NIH, and the National Vaccine Program Office on selecting new influenza viruses to be used in annual vaccine production and in preparing for an influenza pandemic..

- Review extensive manufacturing and clinical information, and conduct several inspections of the manufacturing facilities of additional sponsors of influenza vaccine INDs. ;

- Actively engage with sponsors and manufacturers interested in developing new technologies for influenza vaccine manufacture, including cell-based and recombinant vaccines, in addition to interacting closely and proactively with the four currently licensed influenza vaccine manufacturers, Chiron, GSK, Aventis Pasteur and MedImmune on a variety of issues related to their vaccine manufacturing.

- Expedite lot release of influenza vaccine through the manufacturing time period; the process of manufacturing these vaccines is very complex, and is complicated by the large number of doses administered in a very short time frame.

- Work with manufacturers throughout the year to collect information on the capability of new influenza viruses to be used for large-scale production.



Blood Safety

The blood supply is a critical underpinning of our Nation's health care system and of our emergency preparedness. Our U.S blood system continues to be the world's safest. FDA's goal is to ensure this remains true by minimizing the risk of infectious disease transmission and other hazards. FDA continues to strengthen efforts to protect the blood supply, and to minimize any emerging risk to patients of acquiring HIV, hepatitis, Creutzfeldt-Jakob Disease (CJD), the human form of Mad Cow Disease, West Nile Virus (WNV) and other emerging blood-borne diseases, including potential agents of bioterrorism. These efforts include:

- Promulgating and enforcing standards for blood collection and for the manufacturing of blood products, including transfusible components of whole blood, pharmaceuticals derived from blood cells or plasma, as well as related medical devices and screening tests.

- Facilitating the development and review of innovative products to improve blood safety and availability such as new immunoglobulin and clotting factors, new methods to preserve blood cells and related products, artificial blood substitutes, new blood testing and safety technologies, as well as improved HIV tests for blood and for public health screening.

- Updating existing guidance so it is consistent with new scientific information and eliminate guidance documents where enforcement is either no longer required or not practical.

- Addressing emerging infectious diseases by ensuring compliance of plasma fractionation establishments, blood donor/recipient notification and look back, and FDA emergency and Class I recalls affecting blood safety response procedures.

- Responding to emerging potential threats to the blood supply, such as WNV, SARS, HIV variants; new hepatitis agents; human herpes virus-type 8; and CJD, in a timely and coordinated approach. For example, under the Medical Device User Fee Act FDA has dramatically shortened review times for blood related devices, many of which help test blood or otherwise assure its safety and availability.

- Emphasizing the need to protect the nation's blood supply, and minimizing any risk of acquiring the human form of BSE, CJD, and other blood-borne diseases.

Through enhanced testing and other improvements in blood safety, the risk of transmission of viruses such as HIV, and hepatitis B and C through blood transfusion has been dramatically reduced. The risks of HIV and of HCV have been reduced from 1/100 units in the 1980's to less than 1-in-a-million at present.

Postmarket Monitoring

FDA engages in activities to ensure the continued quality and safety of previously approved biologic products. Because these products are derived from living organisms, they do not have the same manufacturing consistency as pharmaceutical products derived from chemical combinations. FDA must engage in post-approval activities to develop and validate test methods and establish standards for biological products.

Imports, Import Monitoring and Foreign Inspections

The explosion in the number of imports combined with the security concerns raised by terrorism and counterfeiting incidents has increased the need to physically assess the status of imported products, including biologics, as part of the Agency's emerging import strategy. Base funding will enable FDA to improve the safety of imported and domestic biological products and tissues by increasing the surveillance of human tissues and biological products and coordinate domestic field investigational analytical compliance activities.

Prescription Drug User Fee Act (PDUFA)

The Biologics Program has met or exceeded most of its PDUFA performance goals from FY 1994 through 2004. The BT Act reauthorized 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 reauthorization is 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 with sponsors during the review of drugs and biologics intended to treat serious and life-threatening diseases; and, develop principles for improving first-cycle reviews. Review performance monitoring is being done in terms of fiscal-year cohorts. The FY 2006 cohort performance goals include:

- Complete review and action on 90 percent of standard original NDA/BLA submissions within 10 months; and complete review and action on 90 percent of priority original NDA/BLA submissions within six months of receipt.

- Complete review and action on 90 percent of standard efficacy supplements within 10 months; and complete review and action on 90 percent of priority efficacy supplements within six months of receipt.

- Complete review and action on 90 percent of manufacturing supplements within six months of receipt; and complete review and action on 90 percent of manufacturing supplements requiring prior approval within four months of receipt.

- Complete review and action on 90 percent of Class 1 resubmitted original applications within two months; and complete review and action on 90 percent of Class 2 resubmitted original applications within six months of receipt.

Science Based Review

The Center for Biologics Evaluation and Research (CBER) has an experienced staff of research-regulators with expertise in complex biological product evaluation science who works with product sponsors, scientific experts and the public to resolve challenges in development of complex biological products (e.g., vaccines for adults and children, blood and blood products and cell, tissue and gene therapies). CBER science based evaluation activities aimed at ensuring safety and efficacy of complex biological products for the public:

- Improve access to life-saving blood products for trauma victims by developing and evaluating animal and cell-based tests for the safety of blood substitutes.

- Evaluation and qualification of biomarkers predictive of medical product safety to streamline clinical trials and support personalized medicine, e.g., of cancer or autoimmune risk following cellular therapies and of enhanced disease following tuberculosis vaccination.

- Development and evaluation of animal and cell-based models of disease used to predict the safety of gene therapy vectors, e.g., adenovirus gene vector-associated lung disease.

- Ensure safety and availability of the blood supply by evaluating improved blood donor testing kits for detection of malaria and other parasites.

- Development and evaluation of animal and cell-based models of disease used to test the efficacy of vaccines for biodefense, e.g., anthrax, plague, smallpox, ebola.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Science Based Review

CBER science based evaluations develop and evaluate the scientific tools needed to maintain and improve the safety, efficacy and manufacturing quality of the licensed products, and to support efficient and effective evaluation of the novel products that are the fruit of the biotechnology research boon. CBER scientific evaluation activities:

- Ensure that better products reach the patient faster by modernizing and streamlining rapid tests of product quality, e.g., moving from animal-based to non-animal based vaccine potency testing, genomics microarray testing of biodefense vaccines.

- Develop and evaluate tests for contamination of complex biological products, including TSE (Mad Cow Disease), viruses, bacteria in blood, vaccine and cell therapies.

- Evaluate methods to improve consistency of manufacturing and reduce shortages of medical products, e.g., complex protein-carbohydrate meningitis vaccines.

- Develop and evaluate reference standards for biological products, including vaccines such as influenza and blood donor test kits.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

The Agency strategic goal, "Improving FDA's Business Practices," focuses on the critical infrastructure that provides scientific support and administration to FDA's programs. This will ensure a world-class professional workforce, effective and efficient operations, and adequate resources to accomplish the Agency's mission. The managerial and operational efficiencies being pursued under this goal are aligned with the President's Management Agenda, the Secretary's priority of strengthening management by creating a more streamlined, cost-effective, and accountable organization, and the DHHS strategic goal to achieve excellence in management practices.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

West Nile Virus (WNV)

In 2002, FDA and CDC, working together, identified transmission of WNV by blood transfusion. In response, FDA encouraged the development of investigational WNV Nucleic Acid-based Test (NAT) as screening tests and facilitated the widespread study of these investigational tests by blood establishments. Beginning in July 2003, investigational WNV NAT was available throughout the country to screen the blood supply in a minipool format, and more than 95% of the blood supply was tested. In 2005, WNV continued to spread across the lower 48 continental states with about 2,300 cases of WNV illness and 66 deaths reported in the general population. Blood screening for WNV detected more than 350 viremic donors and prevented their donations from entering the blood supply. No cases of transfusion-transmitted WNV were reported in 2005.

Counterterrorism

FDA plays a crucial role in protecting the public health by ensuring the availability of safe and effective medical countermeasures for mitigating the public health consequences of a bioterror event. The Agency's responsibility is to regulate the development and licensure of new biological products, including vaccines, blood and blood products, human tissues and cells and gene therapies. FDA also collaborates closely with other federal agencies, such as DOD, NIH, and CDC to develop protocols, conduct animal studies, and define reference databases on treatment and alternative therapies for infectious diseases caused by the intentional use of biological agents. Major counterterrorism activities during FY 2005 included:

- Issued draft guidance on July 5, 2005 CBER issued addressing FDA's policies for authorizing the emergency use of medical products.

- Issued a direct final rule and accompanying guidance for revision to allow for greater flexibility when manufacturing with spore-forming microorganisms in the production of vaccines and counter-terrorism products.

- Approved two Biologic License Applications (BLAs) for Vaccinia Immune Globulin (VIG), one for DynPort Vaccine Company LLC in February 2005 and the other for Cangene Corporation in May 2005. Both were granted priority review and approved under the accelerated approval mechanism in the regulations.

- CBER reviewed and recommended the authorization of Emergency Use Authorization (EUA) of Anthrax Vaccine Adsorbed for persons in the military at high risk of exposure to a possible attack with anthrax.

- CBER provided extensive support through reviewing and providing technical input on multiple Requests for Proposals for acquisition of additional countermeasures for the SNS (anthrax therapeutics, new smallpox vaccines, botulinum antitoxin, neuropenia), providing information regarding the types of data needed to consider use of unapproved countermeasures under an EUA, and participating in the Project Coordination Team efforts for the first contract awarded under Project Bioshield to VaxGen for Recombinant PA (rPA) Anthrax Vaccine.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

In alignment with the Agency's Critical Path Initiative, the Biologics Program employs science-based approaches to solve current problems and anticipate future barriers to biologics product development and licensure. The Program strives to identify and work collaboratively to develop the scientific knowledge and tools to determine the safety and efficacy of products.

Cell and Gene Therapy: Outreach and Partnerships

The Biologics Program has provided proactive scientific and regulatory guidance in areas of novel product development. Openly communicating regulatory expectations and encouraging dialogue on points of cutting edge product development helps define the best scientific approaches and reduces product development time and risk. Focusing on how to best evaluate the most important issues in safety and efficacy helps avoid unnecessary regulatory burdens. In addition, engaging and supporting broad public interactions helps FDA and product developers to better address difficult issues involving risks and benefits of novel products. Examples during the past year include:

- Held a workshop in October 2004, entitled "From Concept to Consumer: Center for Biologics Evaluation and Research, Working with Stakeholders on Scientific Opportunities for Facilitating the Development of Vaccines, Blood and Blood Products, and Cellular, Tissue, and Gene Therapies."..

- Attended the Cell Therapy/FDA Liaison Meetings on November 5, 2004 and June 24, 2005 . The objectives of the liaison meetings were to discuss emerging manufacturing and regulatory issues related to somatic cell therapy products and to provide an avenue for open discussions and outreach between CBER, industry, and academic sponsors.

- Attended and presented, in April 2005, at a meeting held by the American Society of Gene Therapy in Arlington VA, entitled "Challenges in Advancing the Field of Gene Therapy: A Critical Review of the Science, Medicine and Regulation-Stakeholders Meeting." The objectives of the meeting were to bring members of the gene therapy community together to critically review the issues and consider ways to move the field forward and specifically facilitate the initiation and successful conduct of gene therapy clinical trials.

- Attended and co-chaired, in May 2005, the International Conference on Harmonization (ICH) Gene Therapy Discussion Group (GTDG) meeting held in Brussels, Belgium. At this meeting the group discussed issues related to the potential for inadvertent germline

transmission of gene therapy products and the safety and benefit of using oncolytic viruses for use in oncology clinical trials.

- Attended and co-chaired, on September 22 and 23, 2005, the Korean FDA (KFDA) International Symposium and gave the special lecture entitled, "Current Issues on Xenotransplanation." CBER staff also presented a talk entitled, "Overview of Xenotransplanation Regulation in the US," at the follow-up seminar: Colloquium on the regulatory aspects on Xenotransplanation. This two day meeting allowed the U.S. FDA and KFDA to participate in ongoing discussions on the safety concerns surrounding clinical trials using xenotransplanation products.

Prescription Drug User Fee Act (PDUFA)

PDUFA has provided FDA with needed resources for the review of human drug and biologic applications. Fees collected have been used to help reduce the time required for evaluating human drug and biologic applications and to improve review quality. FDA has submitted annual performance and financial reports to Congress on application review performance and use of PDUFA fees. PDUFA has been amended and extended through September 30, 2007. The amended Act is now referred to as PDUFA III.

In April, 2005, Guidance for Review Staff and Industry entitled "Good Review Management Principles and Practices (GRMPs) for PDUFA Products" was released. The guidance is intended to support the FDA's primary public health mission for human drug and biologic products, help the FDA continue to define processes that fulfill the Agency's PDUFA mandates, promote efficient use of the FDA's resources, and define ways in which both FDA review staff and applicants can further the effectiveness and efficiency of the review process. This guidance is expected to lead to greater consistency and efficiency of the review process within individual review divisions and between CDER and CBER. The GRMPs in this guidance are based on the collective experience of CDER and CBER with review of applications for PDUFA products and are intended to promote the practice of good review management based on sound fundamental values and principles.

Representatives from CBER, CDER, ORA, and OC are currently preparing for negotiations with industry on PDUFA IV.

ACCELERATED APPROVAL PROCESS

On August 31, 2005, FDA approved Fluarix, an influenza virus vaccine. This vaccine is approved for the active immunization of adults 18 years of age or older against influenza disease caused by influenza virus types A and B. The approval of Fluarix broke new ground in that it was the first vaccine approved using the FDA's accelerated approval process. Accelerated approval allows products that treat serious or life-threatening illnesses to be approved based on successfully achieving an endpoint that is reasonably likely to predict ultimate clinical benefit, usually one that can be studied more rapidly than showing protection against a disease. In this case, the manufacturer demonstrated that, after vaccination with Fluarix, the adult body produced levels of protective antibodies in the blood that FDA believes are likely to be effective in preventing flu. Accelerated approval of flu vaccines enabled the manufacturer, GlaxoSmithKline, to get to market in time for the 2005-2006 flu season.

Medical Device User Fee and Modernization Act (MDUFMA)

In the last three years, the Biologics Program has worked intensively and sought input from both inside and outside the Agency to strengthen the quality, efficiency and timeliness of its device review process. The resulting increased effectiveness of device review in CBER is illustrated by the fact that CBER has met FY 2005 MDUFMA goals for all types of submissions in 2004. In many cases, these approvals relate directly to innovations that enhance the safety and efficacy of blood and tissue products. Timely approvals included products for which we received modular pre-market approval applications (PMAs).

Additionally, effective, expert interaction with government partners and industry have facilitated the recent approval of rapid tests for HIV and of tests to monitor HIV drug resistance, examples of successful regulation under the framework established by MDUFMA.

In the spirit of the least burdensome approach to regulating devices, on November 17, 2004, CBER/CDRH issued guidance to industry that provided FDA's recommendations on the timeliest and most effective way to resolve disputes concerning FDA actions that affect payment or refund of a user fee assessed under MDUFMA.

The Biologics Program has met or exceeded the MDUFMA review performance goals, most of which did not become effective until FY 2005. For the first two years of MDUFMA, only two of the performance goals were in place. In FY 2005, 20 MDUFMA goals were in place, and the Agency is collecting data on its performance against these goals. The Agency's MDUFMA performance and finance reports can be accessed at www.fda.gov/oc/mdufma/.

Blood Safety

Bacterial contamination, especially of platelets, remains among the top three causes of transfusion-related fatalities in the United States. To address this problem, FDA has encouraged the development of bacterial detection devices that can be used to release platelets. To date, FDA has approved three devices for quality control monitoring of the platelet collection process (bioMeriuex BacT/Alert, Pall eBDS, Hemosystems Scansystem). In February 2005, the FDA approved Gambro BCT single-donor platelets for 7-day storage. The FDA approved the extension of platelet shelf life from 5 days to 7 days when the Gambro BCT collection bag is used along with the bioMeriuex BacT/Alert Microbial Detection System using both aerobic and anaerobic culture bottles. FDA is also encouraging studies to validate prestorage pooling of platelets derived from platelet-rich plasma.

The Department of Health and Human Services (DHHS), FDA and the Centers for Medicaid and Medicare Services (CMS) received reports that health care providers were having difficulty obtaining immune globulin intravenous (IGIV) for some patients. FDA worked cooperatively with DHHS and the Plasma Protein Therapeutics Association (PPTA) to monitor the IGIV supply and facilitate its availability. While there does not appear to be a severe product shortage, there have been reports of difficulties obtaining the same product in the same treatment center that patients customarily use. Monthly distribution of products has not increased over the last 24 months, while demand has historically increased by 7% – 10% per year. At its July 2005

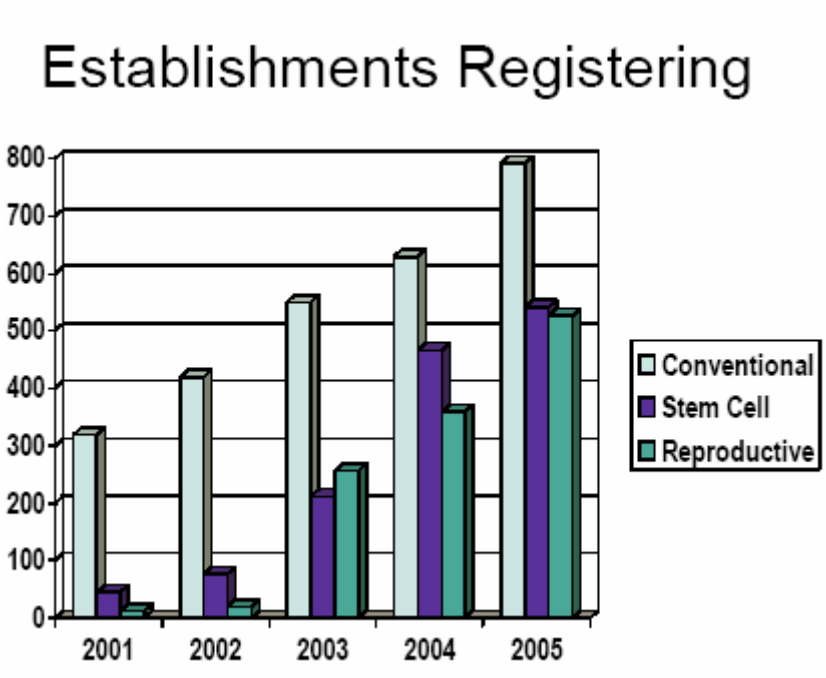
meeting, the Blood Products Advisory Committee (BPAC) announced the closure of the Massachusetts Public Health Biological Laboratories (MPHBL), the primary manufacturer of varicella-zoster immune globulin (VZIG), which is used to treat complications of varicella-zoster infection.) In response, FDA sought the Committee's advice on options for efficacy determination for new BLA applications for VZIG because of concerns about a potential upcoming shortage of this product. The FDA will work with manufacturers to approve other VZIG products or to use investigational mechanisms to make the product available.

Tissue Action Plan

The final rule on current good tissue practice (GTP), the last of three rules to be issued as part of FDA's overall plan to make human cells and tissues even safer, was published in the *Federal Register* on November 25, 2004. GTP governs the methods used in, and the facilities and controls used for, the manufacture of these products. With this final rule, FDA's efforts to establish a new, comprehensive, and risk-based approach to this promising and innovative field of medicine can be realized. The new approach became effective on May 25, 2005.

The new rule, entitled "Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and Enforcement," requires manufacturers to recover, process, store, label, package and distribute HCT/Ps, and screen and test cell and tissue donors, in a way that prevents the introduction, transmission, or spread of communicable diseases. The regulations apply to a broad range of these products including musculoskeletal tissue, corneas, human heart valves, dura mater (lining of the brain) and cellular therapies.

Two other related proposed rules to implement the proposed regulatory approach to HCT/Ps have previously been finalized. The first final rule, "Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing," was issued on January 19, 2001. It became effective on April 4, 2001, and requires HCT/P establishments to register with the FDA and list their products.



The other final rule, "Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products," was issued on May 25, 2004, and focuses on donor screening and testing measures to prevent the unwitting use of contaminated tissues with potential to transmit infectious diseases. It became effective on May 25, 2005. .

Significant Biologics Approvals in FY 2005

One of the goals of the Biologics Program is to provide timely, high quality, cost-effective process for the review of new technologies/pre-market submissions. Several important new Biologics Licensing Applications were approved in FY 2005 as shown in the table below:

Product	Indication/Purpose
Boostrix – Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)	Indicated for active booster immunization against diphtheria, tetanus and pertussis (whooping cough) in a single dose in individuals 10 – 18 years of age. This is the first licensed acellular pertussis containing vaccine with an indication for adolescents.
Adacel – Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine	Indicated for active booster immunization against diphtheria, tetanus, and pertussis (whooping cough) as a single dose in persons 11 through 64 years of age. This is the first licensed acellular pertussis containing vaccine with an indication for adults.
VIGIV – Vaccinia Immune Globulin Intravenous	The first intravenous human plasma-derived product available to treat certain rare complications of smallpox vaccine
ProQuad	Indicated for active immunization against measles, mumps, rubella and varicella (chicken pox) in children 12 months to 12 years of age.

Menactra – Meningococcal Polysaccharide Diphtheria Toxoid Conjugate Vaccine	Indicated for the active immunization of adolescents and adults for the prevention of invasive meningococcal disease. First meningococcal conjugate vaccine approved in the US.
Fluarix	Indicated for the active immunization of adults 18 years of age or older against influenza disease caused by influenza virus types A and B.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

The FDA must ensure that the biological products put on the market for U.S. consumers are both safe and effective. FDA must also ensure the safety of the nation's blood supply by minimizing the risk of infectious disease transmission and other hazards. The Field supports the Biologics Program in improving the safety of both imported and domestic biologics through a variety of activities. Examples of accomplishments and activities appear below organized by strategic goal.

Human Tissue Inspections

The Field inspects human tissue establishments to increase the safety of transplanted human cells, tissue, and cellular and tissue based products, while encouraging the development of new products.

Human Tissue Safety

The Field ensures that clinical safety and efficacy are demonstrated at tissue establishments and that appropriate review is performed for Human Cellular and Tissue Products (HCT/P's).

National Vaccine Stockpile

The Field inspects vaccine manufacturers whose products may be stockpiled as part of the Government's counter terrorism efforts. To ensure that the Government has sufficient quantity of safety and effective vaccines, the Field also monitors and inspects all vaccine stockpile facilities.

Blood Safety Activities

Blood and blood products are vitally important products in medical treatment. The Field monitors the collection of whole blood and the processing of products derived from human blood and assures consumer protection from defective products which may endanger public health.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Biologics Investigational New Drug Management System (BIMS)

The Biologics Investigational New Drug Management System (BIMS) supports high-level tracking and summarization of CBER regulatory efforts associated with Investigational New Drugs (INDs), Master Files (MF), and Investigational Device Exemptions (IDEs). The system was enhanced to support the review, management and tracking of Emergency Use Authorization (EUA) submissions. There were five other software releases implemented providing numerous process modifications, including changes for product data-entry, data quality, and handling original submissions and amendments which greatly reduced processing time by reviewers. BIMS is used by over 600 CDER and CBER medical product reviewers.

Biologics License Application (BLA)

The Regulatory Management System for the Biologics License Application (RMS/BLA) provides an automated system to support the tracking of BLAs, their review, and their associated data. Three major software upgrades were successfully implemented comprising over 100 user and programmer generated change requests, 350 data change requests, 2 data migration related requests, several performance related enhancements, and 15 special report requests. Among these enhancements were modifications to support MDUFMA, promotional materials review, foreign inspections, routing request capability, and additional search and reporting capabilities.

Lot Release System (LRS)

The Lot Release System (LRS) supports the processing of lots and issuance of release notifications. LRS also supports inventory, routing, and laboratory sample tracking. There were two major software releases, comprising of nearly 50 user-requested and programmer-generated improvements. One of the major enhancements, a new Milestones Module for the purpose of tracking and reporting on performance throughout the lot review and approval process, will enable the Product Release Branch (PRB) to track and report on time between events and actions taken for a given lot.

CBER's Electronic Document Room (EDR)

CBER's Electronic Document Room (EDR) functions as an electronic library for reviewers, distributing and storing electronic submissions of IND, BLA, NDA, 510(k), PMA, regulatory correspondence, and other types of submissions defined by CBER. EDR enhancements include the integration of the FDA electronic Common Technical Document (eCTD) review tool that allows for the receipt of eCTD-based submissions, hardware and operating system upgrades, software modifications to the Electronic Secure Email system (ESM), ability to receive and extract data from PDF forms received on physical media, capability to process trans-BLA submissions, and PDF link checking software for the submission processing.

Biologics
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actuals	FY 2006 Estimate	FY 2007 Estimate
Total Original License Application (BLA) Reviews[1/]	35	38	45
BLA Approvals	17	20	25
Median BLA Approval Time (months)	12.9	13.0	13.0
License Supplement (BLA) Reviews[1/]	1,940	2,100	2,250
NDA & NDA Supplement Approvals	15	20	20
ANDA & ANDA Supplement Approvals	8	10	10
PMA & PMA Supplement Reviews[1/]	20	25	25
510(k) Reviews[1/]	86	95	95
Commercial IND/IDE Receipts	146	150	170
IND/IDE Amendments Receipts[2/]	8,581	8,700	9,000
Active INDs/IDEs[2/]	2,687	2,750	2,850
Adverse Event Report Receipts [3/]	21,902	22,000	22,500
Biological Product Deviation Report Receipts	38,769	39,000	40,000

1/Total of approval, and complete decisions. Does not include refuse-to-file decisions or withdrawals.
2/Includes IND, IDE, Master File and license master file receipts.
3/Includes MedWatch, Foreign reports and VAERs reports. Does not include Fatality Reports or Medical Device Reports for CBER-regulated medical devices.

BIOLOGICS FIELD PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	**FY 2005 Actual**	**FY 2006 Estimate**	**FY2007 Estimate**
Bioresearch Monitoring Program Inspections	121	156	156
Blood Bank Inspections	1,439	1,130	1,070
Source Plasma Inspections	188	165	160
Pre-License, Pre-Approval (Pre-Market) Inspections	3	10	10
GMP Inspections	42	36	36
GMP (Device) Inspections	14	35	35
Human Tissue Inspections	270	250	325
Total Above Domestic Inspections	**2,077**	**1,782**	**1,792**
Total Domestic Reinspections (Non-add)	**50**	**50**	**50**
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Blood Bank Inspections	16	24	24
Pre-License Inspections	6	0	0
GMP Inspections	15	24	17
Total Above Foreign FDA Inspections	**35**	**43**	**41**
Total Foreign Reinspections (Non-add)	**4**	**4**	**4**
Import Field Exams/Tests [1]	143	100	100
Import Line Decisions	39,979	44,377	49,258
Percent of Import Lines Physically Examined	0.36%	0.23%	0.20%

Note:

1. CBER staff perform Biologics import analyses, when required.

ANIMAL DRUGS AND FEEDS

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$98,022,000**	**$98,882,000**	**$105,031,000**	**+$6,149,000**
Center	*$62,898,000*	*$64,040,000*	*$69,253,000*	*+$5,213,000*
FTE	*369*	*385*	*406*	*+21*
Field	*$35,124,000*	*$34,842,000*	*$35,778,000*	*+$936,000*
FTE	*241*	*228*	*230*	*+2*
Program Level FTE	**610**	**613**	**636**	**+23**
Budget Authority	**$90,484,000**	**$89,581,000**	**$95,494,000**	***+$5,913,000***
Center	*$55,360,000*	*$54,739,000*	*$59,716,000*	*+$4,977,000*
Field	*$35,124,000*	*$34,842,000*	*$35,778,000*	*+$936,000*
Pandemic Preparedness	*0*	*0*	*$4,868,000*	*+$4,868,000*
FTE	*0*	*0*	*14*	*+14*
Trigger Needs for ADUFA				*+$2,475,000*
FTE				*+17*
Cost of Living				*+$1,299,000*
Strategic Redeployment			*-$2,729,000*	*-$2,729,000*
FTE			*-8*	*-8*
Budget Authority FTE	**571**	**537**	**560**	**+23**
User Fees	**$7,538,000**	**$9,301,000**	**$9,537,000**	**$236,000**
ADUFA				
Center	*$7,538,000*	*$9,301,000*	*$9,537,000*	*+$236,000*
User Fee FTE	**39**	**76**	**76**	**--**

[1/] *Includes a one percent rescission.*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$87,659,000	$87,659,000	$0	596
2004 Actual	$84,441,000	$83,358,000	$1,083,000	595
2005 Actual	$98,022,000	$90,484,000	$7,538,000	610
2006 Enacted	$98,882,000	$89,581,000	$9,301,000	613
2007 Estimate	$105,031,000	$95,494,000	$9,537,000	636

Statement of Budget Request

The Animal Drugs and Feeds Program is requesting $105,031,000 in program level resources to accomplish its mission, including activities:

- 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;

- Process premarket applications as quickly as possible to increase the availability and diversity of safe and effective veterinary products that relieve animal pain and suffering, while ensuring that these products are safe, wholesome and free of drug residue when they reach the consumer; and,

- Monitor marketed animal drugs and feed products to minimize harm to humans or animals that might arise from the use of these products. The Program accomplishes this work through science-based review of drug experience reports, nationwide monitoring systems, and compliance programs conducted by FDA field offices that include inspections, sample collections, analysis, investigations, and appropriate regulatory actions to control volatile goods and firms.

Program Description

The Animal Drugs and Feeds Program is administered by FDA's Center for Veterinary Medicine (CVM) and supported by our Office of Regulatory Affairs (ORA) field force. The authority to regulate animal drugs and medicated feeds is derived from the Food, Drug, and Cosmetic Act, which Congress amended in 1968 to include new authorities relating to animal drugs. These amendments ensure that animal drugs are safe and effective for their intended uses and that the drugs do not result in unsafe residues in foods.

In November 2003, the Animal Drug User Fee Act (ADUFA) provided the authority for FDA to collect user fees for its animal drug review work. ADUFA is intended to supplement the appropriated resources for conducting the animal drug review program. These resources provided by the law will help the Program's scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for animals.

In 2004, Congress enacted the Minor Use and Minor Species Animal Health Act, a statute designed to help make more medications legally available to veterinarians and animal owners to treat minor animal species and also uncommon diseases in the major animal species. The Act is designed to help pharmaceutical companies overcome the financial roadblocks they face in providing animal drugs that have limited demand.

The safety of the food supply is a paramount concern for the Program, as the average American consumes nearly 200 pounds of meat and fish, 30 pounds of eggs, and 585

The Program's scope is far-reaching, its customers include:

- *140 million dogs and cats*
- *6 million horses*
- *9 billion chickens*
- *275 million turkeys*
- *95 million cattle*
- *60 million pigs*
- *6 million sheep*
- *296 million humans in the U.S.*

pounds of dairy products each year. While most of these food products are regulated by the USDA, FDA ensures that animal drugs and feeds used in the care of food producing animals do not result in unsafe residues in food harvested or produced from these animals. ORA supports CVM by conducting preapproval inspections of both domestic and foreign establishments and other premarket-related activities. These activities include bioresearch monitoring of clinical research and laboratory method validations needed for premarket application decisions, and inspections of manufacturing facilities to determine if the factory is able to manufacture the product to the specifications stated in the application.

ORA also supports CVM by conducting post market inspections such as Bovine Spongiform Encephalopathy (BSE) and other high risk inspections on an annual basis. In addition to overseeing regulated products on a surveillance or "for cause" basis, ORA staff also responds to emergencies and investigates incidents of product tampering and terrorist events or natural disasters.

CVM's priorities include, but are not limited to, public and animal health activities such as animal drug review, antibiotic resistance, prevention of BSE and the safety of food derived from genetically modified animals.

Performance Analysis

During the latest performance period (FY 2005), the Animal Drugs and Feeds program expects to successfully achieve the target for its ADUFA performance goal when data becomes available in January 2007, and did meet its two field performance targets for FY 2005. The program met the FY 2004 performance goal when final data became available in January 2006. Additional information about the ADUFA goals and results are provided in the Performance Detail section and will be available in the FY 2005 ADUFA Performance Report.

With the passage of the Animal Drug User Fee Act (ADUFA) of 2003 and the resulting availability of user fees, the Program changed its new animal drug review performance goals to reflect the more ambitious performance target plans under ADUFA. Since the ADUFA fee structure is predicated on supplementing existing appropriated funding, the performance goal target below is dependent upon a sustained level of base and user fee resources. See the Performance Analysis Appendix for detailed discussion of the performance goal and target highlighted below.

Performance Highlight:

FY 2007 Goal Target	FY 2004 Results	*Context*
Complete review and action on 90% of original NADAs & reactivations of such applications received during FY 2007 within 200 days.	CVM completed review and action on 100% of original NADAs & reactivations of such applications received during FY 2004 within 295 days.	The user fee program reflects the implementation of a five (5) year plan to improve the performance for animal drug review.

Program Resource Changes

Pandemic Preparedness: + $4,868,000 and 14 FTE

The National Strategy for Pandemic Influenza, issued by President Bush November 1, 2005, guides our nation's preparedness and response to an influenza pandemic, with the intent of (1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. The Strategy charges the U.S. Department of Health & Human Services with leading the federal pandemic preparedness.

FDA will focus resources on developing an analytical method to detect the two major antiviral drug classes in tissues. The validated method would allow U.S. federal laboratories to detect, quantify the amount and confirm the identity of any of the known and possibly similar black market antiviral agents. Specifically, FDA will:

- Prohibit extra label use of antiviral drugs and ensure that drugs are not used in veterinary medicine that increase drug resistance, compromising the treatment of people for avian influenza;

- Develop methodology for detecting antiviral residues in poultry and coordinate with USDA to sample and test poultry products at import inspection stations, and poultry processing plants for traces of antiviral residues;

- Develop and implement plans for containment and disposal of animal feed that has or may have been contaminated with avian flu agents;

- Participate in exercises with other federal and state agencies to ensure proper policies and programs are in place, and adequate response capabilities are available and educate producers, veterinarians, feed industry and others about the public health threat posed by avian influenza;

- Support research projects, with a focus on analytical methods for detecting illegal use of certain drugs and other compounds;

- Assist with appropriate enforcement actions to protect human and/or animal health (e.g., quarantine of animal products or articles);

- Provide extensive outreach and training in manufacturing quality. Conduct timely and efficient inspections of manufacturing facilities to assure product quality and prevent problems that threaten safety or availability of products essential to respond to the pandemic threat; (Field Activity)

- Improve FDA's capacity to conduct domestic and import surveillance and respond to reports of food or foodborne illness associated with viruses; and, (Field Activity)

- Issue custom alerts to prevent the illegal importation of antivirals. (Field Activity)

Appropriated User Fee Trigger Needs -- Maintaining Animal Drug Review and Medical Device Review Programs: + $ 2,475,000 and + 17 FTE

To meet the statutory requirements for collecting Animal Drug and Medical Device User Fees, FDA must spend a minimum amount of appropriated resources, indexed to the cost of living, on the review process. If the appropriation and/or spending do not meet these minimum requirements (known as user fee triggers), then the agency is unable to receive the supplemental user fee funding and the programs terminate. The additional budget authority is needed to ensure that the trigger requirements are met. The Agency's request amount is $7,425,000 and 45 FTE. For the Animal Drug Review Program, the Center for Veterinary Medicine's portion is $2,475,000 and 17 FTE.

Cost of Living-Pay: + $1,299,000

FDA's request for pay inflationary costs is essential to accomplishing its public health mission. Payroll costs account for over sixty-percent of our total budget, and the Agency is no longer able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Animal Drugs and Feeds portion of this increase is $1,299,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Animal Drugs and Feeds Reductions - $2,729,000 and -8 FTE

To fund FY 2007 priority initiatives such as Pandemic Preparedness, FDA re-deployed resources from base programs. To accomplish this strategic redeployment and fund new, high priority initiatives, Animal Drugs and Feeds reductions include: research, postmarket activities, and the Generally Recognized as Safe (GRAS) notification system.

User Fees

Current Law Fees

Animal Drug User Fee Act (ADUFA): + $236,000

The Animal Drug User Fee Act of 2003 (ADUFA) amends the Federal Food, Drug and Cosmetic Act and authorizes FDA to collect fees for certain animal drug applications, and for the establishments, products and sponsors associated with these and previously approved animal drug applications. ADUFA helps the FDA, through a strengthened animal drug pre-market review program, to provide greater public health protection by ensuring that animal drug products that receive FDA approval as safe and effective are readily available for both companion animals and animals intended for food consumption. Additional resources provided by ADUFA will also help FDA scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for our animals. ADUFA will help provide a cost-efficient, high quality animal drug review process that is predictable and performance driven. In FY 2007, FDA will work with Congress on the reauthorization of the Animal Drug User Fee Act. This increase of $236,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Proposed Fees (Reclassified as Mandatory - Non-Add)

Reinspection User Fee (Mandatory): $2,050,000 and 17 FTE (Non-Add)

The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an amount sufficient to fully fund reinspections. The Animal Drugs and Feeds program component of this user fee is $2,050,000 and 17 FTE.

Food and Animal Feed Export Certification User Fee: $63,000 (Non-Add)

The Administration is proposing legislation authorizing FDA to collect user fees for issuing food and animal feed export certificates. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $3.5 million in revenue, an amount sufficient to fully fund the export certificate program. Private sector exporters would bear the cost of the program, but would reap its benefits through the Agency's enhanced ability to facilitate exports of their products. The Animal Drugs and Feeds program component of this user fee is $63,000.

Justification of Base

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

The Program will use base resources to better enable consumers to make informed decisions weighing benefits and risks of FDA-regulated products as well as to promote improved patient and consumer safety by reducing risks. These activities include safety of animal-derived food and preparation for terrorist actions.

Food Safety

Millions of people get sick annually from contaminated food they eat. Some foodborne illnesses are due to harmful or illegal residues in animal products, while other illnesses are due to microbiological infection. To safely manage animal drug use domestically and internationally and have safe food from farm to table, we must have the knowledge to make proactive, sound science based decisions. In pursuit of this, FDA will:

- Monitor, sample, and investigate reports of pesticide, chemical, and microbiological contamination of animal feed and take enforcement actions as appropriate..
- Screen and survey animal feeds and animal feed components for the presence of bacterial pathogens.

- Review previously approved new animal antimicrobial drug submissions with respect to antimicrobial resistance and human food safety considerations.

- Review new animal food additive submissions to improve safety of edible animal products.

FDA Releases 2003 NARMS Retail Meat Annual Report

FDA has recently published its 2003 National Antimicrobial Resistance Monitoring System (NARMS) Retail Meat Annual Report, which reports on the prevalence of antimicrobial resistance among zoonotic foodborne bacteria. The report provides data on the prevalence of antimicrobial resistant foodborne and commensal bacteria among retail meats, comprising results from nearly 5000 samples. The results generated by the NARMS retail meat program will establish a reference point for analyzing trends of antimicrobial resistance among these foodborne bacteria.

The NARMS retail meat surveillance program is a collaboration that includes the FDA, CDC and 10 participating FoodNet laboratories in the United States.

- Continue to develop a comprehensive risk-based Animal Feed Safety System.

- Continue to support the WHO's Global Salmonella Surveillance.

- Maintain early warning systems by collecting information from Drug Experience Reports and Adverse Event Reports.

Research

FDA is responsible for the post-approval monitoring of retail meats for drug resistant foodborne pathogens under the National Antimicrobial Resistance Monitoring System (NARMS), and molecular typing of those pathogens as part of the national PulseNet program. FDA conducts research to understand the microbiology of animal feeds and the dissemination of resistant organisms via livestock feeds. The Agency also develops analytical methods to detect the presence of toxins, drugs, pesticides and other substances that could be used to intentionally contaminate U.S. animal feed supplies. FDA supports food safety and counterterrorism research activities to:

- Monitor for the prevalence of enteric bacteria in retail meats and the changes in their susceptibilities to a panel of antimicrobial agents that are important in human and animal medicine.

- Identify food animal species that may be associated with transmission of antimicrobial resistance to human bacterial pathogens.,

- Develop and validate multi-residue drug screening methods and methods to detect the presence of prohibited toxic and microbiological substances that could be introduced into U.S. animal feed supplies.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Under this Agency strategic goal, it is FDA's intent to increase the number of safe and effective new animal drug products, including generic drugs, by increasing the predictability, efficiency and effectiveness of development as well as rapid, transparent and predictable review of applications.

Premarket Review

The availability of safe and effective animal drugs assures food animal producers that products will be safe, wholesome, and free of harmful drug residues when they reach the consumer. With the inception of the Animal Drug User Fee Act (ADUFA) of 2003, the Agency has been able to provide greater public health protection by ensuring that an adequate supply of animal drug products are approved to be safe and effective, and readily available for both companion animals and food animals. FDA will:

- Further implement ADUFA and increase the availability of safe and effective animal products while working with regulated industry to minimize drug development time.

- Met all the performance goals defined under ADUFA for FY 2007.

- Conduct pre-submission conferences, meetings, and workshops with industry and develop policy and practical guidance documents as necessary to industry.

- Conduct Bio-Research Monitoring inspections of studies for pending new animal drug applications, including Sponsor-Monitor, Clinical Investigator, and Good Laboratory Practice. Evaluate applications for the Application Integrity Policy to assure the accuracy and conduct of studies to support approval of new animal drugs.

- Continue to work with the generic animal drug sponsors by meeting with the Animal Drug Alliance.

- Continue with the preparation of implementing regulations for the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act) to help make more medications legally available to veterinarians and animal owners to treat minor animal species and also uncommon diseases in the major animal species.

Biotechnology

- Continue work with other Federal agencies to clearly define FDA's role in the regulation of animal biotechnology products.

- Provide educational information on biotechnology products and work with animal biotechnology firms while a policy on transgenic animals is prepared.

Research

FDA supports the drug review function by conducting studies in animal drug safety and efficacy, antimicrobial resistance mechanisms, metabolism, standardization of test methods, and pharmcokinetics/pharmacodynamics. The goal of these efforts is to provide a science base for guideline development. FDA will:

- Conduct method validation for new drug approvals for food producing animals; and,

- Resolve new and emerging scientific issues that impact FDA's ability to make approval decisions.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Base resources will be used to conduct science-based risk management in all FDA regulatory activities; so that FDA's resources can provide the most health promotion and protection at the least cost for the public.

Bovine Spongiform Encephalopathy (BSE)

BSE or "Mad Cow Disease" is a transmissible, slowly progressive, fatal, neurological disease of cattle, caused by an abnormal form of cell protein. It is transmitted when meat and bone meal derived from infected cattle is used as a supplement in cattle feed. To prevent the establishment and spread of BSE through animal feed, FDA finalized a regulation in 1997 entitled "Animal Proteins Prohibited from use in Animal Feed" that prohibits the use of mammalian protein in ruminant feed. FDA will:

- Prepare and implement final regulation that prohibits the use of certain high risk bovine tissues, such as brain and spinal cord in all animal feed.

- Maintain database and a web-based, dynamic report summarizing the most current results of firms subject to BSE inspections.

- Evaluate effects of risk management on the spread and the rate of elimination, with the help of the Harvard BSE Risk Assessment simulation.

- The main focus of FDA's domestic BSE control program continues to be the collaborative program with our state regulatory counterparts to inspect facilities for compliance with the BSE/ruminant feed ban. FDA continues to expand inspection coverage into lower risk firms, while maintaining annual inspections of the higher risk facilities (renderers and feed mills) that process with prohibited material. (Field Activity)

- FDA implemented an advanced analytical procedure for detection of prohibited material in animal feed into an assignment issued for 900 domestic and 900 import feed samples. This novel approach combines light microscopy with polymerase chain reaction (PCR) to determine and detect DNA from ruminants and non-ruminant mammalian species, supporting the BSE/Ruminant Feed Ban. (Field Activity)

- Following the finding of a BSE positive animal in Texas, FDA, USDA/APHIS, the Texas Animal Health Commission (TAHC), and the Texas Feed and Fertilizer Control Service (TFFCS) successfully conducted a feed investigation with two main objectives; to identify all protein sources in the animal's feed history that could potentially have been the source of the BSE agent, and to verify that cattle leaving the herd after 1997 that were identified by USDA/APHIS as animals of concern (e.g. progeny and feed cohorts), were rendered at facilities in compliance with the BSE/ruminant feed ban regulation. (Field Activity)

- Awarded contracts with state and local governments to perform BSE, feed manufacturers and illegal tissue residue inspections. Began designing eSAF to include the feed and BSE programs, which will be piloted in FY06. Auditor training was conducted for feed contracts. Reviewed and awarded Cooperative Agreement grants for BSE infrastructure improvement in eight states. The Agency and the States maintained and continued to develop new partnerships (e.g., BSE inspections) that have contributed to the exchange of inspection and sampling data and have facilitated the receipt of training and distribution of equipment to the states.(Field Activity).

<u>Tissue Residues</u>

- Investigate reports of drug, pesticide, and chemical contaminant residue violations in edible animal tissues and take enforcement actions as appropriate.

- Leverage FDA's Tissue Residue Information Management System with USDA's Residue Violation Information System on residue violators/violations to maintain tissue residue and feed contaminants compliance programs.

- Provide technical support on residue findings of fluoroquinolones in imported seafood.

Animal Drug Compounding

Develop intervention measures over the shipment, receipt, and use of bulk active pharmaceutical ingredients in compounding animal drugs.

Zoonotic Diseases

Zoonotic diseases that have serious impact on human health are on the increase worldwide. Measures to control the spread of disease with a public health impact falls under the Public Health Service Act and the regulation is shared between FDA and CDC.

- Provide educational outreach to veterinarians, pet suppliers, pet and other animal owners about zoonotic diseases such as monkeypox and Salmonella from pet turtles.

- Investigate and take regulatory action where appropriate for violations of Public Health Service Act regulations restricting the sale and movement of animals that serve as a source of zoonotic diseases.

Counterterrorism

FDA's mission includes protecting the health and safety of all food producing, companion and other non-food animals, and assuring that food from animals is safe for human consumption. FDA must work to develop profiles of possible or probable food threats and points of attack. We must have the capacity to quickly and accurately identify outbreaks at any point in the food chain and to take prompt action to mitigate their effects. Base funding will enable FDA to:

- Seek industry input to perform a risk analysis of the vulnerability of livestock and poultry feed.

- Facilitate the sharing of information between existing databases and organizations and fill in any gaps that we identify in this "network" of database systems and other contacts.

- Strengthen relationships with state partners and expand contracting efforts with state labs to provide surveillance and surge capacity related to counter terrorism activities.

- Work with Iowa State University on a database that assists "first responders" by providing: quick identification of labs that have the capability to analyze feed and/or animal tissues for the presence of a chemical or biological agent.

- Maintain a comprehensive inventory of registered animal drug establishments and listed animal drug products to assess the availability or anticipated shortage of animal drug products that would be needed to deal with terrorist attacks.

- Work with CDC on a bioterrorism surveillance system for companion animals that can be used as an early detection mechanism for antibiotic resistant microbes and bioterrorist agents.

Animal Drug Production

Assuring the production, storage, and distribution of animal drugs and feeds containing animal drugs are in conformance with current good manufacturing practice helps to assure drug products are safe and effective and properly labeled. More specifically, FDA will:

- Participate in the risk-based GMP Initiative activities.

- Implement the pilot program for Voluntary Self Inspection Program for medicated feed manufacturers with a history of compliance—permitting the Agency to focus regulatory oversight on firms that are not in compliance or lack inspectional history.

Research

CVM is developing methods to detect material, prohibited by the Bovine Spongiform Encephalopathy (BSE) feed regulation, that could compromise animal feed safety. The availability of practical, validated methods to detect protein from different animal species could improve effectiveness and efficiency in the enforcement of the BSE feed regulation. CVM also supports the Center's illegal tissue residue compliance program through the development of analytical methods and the evaluation of screening tests for detection of drug residues in imported and domestic food products. FDA will:

- Complete the validation of a real-time Polymerase Chain Reaction method that is capable of detecting cattle, swine, sheep, goats, horses, or deer material along with poultry, goose, and turkey to further enhance FDA's ability to detect potentially violative animal feeds. This effort includes the ability to identify up to three or four different prohibited species in a single reaction;

- Evaluate commercially available rapid tests for animal proteins in animal feeds; and,

- Develop and validate multi-residue drug screening methods.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

This includes improvements through the planning, development and implementation of Agency and Center management programs and policies, such as:

- Support and enhance employees' abilities to efficiently work with integrated IT systems to reach CVM goals;

- Enhance the Center's Activity-Based Costing/Activity Time Reporting system, and integrate it into the business culture of the Center's operations in order to manage, define and assign the costs of doing business; and,

- Direct the development and implementation of the competency-based Staff College and accompanying curriculum

Selected FY2005 Accomplishments

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Bovine Spongiform Encephalopathy (BSE)

The U.S. Food and Drug Administration (FDA) announced new measures to help further protect consumers against the agent thought to cause bovine spongiform encephalopathy (BSE, also known as "mad cow disease").

FDA Proposes "Mad Cow" Regulation

The Agency is proposing to amend its animal feed regulations to prohibit from use in the food or feed of all animals certain high risk cattle materials that can potentially carry the BSE-infectious agent. All of the proposed prohibitions, except for those related to tallow, have already applied to cattle feed since 1997.

The proposed regulation builds on a series of firewalls that include FDA's 1997 feed (e.g. for cattle and sheep), but allows these materials to be used in feed for non-ruminant species. The removal of high-risk materials from all animal feed -- including pet food -- will protect against the transmission of the agent of BSE that could occur either through cross-contamination of ruminant feed with non-ruminant feed or feed ingredients during feed manufacture and transport, or intentional or unintentional misfeeding of non-ruminant feed to ruminants on the farm.

Antimicrobial Resistance

FDA Announces Final Decision About Veterinary Medicine

FDA announced the Agency's final decision to no longer allow distribution or use of the antimicrobial drug enrofloxacin, class of drugs known as fluoroquinolones, for the purpose of treating bacterial infections in poultry. Scientific data showed that the use of this drug in poultry caused resistance to emerge in Campylobacter, a bacterium that causes foodborne illness. These resistant bacteria multiply in the digestive tracts of poultry and persist and spread through transportation and slaughter. They are a significant cause of foodborne illness in the U.S. Antimicrobial treatment is recommended for people with severe illness as well as the very young, the elderly, and people with certain medical conditions. Complications of such infections can include reactive arthritis and, more rarely, blood stream infections. Early treatment can mitigate symptoms and may decrease the risk of complications.

Fluoroquinolones used in humans are ineffective if used to treat these bacteria infections that are resistant to them. This failure can significantly prolong the duration of the infections and may increase the risk of complications. The proportion of infections that are resistant to this class of drugs has increased significantly since the use of this antimicrobial drug in poultry was approved in the U.S.

- A database has been developed that is searchable from the web containing a listing of all antimicrobials approved for use in food animals.

- Partnered with scientists at the United States Department of Agriculture (USDA) and relatedness among isolates; Universities in characterizing antimicrobial resistance, susceptibility and genetic.

- Participated in the cooperative agreement with Mexico to determine the prevalence of *Salmonella* species and antibiotic-resistant *E .coli* in humans.

Virginiamycin Risk Assessment

CVM compiled and analyzed comments received on its draft risk assessment of the animal drug virginiamycin, which is used to promote growth and prevent or control disease in chickens, turkeys, swine, and cattle. CVM conducted the assessment, which was released in late November, 2004, to determine whether pathways exist to link food-animal uses of virginiamycin. The risk assessment estimates the risk that humans will acquire a bacterial infection that is resistant to treatment with antibiotics potentially related to the use of virginiamycin in food-producing animals. The review of the risk assessment was not sufficient to warrant revision at this time.

CVM will continue to monitor the scientific literature, the results of surveillance studies, usage patterns of antibiotics in hospital and health care settings, and other relevant data that may affect the findings of the risk assessment. CVM will revisit the risk assessment at a time dictated by the availability of new data and scientific developments in antibiotic resistance.

- Completed development of a standardized in vitro susceptibility testing method for *Campylobacter* and incorporated the method into the NARMS program.

- Completed the laboratory phase of a contract with the American Type Culture Collection to analyze antimicrobial susceptibility among banked historical collections of *Salmonella, E. coli* and *Campylobacter*. This will allow us to examine the

historical susceptibility of pathogens to antimicrobial agents, to better understand the temporal trends of resistance development.

National Antimicrobial Resistance Monitoring System (NARMS)

- The NARMS retail meat surveillance program switched from a convenience sampling scheme to a more statistically robust randomized sampling scheme.

- Continued to improve NARMS testing methods including development and implementation of a *Campylobacter* broth microdilution method approved by the Clinical and Laboratory Standards Institute in 2005. This method is being used in Canada, Europe, Central South America, and WHO training laboratories worldwide.

- Strengthened NARMS program by establishing a DNA fingerprinting database of *Salmonella* and *Campylobacter* isolated from NARMS retail meats. The database will provide useful information on multidrug resistance foodborne pathogens.

- Released the second annual NARMS retail meat report September 30, 2005. This report provides 2003 data on the prevalence of antimicrobial resistant foodborne pathogens and commensal bacterial among retail meat and poultry samples, comprising results from nearly 5000 samples.

- Partnered with other active and passive surveillance systems (e.g. FoodNet, PulseNet) to help public health officials better understand the dynamics of foodborne illness attribution in the United States.

- Continued efforts to maximize cooperation and communication between FDA, USDA, and the CDC to increase efficient use of resources in addressing problems of mutual interest as well as harmonize data reporting.

- Met with panel of outside experts for external review of all three arms of the NARMS program.

Food Safety and Surveillance

- The draft framework for the Animal Feed Safety System was released in February 2005 and a second public meeting was held in April 2005 to present and receive public input. This document covers regulation of the labeling, production and distribution of all feed ingredients and mixed feeds at all stages of manufacture, distribution and use.

- Completed development and instillation of cultural methods to be used in screening feeds and feed commodities for the presence of the *Bacillus cereus* group. This is part of our efforts to investigate issues of importance to animal feed security and support development of the Animal Feed Safety System.

- Conducted Health Hazard Evaluations for several marketed veterinary drug products, determining their recall classifications and recommending the depth of recall based on the seriousness of potential health hazard to animals and/or humans.

- Revised the Feed Contaminants Program 7371.003 Compliance Policy Guide so the agency is now included routinely as a laboratory to receive feed samples from FDA field investigators resulting from their annual feed mill inspections, allowing regular input into the microbiology and residue related issues associated with animal feeds.

Adverse Drug Events (ADEs)

- The FDA Veterinary Medicine Advisory Committee made recommendations on the voluntary recall of the veterinary heartworm prevention drug product PROHEART 6 for dogs. Steps to eliminate or mitigate the safety issues associated with ProHeart 6 could not be found and FDA did not recommend returning the product to the market.

- The Center received over 33,000 adverse experience reports, an increase of approximately 4,700 from FY 2004.

- The Center began participation during the year in a pilot program that is intended to facilitate the electronic submission of adverse drug experiences reports.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Premarket Review

Approved the following noteworthy medicines:

DRUG	PURPOSE
RUMENSIN (monensin)	First drug ever approved for the claim "increased milk production efficiency" in dairy cattle. Cows make more milk consuming less feed. The drug improves energy efficiency by influencing the cow's gut flora toward a more energy efficient digestive population. It was approved previously in different classes (beef cattle, poultry) for different purposes (improved weight gain, treat coccidiosis).
REBALANCE (pyrimethamine and sulfadiazine)	An antiprotozoal product indicated for the treatment of horses with equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona.*
TRIBUTAME (chloroquine phosphate, embutramide, lidocaine)	A euthanasia product for dogs. The product is approved but not yet marketed, pending final product scheduling by DEA.

CYDECTIN f moxidectin)	Injectable Solution for Beef and Nonlactating Dairy Cattle – for the treatment and control of various internal and external parasites in beef and nonlactating dairy cattle.
DRAXXIN (tulathromycin)	Injectable Solution - for 1) treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida*, and *Histophilus somni* and for the control of respiratory disease in cattle at high risk of developing BRD associated with *M. haemolytica, P. multocida*, and *H. somni*; and 2) treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae, P. multocida, Bordetella bronchiseptica*, and *Haemophilus parasuis*.
SPECTRAMAST LC Sterile Suspension (ceftiofur hydrochloride, 125 mg/mL)	For the treatment of clinical mastitis in lactating dairy cattle associated with coagulase-negative staphylococci, *Streptococcus dysgalactiae*, and *Escherichia coli*.
SPECTRAMAST DC Sterile Suspension (ceftiofur hydrochloride, 500 mg/mL)	For the treatment of subclinical mastitis in dairy cattle at the time of dry off associated with *Staphylococcus aureus, Streptococcus dysgalactiae*, and *Streptococcus uberis*.

- Developed guidance to expedite the approval process including revision and republication of a new toxicology section for Guidance for Industry (GFI) #3, *General Principles for Evaluating the Safety of Compounds Used in Food-Producing Animals.* We also published for comment draft GFI #123, *Development of Target Animal Safety and Effectiveness Data to Support Approval of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for Use in Animals*.

Minor Use and Minor Species Animal Health Act of 2004 (MUMSAHA)

- Establishment of the Office of Minor Use and Minor Species Animal Drug Development (OMUMS) early in the fiscal year. By Mid-September, 2005, OMUMS had initiated the review process on more than 50 requests for Designation of drugs intended for minor use or minor species and had granted 5 of those requests. Designation provides for 7 years of marketing exclusivity upon approval of a designated drug, a significant incentive for sponsors to pursue approval.

- On September 27, 2005, the Center published the proposed Designation regulations which establish formal procedures to implement a major portion of the MUMS act. This is the first of three sets of implementing regulations required to be published by the MUMS legislation.

Animal Drug User Fee Act (ADUFA)

- On March 17, 2005, FDA posted the FY 2004 Performance Report to Congress for ADUFA. FDA met or exceeded all the review timeframes defined under ADUFA for

FY 2004 for applications and submissions that were submitted in FY 04. As of September 30th, 2005, FDA has met or exceeded all of the performance goals defined under ADUFA for FY 2005 for applications and submissions that have been acted on.

- FDA has made substantial progress in recruiting for its review staff and will meet its goal of having 50 percent of additional FDA review staff recruited and on-board by the first quarter of FY 2006.

Generics

- Worked with generic animal drug sponsors by meeting on a regular basis with the Animal Drug Alliance.

Biotechnology

- Worked with additional sponsors of animal biotechnology products to ensure that their progress is responsible but not unduly burdened as the Federal government prepares a policy on transgenic animals.

- The Animal Biotechnology Working Group developed seminar programs, courses and a rotating detail program to continue to ensure that personnel are aware of the critical issues, possess the scientific skills, and are familiar with the regulatory environment necessary to address the rapidly evolving and highly technical issues associated with animal biotechnology.

- Continued the development of a transgenic animal policy. The Center participated in on-going White House-level deliberations to evaluate the role of genetically engineered animals in the Coordinated Framework for the Regulation of Biotechnology.

- Worked to update the draft Risk Assessment on Animal Clones and their Progeny, Proposed Risk Management Plan, and a draft Guidance for Industry (GFI) on the use of cloning technology in animal breeding and release of clones and their progeny into the food supply.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Bovine Spongiform Encephalopathy (BSE)

- FDA animal feed experts joined the USDA team to provide technical expertise in an audit conducted by the Canadian Food Inspection Agency in response to the detection of two cases of BSE in Canada in 2004. Records were reviewed, meetings were held and facilities across Canada were inspected. USDA issued a report of its findings on February 25, 2005.

- Issued 10 Warning Letters for animal proteins prohibited in ruminant feed, and 15 class II recalls involving 15 firms and 25 products in response to violations of the BSE rule.

- Provided BSE inspection training to FDA investigators as well as state inspectors during the fiscal year.

- Provided personnel and expertise on BSE and animal feed issues to the U.S. Department of Agriculture in support of its efforts to reopen foreign markets for U.S. beef.

- Continued the development of a real-time Polymerase Chain Reaction (PCR) based method capable of detecting cattle, swine, sheep, goats, horses, or deer material along with poultry, goose, and turkey for use in analyzing samples of animal feeds and feed ingredients in support of the animal protein prohibition. “Real-time” means that we can detect the presence of prohibited material as the reaction is taking place, so we do not have to further process the sample.

- Completed the evaluation of a third commercially available diagnostic test marketed for the detection of ruminant proteins in animal feed. Like the other diagnostic tests previously evaluated, this test was much less sensitive than the methods the Agency uses (microscopy and PCR) for analysis of animal feed.

- FDA implemented an advanced analytical procedure for detection of prohibited material in animal feed into an assignment issued for 900 domestic and 900 import feed samples. This novel approach combines light microscopy with polymerase chain reaction (PCR) to determine and detect DNA from ruminants and non-ruminant mammalian species, supporting the BSE/Ruminant Feed Ban. (Field Activity)

- Following the finding of a BSE positive animal in Texas, FDA, USDA/APHIS, the Texas Animal Health Commission, and the Texas Feed and Fertilizer Control Service successfully conducted a feed investigation with two main objectives. The first objective was to identify all protein sources in the animal's feed history that could potentially have been the source of the BSE agent. The second objective was to verify that cattle leaving the herd after 1997 that were identified by USDA/APHIS as animals of concern, such as progeny and feed cohorts, were rendered at facilities in compliance with the BSE/ruminant feed ban regulation. (Field Activity)

- Awarded contracts with state and local governments to perform BSE, feed manufacturers and illegal tissue residue inspections. Auditor training was conducted for feed contracts. (Field Activity)

- Reviewed and awarded Cooperative Agreement grants for BSE infrastructure improvement in eight states. The Agency and the States maintained and continued to develop new partnerships (e.g., BSE inspections) that have contributed to the exchange of inspection and sampling data and have facilitated the receipt of training and distribution of equipment to the states. (Field Activity)

Tissue Residue

- Completed a major revision of the Tissue Residue Compliance Program and implemented on August 1, 2005 to include instructions for investigating residues in seafood and other animal derived foods such as honey.

- Successfully converted the Residue Violation Information System which contains information on all tissue residue violations/violators identified since 1988, to a web based application that uses an Oracle Relational Database and is shared with FSIS.

- Studied the correlation of drug residue levels in tissues and fluids of beef steers, for use in the development of rapid screening test kits and completed their study of the long-term kidney depletion of gentamicin in beef steers.

- Handled 83 feed recall events during FY 2005. Twenty of these recalls were related to drugs used in feeds, and six were due to BSE feed regulation issues – the feed contained or could have contained prohibited material and did not have the required caution statement.

- Evaluated two commercially available rapid screening test kits, to determine if the tests could detect the presence of aflatoxins in finished feeds. Aflatoxins, a carcinogen, are naturally occurring mycotoxins that can contaminate corn and other grains, a potential for harm to animals consuming the feed.

Animal Drug Compounding

- Inspected compounding pharmacies to reduce the risk of compounded veterinary drug products in food-producing and non-food-producing animals. Outcomes to date resulted in fewer than 40 percent of the completed inspections being considered for some form of regulatory action. Five warning letters have been issued.

- Developed methods for a wide range of animal drug compounds. In the first phase of method development (during FY 2005), we validated a procedure for surveillance of 27 animal drug compounds from nine chemical classes.

- In cooperation with ORA, provided FDA training to compliance officers, program monitors, and investigators on compounding animal drugs and compounding pharmacies, provided in-depth instruction, newly developed training, outreach materials and education on the AMDUCA, attendant regulations, proper drug use and residue avoidance.

Zoonotic Diseases

Salmonella in Turtles

- The FDA amended the current regulation to reflect a change in responsibility for administering the regulation from FDA's Center for Food Safety and Applied Nutrition to FDA's Center for Veterinary Medicine. This action was taken to enable the agency to more effectively administer the provisions of the regulation.

- FDA has investigated reports of salmonella in children ages 2-9 who have been in contact with pet turtles. FDA has issued warning letters in some of these cases and prepared information fact sheets explaining the human health hazards associated with turtles for FDA investigators and consumers.

MonkeyPox

We processed 153 requests for permission to transport animals under an interim final rule adopted by the FDA and the CDC in response to an outbreak of monkeypox. Most of the requests involved the shipment of wild prairie dogs and others were for movement from one zoo to another, moving to research institutions and educational purposes.

Dioxin

Issued an assignment for a nationwide survey to assess dioxin levels in rendered fat from swine, cattle, poultry, and mixed animal species; in yellow grease (restaurant fats/oils); and in agents (such as clay and diatomaceous earth) used to filter and/or bleach mammalian and poultry fats and presented data at an October 2004 scientific meeting on dioxin levels in grains, grain byproducts, fish meal, fish oil and forages.

Aquaculture

Modified the Compliance Program Guidance Manual 7371.006, Illegal Residues in Meat and Poultry to include residues in domestic seafood which will provide guidance to the FDA Field on how to conduct follow-up to residue violations in domestic aquacultured seafood.

Counterterrorism

- Examined the potential use of certain veterinary antimicrobials for human use in a worse case emergency as requested by the National Security Council.

- Trained a segment of the Renderers and Protein Blenders industry on performing risk analysis of their industry to try and prevent deliberate contamination events.

- Participated in TOPOFF 3. One of the challenging agents was plague, which may be transmitted and perpetuated by the companion animal population, with fleas as a vector. Helped to develop a public guide entitled "Controlling Fleas on Your Pet: Recommendations for Pet Owners".

- Assisted the Department of Homeland Security and other agencies in the completion of a draft National Preparedness Goal and the Target Capabilities list that will help states prepare for a wide range of emergencies including accidental or deliberate disease outbreaks, natural disasters, and nuclear and contamination events involving food and livestock.

- Participated in the Agricultural Intelligence Group meeting regularly to exchange information and ideas about food security, and educated constituent organizations how to perform vulnerability assessments of animal feed production facilities.

- Began to develop analytical methods to detect the presence of toxins, drugs, pesticides and other substances that could be introduced into the U.S. animal feed supplies by bioterrorists.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Under this strategic goal, the Program supports the FDA's efforts to strengthen its infrastructure, enhance employee performance, and take other steps to build a high functioning organization. Some of the accomplishments include:

- Played an active role on the Performance Work Statement Team/MEO Team in the effort to ensure that these functions remained in the agency, while working to save money for both the government and the taxpayers.

- The PV Works (Vet) pilot application and database, a commercially-off-the-shelf product that provides an animal health drug safety system designed for both animal and human reactions to veterinary pharmaceuticals, were successfully installed on the CVM server.
    - Test accounts were created for ten FDA reviewers to access and test the PV-Works pilot.
    - Over 25 animal adverse event cases input by two animal drug sponsors were forwarded to FDA and loaded into PV-Works for use by FDA reviewers. Several cases of human exposure input by the two firms were also loaded.

- The Consolidated Reporting Environment (CRE) supports the implementation of the full dataset from the Activity Time Reporting (ATR) system, and the relevant reference data from the Submission Tracking and Reporting System (STARS).
    - Implemented a robust reporting environment supporting the implementation of a dataset with the capability of adding additional source systems.
    - Released the CRE production system.
    - Leveraged the financial and activity characteristics of capture data.

- Continued to support and enhance the partnering of employees and IT by implementing a web content management system (RedDot).

- Played an internal role in the agency's implementation of Unified Financial Management System (UFMS), which replaced five accounting systems that had been used previously across the operating divisions in the agency.

- Continued to implement its Activity-Based Costing program. We made numerous enhancements to improve the information derived from Activity Time Reporting, ensuring that we have the most accurate and up-to-date information available; this improved our reporting and tracking capability.

- The Staff College obtained accreditation through the Maryland State Board of Veterinary Medical Examiners for its Scientific Seminar Series titled Antimicrobial Resistance – Human, Poultry, Swine, Bovine, and Disease Modeling.

- The Staff College has begun the integration of an automated interview tool that is tied to the CVM Competency Model. This will ensure identification and selection of the best-qualified candidates that are learning agile (can continue to learn and remain current with changing medicine, science and technology) and who possess the necessary technical, team, leadership, and management competencies.

- The Staff College enhanced learning activities and educational opportunities by providing seminar series and courses presenting information on new and emerging scientific issues. In addition to ongoing courses, we introduced two new series:
    - The **New Reviewer Training** aimed to reduce the learning curve of new reviewers by 6 to 12 months, from the current 18-month timeframe, and
    - The **Drug Manufacturing Series** implemented to enhance Center employeesunderstanding and application of the drug review process.

Animal Drugs And Feeds
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS [1]	FY 2005 Actuals	FY 2006 Estimates	FY 2007 Estimates
New Animal Drug Applications (NADAs):[2]			
Received	11	10	8
Completed	9	10	10
Approved	7	7	7
Pending[3]	5	5	3
New Animal Drug Application Supplements: [2] [4]			
Received	451	482	482
Completed	449	482	500
Approved	319	362	464
Pending [3]	159	159	141
Abbreviated New Animal Drug Applications (ANADAs): [2]			
Received	49	48	48
Completed	46	50	50
Approved	13	14	14
Pending [3]	50	48	48
Abbreviated New Animal Drug Application Supplements: [2] [4]			
Received	116	118	118
Completed	97	106	111
Approved	71	75	75
Pending [3]	99	111	118
Investigational New Animal Drug (INAD) Files: [5]			
Received	1,888	1,888	1,888
Completed	1,767	1,888	1,900
Pending [3]	386	386	374
Generic Investigational New Animal Drug (JINAD): [5]			
Received	335	335	335
Completed	229	308	335
Pending [3]	173	200	200
Food (Animal) Additive Petitions[6]	9	15	15

[1] ***FY 06 & 07 performance estimates are dependent upon a sustained level of base and user fee resources***. The estimates do not include invited labeling change supplement applications because it is not possible to accurately project sponsor or CVM requests for this type of application.

[2] Includes originals and reactivations. If the application is not approvable, the sponsor may submit additional information until the Agency is able to approve the application.

[3] Reflects submissions (received during the fiscal year) which still require review.

[4] A supplemental application is a sponsor request to change the conditions of the existing approval. They can be significant (a new species or indication), or routine (product manufacturing changes).

[5] An INAD or JINAD file is established at the request of the sponsor to archive all sponsor submissions for a phased drug review including: request for interstate shipment of an unapproved drug for study, protocols, technical sections, data sets, meeting requests, memos of conference and other information.

[6] Non-drug substances added to animal feed are considered Food Additive Petitions and require review and approval.

PROGRAM WORKLOAD AND OUTPUTS 1/	FY 2005 Actuals	FY 2006 Estimates	FY 2007 Estimates
Investigational Food Additive Petitions	31	35	35
Production & Manufacturing Defect Reports			
Received----------→	2,948	2,900	2,900
Reviewed----------→	1,788	1,780	1,780
Adverse Experience Reports (AERs)			
Received----------→	33,183	33,000	33,000
Reviewed----------→	18,591	19,000	19,000
Animal/Medicated Feed Partnership Agreements	27	27	27
PROGRAM OUTPUTS-			
DOMESTIC INSPECTIONS			
Pre-Approval /BIMO Inspections	72	140	110
Drug Process and New ADF Program Inspections	230	210	210
BSE Inspections	3,025	3,760	3,760
Feed Contaminant Inspections	13	15	15
Illegal Tissue Residue Program Inspections	203	245	245
Feed Manufacturing Program Inspections	369	240	40
State Contract Inspections: BSE	3,309	4,562	4,562
State Contract Inspections: Feed Manufacturers	457	347	347
State Contract Inspections: Illegal Tissue Residue	370	750	600
State Partnership Inspections: BSE and Other	988	900	900
Total Above FDA and State Contract Inspections	**9,036**	**11,169**	**10,789**
Total Domestic Reinspections (Non-add)	**173**	**173**	**173**
State Animal Drugs/Feeds Funding	$1,300,000	$1,700,600	$1,800,000
BSE Grant Increase	$3,000,000	$3,000,000	$3,000,000
State Contract for Tissue Residue	$220,000	$220,000	$210,000
Total State Funding	**$4,520,000**	**$4,920,600**	**$5,010,000**
Domestic Laboratory Samples Analyzed	1,841	1,770	1,730
PROGRAM OUTPUTS-			
IMPORT/FOREIGN INSPECTIONS			
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	26	45	45
Foreign Drug Processing and New ADF Program Inspections	12	10	10
Total Above Foreign FDA Inspections	**38**	**55**	**55**
Total Foreign Reinspections (Non-add)	**3**	**3**	**3**
Import Field Exams/Tests	4,298	4,500	4,500
Import Laboratory Samples Analyzed	753	1,120	900
Import Physical Exam Subtotal	5,051	5,620	5,400
Import Line Decisions	212,254	235,602	261,518
Percent of Import Lines Physically Examined	2.38%	2.39%	2.06%

MEDICAL DEVICES AND RADIOLOGICAL HEALTH

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$244,282,000**	**$260,503,000**	**$271,571,000**	11,068,000
Center	*$183,157,000*	*$192,714,000*	*$200,480,000*	7,766,000
FTE	*1,104*	*1,136*	*1,158*	22
Field	*$61,125,000*	*$67,789,000*	*$71,091,000*	3,302,000
FTE	*412*	*407*	*421*	14
Program Level FTE	**1,516**	**1,543**	**1,579**	**36**
Budget Authority	**$214,962,000**	**$220,564,000**	**$229,334,000**	**8,770,000**
Trigger Needs for ADUFA and MDUFMA			*$4,950,000*	$4,950,000
FTE			*28*	28
Cost of Living			*$3,334,000*	*$3,334,000*
Strategic Redeployment			*$486,000*	*$486,000*
FTE			*0*	*0*
Budget Authority FTE	**1,367**	**1,378**	**1,406**	28
User Fees	**$29,320,000**	**$39,939,000**	**$42,237,000**	$16,864,000
MDUFMA	*$16,361,000*	*$22,978,000*	*$24,931,000*	$1,953,000
FTE	*115*	*131*	*139*	8
MQSA	*$12,959,000*	*$16,961,000*	*$17,306,000*	$345,000
FTE	*34*	*34*	*34*	0
User Fee FTE	**149**	**165**	**173**	8

[1/] *Includes a one percent rescission*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	217,285,000	193,350,000	23,935,000	1,485
2004 Actual	$221,506,000	$191,143,000	$30,363,000	1,515
2005 Actual	$244,282,000	$214,962,000	$29,320,000	1,516
2006 Enacted	$260,503,000	$220,564,000	$39,939,000	1,543
2007 Estimate	$271,571,000	$229,334,000	$42,237,000	1,579

Statement of Budget Request

The Center for Devices and Radiological Health is requesting $271,571,000 in program level resources for accomplishing its mission activities including:

- Promoting and protecting the health of the public by ensuring the safety and effectiveness of medical devices and the safety of radiological products.

- Meeting all statutory responsibilities for review of new medical devices.
- Assuring medical product safety by monitoring the use of all medical devices, and the function and use of radiological health.
- Managing emerging hazards to prevent widespread health and safety threats and ensure safe and effective new technologies.
- Applying the Total Product Life Cycle model across the range of Devices and Radiological Health activities, by covering products from concept to obsolescence.
- Connecting to the global public health community, and partner with stakeholders.
- Using science in the regulatory process to the maximum extent.
- Attracting and retaining a diverse and high quality workforce.
- Measuring and setting targets to maximize the program's impact on public health.

Program Description

CDRH regulates a wide array of medical devices, from: artificial hearts, pacemakers, drug-coated stents to deep brain stimulators and spinal implants, mammography and dialysis machines and infusion pumps to intraocular lenses and cochlear implants; as well as robotic surgery devices, stair-climbing wheelchairs, *in vitro* diagnostic devices, radiologic devices and many others. To keep pace with the rapid development of new technology, and to make decisions based on the best scientific information and knowledge available, CDRH routinely consults with experts in the academic community, other government entities, clinical practice, and the military. CDRH also supports initiatives to improve the Nation's ability to respond to bioterrorism and public health challenges, including expediting the review of bioterrorism diagnostics, managing product shortages, supporting safe and effective development and use of battlefield and emergency devices, ensuring safe use of x-ray machines in airports and other security systems, and assessing radiation products for misuse as weapons.

ORA supports CDRH by conducting preapproval inspections of both foreign and domestic establishments and other premarket-related activities such as: bioresearch monitoring of clinical research, preapproval inspections and laboratory method validations needed for premarket application decisions, and inspections of manufacturing facilities to determine if the factory is able to manufacture the product to the specifications stated in the application. ORA conducts risk-based domestic and foreign postmarket inspections, field exams and sampling of medical device manufacturers to assess their compliance with Good Manufacturing Practice requirements, and conducts inspections of reprocessors of single-use devices and radiological health products. To complement the regular field force, the Office of Criminal Investigations investigates instances of criminal activity in FDA regulated industries.

Performance Analysis

During the latest performance period, (FY 2005), the Medical Devices program met four of its seven center performance targets; expects to meet the remaining three when the data becomes available in June FY 2007; and met all three of its field performance targets. For more information about these performance goals and results, please see the Performance Detail section.

The Food & Drug Administration Modernization Act of 1997 gives FDA the mandate to replace universal user facility reporting with the` Medical Product Surveillance Network (MedSun) that is composed of user facilities that constitute a representative profile of user reports. FDA estimates that there may be as many as 300,000 injuries and deaths annually associated with device use and misuse. FDA surpassed by 200% our long-term goal of expanding patient surveillance by 50% by 2008, through increasing the number of patients covered from 17 million to 53 million this year. This will allow for more rapid identification and analysis of adverse events. MedSun is a critical component towards achieving this long-term goal.

Performance Highlight:

FY 2007 Goal Target	FY 2005 Results	Context
Expand actively participating sites in Medsun Network to 76 percent.	FDA recruited, trained and have functioning 354 facilities for the network	MedSun 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.

Program Resource Changes

Budget Authority

Cost of Living-Pay: + $3,334,000

FDA's request for inflationary pay costs is essential to accomplishing our public health mission. Payroll costs account for more than sixty-percent of the FDA budget, and the Agency is not able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Devices portion of this increase is $3,334,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Appropriated User Fee Trigger Needs -- Maintaining Medical Device Review Programs: + $ 4,950,000 and + 28 FTE

To meet the statutory requirements for collecting Medical Device User Fees, FDA must spend a minimum amount of appropriated resources, indexed to the cost of living, on the review process. If the appropriation and/or spending do not meet these minimum requirements (known as user fee triggers), the agency is unable to receive the supplemental user fee funding and the program terminates. The additional budget authority is needed to ensure that the trigger requirements are met. The requested amount for the Medical Device

review Program is $4,950,000 and 28 FTE. The portion for the Center for Devices and Radiological Health is $2,901,000 and 15 FTE, and the portion for the Office of Regulatory Affairs is $2,049,000 million and 13 FTE.

User Fees

Medical Devices User Fee and Modernization Act: +$1,953,000 and + 7 FTE

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amends the Federal Food, Drug, and Cosmetic Act to provide FDA important new responsibilities, resources, and challenges. MDUFMA was signed into law October 26, 2002 and was amended by the Medical Device User Fee Stabilization Act of 2005. MDUFMA has three particularly significant provisions. These provisions allow for the collection of user fees for premarket applications, allow establishment inspections to be conducted by third parties and place new regulatory requirements on reprocessed single use devices. The revenues from these fees, and the appropriated trigger amounts will allow FDA to pursue a set of ambitious performance goals that will provide patients earlier access to safe and effective technology, and will provide more interactive and rapid review to the medical device industry. In FY 2007 FDA will work with Congress on the reauthorization of the Medical Device User Fee and Modernization Act. This increase of $1,953,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Mammography Quality Standards Act (MQSA): +$345,000

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths among American women. Experts estimate that one in eight American women will contract breast cancer during their lifetime. The MQSA, which was reauthorized in October 2004, addresses the public health need for safe and reliable mammography. The Act required that mammography facilities be certified by October 1994, and inspected annually to ensure compliance with national quality and safety standards. The reauthorization codified existing certification practices for mammography facilities and laid the groundwork for further study of key issues that include ways to improve physicians' ability to read mammograms and ways to recruit and retain skilled professionals to provide quality mammograms. The increase of $345,000 will cover inflation.

Proposed User Fees (Reclassified as Mandatory): (Non-Add)

Reinspection User Fee (Mandatory): + $2,616,000 and + 22 FTE (Non-Add)

The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an estimated amount sufficient to fund the FY 2007 reinspections. The Devices Program component of this user fee is $2,616,000 and 22 FTE.

Justification of Base

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

FDA will continue to improve problem detection and the timeliness of risk management actions aimed at preventing harm from regulated products, and will continue its highly-regarded risk communications activities aimed at increasing safe and effective use of medical products. FDA plans to:

Modernize Medicare and Medicaid through Safe Product Use

- Expand the Home Health Care Initiative. This initiative addresses the growing trend of using clinical medical devices in the home setting and advances home health care opportunities. It does this by providing health care practitioners, consumers, and patients with internet-accessible information on the safe and effective operation of devices. Many of these devices were never intended to be used outside the hospital or by lay users. There will be a repository of devices specifically labeled for home use, brochures, references and hyperlinks to other government and private agencies working on home care issues.

Improve Problem Detection and Risk Management to Transform Health Care

- Strengthen the Medical Product Surveillance Network (MedSun). This will be accomplished by increasing by five percent the number of sites sending in device problem reports to the program and recruiting new facilities to replace those that leave the network. This internet-based program is designed to reduce device-related medical errors by disseminating safety information. MedSun also serves as an advance warning system and creates an interactive communication channel between FDA and its system participants.

- Pilot the use of "sub-networks" within MedSun, including hospital laboratories, pediatric ICUs, and catheterization and electrophysiology laboratories. This will allow us to more rapidly evaluate adverse events when they arise.

- Receive process and review an estimated 200,000 medical device adverse event reports Continue to develop an electronic adverse event repository system to accommodate electronic data entry and processing of adverse events for medical devices. This system will facilitate the review, analysis and management of the reports received each year. It will permit more efficient use of FDA analyst resources. It will provide FDA, health care professionals and consumers, and other state and Federal agencies with the information necessary to make faster and more thorough risk management decisions.

- Refine the Alternative Summary Reporting program to ease industry's reporting burden for device-based adverse events. By submitting the reports less frequently and in an abbreviated form, industry is relieved of the individual reporting burden. Yet the Agency can continue to monitor these adverse events on an aggregate basis.

- Provide guidance to industry on the recommended contents of annual reports for premarket approval (PMA) devices. These reports will allow FDA to monitor yearly trends in adverse events and device malfunctions.
- Improve the feedback of post-approval data to premarket reviewers in order to improve the quality and timeliness of premarket reviews.
- Use and improve postmarket communication to mitigate risk from medical device problems. this has been done through:
    - Public health notifications about Ralstonia bacterial contamination of a humidifier used in newborns.
    - Recommendations for clinicians concerning the recalled Enterex implantable device for Gastroesaphogeal Reflux Disease (GERD), information regarding failures with the Guidant Implantable Cardioverter Defibrillator.
    - Recommendations to avoid entr1apment of vulnerable patients in the Vail bed.
- Incorporate human factors risk analysis in premarket and postmarket decision-making. This will enhance the identification of risks associated with the use of medical products and to reduce the occurrence of adverse events related to use error.

<u>Communicating Risks More Effectively to Empower Consumers</u>

- Continue publishing the “FDA & You” electronic newsletter that reaches the secondary schools and health education populations with timely health news. This ongoing collaboration between the FDA Centers is published three times a year.
- Maintain the newly-launched "Maturity Health Matters" online newsletter geared to providing FDA regulated product information of interest to the older adult population. This newsletter will publish three times a year. It will focus on FDA regulated products that help people live longer more productive lives. The inaugural issue primarily addressed medical devices; future issues will include collaboration with all FDA Centers.
- Maintain technical distribution capabilities to allow the content of "FDA Patient Safety News" (PSN) to be readily available as a teaching tool. FDA PSN is an Agency-wide monthly television news show that brings vital information on how to improve the safety of drugs, devices, vaccines, and diagnostic products to physicians, nurses, pharmacists, risk managers and educators across the nation.
- Maintain consumer websites. These provide current and reliable information on issues like cardiovascular disease, pediatric medical devices, radiation emitting electronic products, whole body scanning, personal protective equipment, cosmetic contact lenses, and phakic intraocular lenses—a newly approved, first-of-a-kind device.
- Disseminate public health messages related to medical and diagnostic device use before, during, and after emergencies and natural disasters.
- Maintain the redesigned Medical Device Recall website that provides a web-friendly, plain language overview of medical device recalls. The website now explains the various classes of medical device recalls and the procedures that FDA and companies follow during a recall. The website continues to describe each Class I recall in a plain language format and provides the access to the new recall database.

- Partner with other Federal agencies, states and private-sector organizations to develop and communicate information that will encourage safe use of medical devices. Coupled with this will be technical assistance to small medical device manufacturers and accessible feedback to industry, health professionals, and consumers. This assistance is provided via Device Advice—the CDRH self-service website for medical device and radiation emitting information and feedback. Postmarket communication will be exercised through FDA Press Releases to diminish risk from medical device problems, as has been done through notifications about the potential dangers associated with blood tubing in particular configurations.

National Evaluation of X-ray Trends (NEXT)

The NEXT program is a world-recognized collaboration of FDA with the Conference of Radiation Control Program Directors, the umbrella organization of state radiation control agencies to monitor the radiation doses patients receive during diagnostic x-ray exams.

In April 2005 FDA posted an article on the Radiological Health website titled "Dental Radiography: Doses and Film Speed." The article is a result of the NEXT Dental Survey, major film manufacturer research, and other literature searches, and it documents that dentists who use a higher film speed during dental x-rays can reduce patient radiation exposure by 60 percent. The article is available at: http://www.fda.gov/cdrh/radhlth/dentalradio.html.

Research, Development, and Evaluation Activities

- Increasing safe and effective use of medical products and improving risk communication to consumers. This includes activities to:
  - Study human factors associated with device use error to support appropriate human factor design practices that minimize or eliminate errors. The research supports future guidance, use-related health hazard evaluations, better error reporting and pre-market reviews, and outreach to industry.
  - Conduct usability research to determine how to best provide web-based patient safety information to the public and conduct audience analysis research. Improving access to CDRH's electronic information ensures that the most efficient and cost-effective methods to disseminate high quality, up-to-date information is available to consumers.

Mammography Quality Standards Act (MQSA)

- Maintain the MQSA program to ensure that mammography facilities remain in compliance with established quality standards, including:
  - Certify new mammography facilities and recertify one third of the more than 9,000 existing facilities;
  - Analyze and act on inspection results to ensure compliance with quality standards;
  - Enhance the Mammography Program Reporting and Information System (MPRIS). This system improves the quality, reliability, integrity, and accessibility of facility certification, inspection, and compliance data. It also tracks and monitors the accreditation, certification, inspection, and compliance history of facilities. Facility certification information is available to consumers on the mammography website.

- Fund annual MQSA inspections. Approximately 9 percent of mammography facilities deemed to be governmental entities are funded through budget authority. The other 91 percent of the annual facility inspections are funded through user fees.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

FDA will continue to provide rapid, transparent and predictable review of marketing applications and to increase the number of safe and effective new products—including those for untreated conditions, emerging infectious diseases and counterterrorism—by improving the predictability, efficiency and effectiveness of product development; contributing to standards for performance characteristics of diagnostic devices; and increasing the quality of applications. FDA plans to:

Premarket Review to Advance Medical Research

- Review premarket applications and focus resources on breakthrough medical device products and unmet needs.
- Continue efforts to modernize its information technology infrastructure, which is critical to successful premarket review, postmarket monitoring, and document management activities. The projects include:
  - Premarket database and tracking systems to help FDA better manage review times and processes.
  - A workflow/work management system that supports core and business processes across the entire total product life cycle.
  - Electronic submission systems improvements that will result in premarket reviewer/postmarket analyst savings.
  - Overall system upgrades and other inflationary increases to add new features and improve existing capabilities to obtain work management efficiencies in premarket, postmarket, compliance and administrative areas.
  - Scheduled, systematic upgrading of reviewer personal computers (on a three-year cycle) to ensure data security, compatibility with industry submissions, and more efficient operating systems and program.
- Work with industry and other stakeholders to develop best practice, policy and guidance documents to make premarket applications more consistent, complete, and less subject to multi-cycle reviews.
- Maintain FDA's small business assistance program as required by the Food, Drug & Cosmetic Act.
- Provide professional development opportunities for new and current staff. This will ensure that FDA reviewers develop and maintain the skills necessary to understand and keep pace with technologies that are rapidly developing and becoming more complex.
- Foster education of the workforce on risk management assessment and communication. This will ensure that science-based risk management is used in all regulatory activities. It

will also make sure the Agency's resources can provide the most health promotion and protection at the least cost for the public.

- Hold public workshops to discuss challenging innovative devices for pediatric patients. These will include pediatric mechanical circulatory support devices (ventricular assist devices) and fetal monitoring devices used during delivery.

New DNA-Based Test for Cystic Fibrosis

FDA approved the first DNA-based blood test to help detect cystic fibrosis by directly analyzing human DNA to find genetic variations indicative of the disease. The test will be used to help diagnose cystic fibrosis in children and to identify adults who are "carriers" of the gene variations. FDA was able to take advantage of the automatic reclassification of class III devices (the de novo process) to bring this product to market with an expedited and streamlined 510(k) review despite the lack of a predicate device. The result is the availability of a powerful new diagnostic tool that represents a significant advance in the application of genetic technology and paves the way for similar genetic diagnostic tests to be developed in the future.

Cystic fibrosis is a serious genetic disorder affecting the lungs and other organs that often leads to an early death. It is the number one cause of chronic lung disease in children and young adults, as well as the most common fatal hereditary disorder affecting Caucasians in the U.S. The disease affects about one in 3,000 Caucasian babies. Half of the people with cystic fibrosis die by age 30.

<u>Obesity, Diabetes and Cardiovascular Disease Strategies</u>

Improve the availability of diagnostic devices and consumer information by continuing to:

- Monitor the use and safety of new weight loss technologies through targeted postmarket plans and partnering with NIH and other collaborators.
- Partner with sponsors on new, promising, investigational weight loss devices. These devices support the Secretary's vision of comprehensive and novel early prevention and detection strategies that increase healthy life potential.
- Determine whether more effective but "least burdensome" regulatory mechanisms can be put into place for diabetes devices. This will assist industry in bringing to market new devices to test, monitor, and administer medications for the management and treatment of diabetes.
- Maintain FDA's Diabetes Information website. This site provides detailed consumer information about the products that FDA regulates to diagnose and treat diabetes, with links to additional diabetic information.
- Partner with the diagnostics industry, health professionals and diabetic organizations. This will help assure that safe and effective diagnostics are available, accurate, less invasive and easier for patients to use.
- Maintain FDA's Heart Health Online website. The site provides consumer information about the products FDA uses to diagnose, prevent and treat cardiovascular disease, with links to additional cardiovascular information. This site was selected as one of the Biomaterials Network (Biomat.net) top five internet sites, based on general quality, scientific value and suitability to internet browsing.

- Develop new outreach materials about implantable cardioverter defibrillators (ICDs). This will help consumers understand the risks associated with their underlying health conditions and the benefits and risks of using ICDs.

Third Party Review to Sustain Access to New Products

- Continue the Third Party Review Program established under Food & Drug Administration Modernization Act. The Act was intended to encourage the use of outside scientific and technical expertise and provide an alternative to FDA 510(k) reviews. This option may be faster than reviews performed exclusively by FDA staff. It also gives manufacturers access to specialized expertise by third parties in areas such as device testing, standards, and foreign regulatory requirements. FDA will:
    - Encourage industry's use of third party reviews. Sixty-five percent of all 510(k)s are eligible for third party review, but only seven percent are submitted through this program. In 2005, the number of 510(k) submissions using the third party review program declined by 5 percent (after increasing 34 percent during the prior year).
    - Maintain FDA's third party web site that provides information on the Accredited Persons Program.
    - Maintain the Third Party Recognition Board to advise and assess new applicants, reassess existing Accredited Persons, and monitor FDA's periodic auditing of their work.
    - Encourage ongoing training for third parties to ensure consistency and quality of their reviews.
    - Complete a study based on the experience under the program and submit a report to Congress no later than January 10, 2007 on the findings of the study, as required by section 523(d) of the Federal Food, Drug, and Cosmetic Act.

Science and Standards to Advance Medical Research

- Incorporate epidemiology expertise throughout the application life cycle from review into post-approval investigations.
- Minimize burden to industry and better utilize Center expertise by leading and participating in the development of national and international product standards.
- Promote the use of standards for manufacturing safer and more effective medical products which can speed review and enhance the quality of regulatory decision making.
- Collaborate with National Institute of Standards and Technology (NIST) to ensure medical devices firms that are impacted by standard developments meet the public health needs and maximize medical product quality.

Genetic Testing

The vast majority of genetic tests are currently not regulated by FDA but are being developed as home brew assays under the authority of the Clinical Laboratory Improvement

Amendments of 1988 (CLIA). There is considerable confusion about these two different regulatory mechanisms. There is also ongoing interest in assuring appropriate assessment of technology and communication of information on new genetic tests. FDA plans to work with the Center for Disease Control and Prevention (CDC), the Center for Medicare and Medicaid Services (CMS), the Federal Trade Commission (FTC) and other agencies to:

- Clarify regulatory choices and requirements for development of new genetic tests so that all stakeholders will understand the options available.
- Develop mechanisms for assuring new tests are developed in a timely manner. This will be accomplished with appropriate methods of regulatory oversight; an appropriate combination of FDA, CMS, CDC and stakeholder expertise; and, when relevant, regulatory authority.
- Develop scientific expertise and regulatory strategies for evolving medical device areas such as genetic testing. This will include working with partners such as CDC and NIST to ensure appropriate reference materials and methods are in place to support the cutting edge technologies on which genetic testing is based.
- Ensure consumers understand the nature of tests available to them in over-the-counter settings.
- Participate in the activities of the Secretary's Advisory Committee on Genetics, Health, and Society.

<u>Research, Development, and Evaluation Activities</u>

- Research, development, and evaluation activities support this strategic goal by increasing the predictability, efficiency and effectiveness of product development and application review. This includes activities to:
    - Plan and execute special electrical and software engineering laboratory investigations. These will be used to either confirm a performance claim made by a manufacturer or determine the root cause of a medical device failure that endangers the public health;
    - Develop, using applied mathematics, appropriate methods to evaluate medical imaging system performance and dose. The results will be used in the review of premarket submissions of medical devices such as advanced ultrasound technology for both diagnosis and treatment
    - Maintain ionizing radiation measurement and calibration capabilities to support the review of new safety and security mechanisms. This supports the Agency's counter-terrorism and radiation safety activities.
    - Conduct research and regulatory reviews of possible dangerous malfunctions in devices via electromagnetic interference (EMI) from wireless equipment, such as cellular phones and magnetic-field emitting security devices.
    - Investigate safety issues related to electrophysiology and electrical stimulation medical devices for the heart and nervous system. The work is specifically aimed at forming the scientific basis for regulatory decisions, guidance documents that speed device approvals, and industry safety standards for electrical stimulation.

- Investigate high-priority, minimally invasive optical diagnostic and therapeutic technologies to assist regulatory reviewers in a timely assessment of manufacturer's submissions.
- Conduct laboratory research in:
    - Biological risk assessment and standards development for tissue/material interactions. These activities are designed to provide a scientific basis for regulatory decision-making in the Agency and to develop methods for risk assessment and medical device toxicology.
    - Radiation biology. This research will support the maintenance of existing regulatory standards for radiation emitting electronic products, the development of additional consensus standards, and an understanding of the effects of exposure to radiation.
    - Biomolecular mechanisms. This will help in determining whether new biotechnology developments used in the generation of new devices and diagnostic processes are safe and effective. Proposed studies will address concerns about current and impending medical device combination product submissions and the ways in which new genetic approaches can enhance genomic or genetic testing devices.
    - Mechanics of materials and medical devices. This research will provide reliable, easily interpreted methods for evaluating new heart valve designs. It will also assist in setting standards that may be incorporated into guidance and help expedite product review while maintaining patient safety.
- Develop chemistry and materials science-oriented test methods and performance requirements for devices. This will allow the FDA to study and predict device failure modes and establish performance criteria that will help to ensure safety and effectiveness.

Collaboration Corrects Problems Across An Industry

CDRH issued an inspection assignment to ORA's field investigators after CDRH's review and evaluation of various data determined that many of the cochlear implant manufacturers had hermeticity and moisture problems that led to injuries in patients using these devices. Based on the findings of the inspections, CDRH conducted numerous meetings and discussions with the industry on ways to resolve the problems, including redefining moisture level specifications in the cochlear implants. Through CDRH's efforts, the industry made a number of major hermeticity and moisture level improvements that have led to a decrease in injuries. As a result of CDRH's work, the National Institute of Standards and Technology sponsored an October 2005 workshop on the biocompatibility of microchips, capacitors, and components used in implantable devices.

<u>Research and Clinical Study Ethics and Integrity (Bioresearch Monitoring)</u>

- Maintain an effective, comprehensive inspection and outreach program. This will better assure the quality and integrity of research data upon which regulatory decisions are made and to assure the protection of human research subjects. FDA plans to:

- Promptly evaluate and investigate allegations of research misconduct that may compromise the safety of human research subjects or undermine the quality of research data.
- Develop a "post-approval" inspection program of premarket approval (PMA) holders. The program will assure proper conduct and reporting of CDRH required post approval study commitments.
- Collaborate with non-compliant firms and researchers to develop corrective and preventative actions to improve human subject protection and ensure research integrity.
- Conduct educational outreach activities and develop guidance materials for the medical device research community.
- Develop scientific capabilities through professional staff development and contribute to major breakthroughs and novel technologies in medical device research.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

FDA will continue to prevent harm from regulated products by developing scientific and technical standards and systems aimed at maximizing medical product quality, and by using efficient and effective risk targeting, external partnering and collaboration aimed at detecting and intercepting substandard manufacturing processes and products. FDA plans to:

Risk Management

- Develop and refine a quantifiable risk-based model that effectively manages targeted inspections of device manufacturers who produce products which pose the most significant public health risk. The model will include the use of appropriate follow-up actions to correct problems identified.

Import Monitoring and Inspections

- Maintain inspection coverage for both domestic and foreign medical device as the number of medically and technologically complex devices increases. FDA will:
  - Use risk management to target inspection coverage for Class II and Class III medical device manufacturers. Domestic inspection coverage will be at 20 percent of the estimated 5,550 high-risk device statutory inventory. Foreign inspection coverage will be at 7 percent of the estimated 2,500 high-risk device statutory inventory. This coverage goal does not include any inspections conducted under the "Inspections by Accredited Persons Program".
  - Conduct criminal investigations of reported product tampering, counterfeit products and other fraudulent criminal activities involving FDA regulated products.
  - Conduct emergency operation activities, investigations and respond to incidents involving FDA regulated products.
  - Review approximately 5,700,000 device import lines requesting the admissibility of foreign manufactured devices into domestic commerce.

- Conduct virtual training for foreign firms to assist in their efforts to voluntarily comply with FDA requirements.
- Conduct import field examinations of imported latex products used in the treatment of or as barriers from diseases or terrorist agents.

Bioterrorism and Homeland Security

- Continue to monitor, evaluate, and follow up on the public health needs of new medical devices or their use in counterterrorism preparedness and response. This will enable the FDA to regulate them in a manner that best serves the public health.
- Evaluate the safety and effectiveness of diagnostic test kits that detect biothreat agents as well as other diagnostic and therapeutic devices being developed to address such threats. Also evaluate the performance of diagnostic test kits that detect warfare agents being marketed to the public and the government.
- Predict and manage potential device shortages to ensure there are enough critical, commonly used devices, such as rubber gloves, to aid in rescue efforts. Develop mechanisms to use FDA's medical material shortage experts to assist in acquisition of limited critical medical countermeasures during a terrorist event.
- Develop field expertise to sample for contamination high-risk products such as rubber gloves or surgical masks. Develop test methods for the DOD to test emergency devices for safe use on the battlefield and in civilian emergency care.
- Participate in the development and recognition of standards originated by other agencies and outside organizations for use in reviewing and defining performance for test kits.
- Assess the in vitro diagnostic market to determine the number and type of test kits targeted to detect terrorism activity that are being marketed to the public and government. This will provide FDA with the capability to identify manufacturers that promote diagnostic devices, to monitor their activities and to act appropriately when unsafe practices are detected.
- Expand technical assistance to industry and DOD. In addition, expedite review, and expand outreach to civilian emergency medical professionals to give them more information about new devices in their field.
- Maintain Continuity of Operations (COOP) and emergency response plans and emergency response training, in conjunction with HHS and FDA.

Radiological Counterterrorism and Radiation Safety

- Revitalize the Radiological Health program to focus on standards, monitoring, education, research, and program management in order to:
  - Align CDRH efforts with current and evolving public health needs.
  - Expand focus on patient and consumer product experience.
  - Allow for a more targeted approach to regulation.
  - Increase information dissemination and training.

- Improve coordination across the radiological health community.

- Continue to monitor and assess radiation-emitting products to ensure their safe manufacture and use in existing and in new applications, such as in security or law enforcement deterrence and detection activities. This also includes:
  - Providing support to the Federal security and law enforcement agencies when requesting consult on development of such technology.
  - Ensuring manufacturers do not promote products for misuse or inappropriate use as weapons and to make recommendations and advise the public against such use.
- Conduct Radiological Health Stakeholder Meetings. These meetings provide a forum to address significant stakeholder issues or concerns. They also help FDA obtain feedback regarding opportunities for effective collaboration with CDRH and other members of the radiological health community.
- Continually update the FDA Radiological Emergency Response Plan as needed. Maintain preparedness through participation in interagency emergency response/counterterrorism working groups and exercises.
- Assist the Transportation Security Administration (TSA), U.S. Customs and Border Protection, and the National Institute for Occupational Safety and Health to assure worker safety during use of non-intrusive search products which emit x-rays and the use of x-ray cargo screening and electromagnetic screening products. Provide training and support for development of radiation protection and safety programs and testing of TSA security screening equipment.
- Conduct manufacturer inspection and targeted field testing of x-ray security screening products subject to the FDA cabinet x-ray standard.
- Maintain the electronic reporting system. This system allows manufacturers to submit required radiation safety documentation in electronic format. It permits risk-based prioritization of submissions for review by FDA. It facilitates data analyses and sharing. It also enables more efficient use of FDA and manufacturer resources. And, finally, it helps identify product safety problems to assure the safety of workers and the public.
- Develop a radiation safety consensus standard for cargo screening and other new non-intrusive search products that emit x-rays, neutrons or gamma rays.
- Develop guidance for manufacturers of x-ray personnel security screening systems, and continue to evaluate and monitor new products and manufacturers in this industry.
- Identify safer tanning techniques. FDA's optical radiation laboratory is conducting a human study entitled "Optimization of UV Exposure Patterns". The purpose of the study is to gather data to support a reduction in exposure of the public from artificial tanning devices. This data will be used to modify the present FDA and ISO standards for sunlamp products.
- Collaborate with the Nuclear Regulatory Commission (NRC) on nuclear power plant emergency preparedness and participate in emergency exercises.

- Coordinate with NRC to enable nuclear power plant security contractors to purchase laser products for use in security applications, which are not available on the open market.
- Continue to evaluate the vulnerability of electronic medical implants to new security scanners, and assist in drafting a national safety standard for security screening devices. This work is being adopted by the Federal Aviation Administration in deciding the purchases of walk through metal detectors at all of the nation's airports.
- Through the Interagency Steering Committee on Radiation Standards (ISCOR), encourage discussion among the Federal agencies with radiation control responsibilities to develop consistent policies aimed at reducing exposure for the general public. Efforts will include recommendations for appropriate use of security products and medical imaging equipment that exposes the public to ionizing radiation; continue working with ISCORS to address these radiation control issues.
- Encourage private sector development of radiation measurement instruments to facilitate radiation testing of security screening and non-intrusive search products.
- Prioritize and leverage FDA's radiation protection efforts with state governments, professional societies, and other Federal agencies. This will enable all these organizations to leverage their resources for the common goal of reducing unnecessary radiation exposure to the public.

Electro-Magnetic Interference From Security Systems

In the late 1990s, CDRH identified over 100 reports of injuries in patients with critical active implanted medical devices such as pacemakers/defibrillators and nerve stimulators. Injuries occurred when patients walked through some electromagnetic security devices like metal detectors. Preliminary CDRH measurements confirmed that some devices emitted relatively strong magnetic fields. With no standardized test methods addressing security systems emissions, CDRH engineers developed a new test method and novel simulator to generate electromagnetic fields similar to any security device. The results of this work help biomedical engineers and manufacturers of medical devices and security systems to identify incompatible combinations of emitters and victims early in the development stage, thus preventing injuries for vulnerable medical device patients.

CDRH used the expertise they developed on this subject in numerous premarket reviews, and published the simulator details and test results in peer reviewed journals. They are working with several international standards setting organizations to adopt this FDA-developed technology.

<u>International Activity Collaborations</u>

- Maintain the U.S./European Community (EC) Mutual Recognition Agreement to help reduce the number of foreign firms FDA staff need to inspect. This will be accomplished by relying on FDA inspections conducted by listed European Unions Conformity Assessment Bodies.
- Implement a pilot program to assess the feasibility of using an internationally harmonized format in the review of submissions for device safety and performance.
- Develop and maintain information about EU-based medical device manufacturers. Provide more information about the status of those manufacturers to help expedite product approval.

- Develop a mechanism for recognizing symbols for use in *in vitro* diagnostic labeling to allow for harmonization of package inserts.
- Continue FDA's participation as a member of the Global Harmonization Task Force to ensure a leadership role in the global market.
- Prepare and disseminate information on how FDA will regulate emerging technologies to help support FDA's role in international harmonization on emerging technologies; and,
- Develop and implement a third party pilot program to perform multipurpose audits of medical device manufacturers covering both US and Canadian requirements.

Inspections by Accredited Persons

Maintain the MDUFMA-authorized program to accredit third persons (Accredited Persons) to conduct inspections of eligible manufacturers of Class II and Class III medical devices. This program is independent of third party inspections performed under the current US/EC Mutual Recognition Agreement and offers companies that use the program, if they are doing business globally, the option to coordinate required inspections so that one appropriately certified third party can perform an inspection that may satisfy more than one regulatory authority—thereby limiting the disruption to production that is associated with multiple inspections. FDA will continue to:

- Accept and review applications from establishments wishing to be certified as an Accredited Person (AP) and sponsor classroom training as new firms are accepted into the program;.
- Continue performing joint inspections to qualify APs to perform independent inspections.
- Continue to promote the program to regulated industry.

Bovine Spongiform Encephalopathies (BSE) and Transmissible Spongiform Encephalopathies (TSE)

BSE, also known as "Mad Cow Disease," is a deadly, degenerative disorder of the central nervous system. TSE includes a group of related human and animal diseases that are fatal to humans and animals and for which there is no treatment or preventive vaccine. FDA plans to:

- Maintain current Field Investigator's Guidance for Manufacturing Facilities. The current scientific understanding of TSEs and their potential risks are changing rapidly. Resources are needed for educational activities and document revision as our understanding changes to keep the guidance documents and field investigations scientifically accurate.
- Maintain a device tracking/animal materials data base for identifying/tracking devices containing or manufactured from animal-derived source material.
- Examine ways to prevent the transmission of TSE-related diseases during the use and reuse of medical instruments.
- Evaluate decontamination procedures for device manufacturing processes, including equipment and facilities, and for medical instruments; and to consider the recommendations and deliberations of the advisory panel on this topic.

Clinical Laboratory Improvement Amendments (CLIA)

- This activity is funded by a portion of the CLIA user fees collected by the Centers for Medicare and Medicaid Services. FDA has been assigned the responsibility for developing policy and performing reviews to establish the complexity categorization of all new laboratory tests. This work determines the types of laboratory setting appropriate for each laboratory test and contributes to ensuring both quality and access to important testing technology.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

FDA works to increase the quality, effectiveness, and adaptability of the FDA workforce and to improve capability and capacity for highly coordinated and integrated operations. FDA will:

- Provide leadership to industry in the development of innovative approaches for the evaluation of medical device safety and effectiveness; and,
- Support the President's Management Agenda and competitive sourcing A-76 efforts by performing cost comparison studies for identified functions.

In addition, FDA plans to relocate CDRH's engineering and physics research programs to FDA's consolidated campus at White Oak. FDA needs to allocate funds to provide basic laboratory support equipment, such as biosafety cabinets and autoclaves, and for research instrumentation, such as electron microscopes and lasers.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Modernize Medicare and Medicaid

- *Home Health Care Initiative* - Continued Home Health Care Initiative efforts to address the needs of a growing number of patients using clinical medical devices at home. A prototype was developed and is now under Center review for an electronic repository for manufacturers' infusion pump labels containing pump information and instructions for use.

Improve Problem Detection and Management

- *Postmarket Safety Studies* – Implemented a new system for the oversight of Post-Approval Studies program. This program involves the design and tracking of clinical studies that are required of manufacturers as a condition of approval of a PMA
- *Evaluation of CDRH Postmarket Program* – Conducted an evaluation of the Postmarket program. The evaluation is documented in a report, *CDRH Postmarket Safety Framework.* CDRH established a senior level team who will be responsible for evaluating the recommendations, overseeing the setting of priorities, and monitoring the action items selected for program improvement.

- *Medical Devices Adverse Events* - Received, processed, and analyzed over 180,000 medical device adverse events reported through CDRH's Medical Device Reporting (MDR) system. This system detected and CDRH responded to numerous public health issues ranging from orthodontic headgear, hemodialysis systems and hospital beds, to cochlear implants, deep brain stimulators, and diagnostic tests for heart attack and pregnancy. CDRH began developing an electronic adverse event reporting system that will facilitate processing the reports and also reduce operating costs.
    - **MedSun** is a national network of healthcare facilities trained to recognize and report problems, with an active component that includes targeted surveillance and networks able to provide "real-time" data. MedSun expanded to approximately 350 healthcare facilities. MedSun conducted activities including a pilot program for CBER and MedSun sites to acquire information for that Center on issues involving human cells and tissues; audio conferences for all MedSun sites; a workshop on infusion pump safety; a Device Safety Exchange Program for online sharing of questions and device quality improvement ideas by MedSun reporting sites; and training on problem recognition with laboratory and pediatric devices.
    - MedSun reports contributed to, numerous regulatory actions. In one instance, a patient died when a machine failed in a non-safe mode when a nurse inappropriately responded to an alarm. This report prompted FDA actions including the investigation and finding of a significant design issue related to this continuous renal transfusion device, a public health notification warning of this issue, and cooperative efforts with the company to issue a product recall.

Communicate Risk More Effectively

FDA increased access to information on its websites, in newsletters, through increased outreach efforts, and through internal operational initiatives. Highlights include:

- *Cooperative Relationships* -
    - In conjunction with the Heart Rhythm Society (HRS), held a policy conference on implantable cardioverter defibrillators **(**ICDs) and pacemakers. The conference reviewed current process for recalls. There was also discussion on the important elements of risk communication that can help guide physicians in treating patients with recalled defective devices.
    - Posted a laboratory safety tip on a CDRH webpage as a follow-up to a signal identified from MDR reports and literature. The signal was on falsely elevated results for Troponin, an indicator test for heart attack. As an example of leveraging with industry to address an educational need, AdvaMed, a trade association of medical device manufacturers, drafted the tip in response to FDA concerns.
- *Medical Device Safety Website* – Maintained the Medical Device Safety website for health care professionals. The site consolidates all of CDRH's medical device safety information (recalls, public health notifications, safety tips, etc.) and is updated regularly with high priority risk messages.
- *Public Health Notifications* – Issued notices on the Public Health Notification website (www.fda.gov/cdrh/safety) to mitigate risk from medical device problems. The

notifications covered issues such as Ralstonia bacteria contamination of a humidifier used in neonates, information regarding failures with the Guidant Implantable Cardioverter Defibrillator, and recommendations to avoid entrapment of vulnerable patients in the Vail bed.

- *FDA Patient Safety News (FDA PSN)* – Coordinated the production of FDA Patient Safety News, an award-winning monthly television news show and website (www.fda.gov/psn) distributed to health care practitioners across the nation. FDA PSN covers stories on medical errors, patient safety, recalls and alerts, and newly approved drugs, devices and biological products. The website receives about 8,500 "hits" per month, an increase of about 40% over the previous year.
- *Medical Device Recall Website* - Redesigned the website to provide a web-friendly, plain language overview of medical device recalls. The website explains the various classes of recalls and the procedures followed during a recall. Other highlights include:
  - **E-Consumer Initiative –** Explored ways to improve access to CDRH's electronic information. New features were added to the CDRH website to offer users options for receiving information.

For Youth and Mature Adults… Health Matters

CDRH leads FDA's efforts to reach all consumers—including youth and older adults—with medical information important to maintaining good health. "Maturity Health Matters," a newly-launched online newsletter, is geared toward providing FDA regulated product information of interest to the older adult population. This newsletter focuses on FDA regulated products that help people live longer and more productive lives. www.fda.gov/cdrh/maturityhealthmatters/.

The FDA & You newsletter targets secondary school students and Health Educators. FDA & You provides information on FDA topics of interest to teenagers. www.fda.gov/cdrh/fdaandyou/index.html.

MQSA – Mammography Quality Standards Act

- Commemorated 10 years of MQSA Inspections.
- Completed 93,000 facility inspections nationwide.
- Conducted annual inspections of over 9,000 mammography facilities nationwide.
- Ensured that 98% of mammography facilities met inspection standards. Less than 2% had level 1 problems. FDA worked with each of those facilities to assure adequate corrective action was taken.

Research, Development And Evaluation Activities

CDRH conducted applied research that expanded patient protection, including:

- Developed and validated a method for assigning an accurate expiration date for medical gloves. This work is critical to protect patients and health care workers from transmitting infectious diseases/agents used in terrorist activities.
- Conducted research on mechanical strength improvement in vertebrae following bone glue injections. This is the most common treatment for compression fractures, estimated

to eventually affect a quarter of all women over age 50.

- Measured and modeled exposure to electromagnetic fields and their effects on implanted devices from hand held and walk through security systems, cellular telephones, hand-held computers, and MRI systems. This included models of the head for evaluation of cell phone exposure and of pregnant woman models for 9 gestational ages of the fetus for heating during MRI.

Bioresearch Monitoring(BIMO)
FDA invoked the Application Integrity Policy (AIP) against a manufacturer and distributor of drug of abuse test kits after significant questions arose concerning the integrity of data submitted to the Agency. This achievement effectively removed thousands of potentially inaccurate and ineffective diagnostic drugs of abuse test kits from the marketplace. Because of this action, FDA suspended the substantive review of eight (8) of the manufacturer's pending 510(k) marketing submissions, and the manufacturer subsequently withdrew 18 additional cleared 510(k) marketing submissions due to widespread data inconsistencies and questionable design and research practices

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Medical Device User Fee and Modernization Act of 2002, P.L. 107-250 (MDUFMA)

FDA continued to implement MDUFMA of 2002. FDA used the additional funds to hire staff expertise and develop better systems and infrastructure to support more effective and timely premarket review. The law requires FDA to pursue a complex and comprehensive set of review goals that are more aggressive each successive year. In 2005 CDRH fulfilled the MDUFMA statutory requirements and maintained device review performance in areas not covered by official performance goals.

- *Guidance* - Issued six MDUFMA guidance documents in 2005 to facilitate interactions with industry and ensure effective program implementation. The agency has issued guidance documents on premarket approval applications, premarket assessment of pediatric medical devices, 510(k) submissions, use of validation data in 510(k) submissions for reprocessed single use devices, and the Inspection by Accredited Persons Program. (See http://www.fda.gov/cdrh for specific guidances.)
- *Documents, Notices and Reports* - Developed three Federal Register notices relating to MDUFMA implementation. In addition, CDRH issued three reports to Congress: Annual report to Congress on the Office created to coordinate and monitor the review of combination products – for FY 2004; Annual Financial Report to Congress –for FY 2004; and Annual Performance Report to Congress –for FY 2004. A complete listing is available at http://www.fda.gov/cdrh/mdufma/index.html.
- *Scientific Expertise to Enhance Capability* - Increased MDUFMA hires and brought in 74 new experts under the Medical Device Fellowship Program (MDFP). MDFP reinstituted the National Research Council Associates Program contract to operate a Resident Research Associateship Program and finalized an MOU with Duke University and

Brigham and Women's Hospital. These programs provide doctoral scientists and engineers of unusual ability.

- *Third Party Inspection Program* - Continued implementing the MDUFMA Accredited Persons (APs - Third Party inspection) program. The program is designed to reduce regulatory burden on providers, patients, and consumers of HHS services by increasing efficiency and modernizing regulatory oversight. During 2005, the number of qualifying inspections for APs increased by 10%. Currently, 5 of 16 APs are eligible to conduct independent inspections on behalf of the FDA. CDRH announced, in a letter to 8,600 domestic Class II and Class III device establishments, the publication of the AP Eligibility Guidance and outlined the benefits to manufacturers who use an AP to conduct their AP inspections.

<u>Innovations In Patient Care</u>

The following devices are examples of advanced device technologies that FDA approved or cleared during FY 2005 that have a particular impact on patient care.

- *DuraSeal Dural Sealant System - the first dura mater sealant for neurosurgery:* The DuraSeal Dural Sealant System by Confluent Surgical, Inc. is the first material approved for sealing leaks in the dura mater covering of the brain during neurosurgical procedures. The absorbable sealant is intended to aid in preventing cerebrospinal fluid leakage through suture wound edges of the dura mater.

- *Total Temporomandibular Joint Replacement System* ***- new prosthetic jaw joint:*** The Total Temporomandibular Joint Replacement System, by Walter Lorenz Surgical, Inc., is a prosthetic jaw joint for patients who need a total jaw replacement due to severe arthritis, fused joints, severe fractures, tumors, or severely degenerated joints. The device is a ball and socket joint that may reduce jaw pain, reduce interference with eating and increase the ability to open the mouth.

- *Invader® UGT1A1 Molecular Assay - The first DNA-based test for an enzyme that metabolizes certain drugs:* With the Invader® UGT1A1 Molecular Assay, from Third Wave Technologies, Inc., doctors can use a patient's genetic information to help them determine whether to modify the dose for drugs that are broken down in the body by UGT enzymes. The Invader assay will help to minimize harmful drug reactions and prevent patients from being improperly treated with sub-optimal doses. It joins a growing list of DNA-based tests used for individualized medical care.

- *VeriChip Implantable RF Transponder System – new technology for maintaining patient data:* The VeriChip Implantable Radiofrequency Transponder System, from Applied Digital Solutions, consists of an implantable chip, an introducer, and a reader. After the chip is implanted under the skin, a caregiver is able to retrieve a unique patient identifier and patient medical information from a prescription web site when the patient is otherwise unable to provide this information. The medical information on the websites is supplied by the patient and can only be accessed with appropriate authorization.

- *CoAxia NeuroFlo™ Catheter – approved under the Humanitarian Device Exemption (HDE) program:* The NeuroFlo™ Catheter, from CoAxia, Inc., is used to treat cerebral

ischemia (insufficient blood flow to the brain) resulting from the spasm (squeezing down) of a blood vessel in the brain that results in stroke-like symptoms. The catheter is intended to increase blood flow to the upper body and brain by temporarily reducing blood flow to the lower part of the body.

Rapid, Transparent Device Reviews

- *CDRH approvals* - 38 Premarket Approval Applications (PMAs) and cleared 2,617 510(k) submissions for products that will treat or diagnose a wide variety of medical conditions. FDA used the *de novo* process to automatically reclassify certain class III devices that have no precedent, but whose technology is well understood. This process allows products to come to market through the less burdensome 510(k) review process, and exemplifies FDA's effort to provide the most rapid, cost-effective health promotion and protection for the public.

Leveraging Expertise to Supplement Review Decisions

- *Advisory Committees* - CDRH held 17 Federal Advisory Committee panel meetings in 2005. These panels of external experts reviewed and made recommendations to FDA on 10 PMAs, one humanitarian device exemption (HDE), two 510(k)s, five preamendment device classifications, and six general issues.
- *Third Party Review Program* – CDRH increased the use of the Third Party Review Program for 510(k) submissions. CDRH also made final decisions on 251 "third party" 510(k)s, an increase from the 244 final decisions in FY 2004.

Improving Application Quality

- *Premarket Review Quality Assessment* – CDRH instituted an on-going quality review program for premarket submissions that evaluates the quality of its scientific review in three key areas: biocompatibility, sterilization and statistical analysis. This process allows CDRH to improve the quality of reviews in key scientific areas, thus ensuring that reviewers consistently ask the right questions at the right times.
- *Guidance for Regulated Industry*
    - **Regulations and Guidance Development –** CDRH streamlined guidance development by prioritizing its guidance workload; establishing performance goals and tracking mechanisms; engaging industry stakeholders in the early stages of guidance development; and increasing the use of contract experts. The Center also worked with the Office of General Counsel and the Office of Policy Regulation editorial staff to review and revise the boilerplate Guidance Development Templates for all guidance documents. These templates are available on the Center's web site: www.cdrh.fda.gov/LAWS/GGP/default.htm.
    - **CDRH issued** 28 guidance documents, cleared four draft Guidance documents, drafted nine responses to Citizen Petitions, published 16 final rules, published 47 Notices and issued several device-specific and special control guidance documents, including a guidance for intravascular stents and a guidance providing

clarity on indications for implanted cardioverter defibrillators. CDRH issued key cross-cutting guidance documents related to software used in medical devices and a guidance document on the Format and Content of 510(k) submissions.

- *Workshops*
    - **Significant Item: Glucose Monitoring -** FDA, in conjunction with NIH and the Juvenile Diabetes Research Foundation (JDRF), held an open public workshop entitled "Obstacles and Opportunities on the Road to an Artificial Pancreas: Closing the Loop" on December 19, 2005. Obstacles to development of new technologies for diabetes monitoring were discussed and suggestions made for how to deal with them. FDA offered to review research proposals from JDRF to assist them in launching and managing a new research initiative in the area of non-invasive glucose testing.

- *Small Manufacturers and International Assistance* – CDRH helped small manufacturers and international producers comply with FDA requirements. CDRH answered 44,000 requests for information; 7,000 responses involving international activities; and distributed 82,000 guidance documents on inspection and enforcement procedures, product development, and regulatory submissions.

Research, Development And Evaluation Activities

Applied research advances innovative technologies and consumer health. CDRH research contributes to the internal review process as well as to the development of guidance for industry in the development of innovative technologies:

- Evaluated the effects of optical energy on cellular and intracellular structures and components. This resulted in improved understanding of the effects of light on energy production in cells. This work, supported in part by an interagency agreement with the Air Force Office of Scientific Research, resulted in four journal articles, numerous proceedings and presentations during the past year, and a proposal to the Army's Telemedicine and Advanced Technologies Research Center to evaluate optical methods of stimulation that may enhance the field of neuro-prostheses.

- Enhanced understanding of the device-tissue interface for optical spectroscopy leading to improvements in the efficiency of spectroscopic methods for minimally invasive disease detection. This has the potential to improve the detection of mucosal cancers and the monitoring of changes following therapeutic applications. This work resulted in two journal articles and five proceedings publications during the past year.

Efficient, Effective Predictable Product Development

- *Critical Path*

- **Workshop on Drug-Diagnostics Translational Research – H**eld, In April 2005, the third in a series of national workshops on the co-development of drugs and diagnostics to give stakeholders a public venue for scientific suggestions and concerns about FDA regulatory practices in this important and growing new area. FDA is using the proceedings of this conference to develop guidance to ensure that this type of research translates in a rapid and cost-effective manner to new joint products that can quickly enter the medical marketplace. The new field of pharmacogenetic research will enable pharmaceutical companies to develop drug treatments that precisely target the needs of particular patient populations. By linking drug treatments to diagnostic tests that can accurately identify appropriate receptive patients, pharmaceutical companies aim to decrease drug adverse events, increase drug response rates, and ultimately save healthcare dollars.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Risk–Based Management

Continued to refine the risk-based management program for inspection and enforcement actions. This program not only impacts how inspections are prioritized, but will help identify and prioritize other types of regulatory activities, such as device recalls, that present the greatest risk to public health. CDRH analyses of past inspection data is used to make decisions on inspection priorities and regulatory actions. CDRH analyzed 132 Warning Letters issued to medical device manufacturers, finding 75 percent of the citations related to GMP violations and 24 percent related to MDR violations.

- *Enforcement*
    - Completed administrative and judicial actions to protect the American public. CDRH processed 70 warning letters and 437 product recalls, including 20 highest-risk Class I, 349 Class II, and 68 Class III recalls. Highlights include:
    - Conducted seizure of Baxter Healthcare Corp. infusion pumps because inspections revealed that the firm had continually failed to follow medical device manufacturing controls. Baxter had previously initiated a worldwide recall of the infusion pumps because they could shut down while delivering critical medication and fluids to patients.
    - Class I recall: Abbott Diabetes Care, Inc. recalled its Blood Glucose Meters when an investigation of reported problems showed that the monitor could inadvertently switch the glucose readings from the U.S. to the foreign standard when it is dropped or upon battery replacement. Misinterpreting the results caused by the switch could result in patients developing hyperglycemia, which is particularly harmful to pregnant women and could lead to fetal damage. FDA classified this as a highest-risk Class I recall and dispersed the notice through all of its communications channels.
- *Inspections*

CDRH coordinated with the Office of Regulatory Affairs (ORA) and provided technical support, as necessary, for inspections. The Agency surpassed all inspection goals:

- Exceeded the goal of 20% of 5,520 registered domestic Class II and Class III medical device manufacturers by conducting 1,265 inspections;
- Exceeded the goal of 7% of 2,500 registered foreign Class II and Class III medical device manufacturers by conducting 230 foreign inspections; and
- Exceeded the goal of 295 domestic and foreign BIMO inspections by conducting 335 BIMO inspections with an emphasis on scientific misconduct, data integrity, innovative products, and vulnerable populations.

- *Clinical Laboratories Improvements Act (CLIA)*
    - Established quality standards for all laboratory testing to ensure accurate, reliable and timely patient test results regardless of where a test was performed. Tests are categorized by their complexity (i.e., potential risk to public health,) and laboratories may only purchase and use a particular test based on the laboratory's level of CLIA certification.
    - Completed, during 2004, the delegation of authority to FDA for CLIA complexity determinations and finalized a 5-year Interagency Agreement with the Centers for Medicare and Medicaid Services (CMS) for CLIA waiver authority.
    - Published a draft guidance for the waiver process. Comments have been received and the guidance is currently being revised.

Radiological Health New Direction

CDRH**'s** Radiological Health activities provide expertise for the review and approval of treatment and therapy systems, for preventing excessive radiation exposures from diagnostics examinations such as fluoroscopy, and for monitoring and evaluating radiation emitting products such as security screening devices used to guard against terrorist threats.

- *Protective Activities*
    - **X-rays -** Promulgated amendments to the Federal radiation-safety standard, improving the performance of diagnostic x-ray systems and their major components while significantly reducing unnecessary x-ray exposure, especially in fluoroscopy, and maintaining image quality. The expected improvement in the quality of health care is projected to reduce the annual U.S. population dose by over 7,000 person-sievert, which is associated with a projected annual reduction in over 200 cancer deaths and annual savings of over $300 million.
    - **Lasers** –Briefed House Science Committee staff in January 2005 on its authorities regarding the manufacture and use of laser products. Additionally, in response to reports of green lasers directed at aircraft to distract or temporarily flash-blind the crew, FDA assessed the impact of legal and illegal use of radiation-emitting products and worked with the Federal Aviation Administration (FAA), Department of Homeland Security (DHS) and Department of Defense (DoD) to address this problem. FDA published and contributed to public information regarding safe use of laser pointers and cautioned against internet

sales of laser products through various print media outlets and on the Internet. FDA took action against firms that sell modified green lasers that emit radiation in excess of the limit for general public use.

Emergency Preparedness

CDRH routinely consulted with other government agencies on diagnostic and monitoring devices, radiological counter measures and radiation-emitting devices with potential to be used as weapons (e.g., visible lasers) and on radiation safety issues, including preventing unnecessary radiological exposure from security screening products.

- Formed a working technical group to address the use and rapid approval of diagnostic devices related to influenza and is assisting CDC in making available to the laboratory response network CDC's rapid diagnostic test for avian flu.
- Began, in September 2005, , posting hurricane- and pandemic flu-related emergency information on its website, www.fda.gov/cdrh/emergency/index.html. This was in as a response to the Katrina emergency and to increased national efforts on flu pandemic.
- Posted information on cleared and approved devices for personal protection on its emergency information website, www.fda.gov/cdrh/emergency/flu_qa.html. These devices are integral to minimizing the spread of infectious agents, including those used in bioterrorism.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Improved Management - IT

- Systems development in 2005 included tracking Conditions of Approval postmarket studies, electronic consultations tracking (eConsult), a Device Nomenclature Management System, and enhancements to electronic submissions of in vitro diagnostics (IVD) applications, and implementation of a program for accepting electronic premarket submissions (eCopy).

Devices and Radiological Health
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actual [1/]	FY 2006 Estimate	FY 2007 Estimate
Expedited Original PMA MDUFMA Decision Goal (% of decisions within # of FDA days)	**70% in 300 days**	**80% in 300 days**	**90% in 300 days**
Expedited PMA Received	5	9	9
Expedited PMA Approved	2	9	9
Expedited PMA – Performance	100% in 300 days	80% in 300 days	90% in 300 days
PMA original, panel track supplement and premarket report submissions MDUFMA Decision Goals (% of decisions within # of FDA days)	**NA**	**80% in 320 days**	**90% in 320 days**
PMAs Received (PDP and PMA)	49	50	50
PMAs Approved (PDP and expedited)	38	43	43
Original PMA performance	100% in 320 days	80% in 320 days	90% in 320 days
PMA Supplement Panel Tracks[2/] Received	12	12	12
PMA Supplement Panel Tracks[2/] Approved	9	12	12
Panel track PMA Supple-Ment[2/] performance	100% in 320 days	80% in 320 days	90 % in 320 days
Humanitarian Device Exemptions Received	4	6	6
Humanitarian Device Exemptions Approved	2	5	5
Average HDE FDA Review Time (FDA days approval)	222	150	140
180- day PMA Supplements MDUFMA Decision Goal (% of decisions within # of FDA days)	**80% in 180 days**	**80% in 180 days**	**90% in 180 days**
PMA Supplements Received	97	110	110
PMA Supplements Approved	79	100	100

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actual [1/]	FY 2006 Estimate [3/]	FY 2007 Estimate
180-day PMA supplement performance	97% in 180 days	80% in 180 days	90% in 180 days
510(k) MDUFMA Decision Goal (% of decisions within # of FDA days)	**75% in 90 days**	**75% in 90 days**	**80% in 90 days**
510(k)s Received (Trad., Special, Abbrev., 3rd party)	3,650	3,600	3,600
510(k)s Completed (All Decisions)	2,617	3,500	3,500
510(k) performance	95% in 90 days	75% in 90 days	80% in 90 days
Investigational Device Exemptions Received	232	230	230
Investigational Device Exemptions Decisions	244	220	220
% Acted on Within 30 Days	100%	100%	100%
on IDE Supplements	4,282	4,300	4,300
IDE Supplements (Approved/Total Decisions)	4,249	4,300	4,300
% Acted on Within 30 Days	100%	100%	100%
Total Standards Recognized for Application Review	695	750	775

[1/]Data represents CDRH contributions to the categories listed above and are current as of 1/1/2006. Performance totals for FY 2005 are subject to change as the cohort matures. FDA is committed to meeting the performance goals cited in the MDUFMA legislation. User fees, coupled with the increased appropriated resources for medical device review received in FY 2005, will enable FDA to meet the aggressive premarket goals agreed upon by FDA and its stakeholders. The FY 2005 requested increase will strengthen the capabilities needed to meet the increased performance goals by building the medical device review infrastructure and hiring new reviewers. Outputs are not expected to increase until FY 2006 and FY 2007 when the infrastructure is in place and functioning and the new reviewers are on board and fully trained. Increased outputs in FYs 2006 and 2007 are contingent upon receipt of MDUFMA user fee revenue.

[2/] A "Panel-Tracked" PMA supplement is a supplement to an already approved PMA and is usually for a change in the indications for use statement. The change in indications statement is usually for a new use of the already approved device (not change to the device), for use in a different disease condition, for use in a different anatomical site, or for use in a different patient population. A summary of safety and effectiveness information is prepared and made available to the public.

[3/] Includes filing decisions, review determinations, and approval decisions.

DEVICES FIELD PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	**FY 2005 Actual**	**FY 2006 Estimate**	**FY2007 Estimate**
Bioresearch Monitoring Program Inspections	329	300	300
Pre-Approval Inspections	64	130	130
Post-Market Audit Inspections	63	65	65
GMP Inspections (Levels I, II, III and Accredited Persons)	1,430	1,530	1,530
Total Above Domestic Inspections: Non MQSA	**1,886**	**2,025**	**2,025**
Inspections (MQSA) FDA Domestic (non-VHA)	366	335	371
Inspections (MQSA) FDA Domestic (VHA)	32	32	32
Inspections (MQSA) by State Contract	8,340	7,924	7,700
Inspections (MQSA) by State non-Contract	545	530	530
Total Above Domestic Inspections: MQSA	**9,283**	**8,821**	**8,633**
Total Domestic Reinspections (Non-add)	**237**	**237**	**237**
State Contract Devices Funding	$1,350,000	$250,000	$275,000
State Contract Mammography Funding	$9,800,000	$9,200,000	$9,940,000
Total State Funding	**$11,150,000**	**$9,450,000**	**$10,215,000**
Domestic Radiological Health Inspections	107	130	130
Domestic Field Exams/Tests	944	1,215	1,215
Domestic Laboratory Samples Analyzed	200	217	217
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Foreign Bioresearch Monitoring Inspections	6	10	10
Foreign Pre-Approval Inspections	17	34	34
Foreign Post-Market Audit Inspections	26	27	27
Foreign GMP Inspections	225	207	189
Foreign MQSA Inspections	16	15	15
Foreign Radiological Health Inspections	9	19	19
Total Above Foreign FDA Inspections	**299**	**312**	**294**
Total Foreign Reinspections (Non-add)	**24**	**24**	**24**
Import Field Exams/Tests	6,901	5,000	5,000
Import Laboratory Samples Analyzed	1,333	1,440	1,440
Import Physical Exam Subtotal	8,234	6,440	6,440
Import Line Decisions	3,484,393	4,460,023	5,708,829
Percent of Import Lines Physically Examined	0.24%	0.14%	0.11%

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

	FY 2005 Actual	FY 2006 Enacted [1/]	FY 2007 Estimate	Increase or Decrease
Total Program Level	**$40,206,000**	**$40,740,000**	**$34,240,000**	**-$6,500,000**
Center	*$40,206,000*	*$40,740,000*	*$34,240,000*	*-$6,500,000*
FTE	*187*	*206*	*199*	*- 7*
Budget Authority	**$40,206,000**	**$40,740,000**	**$34,240,000**	**-$6,500,000**
Cost of Living-Pay			*$533,000*	*+ $533,000*
Strategic Redeployment			- $7,033,000	*- $7,033,000*
FTE			*- 7*	*- 7*
Budget Authority FTE	**187**	**206**	**199**	**- 7**

[1] *Includes a one percent rescission.*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$40,403,000	$40,403,000	0	226
2004 Actual	$39,869,000	$39,869,000	0	207
2005 Actual	$40,206,000	$40,206,000	0	187
2006 Enacted	$40,740,000	$40,740,000	0	206
2007 Estimate	$32,240,000	$34,240,000	0	199

Statement of the Budget Request

The National Center for Toxicological Research (NCTR) is requesting $34,240,000 to conduct peer-reviewed translational research that supports and anticipates the FDA's current and future regulatory needs. The mission of NCTR is to:

- Conduct fundamental and applied research aimed at understanding critical biological events, such as adverse drug reactions and/or antibiotic resistance, to determine how people are adversely affected by exposure to products regulated by FDA.

- Conduct peer-reviewed scientific research that provides the basis for FDA to make sound, science-based regulatory decisions, and to promote the health of the American people through the Agency’s core activities of pre-market review and post-market surveillance.

- Develop methods to measure human exposure to products that have been adulterated or to assess effectiveness and/or the safety of a product.

- Provide the scientific findings used by the FDA product centers for pre-market application review and product safety assurance for the betterment of public health.

Program Description

The NCTR conducts translational applied research specifically designed to define biological mechanisms of action underlying the toxicity of FDA-regulated products. This research aims at understanding critical biological events triggered by exposure to toxins and at developing methods to improve assessment of human exposure, susceptibility, and risk. This is particularly pertinent in supporting FDA's role in developing medical counter-measures and other preparatory efforts for the Department's bioterrorism activities.

Research performed at NCTR targets fulfillment of three program strategic research goals in support of FDA's public health mission:

- *Risk Assessment for Regulated Products* includes the development of new strategies and methods to test/predict toxicity and assess/detect risk for FDA regulated products, both new and on the market - this includes new genetic systems and computer-assisted toxicology for use in application review and development of gene chip and gene array technology.

- *Knowledge Bases that Predict Human Toxicity* takes in the development of computer-based systems as knowledge bases that predict human toxicity to enhance efficiency and effectiveness of premarket reviews.

- *Methods for Use in FDA Standard Development and Product Risk Surveillance* covers the conduct of fundamental research to understand mechanisms of toxicity assess new product technology and provide methods for use in FDA standards development and product risk surveillance.

NCTR conducts research that supports FDA's core mission areas through the dedicated efforts of staff in NCTR's Office of Research whose primary focus is on the study of systems biology, biochemical and molecular markers of cancer, neurotoxicity, applied and environmental microbiology. The divisions work closely in a seamless effort supporting FDA's mission to bring safe and efficacious products to the market rapidly and to reduce the risk of adverse health effects from products on the market.

Translational Research

Research performed by NCTR is "translational" – meaning basic information derived from studies and then further modified to apply to a specific question that supports FDA's public heath mission. An example of this is the basic research developed to create a mutant mouse or rat. FDA scientists use this capability and apply it to specific rodent strains to assess the safety of a human or animal drug, or to understand the mechanism of action of a food additive or medical device. Studies include the nature, effects and detection of poisons and the treatment of poisonings—toxicology.

NCTR is co-located with the Office of Regulatory Affairs' Arkansas Regional Laboratory on a large campus to form the Jefferson Laboratories (an FDA owned facility) located in Jefferson, Arkansas, situated near the city of Little Rock, Arkansas. The research work performed by NCTR occurs in 34 buildings and 4 trailers.

Performance Analysis

During the latest performance period, (FY 2005), the National Center for Toxicological Research successfully met all of the targets for the Center's four performance goals. For more information about these performance goals and results, please see the Performance Detail section.

NCTR continues to support the Agency's counterterrorism efforts by conducting research in the effort to protect the Nation's food supply from a terrorist's attack. The center has set ambitious targets in support of these efforts.

Performance Highlight:

FY 2007 Goal Target	FY 2005 Results	Context
Develop risk assessment methods and build biological dose-response models in support of Food Security by using flow cytometry to facilitate isolation of single bacteria from contaminated samples for rapid bacterial identification and for pyrolysis mass spectrometry.	In collaboration with CFSAN, scientists in the Division of Microbiology developed and validated a *Salmonella* biochip using microarray technology for rapid and accurate identification of virulence and antimicrobial resistance genes in Salmonella.	To protect the public from the threat that anti-microbial resistant organism pose, FDA conducts research to investigate the relationship between anti-microbial resistance and foodborne diseases.

Program Resource Changes

Budget Authority

Cost of Living-Pay: + $ 533,000
FDA's request for pay inflationary costs is essential to accomplishing its public health mission. Payroll costs account for over sixty-percent of our total budget, and the Agency is no longer able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The

NCTR's portion of this increase is $533,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

NCTR Redeployment: - $7,033,000 and - 7 FTE

To fund FY 2007 priority initiatives such as Food Defense, Pandemic Preparedness, and Human Tissues Initiatives, FDA re-deployed resources from base programs. To accomplish this strategic redeployment and fund new high priority initiatives, NCTR reductions include: infrastructure and contract support, and research support services including animal care/diet preparation, pathology and scientific information technology. NCTR is also reducing studies in the areas of systems biology, genetic and reproductive toxicology, and rapid identification methods for biohazards.

Justification of Base [1]

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

NCTR supports the strategic goal by developing new scientific tools and biomarkers to expedite FDA's critical path research in medical product discovery, development and assessment. NCTR will continue to:

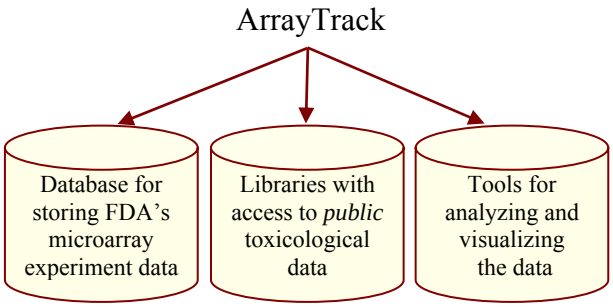
- Develop a unique and sophisticated analytical infrastructure to assess the safety of FDA-regulated products using genomics, proteomics and metabolomics in conjunction with traditional biomarkers of safety. A systems biology approach to toxicity testing will provide data that are more easily extrapolated to humans, making data interpretation easier and relevant. Scientists believe these developments may prove that new disease markers and drug targets can be identified that will help design products to prevent, diagnose and treat disease.

Microarray Quality Control Project

FDA is promoting the use of omics technologies (e.g. microarrays) in medical product development and personalized medicine. Specifically, FDA is establishing standard metrics and thresholds for assessing the performance of different microarray platforms and evaluating microarray data analysis methods. These standards are vital to the validation and proper application of microarray data in the discovery, development and review of FDA regulated products. Cross laboratory/platform comparability is essential to moving microarrays from a research to clinical practice. NCTR scientists initiated and are participating with other FDA Centers and the microarray industry providers in the Microarray Quality Control project.

[1] Congressional Appropriation Report 109-255 directed FDA to include additional justification on its research, development, and evaluation (RD&E) activities. In response to this report language, FDA is providing explanatory paragraphs detailing each program's RD&E activities. Because NCTR performs RD&E as its main activity, the justification of base also serves as the RD&E paragraphs for this program narrative. Other FDA programs include RD&E paragraphs within their justification of base activities, and these paragraphs are aligned by FDA strategic goal.

- Provide software systems and analysis capability to manage and integrate data from new technologies (such as microarrays, proteomics, and functional genomics) with traditional toxicological data. NCTR computational scientists have developed ArrayTrack, a data management and analysis software used to store and analyze the thousands of data points generated by a single microarray experiment to provide a scientific basis for FDA regulatory standards.



- Analyze, using advanced proteomic technology, changes in a given sample after exposure to a toxicant allowing the identification of function and quantification of all proteins in the sample. A mass spectrometer analyzes the changes in proteins due to toxicant exposure in order to identify possible disease states in the brain, liver, prostate, and blood.

- Develop methods to measure human exposure to adulterated products and enhance the understanding of acute and chronic liver disease. This research is used by FDA's product centers for premarket application review and product safety assurance to improve product quality and better predict the toxicity of new drugs; thereby, managing public health risk.

- Determine, using chemical probes, if bacteria in food and food producing animals or their environment have developed resistance to commonly used antibiotics.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

NCTR supports this strategic goal by identifying risks associated with the use of medical products. NCTR also supports this goal by developing methods to manage or assess risks associated with products that have been adulterated, intentionally contaminated, or found to be detrimental to human health. These activities support the Department's goal to enhance the ability of the Nation's health care system to respond to bioterrorism and other public health challenges. At NCTR, FDA will continue to:

Simulated solar light

- Address the potentially hazardous effects of sunlight with products used by the public. NCTR has one of only two phototoxicology laboratories in the world with the capacity to expose large numbers of animals to simulated solar light – almost any light to which humans are exposed. Studies of particular concern being conducted at NCTR include:

  - Interaction of sunlight and cosmetics;
  - Safety of products (such as dietary supplements, sports drinks, or skin creams) containing aloe vera; and,
  - Stability and toxicity of tattoo ink ingredients.

- Conduct studies to assess the toxicity of nanoscale materials (miniscule particles that measure less than 100 nanometers) and to assist the FDA in evaluation of nanotubes (extremely small tubes made from pure carbon) as safe delivery platforms for drugs.

- Conduct fundamental applied research, including animal and microbial bioterrorism research and analytical studies aimed at understanding critical biological events. This will assist determining adverse effects on people exposed to FDA-regulated products. It will also help develop a means for rapidly detecting potential biowarfare agents

- Conduct research studies of bacterial strains. This will enable the FDA to support the rapid detection and identification of biological warfare agents or foodborne contaminants through methods developed in a state-of-the-art Biosafety Level-3 laboratory facility located in Jefferson, Arkansas.

In vitro culture system of human colon

- Conduct studies, developing methods and recommending industry guidelines to evaluate the safety of antimicrobial agents for human health risks. Studies of emerging interest to FDA under the food security/counter terrorism initiative continuing at NCTR include:

  - Human flora-associated mouse model and *in vitro* cell-culture model evaluations of antimicrobial drug residue effects on colonization resistance and host immunity.

  - Development of a DNA microarray method for the detection of intestinal bacterial species and foodborne pathogens in human fecal samples to monitor drug-mediated perturbations in these indigenous populations.

Toxicant-Induced Exposure

FDA conducts studies to evaluate tissues and biological fluids for changes in metabolite levels that result from toxicant-induced exposure. This exposure could stem from adulteration of a product through the manufacturing process or as a result of a biological agent.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

NCTR supports this strategic goal by developing policies and strategies to enhance its resource utilization, while building its human capital capability to meet the critical needs of the Agency. NCTR will continue to:

- Reward and retain state-of-the-art scientists and health professionals.
- Increase the use of existing formal and informal training programs such as postdoctoral programs, student intern programs and mentorship experiences.
- Maintain state-of-the-art expertise by training scientists in emerging technologies.
- Redirect resources to programs more critical to FDA's research mission.
- Leverage NCTR's resources and scientific expertise with other agencies [through interagency agreements] and non-government groups [through cooperative research and development agreements] to support FDA critical research needs.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

A key NCTR strength is our cadre of interdisciplinary research teams working with colleagues across the FDA and leveraging other agency resources to conduct research to develop new scientific tools. These tools include database and bioinformatics tools, genetic tools to assess populations susceptible to disease biomarkers, and systems tools (integration of genomics, proteomics, metabonomics, and bioinformatics). These tools will provide FDA with improved means of monitoring drug safety, the ability to advance personalized medicine through a better understanding of individualized responses based on genetics, and validated technologies for ultimate use by the reviewer in FDA.

Translational Research[2]

- Implemented ArrayTrack for interpretation of data received from DNA chromosome test studies. ArrayTrack is an integrated software package that plays a critical role in managing, analyzing and interpreting microarray data to study toxicology in human drug and food programs.

[2] In the past five years, NCTR has been developing and standardizing new technologies that will be used in developing biomarkers, micro-array data, and other models for FDA-regulatory applications. This precursory work supports the new Critical Path Initiative.

- Collaborated with NIH's components and commercial vendors to integrate ArrayTrack with a variety of tools and expanded the user base for the software to over 50 companies/institutions.

- Initiated the MicroArray Quality Control Project (MAQC), collected data from over 600 arrays, served as a test site for the MAQC project and held a conference with over 100 participants from government and industry.

- Collaborated with NIH to develop a draft document on standards in metabolomics and aid in dissemination of best practices for metabolomics.

- Identified with other Agency collaborators metabolic patterns of toxicity that correlated with cisplatin and gentamicin toxicity.

- Developed Protein Track software for the analysis of proteomic data.

- Examined utility of gene expression microarray data for providing toxicological insights for drug safety evaluations through the FDA's Interdisciplinary Pharmacogenomics Review Group and the Voluntary Genomics Data Submission group.

- Demonstrated the importance of optimal microarray scanner calibration on the quality of microarray data.

<u>Toxicology Research</u>

- Participated in international efforts that resulted in harmonization of guidance for the conduct of and interpretation of data from genetic toxicology assays. FDA used the information from genetic toxicology assays for drug, food additive and other product safety assessments.

- Conducted studies (under the FDA-NCTR/National Toxicology Program Interagency Agreement) to evaluate the possible genotoxic mode of action for the carcinogen acrylamide. The mode of action will impact the choice of low dose extrapolation model used for the quantitative risk assessment of acrylamide, produced as a by-product of the high heat cooking of starchy foods such as potatoes.

- Established a rodent model for studying the consequences of lifetime exposure to low doses of acrylamide (a common contaminant of carbohydrate-based foodstuffs cooked at high temperatures).

- Developed a new approach to using a quantitative evaluation of *in vivo* mutation data to better inform the decision as to whether a particular chemical is a mutagenic or non-mutagenic carcinogen, thus impacting the choice of low dose extrapolation model or providing evidence that there may be limited risk at low dose exposures.

- Discovered that individuals with a mutation in the CYP3A43 gene were at three-fold increased risk of prostate cancer than individuals without the mutation. This mutation

was more common in African-Americans than in Caucasians suggesting that the CYP3A43 gene mutation may contribute to the disparity in prostate cancer risk. Additional common mutations continue to be studied to further understand the genetic causes of the disparity in prostate cancer risk.

- Obtained data from both *in vivo* and *in vitro* rodent and nonhuman primate models for assessing the consequences of developmental exposure to commonly used anesthetic agents (ketamine, benzodiazepines) on brain development. These data are critical for establishing Agency guidelines and labeling.

- Completed research on the toxicity of cosmetic ingredients due to their interaction with light. Research included studies on the combined effects of light with α- and β-hydroxy acids, *Aloe vera*, retinyl palmitate, nanoscale titanium dioxide, and several coloring agents including iron oxide, Pigment Orange 13, Pigment Yellow 83, Pigment Orange 36, and Pigment Red 22. Experiments are continuing on tattoo dyes to determine the effect of light on the chemicals in those dyes, their metabolism in the body, and how they react with DNA following their metabolism.

- Assessed the effects of transplacental exposure of the anti-retroviral drugs (zidovudine and lamivudine) in combination with nevirapine and nelfinavir. In addition, range-finding studies were conducted in which the drugs were administered transplacentally and neonatally. Investigators have been measuring other endpoints (DNA incorporation, mutagenicity, and micronuclei induction) to determine the mechanisms for the adverse effects of these drugs.

- Developed Windows-based software for simultaneously implementing and linking as many as four physiologically based pharmacokinetic (PBPK) models, each of which incorporates postnatal growth and includes linkage for simulation of pharmacodynamic (PD) effects, such as DNA-adduct formation or cholinesterase inhibition. The user-friendly software will soon be made available to FDA researchers and reviewers, as well as to the scientific community.

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Working with colleagues within the agency, NCTR researchers conduct studies to assess the toxic effects of compounds in foods including antibiotics, pathogens, adulterants, etc. to develop risk identification standards for use in FDA guidance documents.

Nutrition Research

- Initiated under the FDA-NCTR/NTP IAG, a study investigating the hazardous effects of exposure to bitter orange, a dietary supplement chemically similar to ephedra.

Food Defense

- Developed, in collaboration with the Center for Veterinary Medicine (CVM), oligo-based microarray and recombinant DNA technology methodologies for the detection of antibiotic resistance genes in bacteria isolated from chicken and turkey farms.

- Assessed the safety of drugs and other compounds and their effects on the gastrointestinal tract microbiota. NCTR scientists played a critical role in the development of a decision tree for determining the limits on Acceptable Daily intake of antimicrobials in foods, which was adopted by the World Health Organization and recently used in the FDA/CVM Guidance for Industry #52.

- Investigated the ecology, epidemiology, virulence and molecular characteristics of foodborne pathogen populations of *Salmonella, Vibrio, Campylobacter* and *E. coli* for source tracking, delineating transmission pathways and better identifying targeted control measures in poultry, cattle, aquaculture and clinical environments. NCTR scientists used various molecular typing methods (such as pulsed-field gel electrophoresis, antibiogram patterns, multi-locus sequence typing, PCR-restriction fragment length polymorphism, ribosomal rRNA operon typing and ribotyping,) to create databases of bacterial DNA fingerprints.

- Published in the *Risk Analysis Journal* developed model-averaging techniques for benchmark-dose estimation in risk/safety assessment and other novel hierarchical models for probabilistic dose-response assessment and for proper propagation and management of uncertainty in inter- and intra-species extrapolations.

NCTR
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2005 Actuals	FY 2006 Estimate	FY 2007 Estimate
Research Publications	200	200	215
Scientific Presentations	286	285	250
Patents (Industry)	6	6	5
Interagency Agreements (IAG)	11	8	5
Cooperative Research & Development Agreements (CRADA)	11	11	11
Total Active Research Projects	196	210	192

FIELD ACTIVITIES - OFFICE OF REGULATORY AFFAIRS [1]

	FY 2005 Actual	FY 2006 Enacted [2/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$493,258,000**	**$503,951,000**	**$526,259,000**	**$22,308,000**
FTE	*3,633*	*3,488*	*3,488*	*0*
Budget Authority	**$477,568,000**	**$482,458,000**	**$504,029,000**	**$21,571,000**
Foods	$283,257,000	$285,153,000	$301,324,000	$16,171,000
Human Drugs	$81,003,000	$79,919,000	$79,794,000	- $125,000
Biologics	$26,514,000	$27,184,000	$28,776,000	$1,592,000
Animal Drugs & Feed	$35,124,000	$34,842,000	$35,778,000	$936,000
Medical Devices	$51,670,000	$55,360,000	$58,357,000	$2,997,000
Budget Authority				
Pandemic Preparedness			*$4,031,000*	*$4,031,000*
FTE			*18*	*18*
Food Defense	*$12,270,000*	*$33,903,000*	*$51,301,000*	*$17,398,000*
FTE			*4*	*4*
Tissues			*$1,238,000*	*$1,238,000*
FTE			*10*	*10*
Trigger Needs for ADUFA and MDUFMA 3			*$2,049,000*	*$2,049,000*
FTE			*13*	*13*
Cost of Living			*$8,297,000*	*$8,297,000*
Strategic Redeployment			*($11,442,000)*	*($11,442,000)*
FTE			*(48)*	*(48)*
User Fees	**$15,690,000**	**$21,493,000**	**$22,230,000**	**$737,000**
PDUFA	*$6,138,000*	*$8,675,000*	*$9,074,000*	*$399,000*
FTE	*32*	*41*	*43*	*2*
MDUFMA	*$966,000*	*$1,194,000*	*$1,295,000*	*$101,000*
FTE	*8*	*9*	*10*	*1*
MQSA	*$8,586,000*	*$11,624,000*	*$11,861,000*	*$237,000*
FTE	*8*	*8*	*8*	*0*

[1] This program narrative is shown for illustrative purposes only. The five program narratives (Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Devices and Radiological Health) have a Field component included in them.

[2] Includes a one-percent rescission.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$471,065,000	$456,148,000	$14,917,000	4,003
2004 Actual	$528,853,000	$513,906,000	$14,947,000	3,872
2005 Actual	$493,258,000	$315,562,000	$15,690,000	3,633
2006 Enacted	$503,951,000	$482,458,000	$21,493,000	3,488
2007 Estimate	$526,259,000	$504,029,000	$22,230,000	3,488

Program Description

The Office of Regulatory Affairs (ORA) is the lead office for all FDA field activities. ORA supports each of FDA's five Centers by inspecting regulated products and manufacturers, conducting sample analysis on regulated products, maintaining import data entry systems, and advising key officials on regulations and compliance-oriented matters that have an impact on policy development and execution, and long-range program goals.

In FY 2007, ORA's budget will support approximately 3,300 people in the field and 170 people in the Office of Shared Services. Newly proposed Reinspection and Export Certification User Fees will support 120 of these FTE. Over 85 percent of ORA's staff works in five Regional Offices, 20 District Offices, 13 Laboratories, and 150 Resident Posts and Border Stations. The Office of Criminal Investigations (OCI) personnel are located throughout the field organization in Field Offices, Resident Offices and Domiciles, which are located in 25 cities throughout the U.S. FDA maintains offices and staff in the D.C., the U.S. Virgin Islands, Puerto Rico, and in all states except Wyoming. FDA also monitors imported products traveling through 12 international mail facilities and 22 courier ports.

ORA's work involves conducting foreign and domestic pre-market and post-market inspections. Pre-market activities can include bioresearch monitoring of clinical research; pre-approval inspections and laboratory method validations needed for premarket application decisions; and, inspections of manufacturing facilities to determine if the factory is able to manufacture the product to the specifications stated in the application. To complement these pre-market activities, the largest portion of ORA's work involves post-market inspections of foods, human drugs, biologics, animal drugs and feeds, and medical device manufacturers. These inspections assess their compliance with Good Manufacturing Practice and biennial inspection requirements. ORA's radiological health activities include inspecting certified mammography facilities for compliance with the Mammography Quality Standards Act (MQSA). It also includes inspecting radiological health products such as lasers, sunlamps, and x-ray equipment to ensure they are in compliance with performance standards. ORA also monitors and samples imports to ensure the safety of the food supply and medical products.

In addition to overseeing regulated products on a surveillance or "for cause" basis, ORA staff also respond to emergencies and investigate incidents of product tampering and terrorist events or natural disasters that may impact FDA regulated goods. To complement the regular field force, the OCI investigates instances of criminal activity in FDA-regulated industries.

FDA relies heavily on its post-market investigation, inspection, and compliance activities to assure the safety and quality of the products it regulates. ORA's Counter Terrorism (CT) program role includes safety and security of the food and feed supply; support of the development and manufacturing of vaccines and medical counter measures; the assessment of drugs and other medical products included in the Strategic National Stockpile Program; and, participation in and support for exercises and security preparations for public events such as the Olympics and National political conventions. FDA's responsibilities for radiation safety and health give it a role in assessing x-rays used for security screening of packages and other radiation emitting products with medical or CT uses. The Field provides emergency responses to illness and injury potentially linked to FDA regulated products; and, coordinates its activities with the Centers for Disease Control (CDC). In addition, ORA inspections and investigations are essential to human tissue safety; BSE feed contamination prevention; counterfeit drug, infant formula and other product investigations; and, dietary supplement safety enforcement.

The Field coordinates import activities with the Department of Homeland Security's Customs and Border Protection (CBP) Agency. The number of FDA regulated imported products is increasing exponentially. This would challenge FDA's ability to provide an appropriate response even if security concerns were not taking an ever increasing role. In FY 2007, FDA is projecting a total of 19.8. million import lines. These are 60 percent food products; 8 percent cosmetic products; 2 percent human drugs and biologic products; 1 percent animal drugs and feeds products; and, 29 percent medical device and radiological health products. ORA uses a combination of electronic information technology for risk based screening and staff intensive surveillance; physical examinations; and, laboratory analysis to make import entry decisions.

Performance Analysis

During FY 2005, which was the latest performance period, the Office of Regulatory Affairs (ORA) successfully achieved or exceeded all 14 targets for its FY 2005 performance goals. For more information about these performance goals and results, please see the Performance Detail section.

For FY 2006, ORA adjusted the performance goal targets due to the catastrophic natural disasters that affected the southeastern portion of the United States. This allows the field personnel in the affected area to focus on disaster recovery and revitalization rather than on traditional performance goal activities.

For FY 2007, it is assumed the field will return to normal operations for performance goals except in the Import Food Field Exams goal which decreased by 4,000 exams as a result of redirection of funds to other food defense priorities.

ORA added a new performance goal target to the existing biologics performance goal to highlight the accomplishments in the Human Tissue inspection area. In Medical Devices, the two performance goals, foreign inspections and domestic inspections, were combined into one performance goal to better reflect the overall inspectional coverage.

The FY 2007 Human Tissues budget increase permits FDA to maintain and increase the human tissues goal. The MDUFMA trigger increase allows an increase in device inspections.

Performance Highlight:

FY 2007 Goal Target	FY 2005 Results	Context
Perform prior notice import security reviews on 60,000 food and animal feed line entries considered to be at high risk for bioterrorism and/or present the potential of a significant health risk.	In FY 2005, FDA exceeded the goal of 38,000 by performing 86,187 prior notice import security reviews.	FDA will continue to focus much of its resources on intensive prior notice import security reviews of products that pose the highest potential bioterrorism risks to the U.S. consumer and market. The Prior Notice Center will receive feedback from import field exams and filer evaluations and begin targeting those individuals that continuously violate the law. They will also target commodities based on immediate and potential threats to the integrity and security of the intact food supply chain.

Program Resource Changes

Budget Authority

Pandemic Preparedness: + $ 4,031,000 and + 18 FTE

FDA plays a unique and vital role in the Nation's preparedness for an influenza pandemic. We facilitate the development and availability of safe and effective vaccines and we safeguard America's animal health and food safety systems in the event of an outbreak of avian and pandemic influenza. FDA is requesting resources for an enhanced and sustained preparedness effort to:

- Provide extensive outreach and training in manufacturing quality.

- Conduct timely and efficient inspections of manufacturing facilities to assure product quality and prevent problems that threaten safety or availability of products essential to respond to the pandemic threat.

- Issue Custom Alerts to prevent the illegal importation of antivirals into the U.S.

- Improve FDA's capacity to conduct domestic and import surveillance and respond to reports of food or foodborne illness associated with viruses.

- Equip field labs and support technology transfer and training of field scientists to ensure adequate capacity to respond to outbreaks of avian influenza.

Food Defense: + $17,398,000 and + 4 FTE

The food supply is part of the Nation's critical infrastructure and contributes about 20 percent to the U.S. Gross National Product. A terrorist attack on the food supply could have catastrophic public health and economic consequences. The funds requested would continue to enhance laboratory preparedness, food defense research, surveillance, and incident management capabilities. Through this initiative, FDA will enhance its capacity to prevent, prepare for, respond to and mitigate the effects of a terrorist attack, a major disaster or other emergency on the food supply. The Field will use the additional resources for the following activities:

- Expand the FERN system to 16 State laboratories. Also provide cooperative agreements and technical support to these laboratories and build analytic surge capacity to respond to a terrorist attack.

- Target potentially high-risk imported foods through Prior Notice Import Security Reviews. The reviews are based on intelligence, FDA inspection reports, discrepancies in prior notice reporting and sample collection and analysis.

- Manage the FERN laboratory response for a terrorist attack on (or threat to) the food supply or other food-related emergency.

Human Tissues Safety: + $1,238,000 and + 10 FTE

FDA is implementing a new, risk-based approach to assure the safety of the human cells, tissues, and cellular and tissue-based products (HCT/Ps) involved in these tissue implants. This initiative will allow FDA to address issues related to safety and effectiveness of a rapidly growing industry. The current good tissue practice rule became effective May 25, 2005. This rule requires manufacturers to recover, process, store, label, package and distribute HCT/Ps in a way that prevents the introduction, transmission, or spread of communicable diseases. These rules are critical new tools that give FDA the ability to monitor human tissue adverse reactions to target more effectively the products with the highest risks. This initiative will fund monitoring and follow-up of adverse events and deviation reports, inspections of HCT/P establishments, and development of guidance and conducting outreach activities. The human tissue safety initiative is funded at $2.5 million. The Field portion supporting CBER is $1.238 million and 10 FTE. FDA is requesting resources to implement the new risk-based comprehensive approach for assuring the safety of HCT/Ps. The Field will use the additional resources for the following activities.

- Conduct 75 additional tissue inspections and thereby significantly increase coverage among the approximately 2,000 registered firms.

- Training of FDA investigators and staff.

- Compliance activities for manufacturing and processing facilities.

Appropriated User Fee Trigger Needs -- Maintaining Animal Drug Review and Medical Device Review Programs: + $ 2,049,000 and + 13 FTE

To meet the statutory requirements for collecting Animal Drug and Medical Device User Fees, FDA must spend a minimum amount of appropriated resources, indexed to the cost of living, on the review process. If the appropriation and/or spending do not meet these minimum requirements (known as user fee triggers), then the agency is unable to receive the supplemental user fee funding and the programs terminate. The additional budget authority is needed to ensure that the trigger requirements are met. The request amount is $7,425,000 and 45 FTE. For the Medical Device Review Program, the portion for the Center for Devices and Radiological Health is $2.9 million and 15 FTE and the portion for the Office of Regulatory Field is $2.0 million and 13 FTE.

Cost of Living-Pay: + $8,297,000

FDA's request for inflationary pay costs is essential to accomplishing our public health mission. Payroll costs account for more than sixty-percent of the FDA budget, and the Agency is not able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Field Activities share of this increase is $8.297 million. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Field Activities Reduction[1]: - $11,442,000 and – 48 FTE

ORA (Field) support the five major program areas regulated by FDA, including Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Medical Devices. The Field redeploy base activities in certain program areas in order to support activities under the Agency's high priority initiatives: Pandemic Preparedness, Food Defense, and Human Tissues Initiatives. Field reductions include: the analysis of domestic and import samples of food; the analysis of laboratory samples of human and veterinary drug products; inspection of pre-approval and bioresearch monitoring inspections of veterinary drugs; inspections of veterinary feed manufacturers; inspection of human drugs manufacturers; regulatory research related to the development of laboratory analytical methods for foods, human drug, and animal feed products; compliance and recall functions involving food, human drugs, and

[1] The amount shown in the Strategic Redeployment paragraph is shown for illustrative purposes. The Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Devices and Radiological Health programs include the Office of Regulatory Affairs – Field Activities portion in the Strategic Redeployment paragraphs of these programs.

animal drugs and feeds; and the management, supervisory, and coordination of personnel at multiple locations involved in the food, human drugs, and animal drug and feeds areas.

User Fees

Prescription Drug User Fee Act: +$399,000 and +2 FTE

PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These fees expand the resources available for the process of reviewing human drug applications including reviewers, information management, space costs, acquisition of fixtures, furniture, equipment and other necessary materials so that safe and effective drug products reach the American public more quickly. In 2002, the Bioterrorism Act included reauthorization 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 (PDUFA III). The reauthorization directs FDA to strengthen and improve the review and monitoring of drug safety; consider greater interaction with 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. The increases will contribute to meeting these mandated directives. In FY 2007 FDA will work with Congress on the reauthorization of the Prescription Drug User Fee Act. This increase of $399,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Medical Devices User Fee and Modernization Act: +$101,000 and + 1 FTE

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amends the Federal Food, Drug, and Cosmetic Act to provide FDA important new responsibilities, resources, and challenges. MDUFMA was signed into law October 26, 2002 and was amended by the Medical Device User Fee Stabilization Act of 2005. MDUFMA has three particularly significant provisions. These provisions allow for the collection of user fees for premarket applications, allow establishment inspections to be conducted by third parties and place new regulatory requirements on reprocessed single use devices. The revenues from these fees, and the appropriated trigger amounts will allow FDA to pursue a set of ambitious performance goals that will provide patients earlier access to safe and effective technology, and will provide more interactive and rapid review to the medical device industry. In FY 2007 FDA will work with Congress on the reauthorization of the Medical Device User Fee and Modernization Act. This increase of $101,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Mammography Quality Standards Act (MQSA): +$237,000

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths among American women. Experts estimate that one in eight American women will contract breast cancer during their lifetime. The MQSA, which was reauthorized in October 2004, addresses the public health need for safe and reliable mammography. The Act required that mammography facilities be certified by October 1994, and inspected annually to ensure compliance with national quality and safety standards. The reauthorization codified existing certification practices for mammography facilities and laid the groundwork for further study

of key issues that include ways to improve physicians' ability to read mammograms and ways to recruit and retain skilled professionals to provide quality mammograms. The increase of $237,000 will cover inflation.

Proposed User Fees (Reclassified as Mandatory): (Non-Add)

Reinspection User Fee (Mandatory): + $12,300,000 and + 102 FTE (Non-Add)
The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an estimated amount sufficient to fund the FY 2007 reinspections. The Field – Office of Regulatory Affairs component of this user fee is $12,300,000 and 102 FTE.

Justification of Base

In FY 2007, FDA has directed its resources to support the highest risk, highest impact, and highest priority initiatives. The following activities which are grouped by strategic goal provide more information about FDA's field base activities. They include noteworthy examples to illustrate base activities. Activities supporting counter terrorism and food defense appear throughout the following sections.

FDA Strategic Goal: Improve Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Base resources will be used to conduct science-based risk management in all agency regulatory activities, so that the most health promotion and protection can be provided at the least cost for the public.

FDA must have the capacity to quickly and accurately identify and respond to potential terrorist events occurring at any point in the food chain, or in the distribution chain of other FDA-regulated products and take prompt action to mitigate their effects. In the event of an identified threat, FDA will work with other Federal, state, and local agencies to eliminate or contain the hazard, reduce public health risk, and identify those who perpetrated the attack.

- Continue to implement regulations issues under the Bioterrorism (BT) Act, such as detaining suspect food when the agency has credible evidence or information that it presents a threat to humans or animals.

- Strengthen relationships with State partners through the FERN, a national laboratory network that enables FDA to test thousands of food samples within a matter of days if there is a food terrorism event, or a foodborne illness outbreak.

- Fund FERN state Cooperative Agreements for increased laboratory surge capacity and the National Surveillance Sampling Program.

- Operate a National Sampling Surveillance Program using FERN to build the capacity to effectively monitor the food supply.

- Conduct training and proficiency testing of FERN laboratories to assure that these laboratories can achieve consistent testing results.

Electronic Laboratory Exchange Network (eLEXNET) Expansion

eLEXNET has been identified as a candidate system to participate in the National Biosurveillance Integration System (NBIS). NBIS is being developed by the Department of Homeland Security as a program that will integrate systems that monitor health, environment, and intelligence information across government agencies. In order to provide food sector-specific information to NBIS, FDA has begun work to develop statistical tools and algorithms for detecting signals that analytes or agents are atypical from normal trends. This activity will enhance eLEXNET's progression toward the achievement of FDA's strategic goal "to improve the coordination and integration of existing food surveillance capabilities with the Department of Homeland Security's (DHS) integration and analysis function, as part of the government wide Bio-Surveillance Initiative."

- Expand the use of eLEXNET. It collects lab analytical data on chemical, microbiological, and other contaminants and links federal, state, and other laboratories. This data capture and exchange system provides the necessary infrastructure for an early-warning system that identifies potentially hazardous foods and enables health officials to assess risks and analyze trends.

- Develop effective prevention strategies to "shield" the food supply from terrorist threats, including the capacity for rapid, coordinated responses to a food borne terrorist attack.

- Intensify the review of products offered for import into the U.S. for safety and security issues.

- Expand field laboratory and contract activities to evaluate and develop existing and potential laboratory and field test kits for product contaminants.

- Inspect drug and vaccine manufacturers whose products may be stockpiled as part of the Governments' counter terrorism efforts.

- Provide training, equipment, facilities, and information technology support to field staff to work on counter terrorism initiatives with a focus on imports.

- Support the requirements of the Bioterrorism Act of 2002. This is accomplished by the FDA Unified Registration and Listing System (FURLS) as it relates to Food Facility Registration, Drug Facility Registration and Listing, and Prior Notice of Food Shipments into the U. S. FDA began this effort by identifying opportunities for unification between the FDA Drug Facility Registration and Listing requirements with those of the Food Facility Registration Requirements.

- Continue to develop the Food Registration and Prior Notice systems that became operational in the first quarter of FY 2004.

- Collaborate with CBP to monitor the importation of regulated products and follow-up on the status of products refused entry.

- Evaluate the accuracy of information import filers provided to the FDA automated entry review system regarding regulated products offered for entry into domestic commerce.

- Continue to conduct food import exams of food products offered for import into the country.

- Expand import surveillance at international mail facilities and courier hubs.

- Continue development of the National Biosurveillance Integration System. The Health Level-7, the departmentally recognized standard for communication in the health arena, was added that will allow eLEXNET to generate standardized messages and use other government recognized terminologies for health and laboratory information.

Research, Development, and Evaluation Activities

ORA's research, development, and evaluation activities support the strategic goal through the Method Validation/Development Program. This program supports the vision of providing a convincing and prevailing scientific and analytical base for regulatory decisions that protect and promote public health. Vital to carrying out this mission is the development, improvement, and validation of methods that support the agency's regulatory responsibilities. Specifically, the laboratory techniques developed and validated through the ORA Method Validation/Development Program allow FDA to: (1) evaluate the safety and effectiveness of regulated products; and (2) to detect and respond to threats to public health from foods and medical products. The primary focus of this program is to enhance FDA Center programs through projects in the following two categories.

- *Method Validation:* projects designed to evaluate existing methodologies in the regulatory laboratory via peer reviewed assessment and inter-laboratory collaborations.
- *Method Modification, Enhancement, and Extension:* projects designed to extend an existing method to one or more additional matrices or analytes; projects designed to improve an existing method.

In coordination and collaboration with FDA Centers, this program also supports projects in the following three categories:

- Method Development: Projects designed to develop and implement new methods in the regulatory laboratory.

- Technology Exploration: Projects designed to investigate and evaluate the usefulness and applicability of new technologies for the regulatory laboratory and increase our base expertise in these new technologies.

- Applied Studies: Projects designed to test hypotheses related to FDA's mission such as food safety, quality mechanisms, contaminants, analyte/matrix interactions, metabolism studies, degradation/depletion studies, and stability studies.

Many ORA research studies aim to apply existing methods to complex and highly varied food commodities. Examples of these activities include:

- Validation of methods for the detection of high risk pathogens in food such as Shigella, Escherichia coli, and Clostridium botulinum toxins.

- Validation of methods to analyze fruits and vegetables for pesticides including evaluation of a faster, more precise carbamate detection method.

- Rapid Methods for pathogen detection such as Pathatrix, Polymerase Chain Reaction (PCR), and multiplex PCR to increase productivity and decrease sample analysis time in the regulatory laboratory.

- Methods for improved detection of mycotoxins toxins produced by fungi that grow in grains and produce, often during storage, in a wider variety of food commodities.

- Methods to detect antibiotic residues in milk and fish intended for human consumption in order to protect against human exposure to antibiotic drugs.

Examples of food defense research activities include:

- Method development and validation for the detection of potential bioterrorism agents in food such as Bacillus anthracis, Clostridium botulinum neurotoxin, and Yersinia pestis.
- Method development and validation for the detection of potential chemical contaminants such as cyanide, ricin, T2 toxin, and radionuclides.

- In addition to increasing FDA's ability to respond to threats in the food supply, the food defense projects also support activities of the Food Emergency Response Network (FERN).

Import Entry Evaluations, Investigations, and Laboratory Analyses

Since the emergence of the "global marketplace" imported foods have grown increasingly important to the U.S. food supply. At the current rate of increase, FDA estimates that by FY 2007 the number of imported food lines will have nearly quadrupled since 1999. This rapid growth combined with ever present security concerns has increased the need to assess the status of imported products. FDA electronically screens imports through OASIS. OASIS is an automated system for processing and making admissibility determinations for FDA regulated products that are offered for import. FDA's electronic screening of imports will be enhanced enhanced by the completion of the Mission Accomplishment and Regulatory Compliance System (MARCS). Other program objectives include:

- Review more than 19 million import lines for admissibility into domestic commerce by the end of FY 2007.

- Expand the use of information on manufacturer, supplier, source country, and past violations to make enhanced admissibility decisions.

- Continue to perform laboratory analysis on products offered for import into the United States.

- Continue to conduct inspections of foreign establishments as part of the Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Devices and Radiological Health programs.

- Perform periodic filer evaluations ensure that the data being provided to FDA is accurate.

Domestic Inspections and Laboratory Analyses

Inspections and surveillance are the primary means of assuring the safety of marketed products. Consumers rely on the FDA to prevent dangerous and unreliable products from entering commerce. Related activities include:

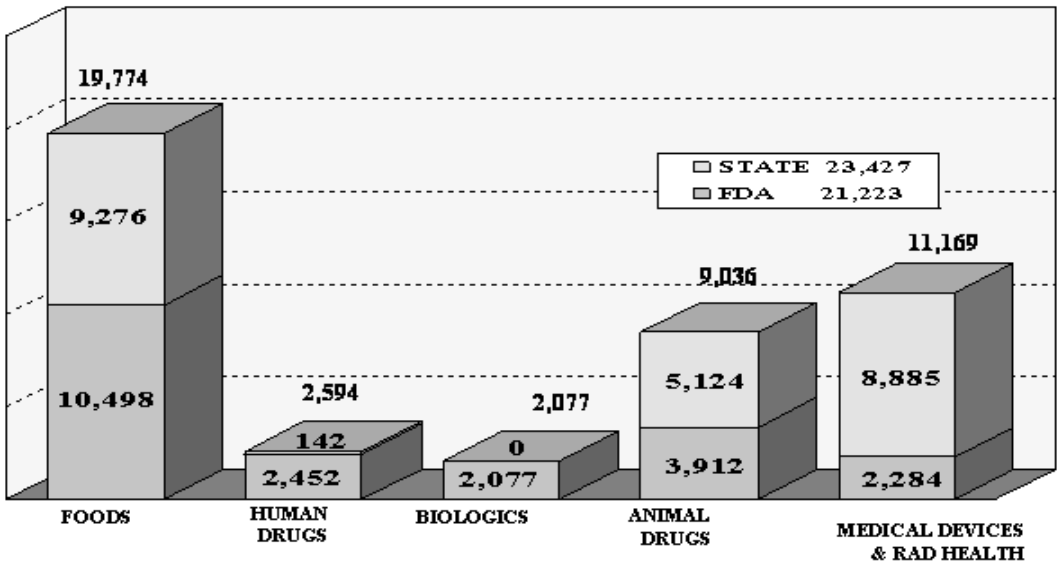
- Identify the food source and contaminant of food borne illness outbreaks ranging from chemical and microbiological to physical hazards.

- Perform engineering, biological and chemical analysis to prevent the exposure of the public to potentially unsafe or ineffective medical devices, electronic products, radionuclide, and radiopharmaceuticals.

- Develop laboratory analytical methods to permit the analyses of products for chemical and microbiological hazards.

- Continue to analyze food samples for pesticides and environmental contaminants.

FY 2005 DOMESTIC INSPECTIONS



44,650 Total Domestic Inspections

- Funding state contracts, partnerships and grants to permit the states to inspect the foods and animal feeds industry; conduct state contract audit inspections to ensure consistent application of regulations during FDA and state inspections of food and animal feed establishments.

- Providing criminal investigations of reported product tampering, counterfeit products and other fraudulent criminal activities involving regulated products.

Bovine Spongiform Encephalopathy (BSE)

FDA works closely with USDA and State agricultural and veterinary agencies to implement BSE regulations and control imported products that may put the public at risk. FDA regulates many products that could contain specified risk materials, including vaccines, foods, dietary supplements, cosmetics, animal drugs, and animal feeds, and has established a comprehensive monitoring system to identify products that may pose a health risk and ensure that they do not enter the U.S. Examples of BSE activities are:

- Providing Federal and state inspectors with up-to-date information on the BSE feed regulation; the FDA Interim Final Rule on BSE and human food and cosmetics; EU regulatory issues; Animal Plant and Health Inspection Service authority; and, best sampling practices.

- Leveraging with state agencies by funding contract and cooperative agreement inspections of feed mills and renderers, and conduct compliance, follow-up, and audit inspections to state contracts.

- Collecting and analyzing domestic and import feed and feed component samples for BSE-related contaminants to ensure proper labeling of animal feeds and feed components.

- Conducting annual BSE inspections of all known renderers and feed mills processing products containing prohibited material. Any firm found to be in violation of the requirements of the regulation will be re-inspected, and other potentially affected firms will be inspected to determine compliance with the regulation.

- Conducting annual BSE inspections domestically, and review records at U.S. ports of entry of human foods, including dietary supplements and cosmetic manufacturers and processors to confirm compliance with the ban on the use of prohibited material.

- Conducting a sampling program for animal feeds domestically and those detained at U.S. ports of entry that contain ingredients possibly derived from contaminated animals.

Bovine Spongiform Encephalopathy (BSE)

The main focus of the BSE-feed control program has been annual inspections of all renderers and feed mills in the U.S. that process with prohibited material. FDA continues to find a very high level of compliance with the 1997 rule that prohibits the inclusion of most animal protein in feeds for cattle and other ruminants. USDA tested more than 500,000 animals and only two animals have been found to be positive. The most recent positive animal was disposed of by incineration and did not enter into the human food or animal feed chain.

FDA issued the first BSE cooperative agreements to eight states with a total value of $2 million. These cooperative agreements are designed to enhance the infrastructure of State BSE control programs. FDA also plans to expand its inspection activities to lower risk enterprises, such as salvage operations, on-farm mixers and transporters of animal feed.

- Enhancing the ability of our public health system to detect prohibited materials in animal feed, human food, and cosmetics, so FDA will continue to support the development and evaluation of diagnostic tests to identify prohibited materials.

- Continuing to develop regulations to help prevent the establishment or amplification of BSE in cattle and prevent the potential for development of vCJD in humans.

- Continuing to develop a real-time PCR (Polymerase Chain Reaction) method that is capable of detecting cattle, swine, sheep, goats, horses, or deer material, along with fowl, to further enhance FDA's ability to detect potentially violative animal feeds. Part of this effort includes the ability to identify up to three or four different prohibited species in a single reaction.

- Utilizing validated real-time PCR methodology to identify prohibited animal proteins in rendered materials from non-United States sources as well as materials rendered in the U.S.

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Base resources will be used to better enable consumers to make informed decisions weighing benefits and risks of FDA-regulated products. These activities include:

Health Fraud and Dietary Supplements

The Consumer Health Information for Better Nutrition initiative is designed to foster two complementary goals concerning the labeling of food and dietary supplements:

- Encourage makers of conventional foods and dietary supplements to make accurate, science-based claims about the health benefits of their products.

- Help to eliminate bogus labeling claims by taking on those dietary supplement marketers who make false or misleading claims.

The Field will ensure that enforcement activities focus on products with the following marketing strategies: herbal products illegally promoted as alternatives to illicit street drugs; unapproved new drugs containing prosteroids and precursor steroids such as dietary supplements; items which are unapproved new drugs marketed as "natural" treatment for viruses, including the herpes virus, and for cold and flu protection; dietary supplements with unsubstantiated structure function claims (examples include treatments for autism, treatments for mental retardation and epilepsy, sports performance enhancement, and aging); and, dietary supplements containing prescription drug ingredients.

Medical Product Safety

FDA believes that roughly half of the deaths and injuries associated with medical errors can be avoided by fully implementing its strategies. The Field's role in reducing these injuries and deaths is as follows:

- Reviewing adverse event and complaint files at manufacturers during inspections for compliance with FDA reporting regulations and to conduct follow up inspections on adverse event reports when information from the manufacturer is needed to evaluate the risks involved.

- Conducting investigations of reported errors and product recalls so that program managers can collect information needed to assess the error, and develop error reduction strategies with manufacturers and the medical community.

- Inspecting hospital device reprocessors to determine compliance with regulatory requirements.

- Providing training for field staff to improve the information gathered through investigation of consumer complaints and reports of medical errors.

Internet Drug Sales

At present, there are an exploding number of new web sites marketing FDA regulated products to the U.S. consumer and medical professionals. FDA currently conducts only minimal levels of web-based oversight. The Office of Criminal Investigations is expanding its efforts to develop cases that address the marketing of counterfeit products. The following is an example of those efforts.

Office of Criminal Investigations: Drug Safety Activities

- *Approximately 70% of OCI criminal investigative activity is in support of FDA's Center for Drug Safety Evaluation and Research.*
- *These investigations primarily involve counterfeit or unapproved/misbranded drugs, fraudulent drug approval studies, illicit internet drug sales, or tampering.*
- *A large percent of these drugs of unknown safety and efficacy are distributed through illicit drug diversion networks.*
- *In FY 2005, OCI initiated over 350 criminal investigations, and achieved over 325 arrests, 225 convictions, and over $55,000,000 in fines and restitution.*
- *OCI is currently actively investigating the issue of internet and other solicitations for fraudulent medications relating to public concerns about bird flu.*
- *In FY2004, FDA's Office of Criminal Investigations initiated 58 counterfeit drug investigations. OCI's counterfeit drug investigations typically do not involve inspections.*
- *In addition to counterfeit drug cases involving Viagra, Cialis, Lipitor, Celebrex, and Serostim, OCI initiated a growing number of investigations involving illicitly diverted high-cost drugs, such as Zyprexa (an anti-anxiety medication) and Epivir (an AIDS treatment) which has been misbranded by relabeling them to disguise their actual source.*
- *OCI has initiated 148 counterfeit drug cases since October 1996.*
- *Investigations so far have netted 108 arrests and 58 convictions to date with fines and/or restitution totals in excess of $4,371,675.*

- Monitoring potentially fraudulent Internet sites to identify targets for investigation and sampling of products.

- Conducting "undercover only" purchases of prescription drugs from Internet sites suspected of engaging in illicit drug sales, distribution, and/or marketing.

- Providing oversight of mail and courier packages entering the U.S. from foreign sources.

FDA Strategic Goal: Transform FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Information Technology

ORA is currently in the midst of a major realignment of its software projects. Burdened with a legacy of stove-piped systems that use outmoded technology, ORA's automated systems cannot provide the support necessary to ensure that FDA can continue to meet its performance goals. ORA strategy to address this challenge is to combine its IT development

efforts into three major programs: Automated Regulatory Management, Data Warehousing and Reporting, and Laboratory Automation. Grouping existing and new IT initiatives into just three areas helps focus resources and management attention on ORA's growing business needs. It also helps ensure that these programs will work together to capture, maintain, and report the information needed to identify and manage health and safety risks while using scarce resources more effectively.

Automated Regulatory Management: This program encompasses the Mission Accomplishment and Regulatory Compliance System (MARCS). The MARCS will establish an electronic environment that can dramatically improve the efficiency of FDA field staff. Benefits include: improved import screening; management of foreign inspections; tracking of violative products and BSE firms to improve the safety of the food supply; more sharing of information with states; better integration with FDA laboratories; efficient work-load management; the flexibility to address drug importation if required, and the ability to meet the prior notice requirements for 24/7 support.

Data Warehousing and Reporting: ORA Reporting Analysis and Decision Support System (ORADSS) is a centralized data warehouse that provides integrated decision support to help FDA identify and manage health and safety risks. This will consolidate ORA's reporting functions. When fully implemented, ORADSS will be a comprehensive repository of information about FDA regulated facilities and the enterprises that are part of the supply chain for regulated products. ORADSS' information will allow FDA Centers and management to statistically correlate and analyze multi-year data on geographic areas, firms, products, inspections, and shipments of interest to the FDA.

The Laboratory Automation: The Laboratory Automation Program, including eLEXNET integration, is an emerging ORA program designed to improve the efficiency of the FDA lab staff the quality of the information the labs provide, and the ability of FDA to share this information with its own centers and other public health labs. In spite of the importance of FDA's labs to critical FDA regulatory activities. ORA's labs currently depend on manual and semi-automated processes which limit the number and scope of the analyses FDA staff can perform. This program would enable FDA labs to improve chain-of custody tracking, including assignments and sample status; automate collection and processing of analytical data; and track calibration and scheduling to improve the quality of the data produced. The Lab Automation Program will also integrate with eLEXNET, the network developed jointly by USDA, CDC, and DoD, to communicate unusual findings from laboratory analyses about food-borne pathogens.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

ORA conducts premarket activities such as bioresearch monitoring of clinical research, preapproval inspections and laboratory method validations needed for application decisions, and inspecting facilities to ensure their ability to manufacture the product to the specifications stated in the application. Specifically, these activities include:

- Continuing to develop a program to conduct pre-approval inspections and pre-operational visits in support of the Presidential Emergency Plan for Aids Relief.

- Conducting bioresearch monitoring inspections to support the drugs, biologics and device pre-approval programs.

- Supporting the generic drug program through the performance of pre-approval inspections to verify the data submitted in Abbreviated New Drug Applications and to assess firm's ability to manufacture products in accordance with Current Good Manufacturing Practices).

Selected FY 2005 Accomplishments

FDA Strategic Goal: Improving Product Quality, Safety, and Availability through Better Manufacturing and Product Oversight

Food Emergency Response Network (FERN)

- 123 laboratories representing 50 States and Puerto Rico that have satisfactorily completed the FERN Laboratory Qualification Checklist.

- Awarded eight cooperative agreements to state laboratories to support additional capacity for food analysis related to chemical terrorism and to enhance state, local, and tribal food safety and security efforts.

- Participated in two FDA surveillance assignments, the Food Security Surveillance Assignment and the Interstate Travel Program Water Assignment.

- Issued six proficiency test samples including one joint proficiency test sample with CDC/LRN for microbiology laboratory testing of *Bacillus anthracis*; three chemistry proficiency test samples; and, two radiological proficiency test samples.

- Conducted five FERN training courses.

Food Security Surveillance Assignment

- Conducted in collaboration with forty-four states and the Commonwealth of Puerto Rico, a Food Security Surveillance Assignment (FSSA) for six weeks. The primary goals of the FSSA were to deter intentional contamination of the food supply through heightened and targeted preventive activities at various points in the food distribution chain and to exercise the systems and networks for responding to a food related emergency during a period of increased food security risk.

Laboratory Response to BSE

- Implemented an advanced analytical procedure for detection of prohibited material in animal feed into an assignment issued for 900 domestic and 900 import feed samples. This novel approach combines light microscopy with polymerase chain reaction (PCR) to determine and detect DNA from ruminants and non-ruminant mammalian species, supporting the BSE/Ruminant Feed Ban.

BSE Surveillance

- Continued collaborative program with our state regulatory counterparts to inspect facilities for compliance with the BSES/ruminant feed ban.

Response to BSE Positive

- Conducted, following the finding of a BSE positive animal in Texas, a feed investigation. It was joint operation with USDA/APHIS, the Texas Animal Health Commission, and the Texas Feed and Fertilizer Control Service. FDA accomplished our two main objectives:
    - Identify all protein sources in the animal's feed history that could potentially have been the source of the BSE agent.
    - Verify that cattle leaving the herd after 1997 that were identified by USDA/APHIS as animals of concern (e.g. progeny and feed cohorts), were rendered at facilities in compliance with the BSE/ruminant feed ban regulation.

Operation Safeguard Pharmaceutical

- Conducted with Customs and Border Protection, blitzes of several international mail facilities across the country. The blitzes revealed substantial numbers of shipments of unapproved drugs, and provided useful information for future targeting efforts.

State Contracts Program

- Awarded 153 contracts with state and local governments to perform MQSA, feed, tissue residue, food, and medical device inspections.

- Implemented electronic State Access to FACTS (eSAF) in 15 state food programs and conducted the associated training for FDA and state personnel. ORA began designing eSAF to include the feed and BSE programs, which will be piloted in FY 2006.

- Conducted auditor training for FDA and state personnel for food and feed contracts.

- Completed audits of all state food inspectors working under contract.

- Pilot tested an audit program for contracts with New York State.

50 State Conference Calls

- Continued the 50 State Call, which is one of our most effective communication tools to share critical regulatory information with our state counterparts. Calls were held covering such topics as food defense, CDC updates, seafood HACCP, and State legislation on ephedra, BSE rule changes, decorative contact lenses, infant formula, food safety task forces, and dietary supplements.

State Grants Program

- Reviewed and awarded Cooperative Agreement grants for BSE infrastructure improvement in eight states and Food Emergency Response Network (FERN) infrastructure improvement in eight states.

- Reviewed, renewed, and awarded new grants for Food Safety projects in 34 states and Health Fraud prevention projects in 11states.

State Partnership Program

- Continued to develop new partnerships that have contributed to the exchange of inspection and sampling data and have facilitated the receipt of training and distribution of equipment to the states.

- Coordinated Partnership Agreements for x-ray inspections in over 20 States.

- Conducted BSE and Seafood HACCP inspections under State Partnership.

Risk-Based Screening of Imports

- Funded a proof-of-concept by the University of New Mexico, completed in May 2005, for an electronic system to use artificial intelligence and extensive data mining to perform risk-based screening of import entries.

- Funded, in September 2005, the expansion of that work into a functional prototype which, once operational, could enhance the effectiveness of the import entry review process.

Shelf-Life Extension Program

- Utilized an inter-agency agreement with the Department of Defense to acquire new equipment for the shelf-life extension program. This new equipment not only provided necessary resources for the continuation of the program, but also allowed ORA to broaden the scope of the shelf-life testing to include new products never tested before.

MDUFMA Accredited Persons Inspection Program

- Continued assistance in the Agency's implementation of the Medical Device User Fee and Modernization Act's (MDUFMA) Accredited Persons Inspection Program by providing an FDA inspection course for AP auditors in May 2005.

- Coordinated, conducted and tracked training in the form of performance audits has been coordinated, conducted and tracked throughout the year.

- Promoted the program has also been promoted to industry groups in the form of presentations.

Hurricanes Katrina and Rita: August – September, 2005

The Gulf Coast of the United States, and specifically New Orleans, LA and Gulf Port, MS, have large port operations and are home to major FDA regulated industries, especially seafood harvesting, processing, storage and distribution. There were approximately 1,700 FDA regulated firms in the most heavily storm-impacted counties of Louisiana, Mississippi, Alabama and Florida. To conduct our public health responsibilities in the region, FDA/ORA:

- *Re-established the New Orleans District at the Continuity of Operations site in Nashville, TN and coordinated FDA deployments to assist the CDC teams in Texas to support the evacuee efforts.*

- *Worked with the affected states to inspect 417 pharmacies, as well as retail food establishments. In Louisiana alone, FDA contacted 1,461 establishments and assisted 518 retail establishments to reopen, i.e. schools, nursing homes, restaurants, etc.*

- *Examined FDA regulated products to assure safety, purity and /or effectiveness; evaluated products to determine whether or not the product was suitable for distribution due to spoilage, contamination, etc.; and, supervised the reconditioning or destruction of those products deemed unsuitable for their original intended use.*

- *Provided education outreach materials to assist consumers returning to their homes.*

- *The Prior Notice Center provided staff for a 24/7 office coordinated by the USAID Office of Foreign Disaster Assistance (OFDA) Response Management Team set up to receive and distribute foreign-donated humanitarian relief supplies. Fifty-three (53) State Department authorized shipments of FDA-regulated products were identified and reviewed. FDA advised OFDA of decisions regarding the dispensation of the shipments.*

- *At the land borders, we worked with local Customs and Border Protection personnel to review and clear non-government donations of humanitarian relief supplies from unofficial sources and non-profits as well as expediting emergency bottled water shipments imported from FEMA contractors so that needed supplies could proceed to destination.*

Mobile Laboratories

- Took possession of the completed mobile laboratories in April 2005. Currently, 30 FDA laboratory personnel have been trained in the mobile laboratory platform.
- Ran a test deployment of the mobile laboratories at NCTR to demonstrate that analysts were able to set up the laboratories on a location site and run sample analyses using only the mobile laboratory facilities.

- Deployed FDA Mobile Laboratories deployed on Monday October 3rd to Thibodaux, Louisiana in response to the Louisiana Department of Health and Hospitals (LDHH) request for assistance. LDHH water testing laboratories were completely disabled and unable to perform laboratory testing to assess the quality of shellfish growing waters forcing them to remain closed until water testing resumed. During the one month deployment, a total of 417 samples were collected and analyzed by a team of FDA and LDHH analysts to assess the fisheries of Lake Pontchartrain and outfall receiving waters of Lake Borgne. See adjacent picture.

The data from these analyses has enabled the LDHH to reopen numerous growing areas for the shellfish industry. This assistance has also allowed the LDHH time to set-up their laboratory facilities so that their staffs were able to return and begin classification of the waters.

Operation Bait and Switch

- Conducted a multi-district operation to detect import parcels which had been shipped via postal service from a country other than Canada, and which contained pharmaceutical products labeled or identified as coming from a Canadian pharmacy. FDA found that such products sourced from 39 different countries.

- Analyzed a total of 487 samples and found 28 products that were found to be counterfeit (not consistent with authentic product) and one sample significantly sub potent. In addition, label reviews found some products labeled entirely in a foreign language.

- Confirmed, through Operation Bait and Switch, that U.S. consumers have no assurance of quality when purchasing medications from sources outside the normal distribution channels in the U.S.

Tsunami Response

- Utilized FDA data and data from the National Geospatial Intelligence Agency to identify approximately 2,600 exporters of foods, drugs, and medical devices in the areas affected.

- Demonstrated Prior Notice Center capabilities to target specific imported food commodities for further scrutiny and/or exam as needed to respond to a specific event. Prior notice targeting criteria were established based on commodity type, previous regulatory history, intelligence, and geographic areas of concern. A sampling assignment was issued for fresh seafood products that were analyzed for biological hazards and decomposition.

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Ephedra-Containing Dietary Supplements

- Identified more than thirty internet and retail firms selling banned ephedra products

- Conducted investigations to identify physical locations and other information for regulatory action to uphold the ban on ephedra containing products.

Internet Storefront Drugs

- Obtained a preliminary injunction against one storefront operation facilitating the Internet sale and importation of unapproved prescription drugs from Canada.

- Coordinated regulatory activities with state regulatory bodies and national regulatory organizations against internet and storefront operations that import unapproved prescription drugs.

GlaxoSmithKline, Inc.

- Announced on April 28, 2005, that GlaxoSmithKline, Inc. had signed a Consent Decree of Condemnation and Permanent Injunction with FDA to correct manufacturing deficiencies at its Cidra, Puerto Rico facility. FDA was concerned that GSK's violation of manufacturing standards may have resulted in the production of drug products that could potentially pose risks to consumers.

Vail Products, Inc.

- Initiated seizures on March 22, 2005, of all finished Enclosed Bed Systems made by Vail Products, Inc. This was in a response to ongoing concerns about manufacturing quality and labeling, the FDA and the Department of Justice. Use of these systems poses a public health risk because patients can become entrapped and suffocate, resulting in

severe neurological damage or death. On August 23, 2005, an order of condemnation and injunction was entered against the seized enclosed bed systems.

ATF Fitness – Dietary Supplement Containing Ephedrine Alkaloids

- Announced on February 25, 2005, that the Agency had requested the U.S. Attorney's Office for the Western District of Pennsylvania to file a Complaint for Forfeiture against $13,500 worth of adulterated and misbranded dietary supplement containing ephedrine alkaloids that were located at ATF Fitness Products, Inc. in Oakmont, PA. The U.S. Marshals seized the products in response to a warrant issued by the court. The seizure followed an FDA investigation that determined the products either contained prohibited ephedrine alkaloids or claimed to contain ephedrine or ephedrine alkaloids but did not.

Asia MedLabs, Inc.

- On November 23, 2004, FDA investigators accompanied the U.S. Marshals Service in a seizure of more than 2.1 million VITERA-XT capsules in the possession of Asia MedLabs, Inc., located in Houston, Texas. Of the total products seized, one million were yet unpackaged capsules; the remainder was contained in more than 14,000 labeled bottles. The articles were seized because they contained an ephedra-containing dietary supplement marketed by Houston-based Asia MedLabs, Inc.

Pharmakon Labs

- On July 27, 2005, FDA announced a permanent injunction shutting down operations at Pharmakon Labs of Florida. The company manufactured and distributed cough and cold liquids, tablets and caplets. Following inspections by FDA and a trial in U.S. District Court, it was determined that drug products sold by Pharmakon Labs, Inc., its president Abelardo L. Acebo, and its secretary/ treasurer Edward R. Jackson (the defendants) did not meet current good manufacturing practice (CGMP) standards and other legal requirements. The government's request for a permanent injunction was based on the defendants' demonstrated unwillingness to comply with the law.

Genendo Pharmaceutical N.V

- On August 22, 2005, U.S. District Judge James F. Holderman entered an order of permanent injunction against Genendo Pharmaceutical N.V., a drug importer located in Curacao, Netherlands, Antilles. The Order, which followed nearly two years of intense litigation and a trial on the merits, held that Genendo violated the Federal Food, Drug, and Cosmetic Act when it imported name-brand drugs that were labeled in foreign languages and manufactured and/or packaged in facilities not identified in FDA-approved new drug applications.

Boston Scientific Agrees to Pay $74 Million to Resolve Allegations of Violations

- On June 24, 2005, the U.S. Department of Justice announced that Boston Scientific Corporation, Inc., agreed to pay $74 million to the United States to resolve an ongoing investigation concerning its 1998 distribution and subsequent recall of one of its coronary stent delivery systems. A Civil Complaint was filed in federal district court charging BSC with distributing in interstate commerce 34,589 medical devices that were adulterated and misbranded during August 12, 1998 through October 5, 1998. To resolve the allegations in the civil complaint, BSC, without admitting liability, agreed to pay $74 million to the United States.

FDA Strategic Goal: Transforming FDA Business Operations, Systems and Infrastructure to Support FDA's Mission in the 21st Century

Prior Notice Center (PNC)

- Began full enforcement of the Prior Notice Interim Final Rule in FY2005, which resulted in the refining of Prior Notice (PN) data targeting criteria and edits to assure the accuracy of the submitted data. The accuracy is critical to help assure that FDA is able to detect and prevent food that may be intentionally contaminated with biological, chemical, or radiological agents, or which may pose significant health risks, from entering the U.S. Thousands of entries were rejected or refused based on inaccurate or incomplete prior notice data submissions, and required resubmission before allowing the subject imported food cargo to transit the U.S.

OASIS Import Data System

- Enhanced the Operational and Administrative System for Import Support (OASIS). Examples include modifications to improve receipt and processing of prior notice submissions; conversion of the database to ORACLE 9i to support migration from a client application to a direct web application; and modifications to better record the basis for decision-making when releasing or refusing admission to shipments after sampling and analysis, particularly in relation to the risk of bovine spongiform encephalopathy (BSE). These enhancements will improve system performance, user accountability, and overall productivity for risk-based screening of import entries.

ORADSS Upgrades

- Upgraded its enforcement data warehouse, the ORA Reporting Analysis and Decision Support System (ORADSS) by migration to Business Objects v. 6.5 and by providing extensive training for users. This will significantly improve the ability of field, ORA headquarters, and Center offices to do in-depth, customized analyses of the effectiveness of compliance programs and enforcement initiatives, and to detect patterns of violations.

Mission Accomplishment and Regulatory Compliance System (MARCS)

- Completed a comprehensive design plan of the MARCS suite of applications. The plan includes recommendations for the priority and sequence for application rollout, as well as the associated cost and time estimates. In addition, a Process Control Board was established to validate and prioritize business requirements.

Identity and Trust Management System

- Implemented the Identity and Trust Management System. Twelve hundred ORA field inspectors and investigators are now working within a high level of trust assurance. Using the Turbo EIR application, users are issued digital certificates that protect the confidentiality and integrity of their information. The system also provides digital signature capability where required. Based on strong ORA compliance advocacy, the certificate authority is maintained and operated at the highest level of assurance.

Electronic Laboratory Exchange Network (eLEXNET)

- Continued to expand the system. Of the 113 laboratories in the eLEXNET system, 95 are actively submitting data, an increase of 16 laboratories from the previous year. The number of FERN laboratories is at 106, an increase of 38, with 60 submitting data, an increase of 26. In addition, the eLEXNET HL7 Implementation Guide was developed which provides exchange of food laboratory analysis data using the HL7 message format.

Tactical Work Planner (TWP)

- Implemented TWP, the first component of MARCS. The TWP is a Web application providing specialized work assignment support for District managers and staff. The application provides the ability to view, create, and track the ORA Annual Work Plan and Performance Goals, and also plan, report, and create group assignments that support the compliance program.

Electronic State Access to FACTS (eSAF)

- Expanded the system to include seventeen states that are now trained and using eSAF. The eSAF allows the FDA to expand inspections of facilities by utilizing staff from the state level to enter inspection data directly into FACTS, thus increasing the number of inspections available for review by the agency.

Training

- Developed and delivered:
    - One course (Advanced non-Clinical BIMO) to 60 students to provide training on emerging issues, new technology and interpreting laboratory data and ECGs that may be reviewed during complex Clinical Bioresearch Monitoring inspections.

- 43 food related courses to 1,700 state and local regulators to help assure that they have the knowledge and skills to conduct risk based approach inspections.

- Four BSE related courses to 95 ORA and state regulators in order for them to conduct inspections of animal feed firms; delivered one Microscopic Analysis of Feeds for Processed Animal Proteins course to 20 FDA and state analysts.

- BSE Inspection training course to state contracted feed control inspectors.

- FDA employees and state, local and tribal regulators have completed more than 200,000 Web-based training modules.

- ORA provided FERN training to laboratory analysts to 27 State and 15 FDA employees.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

ORA developed a program to conduct pre-approval inspections and pre-operational visits in support of the Presidential Emergency Plan for Aids Relief.

Combined Field Activities – ORA
Program Activity Data

FOODS FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	FY 2005 Actual	FY2006 Estimate	FY2007 Estimate
Domestic Food Safety Program Inspections	4,573	3,400	3,400
Imported and Domestic Cheese Program Inspections	477	400	400
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	481	400	400
Domestic Fish & Fishery Products (HACCP) Inspections	2,467	2,480	2,480
Import (Seafood Program Including HACCP) Inspections	500	500	500
Juice HACCP Inspection Program (HACCP)	490	375	375
Interstate Travel Sanitation (ITS) Inspections	1,510	1,700	1,700
State Contract Food Safety (Non HACCP) Inspections	6,992	8,130	8,130
State Contract Domestic Seafood HACCP Inspections	953	1,135	1,135
State Contract Juice HAACP	47	35	35
State Partnership Inspections	1,284	1,300	1,300
Total Above FDA and State Contract Inspections	**19,774**	**19,855**	**19,855**
Total Domestic Reinspections (Non-add)	**523**	**523**	**523**
State Contract and Grant Foods Funding	$6,825,000	$7,100,000	$6,940,000
Number of FERN State Laboratories	8	10	16
Annual FERN State Cooperative Agreements/Operations	$12,270,000	$7,037,000	$12,236,000
Total State & Annual FERN Funding	**$19,095,000**	**$14,137,000**	**$19,176,000**
Domestic Field Exams/Tests	3,528	5,000	5,000
Domestic Laboratory Samples Analyzed	15,390	11,425	9,425
All Foreign Inspections	129	200	100
Total Foreign Reinspections (Non-add)	**15**	**15**	**15**
Import Field Exams/Tests	84,997	75,000	71,000
Import Laboratory Samples Analyzed	25,549	31,600	29,600
Import Physical Exam Subtotal	110,546	106,600	100,600
Import Line Decisions	8,672,168	10,059,715	11,669,269
Percent of Import Lines Physically Examined	1.27%	1.06%	0.86%
Prior Notice Security Import Reviews (Bioterrorism Act mandate)	86,187	45,000	60,000

COSMETICS FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	**FY 2005 Actual**	**FY2006 Estimate**	**FY2007 Estimate**
All Inspections	138	100	100
Total Domestic Reinspections (Non-add)	**7**	**7**	**7**
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Import Field Exams/Tests	1,983	2,000	2,000
Import Laboratory Samples Analyzed	241	200	200
Import Physical Exam Subtotal	2,224	2,200	2,200
Import Line Decisions	1,146,049	1,398,180	1,705,779
Percent of Import Lines Physically Examined	0.19%	0.16%	0.13%

DRUGS FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	FY 2005 Actual	FY2006 Estimate	FY2007 Estimate
Pre-Approval Inspections (NDA)	149	130	130
Pre-Approval Inspections (ANDA)	81	135	135
Bioresearch Monitoring Program Inspections	562	520	520
Drug Processing (GMP) Program Inspections	1,365	1,500	1,440
Compressed Medical Gas Manufacturers Inspections	125	155	150
Adverse Drug Events Project Inspections	106	135	135
OTC Monograph Project Inspections and	11		
Health Fraud Project Inspections [1]	53	45	45
State Partnership Inspections: Compressed Medical Gas Manufacturers Inspections	85	110	110
State Partnership Inspections: GMP Inspections	57	50	50
Total Above FDA and State Partnership Inspections	**2,594**	**2,780**	**2,715**
Total Domestic Reinspections (Non-add)	**220**	**220**	**220**
Domestic Laboratory Samples Analyzed	1,446	1,735	1,600
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Foreign Pre-Approval Inspections (NDA)	163	180	180
Foreign Pre-Approval Inspections (ANDA)	77	60	60
Foreign Bioresearch Monitoring Program Inspections	85	65	65
Foreign Drug Processing (GMP) Program Inspections	217	195	195
Foreign Adverse Drug Events Project Inspections	10	25	25
Total Above Foreign FDA Inspections	**552**	**525**	**525**
Total Foreign Reinspections (Non-add)	**17**	**17**	**17**
Import Field Exams/Tests	4,288	4,400	4,400
Import Laboratory Samples Analyzed	1,045	355	300
Import Physical Exam Subtotal	4,850	4,850	4,700
Import Line Decisions	264,559	317,471	380,965
Percent of Import Lines Physically Examined	1.83%	1.53%	1.23%

Note:

1. The OTC Monograph and Health Fraud Inspections will no longer be planned separately in FY 2006.

BIOLOGICS FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	**FY 2005 Actual**	**FY 2006 Estimate**	**FY2007 Estimate**
Bioresearch Monitoring Program Inspections	121	156	156
Blood Bank Inspections	1,439	1,130	1,070
Source Plasma Inspections	188	165	160
Pre-License, Pre-Approval (Pre-Market) Inspections	3	10	10
GMP Inspections	42	36	36
GMP (Device) Inspections	14	35	35
Human Tissue Inspections	270	250	325
Total Above Domestic Inspections	**2,077**	**1,782**	**1,792**
Total Domestic Reinspections (Non-add)	**50**	**50**	**50**
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Blood Bank Inspections	16	24	24
Pre-License Inspections	6	0	0
GMP Inspections	15	24	17
Total Above Foreign FDA Inspections	**35**	**43**	**41**
Total Foreign Reinspections (Non-add)	**4**	**4**	**4**
Import Field Exams/Tests [1]	143	100	100
Import Line Decisions	39,979	44,377	49,258
Percent of Import Lines Physically Examined	0.36%	0.23%	0.20%

ANIMAL DRUGS & FEEDS FIELD

PROGRAM OUTPUTS- **DOMESTIC INSPECTIONS**	**FY 2005** **Actual**	**FY2006** **Estimate**	**FY2007** **Estimate**
Pre-Approval /BIMO Inspections	72	140	110
Drug Process and New ADF Program Inspections	230	210	210
BSE Inspections	3,025	3,760	3,760
Feed Contaminant Inspections	13	15	15
Illegal Tissue Residue Program Inspections	203	245	245
Feed Manufacturing Program Inspections	369	240	40
State Contract Inspections: BSE	3,309	4,562	4,562
State Contract Inspections: Feed Manufacturers	457	347	347
State Contract Inspections: Illegal Tissue Residue	370	750	600
State Partnership Inspections: BSE and Other	988	900	900
Total Above FDA and State Contract Inspections	**9,036**	**11,169**	**10,789**
Total Domestic Reinspections (Non-add)	**173**	**173**	**173**
State Animal Drugs/Feeds Funding	$1,300,000	$1,700,600	$1,800,000
BSE Grant Increase	$3,000,000	$3,000,000	$3,000,000
State Contract for Tissue Residue	$220,000	$220,000	$210,000
Total State Funding	**$4,520,000**	**$4,920,600**	**$5,010,000**
Domestic Laboratory Samples Analyzed	1,841	1,770	1,730
PROGRAM OUTPUTS- **IMPORT/FOREIGN INSPECTIONS**			
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	26	45	45
Foreign Drug Processing and New ADF Program Inspections	12	10	10
Total Above Foreign FDA Inspections	**38**	**55**	**55**
Total Foreign Reinspections (Non-add)	**3**	**3**	**3**
Import Field Exams/Tests	4,298	4,500	4,500
Import Laboratory Samples Analyzed	753	1,120	900
Import Physical Exam Subtotal	5,051	5,620	5,400
Import Line Decisions	212,254	235,602	261,518
Percent of Import Lines Physically Examined	2.38%	2.39%	2.06%

DEVICES FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	FY 2005 Actual	FY 2006 Estimate	FY2007 Estimate
Bioresearch Monitoring Program Inspections	329	300	300
Pre-Approval Inspections	64	130	130
Post-Market Audit Inspections	63	65	65
GMP Inspections (Levels I, II, III and Accredited Persons)	1,430	1,530	1,530
Total Above Domestic Inspections: Non MQSA	**1,886**	**2,025**	**2,025**
Inspections (MQSA) FDA Domestic (non-VHA)	366	335	371
Inspections (MQSA) FDA Domestic (VHA)	32	32	32
Inspections (MQSA) by State Contract	8,340	7,924	7,700
Inspections (MQSA) by State non-Contract	545	530	530
Total Above Domestic Inspections: MQSA	**9,283**	**8,821**	**8,633**
Total Domestic Reinspections (Non-add)	**237**	**237**	**237**
State Contract Devices Funding	$1,350,000	$250,000	$275,000
State Contract Mammography Funding	$9,800,000	$9,200,000	$9,940,000
Total State Funding	**$11,150,000**	**$9,450,000**	**$10,215,000**
Domestic Radiological Health Inspections	107	130	130
Domestic Field Exams/Tests	944	1,215	1,215
Domestic Laboratory Samples Analyzed	200	217	217
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS			
Foreign Bioresearch Monitoring Inspections	6	10	10
Foreign Pre-Approval Inspections	17	34	34
Foreign Post-Market Audit Inspections	26	27	27
Foreign GMP Inspections	225	207	189
Foreign MQSA Inspections	16	15	15
Foreign Radiological Health Inspections	9	19	19
Total Above Foreign FDA Inspections	**299**	**312**	**294**
Total Foreign Reinspections (Non-add)	**24**	**24**	**24**
Import Field Exams/Tests	6,901	5,000	5,000
Import Laboratory Samples Analyzed	1,333	1,440	1,440
Import Physical Exam Subtotal	8,234	6,440	6,440
Import Line Decisions	3,484,393	4,460,023	5,708,829
Percent of Import Lines Physically Examined	0.24%	0.14%	0.11%

OTHER ACTIVITIES

	FY 2005 Actual	FY 2006 Enacted[1]	FY 2007 Estimate	Increase or Decrease
Program Level	**$104,504,000**	**$117,414,000**	**$120,341,000**	**+ $2,927,000**
Total FTE	*652*	*706*	*695*	*- 11*
Budget Authority	**$87,230,000**	**$84,905,000**	**$88,236,000**	**$3,331,000**
Pandemic Preparedness		*$2,000,000*	*$2,354,000*	*$354,000*
FTE		*3*	*0*	*0*
Food Defense	*$1,488,000*	*1,473,000*	*$1,485,000*	*$12,000*
FTE	*2*	*2*	*2*	*2*
Drug Safety			*$396,000*	*$396,000*
FTE			*2*	*2*
Cost of Living			*$1,413,000*	*$1,413,000*
UFMS			*$1,180,000*	*$1,180,000*
Strategic Redeployment			*($5,497,000)*	*($5,497,000)*
FTE			*(19)*	*(19)*
Budget Authority FTE	**508**	**581**	**531**	**- 50**
Total User Fees	**$15,499,000**	**$26,779,000**	**$32,105,000**	**$1,596,000**
PDUFA	*$14,020,000*	*$25,116,000*	*$26,272,000*	*$1,156,000*
FTE	*124*	*133*	*136*	*- 14*
MDUFMA	*$2,644,000*	*$4,535,000*	*$4,921,000*	*$386,000*
FTE	*15*	*19*	*20*	*12*
ADUFA	*$384,000*	*$646,000*	*$696,000*	*$50,000*
FTE	*3*	*6*	*6*	*0*
MQSA	*$226,000*	*$212,000*	*$216,000*	*$4,000*
FTE	*2*	*2*	*2*	*0*
User Fee FTE	**144**	**160**	**164**	**4**

[1] Includes the rescission of 1 percent.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2003 Actual	$107,675,000	$84,685,000	$22,990,000	813
2004 Actual	$114,296,000	$98,597,000	$15,4699,000	709
2005 Actual	$104,504,000	$87,230,000	$15,499,000	652
2006 Enacted	$117,414,000	$84,905,000	$26,779,000	706
2007 Estimate	$120,341,000	$88,236,000	$32,105,000	695

Statement of Budget Request

The Other Activities program is requesting $120,341,000 in program level resources for accomplishing its mission activities including:

- Providing centralized program direction and management services for agency programs to ensure FDA's public health hazard prevention efforts are effectively managed within its regulatory framework.

- Providing management expertise and direction to support standards development for regulated products to effectively serve consumers and our industry stakeholders.

- Developing agency-wide policy in legislation, consumer communications, public information, scientific coordination and regulatory requirements.

- Providing direction in the management of financial, human and information systems resources, knowledge management and other critical infrastructure needs in support of our science-based work.

Program Description

Through the Office of the Commissioner, Other Activities provides agency-wide program direction and administrative services to ensure that FDA's consumer protection efforts are effectively managed and that available resources are put to the most efficient use. The Office of the Commissioner consists of nine subordinate offices that provide policy making, program direction, coordination and liaison, and expert advice to agency leadership and programs. The following table provides a description of each office's functions.

OC Office	Description
Office of the Chief Counsel	Provides expert legal advice and review on statutory and regulatory interpretations affecting FDA enforcement and administrative actions.
Office of Crisis Management	Serves as FDA's focal point for coordinating emergency and crisis response activities, counter terrorism activities, interagency and intra-agency coordination of emergency and crisis planning and management, and internal and external security.
Office of Equal Employment Opportunity and Diversity Management	Advises and assists key officials on equal employment opportunity (EEO) and Civil Rights activities; develops, implements, and monitors the FDA's Affirmative Employment Plan and directs the Affirmative Employment Program; develops labor-management partnerships on EEO matters; and develops and oversees diversity initiatives.
Office of External Relations	Advises FDA leadership on activities and issues affecting FDA programs, projects, and strategies impacting on various constituencies – including the public, consumer groups, industry and trade association, stakeholders, and governmental bodies.
Office of International Affairs and Strategic Initiatives	Advises FDA leadership on international activities including the coordination of the international conference on harmonization and World Health Organization functions; and fosters the development of and administers mutual recognition agreements and other policy documents with foreign countries and multi-national governmental organizations. The office also administers the combination products and pediatric therapeutics programs.

OC Office	Description
Office of Legislation	Coordinates FDA's response to authorizing committees' requests, reviews proposed legislation, prepare agency testimony and facilities clearance by the Department and OMB.
Office of Management	Provides variety of administrative and program support services, assures strategic and operational management of information technology, financial management expertise, and administrative support services to FDA employees.
Office of Planning and Policy	Provides advice and assistance in policy development and oversees FDA rulemaking; serves as focal point for coordinating agency strategic, performance and business-process planning and evaluation; ensures that internal and external stakeholders clearly understand FDA's challenges, achievements, and future directions.
Office of Science and Health Coordination	Advises key officials on scientific issues that impact policy, direction, and long-range goals; coordinates the responsibilities for women's health issues, good clinical practices program, and orphan product development program.

Performance Analysis

During the latest performance period, (FY 2005), the Other Activities Program met the targets for all four performance goals. For more information about these performance goals and results, please see the Performance Detail section.

The FDA supports the Department in establishing a Unified Financial Management System (UFMS). The goal of the UFMS project is to reduce costs, mitigate security risks, and provide timely and accurate information across DHHS. 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 Highlight:

FY 2007 Goal Target	FY 2005 Results	Context
Through FDA's implementation of HHS's Unified Financial Management System, the FDA will finalize its decision on an activity-based costing application and make it operational for its user fee programs.	Major components of data cleanup have been completed. Travel Manager implementation has been completed throughout the Agency in preparation of UFMS.	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.

Program Resource Changes

Budget Authority

Pandemic Preparedness: + $ 2,354,000
FDA plays a unique and vital role in the Nation's preparedness for an influenza pandemic. The agency facilitates the development and availability of safe and effective vaccines and we safeguard America's animal health and food safety systems in the event of an outbreak of avian and pandemic influenza. This funding will enhance the Agency's crisis management office located in the Other Activities program to coordinated the Agency's preparedness efforts and provide the necessary coordination to respond to a pandemic influenza outbreak.

Food Defense: + $1,485,000 and + 2 FTE
The food supply is part of the Nation's critical infrastructure and contributes about 20 percent to the U.S. Gross National Product. A terrorist attack on the food supply could have catastrophic public health and economic consequences. The funds requested would continue to enhance laboratory preparedness, food defense research, surveillance and incident management capabilities. These enhancements would expand FDA's capacity to prevent, prepare for, respond to and mitigate the effects of a terrorist attack, a major disaster or other emergency on the food supply. The Other Activities program component of this initiative is $1,485,000 and 2 FTE.

Improved Drug Safety: + $ 396,000 and + 2 FTE
This initiative will enable FDA to continue its efforts to transform healthcare by reducing occurrences of drug side effects and increasing the number of more affordable drug treatment options. Specifically, funding for this initiative will make possible our continued efforts to modernize the Adverse Event Reporting System (AERS) to create "AERS II", the primary source for drug product adverse event data. To further augment AERS data, FDA will advance its integration efforts with the Centers for Medicaid and Medicare (CMS) to obtain access to very valuable drug safety information housed in CMS population-based databases. The initiative is $3,960,000 and 8 FTE. The Other Activities' share is $396,000 and 2 FTE.

Cost of Living-Pay: + $1,413,000
FDA's request for pay inflationary costs is essential to accomplishing its public health mission. Payroll costs account for over sixty-percent of our total budget, and the Agency is no longer able to absorb this level of inflation on such a significant portion of its resources. The increase will allow FDA to maintain staffing levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $20,267,000. The Other Activities' portion of this increase is $1,413,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.

Unified Financial Management System: +$1,180,000
FDA continues to implement the Unified Financial Management System (UFMS), an enterprise-wide financial management system that will provide qualitative and quantitative benefits. UFMS will enable FDA to maintain its clean audit record, meet the accelerated time frames established by the Reports Consolidation Act and satisfy various Federal financial management laws and regulations. Specifically, the funding will provide:

- Support to the UFMS Global Program Management Office and the Operations and Maintenance Center of Excellence in all testing activities associated with new releases.

- Support for system enhancements and updates.

- Training for new and current users throughout the Agency.

- Vendor support for reporting tools and licenses.

- Ongoing stabilization efforts in FY 2007.

Other Activities Reduction: - $5,497,000 and - 19 FTE
To fund FY 2007 priority initiatives such as activities such as Pandemic Preparedness, Food Defense, and Drug Safety, the Other Activities program will reduce the number of the FTE through attrition, selective replacement of vacant positions, and other workforce restructuring strategies.

User Fees

Prescription Drug User Fee Act: +$1,156,000 and + 3 FTE
PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These fees expand the resources available for the process of reviewing human drug applications including reviewers, information management, space costs, acquisition of fixtures, furniture, equipment and other necessary materials so that safe and effective drug products reach the American public more quickly. In 2002, the Bioterrorism Act included reauthorization 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 (PDUFA III). The reauthorization directs FDA to strengthen and improve the review and monitoring of drug safety; consider greater interaction with 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. The increases will contribute to meeting these mandated directives. In FY 2007 FDA will work with Congress on the reauthorization of the Prescription Drug User Fee Act. This increase of $1,156,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Medical Devices User Fee and Modernization Act: +$386,000 2 FTE
The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amends the Federal Food, Drug, and Cosmetic Act to provide FDA important new responsibilities, resources, and challenges. MDUFMA was signed into law October 26, 2002 and

was amended by the Medical Device User Fee Stabilization Act of 2005. MDUFMA has three particularly significant provisions. These provisions allow for the collection of user fees for premarket applications, allow establishment inspections to be conducted by third parties and place new regulatory requirements on reprocessed single use devices. The revenues from these fees, and the appropriated trigger amounts will allow FDA to pursue a set of ambitious performance goals that will provide patients earlier access to safe and effective technology, and will provide more interactive and rapid review to the medical device industry. In FY 2007 FDA will work with Congress on the reauthorization of the Medical Device User Fee and Modernization Act. This increase of $386,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Animal Drug User Fee Act (ADUFA): + $50,000

The Animal Drug User Fee Act of 2003 (ADUFA) amends the Federal Food, Drug and Cosmetic Act and authorizes FDA to collect fees for certain animal drug applications, and for the establishments, products and sponsors associated with these and previously approved animal drug applications. ADUFA helps the FDA, through a strengthened animal drug pre-market review program, to provide greater public health protection by ensuring that animal drug products that are approved to be safe and effective are readily available for both companion animals and animals intended for food consumption. Additional resources provided by ADUFA will also help FDA scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for our animals. ADUFA will help provide a cost-efficient, high quality animal drug review process that is predictable and performance driven. In FY 2007 FDA will work with Congress on the reauthorization of the Animal Drug User Fee Act. This increase of $50,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

Mammography Quality Standards Act (MQSA): +$4,000

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths among American women. Experts estimate that one in eight American women will contract breast cancer during their lifetime. The MQSA, which was reauthorized in October 2004, addresses the public health need for safe and reliable mammography. The Act required that mammography facilities be certified by October 1994, and inspected annually to ensure compliance with national quality and safety standards. The reauthorization codified existing certification practices for mammography facilities and laid the groundwork for further study of key issues that include ways to improve physicians' ability to read mammograms and ways to recruit and retain skilled professionals to provide quality mammograms. The increase of $4,000 will cover inflation.

Proposed User Fee Proposals

Reinspection User Fee (Mandatory): + $7,100,000 and + 16 FTE (Non-Add)

The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would

generate $22.0 million in revenue, an amount sufficient to fully fund reinspections. The Other Activities program component of this user fee is $7,100,000 and 16 FTE.

Justification of Base

Base resources support a many critical activities servicing various stakeholders (DHHS, OMB, Congress, and others) and agency components. The following activities are arrayed by FDA strategic goal.

FDA Strategic Goal: Enhancing Patient And Consumer Protection and Empowering Them with Better Information about Regulated Products

Base resources supports the strategic goal by planning and preparing for emergency events; monitoring the integrity of clinical research to ensure adequate human protection; promoting outreach programs that explain consumer choices for better health; and ensuring that women's needs are considered in the review of FDA-regulated products.

Emergency Response and Preparedness

FDA must have the capability to assess and effectively prepare for and respond to public health emergencies and other incidents known or suspected to be terrorist-related. The Agency plays a vital role in homeland security through measures to safeguard regulated food and medical products from attack and to speed the availability of medical countermeasures. The unpredictable and varied ways acts of terror can be launched complicate preparedness and the agency's ability to respond quickly and effectively. As a result, FDA is developing a robust system to manage incidents. The Agency also is expanding the exercise program that periodically tests our response capabilities.

FDA has several major objectives that address these challenges:

- Enhance public protection against the effects of a terrorist attack by facilitating the development and use of safe and effective medical countermeasures. For example, assist DHHS with Project Bioshield and the Strategic National Stockpile.

- Implement and enhance procedures for Emergency Use Authorization (EUA) requests including proactive review of candidate products before an emergency to expedite availability in crisis situations.

- Enhance the security of America's food supply by enhancing food defense preparedness and research. For example, implement key provisions of the Bioterrorism Act including prior notice of imported foods, registration of certain types of food facilities, records maintenance, and administrative detention.

- Improve prevention and detection of product tampering through development and use of needed methodologies.

Consumer Out-Reach and Education Programs

FDA directs an array of public outreach programs to better enable consumers to make informed decisions weighing benefits and risks of FDA-regulated products. These activities include:

- Development and implementation of an FDA-wide consumer communication infrastructure and consumer-media outreach strategy to help both consumers and patients understand how to live better, healthier lives.

- Create and leverage collaborations with healthcare providers, and public and private healthcare organizations and institutions.

- Seek out speaking opportunities for FDA to communicate directly with diverse consumer segments.

Good Clinical Practice Program

This program is the focal point within FDA for Good Clinical Practice (GCP) and Human Subject Protection (HSP) issues arising in human research trials regulated by FDA. To improve and enhance protection for human subjects, the Program:

- Coordinates FDA policies, develops guidance, and provides advice on HSP and GCP.

- Provides leadership and direction through the administration of FDA's Human Subject Protection/Good Clinical Practice Steering Committee.

- Coordinates FDA's Bioresearch Monitoring program with respect to clinical trials.

- Contributes to international GCP harmonization activities.

- Plans and conducts training and outreach programs for internal and external audiences.

- Serves as FDA's liaison with the HHS Office of Human Research Protection and other federal agencies and external stakeholders committed to the protection of human research participants.

- Contributes to the HSP/Bioresearch Monitoring Steering Committee's initiative to implement a quality systems framework for the agency's GCP activities and Bioresearch Monitoring program.

Office of Women's Health

The Office of Women's Health works to identify key agency priorities regarding women's health and sex differences and to effectively deliver health messages to women around the nation; and develops partnerships and collaborations with stakeholder organizations to best facilitate outreach and consumer information dissemination. These partnerships have resulted in unprecedented free publicity for and duplication of millions of FDA/OWH materials using a variety of media venues (e.g., print, radio, television). Specifically, OWH continues to:

- Develop and disseminate consumer and health provider information about FDA regulated products that will result in improved health for consumers including women.
- Conduct outreach campaigns related to menopause and hormone therapy and roll out developing campaigns in cardiovascular disease, health fraud and safe medication use.
- Update the OWH website with current products, contacts, and information.

Science and Health Coordination Responsibilities

- Manages two OC advisory committees, the FDA Science Board, the Senior Science Council and the Committee for the Advancement of FDA Science.
- Manages the FDA Research in Human Subjects Committee and Quality Assurance Program.
- Coordinates standards development and science initiatives across agency.
- Manages the annual Science Forum.
- Serves on several interdepartmental committees of OSTP addressing scientific issues.
- Coordinates Commissioned Corps activities for the FDA, oversees implementation of Corps transformation for FDA, implements Corps policy and regulations for FDA's 700-plus officers and serves as the FDA representative to the Surgeon General's Policy Advisory Council.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Base resources support the strategic goal by ensuring administration of two statutorily established programs addressing combination products and pediatric drugs.

Office of Combination Products

The Office of Combination Products (OCP) is a statutorily mandated Office with wide-ranging and specific regulatory responsibilities to ensure the consistent and appropriate assignment, premarket review and postmarket regulation of combination products. OCP responsibilities cover the regulatory life cycle of combination products, and oversight of product jurisdiction decisions and specific premarket and postmarket processes. Its responsibilities directly contribute to FDA's strategic goals to (1) increase access to innovative technologies to advance health, (2) improve product quality and safety through better manufacturing oversight, and (3) expand patient protection and empower consumers for better health. OCP activities include:

- Conducting the FDA product jurisdiction program.
- Facilitating the timely and effective premarket review of combination products.

- Ensuring consistent and appropriate postmarket regulation of combination products.

- Developing cross-cutting regulations, guidance documents, procedures and processes to clarify the regulation and assignment of combination products.

- Serving as FDA's focal point on matters related to combination products for internal and external stakeholders.

Office of Pediatric Therapeutics

The Best Pharmaceuticals for Children Act directed HHS to establish an Office of Pediatric Therapeutics within FDA's Office of the Commissioner. The Pediatric Research Equity Act of 2003 authorizes FDA to require pediatric studies and establish a Pediatric Advisory Committee. The Office of Pediatric Therapeutics has five areas of responsibility: pediatric ethics, safety review and reporting for certain pediatric products, agency-wide scientific coordination, external communications, and the Pediatric Advisory Committee. Office activities include:

- Overseeing the safety of all drugs granted pediatric exclusivity.

- Enhancing the ethical conduct and quality of pediatric clinical trials.

- Assuring ethical pediatric research and child subject protection across all FDA centers.

- Reviewing, evaluating and advising on Subpart D (additional protections for children) referrals from Institutional Review Boards.

- Developing cross-cutting pediatric scientific issues and coordinate activities pertaining to the pediatric population across all FDA product Centers.

- Enhancing communication of pediatric issues and new pediatric information for FDA regulated products with consumers, advocacy groups, and healthcare providers.

- Serve as the pediatric liaison to external organizations.

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Base resources support this strategic goal by providing administrative policy, support and delivery of services to FDA components.

Shared Services Activities

The Office of Shared Services and Office of Information Technology Shared Services provide a portfolio of administrative and information technology services to components agency-wide. The shared services concept employs innovative management techniques such as customer advocacy, negotiated service level agreements, engaged performance planning, active governance boards

and integrated strategic planning that leverages the best of centralized and decentralized organization structures. Key activities include:

- Providing advisory services to program and management personnel in the business and administrative aspects of the contracting program.

- Managing contracts, grants, purchase card and interagency agreement programs.

- Performing day-to-day operations for financial services related to accounts payable, travel payments, invoice payments, payroll, fleet and claims management.

- Directing the management of programs and systems leading to the acquisition, alteration, maintenance, and utilization of leased and owned facilities nationwide.

- Directing building operations functions for all FDA facilities nationwide.

- Providing medical library services to FDA employees.

- Providing consolidated management of all common IT infrastructure organizations across the agency as required under the Clinger-Cohen Act of 1996 and HHS "One Department" goals.

- Operating a modern contact center (Employee Resource and Information Center) to provide information and services to over 10,000 employees nationwide for obtaining a wide array of administrative and IT assistance.

Financial Management

FDA financial systems support all agency financial activities and are mission critical needs for our public health mission. Improved financial performance includes initiatives to reduce erroneous payments and roll-out an activity based cost application for FDA's user programs. FDA moved into an environment that resolved outstanding audit findings, met modern Federal financial requirements, maintained a clean audit opinion, and provided timely financial information to support strategic and resource allocations. These activities include:

- Monitoring and ensuring that financial operating plans and budget execution reports meet Federal requirements while providing timely financial information to Agency leadership.

- Formulating user fee projections used in the budget submission; execute and monitor user fees resources that were provided to FDA programs; report annually on agency expenditures to the Congress.,

- Preparing quarterly financial statements and annual financial reports, and liaison with the Office of Inspector General's independent auditor conducting the audit on FDA's financial statements, and perform necessary audit follow-up.

User Fees Programs: Prescription Drug User Fee Act (PDUFA), Medical Devices User Fee and Modernization Act (MDUFMA), Animal Drug User Fee Act (ADUFA), and Mammography Quality Standards Act (MQSA)

The Other Activities share of the user fee programs provides the financial management infrastructure for the collection, receipt, payment, accounting, and reporting of user fee revenues and expenses for PDUFA, MDUFMA, ADUFA, and MQSA. It also coordinates the acquisition and management of the additional space, and provides information technology support.

Other Activities coordinates the preparation of the annual fiscal report to the Congress for PDUFA, MDUFMA, and ADUFA, and is also responsible for the annual PDUFA performance report to Congress and for assisting with other management responsibilities including the PDUFA III goal for improved performance management and the various associated contracts.

Management Programs

FDA management programs support the agency by providing specialized workforce programs, administering the FDA ethics program, implementing programs on the Privacy Act, Freedom of Information Act, and Paperwork Reduction Act, and providing management analysis support to the Office of Commissioner. FDA management programs provide leadership and direction regarding all aspects of a variety of essential agency management programs. These activities include:

- Managing the agency Ethics program to ensure that all FDA employees are in compliance with regulations to maintain high standards of ethical conduct.

- Coordinating the implementation of the Federal Manager's Financial Integrity Act in the agency and preparing the annual assurance statement that internal controls are providing reasonable assurance against waste, fraud, and abuse.

- Acting as liaison with the Department's Office of Inspector General regarding the conduct of audits and evaluations, and providing coordination of agency responses to audit reports and audit follow-up.

- Directing FDA's organizational management and delegations of authority program in conformance to government-wide regulations and departmental policies.

- Establishing and overseeing implementation of the FDA policy, procedures and processes to ensure agency conformance with the Paperwork Reduction Act.

- Providing leadership and direction to FDA's Freedom of Information (FOI), Privacy Act, and regulatory dockets and rule-making activities.

- Overseeing the agency's competitive sourcing (A-76) program.

- Conducting specialized workforce planning and development programs including the Quality of Work Life, Reward & Recognition, Performance Management, Scientific and Regulatory Peer Review Program.

- Acting as liaison with the Commissioned Corps and the Department's Human Resources Offices to ensure FDA personnel issues are addressed.

Information Technology

FDA's Information Technology (IT) program enables FDA's strategic efforts by transforming and improving the systems and infrastructure needed to support critical agency operations. Specific initiatives of the program include:

- Consolidating and modernizing the FDA's IT infrastructure thereby ensuring a stable and robust environment for critical health initiatives such as Health Information Technology (HIT) that rely heavily on IT to operate effectively.

- Enhancing the implementation of enterprise-wide management systems, including integrated data warehousing of financial and program performance information through the alignment of financial information with program and FDA performance measures.

- Optimizing data and systems security measures to strengthen the reliability, integrity, survivability, and continuity of all FDA information technology operations.

- Providing support and tools for ongoing business process planning by making available IT management and technical expertise across FDA programs.

- Maximizing the availability and use of information technologies that increase or enhance electronic access for the public, as well as for the full span of FDA external and internal customer base, while maintaining security by achieving the E-Gov goals of the PMA in a fashion that meets FDA business needs.

- Aligning IT investments to business goals in a manner that reduces costs of existing legacy systems by ensuring the FDA IT Portfolio effectively aligns and fully supports core mission and business priorities.

OC Information Technology Initiatives

- *Office of Women's Health Demographic Information and Data Repository Development (DIDR) Program* – The DIDR Program is an information management system to develop new systems for the collection of demographic data in clinical studies submitted to the Agency. The system will eventually allow for an Agency wide information management infrastructure intended to improve the analysis and reporting of subpopulation data (e.g., sex, race, ethnicity and age) in clinical trials and product labeling. This program requires the creation of additional electronic warehouses, standards for electronic submission of data, standards for reviewer analysis and templates for reviews that can feed directly into a database that can provide the basis for demographic data analyses across studies, products, and Centers. Specifically, the program will:

    - Continue the CDER pilot of a "SMART" document approach to select reviews.

- Expand the "SMART" document approach to other CDER and CBER review templates.
- Continue development and testing and explore storage and reporting components of the Template Warehouse System.
- Prepare report to CDER on findings of the pilot "SMART" document program.

Enterprise Information technology Fund

The Food and Drug Administration's request includes funding to support the President's Management Agenda Expanding E-Government and Departmental enterprise information technology initiatives. Operating Division funds will be combined to create an Enterprise Information Technology (EIT) Fund to finance specific information technology initiatives identified through the HHS strategic planning process and approved by the HHS IT Investment Review Board. These enterprise information technology initiatives promote collaboration in planning and project management and achieve common HHS-wide goals. Examples of HHS enterprise initiatives funded by the EIT Fund are Enterprise Architecture, Capital Planning and Investment Control, Enterprise E-mail, Grants Management Consolidation, and Public Key Infrastructure."

Research, Development, and Evaluation (RD&E) Activities

The Office of Women's Health Scientific Research Program addresses gaps in current knowledge, uses novel approaches for conducting research, and sets new standards of excellence for women's health research. The program funds research projects at FDA and academic institutions through intramural and extramural research programs and special funding initiatives. Some of the program's key activities include:

- Using a peer review process to select the highest quality scientific research projects of regulatory significance to FDA.
- Implementing a process to identify the women's health research needs of highest priorities in the Centers to advance a science program, including the review and awarding processes, that directly reflects these priorities and integrates them with the Critical Path Initiative.
- Partnering with other HHS organizations to identify gaps in women's health research and to leverage current funding to best fill those research needs.
- Seeking out opportunities to present the OWH scientific programs and facilitate discussion in cross cutting women's health scientific issues and research needs.
- Updating the OWH Pregnancy Registry website with current information.

Selected FY 2005 Accomplishments

FDA Strategic Goal: Enhancing Patient and Consumer Protection and Empowering Them with Better Information about Regulated Products

Office of Counterterrorism Policy and Planning

FDA's Office of Counter Terrorism Policy and Planning serves as FDA's focal point for the development and implementation of policies that safeguard food and medical products from intentional adulteration or disruption of supplies, and policies to facilitate the availability of safe and effective medical countermeasures. Specific accomplishments include:

- Issued the Draft Guidance on Emergency Use Authorization of medical countermeasures during declared emergencies involving a heightened risk of attack.

- Coordinated issuance of an Emergency Use Authorization to DoD for the use of the Anthrax Vaccine Adsorbed.

- Ensured that recommendations of the Weapons of Mass Destruction Medical Countermeasures Senior Steering Committee on purchases for the Strategic National Stockpile are based on sound information, reflect FDA professional judgment and expertise, and are consistent with FDA policies and regulations.

- Provided scientific and policy expertise while serving as an *ex officio* member of the National Scientific Advisory Board on Biosecurity.

- Led the development and implementation of crosscutting counterterrorism policies, such as FDA's portion of the Interagency Security Plan and the National Infrastructure Protection Plan.

Office of Women's Health

- Supported five new and fourteen continuing intramural research projects of relevance to women's health and sex differences.

- Supported one new and twelve continuing extramural research projects addressing issues related to FDA products and women's health and sex differences.

- Conducted three site visits and two Office of Inspector General audits at OWH funded institutions to ensure extramural funded studies are consistent with contractual and human subjects protection obligations.

- Continued the Take Time to Care Campaign, a multi-faceted campaign that focuses on dissemination of health education materials for consumers through activities and collaborative partnerships. A Dear Abby announcement generated 2.2 million requests for this information.

- Implemented Phase 2 of the Menopause and Hormones Education Campaign to bring clear and useful information to women about the use of hormones during menopause. This program reached approximately 15.1 million English and Spanish speaking women (ages 40 to 59) via newspaper, magazine, radio, Internet, and mass e-mail.

- Increased the frequency of distribution of the OWH E-newsletter from 4 to 6 times per year to our network of stakeholder organizations.

- Participated on thirty-two national medical, scientific, and health care conferences with an estimated outreach of 225,000.

- Translated OWH consumer information and publications into fourteen different languages.

Other Office of Science and Health Coordination Accomplishments

- *Committee for the Advancement of FDA Science.* Conducts twenty-four meetings per year; reports to the Council for Environmental Quality. Represents the agency on OSTP Committees on nanotechnology, deemed export, science in food and agriculture modernizing NEPA.

- *Management of Agency Institutional Review Board (RIHSC) and Quality Assurance Program.* These activities included approximately 200 protocols submitted for initial review, about 250 protocols submitted for continuing review, twelve meetings of the FA IRB, approximately five requests for audits of ongoing studies, 150 information requests/consultations on various human subject protection issues by the Centers.

- *Management of OC Advisory Committees.* The scientific peer review of the ORA pesticide program was completed, two meetings of the Science Board were held, and 5-6 meetings of the Pediatric Advisory Committee and the Pediatric Ethics Subcommittee. For each Committee, annual reports to Congress were submitted.

- *Coordinating with the Office of the Surgeon General FDA's Commissioned Corps response to public health emergencies.* FDA deployed over 500 Commissioned Corps officers to respond to Hurricanes Katrina and Rita, the largest number of officers from any of the Public Health Service agencies and almost 75% of FDA's total Corps strength.

- *2005 Science Forum.* There were over 2000 attendees, including 200 from industry and academia; 450 posters with about 65 from non-FDA participants.

- *Coordination of Standards Development Across Agency.* The OSHC Director attended 4 meetings of the Interagency Committee on Standards Policy, three meetings of the ANSI Board of Directors and three of the ANSI Government Members Council, four meetings of the FDA Standards Committee, coordinated sixballots on voluntary standards, and published the annual report to Congress on FDA utilization of voluntary standards in lieu of government unique standards.

- *Coordination of Science Initiatives, Science Training and Science Information Across Agency.* This activity included developing initiatives on nanotechnology and genomics; discussion of FDA-wide issues through the Senior Science Council and Leadership Council.

Good Clinical Practice Program

- Published a draft guidance document, Guidance for Industry on Using a Centralized Institutional Review Board Process in MultiCenter Clinical Trials.

- Co-organized a public hearing under 21 CFR Part 15 to obtain input on adverse event reporting to Institutional Review Boards in order to develop guidance for industry on this issue.

- Conducted numerous Good Clinical Practice and Human Subject Protection Education and Outreach Programs.

- Developed and continued to maintain the agency Clinical Trials/Good Clinical Practice webpage for research professionals.

- Responded to over 1500 queries annually received in a dedicated GCP e-mail account or by telephone, and implemented a Katrina clinical trials hotline.

- Contributed to international working groups on good clinical practice (GCP) and human subject protection (HSP) projects.

- Participated as FDA representative to the (1) US-China Health Care Forum; and (2) Clinical Trials Congress.

FDA Strategic Goal: Increasing Access to Innovative Products and Technologies to Improve Health

Office of Combination Products

The Office of Combination Products directly contribute to FDA's strategic goals to (1) increase access to innovative technologies to advance health, (2) improve product quality and safety through better manufacturing oversight, and (3) expand patient protection and empower consumers for better health. Specific accomplishments include:

- Issued 37 decisions in response to formal Requests for Designation (RFD) under the agency's product jurisdiction program. The average RFD review time was 42.9 days of the 60 days provided by statute, and 100 percent of the decisions were issued on time.

- Published a final rule defining the primary mode of action of a combination product.

- Responded to over 195 stakeholder inquiries on issues ranging from the assignment process itself to jurisdictional issues on a wide range of specific combination products.

- Facilitated the premarket review process for a wide variety of combination products presenting complex regulatory issues.

- Published three final guidance for industry and agency review staff: Application User Fees for Combination Products; Submission and Resolution of Formal Disputes Regarding the Timeliness of Premarket Review of a Combination Product; and How to Write a Request for Designation (RFD).

- Monitored and actively facilitated 275 inter-center consulting requests for combination products to ensure the requesting center received timely and effective feedback. This represents a 31% increase over FY 2004.

Office of Pediatric Therapeutics (OPT)

- Reviewed and presented fifty products studied in children to the Pediatric Advisory Committee (PAC) in a public forum as of November 2005.

- Provided advice and consultation on ethical issues across the agency and to external stakeholders.

- Developed, with the Department's Office for Human Research Protection (OHRP), a collaborative Subpart D process to address the ethical issues of testing drugs in children.

- Coordinated and participated in international pediatric regulatory activities

Pediatric Advisory Committee Adverse Event Meetings and Drugs Discussed

February 2005	June 2005	November 2005
Lotensin (benazepril)	Arava (leflunomide)	Imitrex (sumatriptan)
Malarone (atovaquone/proguanil)	Concerta (methylphenidate)	Camptosar (itinotecan)
Brevibloc (esmolol)	Zemplar (paricalcitol)	Carboplatin (paraplatin)
Viracept (nelfinavir)	Zomig (zolmitriptan)	Vioxx (rofecoxib)
Xenical (orlistat)	Ortho-Tri-Cyclen (ethinyl estradiol;norgestimate)	Ferrlecit (sodium ferric gluconate)
Gluvovance (glyburide/metformin)	Cipro (ciprofloxacin)	Diflucan (fluconazole)
	Trusopt (dorzolamide)	Tamiflu (oseltamivir)
	Detrol (tolterodine)	Agrylin (anagrelide)

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Shared Services

- Supported implementation of the Unified Financial Management System (UFMS) and iProcurement.

- Implemented grant processing system eRA/IMPAC II.
- Met HHS goal for electronic posting of federal grants applications on grants.gov.
- Met HHS small business contracting goals.
- Reduced misuse and delinquencies on travel card purchases.
- Improved vendor payment processes.
- Implemented facility management system.
- Created the Division of Logistics Services to provide facilities services to the FDA White Oak Campus.
- Implemented processes to improve timeliness of service ticket resolution.

Financial Management

- Completed implementation of the financial management user fee solution. These included PDUFA, MDUFMA, ADUFA, MQSA, Color certification, and export certification payment information.
- Completed the implementation of the Purchase Request Information System (PRISM)

Management Programs

- Completed the FDA Federal Activities Inventory Reform (FAIR) Act of 1998, which identified 1,495 FTE as commercial and 8,815 FTE as inherently governmental.
- Completed development of the Most Efficient Organization (MEO) for the 350 FTE Clerical Support Services Study with a performance decision announced in February 2005 awarding the competition to the FDA's MEO. A formal transition process began in May 2005 with the expectation that the MEO will be operational by the second quarter of FY 2006.

Information Technology

- Commenced on October 1, 2004, the Single Source Infrastructure Service Support which consolidated 15 IT Infrastructure Service contracts, which will result in nearly $10 million in savings over the next five years.
- Awarded the contract to develop the Electronic Submissions Gateway (e-Submissions Gateway), which will provide a single point of entry for electronic regulatory submissions to the FDA.

- Awarded the contract to implement electronic standards for structured product labeling (SPL).

- Led, as project manager, the HHS-Net project by designing the solution and directing the successful implementation across all Operating Divisions.

- Partnered with HHS to achieve an Enterprise Email Systems (EES) design that met both HHS and FDA-specific needs and began the conversion project.

- Provided HHS with a proven model for an HHS-wide tool (Prosight) for Capital Planning and Investment Control (CPIC) process.

- Fully met HHS SecureOne Goals (100 percent C&As and PIAs accomplished; 100 percent employees received IT security training).

- OMB recognized FDA as one of the lead federal EA programs with a Level 3 maturity rating; FDA also received the Excellence in Enterprise Architecture Award for its leadership in this area.

- Achieved greater than 25% reduction in last year's FISMA reportable conditions, and have no significant deficiencies; commended by the IG for a strong security posture within HHS, as exemplified by performance in combating the Zotob worm, in which we were able to report no incidents.

- Successfully implemented automated patch management this year, and now have the capability to "push" new software and patches onto 100% of FDA desktops in order to ensure a standard configuration.

- Fully tested Disaster Recovery Plan by September 30, 2005.

INFRASTRUCTURE
GSA RENT, OTHER RENT AND WHITE OAK

	FY 2005 Actuals	FY 2006 Enacted[1/]	FY 2007 Estimate	Increase or Decrease
Program Level	**$192,995,000**	**$191,615,000**	**$208,020,000**	**+$16,405,000**
GSA Rent	$127,617,000	$133,677,000	$146,013,000	+$12,336,000
Other Rent	$44,532,000	$36,183,000	$36,455,000	+$272,000
White Oak	$20,846,000	$21,755,000	$25,552,000	+$3,797,000
Budget Authority	**$167,083,000**	**$173,558,000**	**$187,823,000**	**+$14,265,000**
GSA Rent	$113,479,000	$116,403,000	$126,871,000	+$10,468,000
Other Rent	$35,758,000	$35,400,000	$35,400,000	$0
White Oak	$17,846,000	$21,755,000	$25,552,000	+$3,797,000
User Fees	**$22,912,000**	**$18,057,000**	**$20,197,000**	**+$2,140,000**
GSA Rent	***$14,016,000***	***$17,274,000***	***$19,142,000***	***+$1,868,000***
PDUFA [2/]	*$11,212,000*	*$12,700,000*	*$14,501,000*	*+$1,801,000*
MDUFMA	*$2,237,000*	*$3,203,000*	*$3,270,000*	*+$67,000*
ADUFA	*$567,000*	*$1,371,000*	*$1,371,000*	*$0*
Other Rent	***$8,896,000***	***$783,000***	***$1,055,000***	***+$272,000***
PDUFA	*$8,334,000*	-	-	-
MDUFMA	*$562,000*	*$783,000*	*$1,055,000*	*+$272,000*
White Oak	***$3,000,000***			
PDUFA	*$3,000,000*			

[1/] *Contains budget authority rescission of 0.8 percent.*

[2/] *Excludes $12,092,000 in FY 2005 and $8,188,000 in FY 2007 in PDUFA carryover fees to fund the White Oak Consolidation Project.*

Historical Funding and FTE Levels – GSA Rent

Fiscal Year	Program Level	Budget Authority	User Fees
2003 Actual	$114,152,000	$105,033,000	$9,119,000
2004 Actual	$121,680,000	$114,354,000	$7,326,000
2005 Actual	$127,617,000	$113,479,000	$14,138,000
2006 Enacted	$133,677,000	$116,403,000	$17,274,000
2007 Estimate	$146,066,000	$126,871,000	$19,195,000

Historic Funding and FTE Levels – Other Rent and Rent Related Activities

Fiscal Year	Program Level	Budget Authority	User Fees
2003 Actual	$36,359,000	$36,259,000	$100,000
2004 Actual	$36,330,000	$36,043,000	$287,000
2005 Actual	$44,532,000	$35,758,000	$8,774,000
2006 Enacted	$36,183,000	$116,403,000	$783,000
2007 Estimate	$36,402,000	$126,871,000	$1,002,000

Historic Funding and FTE Levels – White Oak

Fiscal Year	Program Level	Budget Authority	User Fees
2003 Actual	$3,138,000	$3,138,000	$0
2004 Actual	$6,131,000	$2,361,000	$3,770,000
2005 Actual*	$20,846,000	$17,846,000	$3,000,000
2006 Enacted	$21,755,000	$21,755,000	$0
2007 Estimate*	$25,552,000	$25,552,000	$0

** Excludes $12,092,000 in FY 2005 and $8,188,000 in FY 2007 in PDUFA carryover fees to fund the White Oak Consolidation Project.*

Statement of Budget Request

FDA requests $208,020,000 in program level resources for rent activities and the resources needed to move to White Oak in FY 2007. Rent Activities and White Oak are a part of the Salaries and Expenses Appropriation and include Rental Payments to GSA and Other Rent and Rent-Related Activities such as guard services, security systems and grounds maintenance. White Oak funding will pay for the fit-out and move to newly constructed buildings for the FDA consolidation at White Oak, Maryland.

Program Description

FDA rental properties provide office and laboratory space for the Agency's 10,000 employees. These are essential facilities that allow FDA to perform its vital public health mission. GSA Rental Payments includes charges for all of GSA space. The Other Rent and Rent-Related account includes rent and rent-related charges that are not part of the GSA account. These include Commercial Rent and Related Services, GSA Rent-Related Services and GSA Building Delegation Services account. The agency currently occupies over 6.7 million square feet of GSA space, including parking. Approximately half of the GSA rent charges for government-owned or GSA-leased space are for facilities in the Washington, DC area. The largest amounts include

charges for the Parklawn complex, Module II in Beltsville, CFSAN's College Park complex and the newly occupied buildings at the White Oak, Maryland campus. In addition, FDA-occupied space includes over 200 leased offices, including District Offices, Regional Offices, laboratories and resident posts that are strategically placed across the nations.

The White Oak campus will replace existing fragmented facilities with new, state-of-the art laboratories, office buildings and support facilities. The consolidation of the remaining FDA headquarters is occurring at the government-owned White Oak site. The design and construction of the new buildings at White Oak are funded through General Services Administration (GSA) appropriations, with FDA paying for building fit-out and move costs.

The consolidation at White Oak will allow FDA to standardize and modernize document handling and shared use activities such as libraries and conference areas. We will also reduce redundancies in a wide range of administrative management tasks and achieve conversion to a single computer network. This will create a stronger FDA by reducing operating costs, reducing travel time between FDA organizations and increasing convenient access to FDA by the public. To date, approximately 1,850 employees are onsite at White Oak, and the last phase of the consolidation is currently scheduled for FY 2010.

Program Resource Changes

Budget Authority

GSA Rent: +$10,468,000
FDA requests an increase of $10,468,000 over the FY 2006 level for GSA Rent. This increase will help cover inflation on FDA's current GSA leased facilities and the increased rental costs for the White Oak facility. The proposed increase will allow FDA to improve management and provide for rising GSA rent, without redirecting resources from core, mission-critical public health activities.

White Oak Consolidation Project: +$3,797,000
FDA requests an increase of $3,797,000 over the FY 2006 level for the White Oak Consolidation Project. The proposed increase, along with the base funding and PDUFA carryover funds of $8,188,000, will allow FDA to continue core, mission-critical public health activities. These funds will provide funding for the CDER Office II building, Shared Data Center and Auxiliary Facilities. Detailed activities include:

- *CDER Office Building II component:* To fund relocation costs including: decommissioning vacated office space, relocation coordination and moves, furniture, document management equipment and, audio/video equipment. It will also fund internal communications costs such as equipment, cabling, IT engineering support and desktop computer preparation and relocation.

- *Consolidated Data Center component:* To fund Phase II of the Central Shared Use I Building Data Center including communications equipment and services, project management services, uninterrupted power supply and data equipment services.

- *Auxiliary Facilities component:* To fund parking garage security and for furniture, move and security costs for Phase II of the Central Shared Use I Building.

User Fees

Current Fees

Prescription Drug User Fee Act: +$1,801,000 for GSA Rent

PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These fees expand the resources available for the process of reviewing human drug applications. Fee resources pay for the salaries of scientists and other professionals who review drug applications, and for information management, space costs, acquisition of fixtures, furniture, equipment and other materials necessary to conduct drug product reviews and to ensure that safe and effective drug products reach the American public more quickly. In 2002, the Bioterrorism Act included PDUFA III, which reauthorized FDA to collect user fees to enhance the review process of new human drugs and biological products. PDUFA III also reauthorized fees for applications, establishments and approved products. The GSA Rent and White Oak costs coved by PDUFA fees directly support the drug review process. In FY 2007, PDUFA carryover fees will be used to cover costs associated with the White Oak project by supporting CDER review staff and a portion of the Central Shared Use building. The increase of $1,801,000 will cover inflationary costs associated with the GSA Rent that is attributable to the drug review process. In FY 2007, FDA will use $8,188,000 in PDUFA carryover fees to fund the White Oak Consolidation Project.

Medical Devices User Fee and Modernization Act: +$67,000 for GSA Rent and $272,000 for Other Rent and Rent Related Activities

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amends the Federal Food, Drug, and Cosmetic Act to provide FDA important new responsibilities, resources and challenges. MDUFMA was signed into law October 26, 2002 and was amended by the Medical Device User Fee Stabilization Act of 2005. MDUFMA has three particularly significant provisions. These provisions allow for the collection of user fees for premarket applications, allow establishment inspections to be conducted by third parties and place new regulatory requirements on reprocessed single use devices. The revenues from these fees and the appropriated trigger amounts will allow FDA to pursue a set of ambitious performance goals that will provide patients earlier access to safe and effective technology, and will provide more interactive and rapid review to the medical device industry. The GSA Rent and Other Rent costs coved by MDUFMA fees directly support the device review staff. This increase of $67,000 for GSA Rent and $272,000 for Other Rent and Rent Related Activities will cover inflationary costs associated with the rent activities that are attributable to the device review process.

Proposed User Fees [Non-add]

Reinspection User Fee (Mandatory): $1,800,000 for GSA Rent and $800,000 for Other Rent and Rent Related Activities

The Administration is proposing authorizing legislation that requires establishments to pay the full costs of reinspections and associated follow-up work when FDA reinspects facilities due to failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. Under this proposal, these activities will be reclassified as mandatory user fees in FY 2007. FDA currently funds this activity through discretionary appropriations. Imposing a fee would generate $22.0 million in revenue, an amount sufficient to fully fund reinspections. The Rent Activities program component of this user fee is $1,800,000 for GSA Rent and $800,000 for Other Rent and Rent Related Activities and directly supports the reinspection program.

Justification of Base

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

GSA Rent

Through improving FDA's business practices, the Agency will ensure a world-class professional work force, effective and efficient operations and adequate resources to accomplish the mission. The Agency currently occupies over 6.7 million square feet of GSA space, including parking. Approximately half of the GSA rent charges for government-owned or GSA-leased space are for facilities in the Washington, DC area. The largest amounts include charges for the Parklawn complex, Module II in Beltsville, CFSAN's College Park complex and the newly occupied buildings at the White Oak, Maryland campus. In addition, FDA-occupied space includes over 200 leased offices, including District Offices, Regional Offices, laboratories and resident posts that are strategically placed across the nation.

Other Rent and Rent-Related Activities

- *Commercial Rent and Related Services:* Recurring activities that FDA pays directly to non-Federal sources under the delegation of direct lease and service authority. Services include rental of space and all recurring services for building operations.

- *GSA Rent-Related Services:* Recurring reimbursable services provided by GSA that are over and above the standard ten hour period that GSA covers in its rent charges. Services include security systems, guard services, and HVAC beyond the standard level funded by GSA.

- *GSA Building Delegation Services:* Recurring services and one-time repairs to operate and maintain buildings delegated to FDA by GSA for management of day-to-day operations. Services include utilities and all recurring services for building operation, such as janitorial, guard, grounds maintenance, and operation and maintenance of HVAC systems.

White Oak Consolidation Project

The White Oak Consolidation Program continues its coordinated efforts to execute the 2002 Master Plan design and to update the Master Plan to reflect and provide a new state of the art campus for the FDA at White Oak. The campus will replace existing fragmented facilities with new, state-of-the art laboratories, office buildings and support facilities. To date, approximately 1,850 employees are onsite at White Oak, and the final phase of the consolidation is currently scheduled for FY 2010. The proposed increase, along with the use of base funding and PDUFA carryover funds of $8,188,000, will allow FDA to improve management, without redirecting resources from core, mission-critical public health activities. These funds will provide funding for the CDER Office II building, Shared Data Center and Auxiliary Facilities and the decomissioning of leased laboratories vacated by CDRH.

Selected FY2005 Accomplishments

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

Rent Activities

FDA is continually striving to improve its business practices. This will help ensure a world class professional workforce, effective and efficient operations and adequate resources to accomplish the mission. Accomplishments in Rent Activities include:

- Negotiated with GSA to delay rent start for the White Oak CDER Office Building I until August 1. This saved FDA approximately $2,166,000 in FY 2005.

- Negotiated a settlement agreement with the lessor for termination of the direct lease for 1521 West Pico Blvd in Los Angeles. This saved FDA $122,000 in FY 2005.

- Negotiated with GSA and the lessor for a succeeding lease at Crawford and Annex I in Atlanta. This saved FDA $14.7 million over the 12-year remaining lease term, averaging $1.2 million per year.

- Turned back space to GSA and renovated the remaining space at two locations, saving the Agency $431,300 annually in rent.

- Relocated nine ORA Resident Posts due to lease expirations. Space was also acquired for three new Resident Posts and one resident post was expanded.

- Acquired expansion space and built out CVM document control unit related to animal drug review at 7519 Standish Place.

- Expanded Moffett Center in Bedford Park, IL.

- Expanded Office of Criminal Investigation's San Diego Field Office.

- Expanded Bio Safety Level 3 laboratory in Cincinnati, OH. Certification for the laboratory was received.

- Acquired temporary emergency replacement space in Nashville, Lafayette, Mandeville, and Metairie to accommodate ORA District Office staff evacuated from New Orleans following Hurricane Katrina;

- Completed decommissioning at 12709 Twinbrook Parkway in order to turn the lease upon its expiration on December 31, 2005.

White Oak Consolidation Project

The White Oak campus will replace existing fragmented facilities with new, state-of-the art laboratories, office buildings and support facilities. The consolidation of the remaining FDA headquarters is occurring at the government-owned White Oak site. The design and construction of the new buildings at White Oak are funded through General Services Administration (GSA) appropriations with FDA paying for building fit-out and move costs. The LABQUEST coalition was established to support community planning and redevelopment of the White Oak site after the BRAC Commission announced the closure of the Federal Research Center (FRC) at White Oak in 1994. FDA participates in LABQUST by:

- Attending monthly meetings that bring together the local community, members of the Maryland Delegations, local business representatives, NTEU representatives, and FDA and GSA employees.

- Discussing the relocation of the FDA to the FRC; the necessary transportation; housing; and, amenities to accommodate FDA's employees, scientists, vendors and visitors to the area.

The White Oak Consolidation Program Continues its coordinated efforts to execute the 2000 Master Plan design to provide a new state of the art facility for the FDA at White Oak.

- Dedicated the Life Sciences Laboratory, a state-of-the-art chemistry, bioscience and animal research facility dedicated in December 2003. It was the first building to be occupied on the site. This laboratory provides approximately 124,000 gross square feet of research space, for 120 employees from the Center for Drug Evaluation and Research (CDER) and the Center for Devices and Radiological Health (CDRH).

- Completed relocation of employees to the CDER Office Building I in fall 2005. This building provides 560,000 gross square feet of modern office space to accommodate the Office of New Drugs, comprised of approximately 1,700 scientists, medical reviewers and support staff. The facility also includes a 60,000 square foot efficient document storage center, mail room and support space.

- Continued construction of the Engineering and Physics Laboratory; completion expected in early 2007. This building will provide approximately 128,000 square feet of high tech

laboratories engaged in evaluating electromagnetic and medical devices, radiological instruments and radiation-generating consumer appliances. The facility consists of numerous vibration isolation slabs, electromagnet shielding, an anechoic chamber and laser devices especially dedicated to the program science.

- Commenced construction of the CDER Office Building II; completion expected in early 2008. This approximately 291,000 gross square foot facility will accommodate the Center Director's office and the balance of the CDER scientific and support staffs. This uniquely designed office building will be equipped with an under-floor ventilation system. This design feature provides for more offices benefiting from natural daylight, taller windows, more efficient distribution of air and electrical wiring along with IT/Telecom and security wiring.

GSA History of Funding for White Oak Consolidation Project

Fiscal Year	Appropriation	Purpose
1992-96	$ 4.6M	Planning, Technical Support, Utilities
2000	$35.0M	Life Sciences Lab [formerly Center for Drug Evaluation & Research (CDER) Lab] construction; design of Lab and CDER Office Building. Life Sciences Lab dedicated 12/11/03.
2001	$92.1M	CDER Office Building construction.
2002	$19.06M	Planning/design for Engineering/Physics Lab [formally Center for Devices and Radiological Health (CDRH) Lab], for Central Shared Use Building; misc. construction.
2003	$37.6M	Central Shared Use facility construction, fit-out third and fourth floors of Life Sciences Laboratory for use by CDRH, design of second CDER Office Building.
2004	$ 42.0M	Construction of Engineering/Physics Lab.
2005	$ 88.71M	Construction of second CDER Office Building ($53.4 M); internal roads/bridge ($14.2M); construction of parking garage ($8M); fit-out for Central Shared Use Building ($7M); design of CDRH Office Building ($3.1M); infrastructure, site prep for Engineering Physics Lab ($3M).
2006	$127.6M	Infrastructure design; infrastructure construction phases 1-5; CBER labs design; Central Shared Use II/auditorium; CDRH Office construction; parking garage, design of the OC/ORA office complex.2007 Office of the Commissioner and Office of Regulatory Affairs office complex and infrastructure, Construction of the SW Parking Garage, Building One Renovation for Office of the Commissioner, Fitout for the Central Shared Use I and Construction of the CDRH High Bay Area.

BUILDINGS AND FACILITIES

	FY 2005 Actual	FY 2006 [1/] Enacted	FY 2007 Estimate	Increase or Decrease
Program Level	**$2,199,000**	**$7,920,000**	**$4,950,000**	**- $2,970,000**
Budget Authority	**$2,199,000**	**$7,920,000**	**$4,950,000**	**- $2,970,000**

[1/] *Contains budget authority rescission of 0.8 percent.*

Historical Funding

Fiscal Year	Program Level	Budget Authority	User Fees
2003 Actual	$7,948,000	$7,948,000	$0
2004 Actual	$6,958,700	$6,958,700	$0
2005 Actual	$2,199,000	$2,199,000	$0
2006 Enacted	$7,920,000	$7,920,000	$0
2007 Estimate	$4,950,000	$4,950,000	$0

Program Description

The Building and Facilities appropriation provides funding for new construction and for special-purpose laboratories and other facilities and for needed repairs and improvements to existing facilities across the U.S.

Program Resource Changes

Budget Authority

Buildings and Facilities: -$2,970,000
Buildings and Facilities is requesting $4,950,000 in program level resources to accomplish its mission activities, a decrease of -$2,970,000 from the previous year. FDA will provide for the repair and maintenance of its facilities through the FY 2007 Budget request of $4,950,000 and remaining unobgligated balances.

Justification Of Base

FDA Strategic Goal: Transforming FDA Business Operations, Systems, and Infrastructure to Support FDA's Mission in the 21st Century

A strong FDA will ensure a world-class professional work force, effective and efficient operations and adequate resources to accomplish the mission of FDA. The Agency will continue to use base resources to cover the costs of repairs and improvements to FDA and Government owned facilities. Managing a nationwide inventory of leased and owned real property assets that

include a substantial amount of laboratory facilities requires regular repair, improvement and maintenance activities on a preventative, as needed and emergency basis. Modifying these spaces to accommodate programs and maintaining the buildings as they age allows FDA employees to perform their duties in a safe, healthful and productive work place.

Included in the FDA's real property inventory are the Washington area headquarters components which are now located in 40 buildings that are government owned and leased and are in 18 separate location; plus five regional offices, 19 field District complexes including 19 administrative and 13 specialized laboratory facilities nationwide; more than 120 resident posts, eight field criminal investigation offices, two distinct program laboratory complexes outside the Washington metropolitan area and the National Center for Toxicological Research in Jefferson, Arkansas. With all of these Field facilities combined, FDA maintains offices and staff in 49 of the 50 States, and in the District of Columbia and Puerto Rico.

The repair and maintenance of these facilities is fundamental to the FDA's mission. Specific facilities must be fully accredited in order to support ongoing scientific protocols. Without fundamental base resources to maintain these facilities the Agency's ability to ensure properly functioning buildings and laboratories is greatly diminished. While industry components that FDA regulates spend between nine and 12 percent of the replacement value of their physical plants on maintenance, alteration, and repair, FDA has been spending less than two percent of the replacement value of its physical plant for the same purpose. Further reductions would hasten the degradation of the work environment for FDA scientists, aggravating the FDA's ability to retain the expertise that is necessary to keep pace with the technological advances that fuel incoming premarket applications.

The following are planned repairs and improvement projects, and their estimated costs, that will be prioritized and initiated based upon greatest need:

R&I Projects	**$**	**4,950,000**

Center & Project Description	**by Center**	
ORA - Nationwide -- Miscellaneous Repair and Improvement.	$	1,028,000
CFSAN - Dauphin Island, AL; Laurel, MD. -- Miscellaneous Repair and Improvement.	$	803,000
NCTR - Jefferson, AR. – Miscellaneous Repair and Improvement.	$	2,769,000
CDRH - Rockville, Maryland -- Decommissioning of Laboratories	$	350,000
B&F PROJECT SUBTOTAL	**$**	**4,950,000**

Status Of Major Field Lab Projects

Arkansas Regional Laboratory (ARL)

As a part of FDA's plan to restructure its eighteen field laboratories, ARL is one of five multi-disciplined laboratories and will provide laboratory support for a seventeen statewide area and

for the U.S-Mexican border stretching from Otay Mesa, California to Brownsville, Texas. The ARL provides analytical support in chemistry and microbiology. The ARL scientists are testing products regulated by the FDA to ensure compliance with the Federal Food, Drug and Cosmetic Act, which will include products produced in the U.S. and imported.

ARL - Laboratory Facility Status

A building dedication ceremony for Phases I & II, the laboratory portion, was held on February 17, 2000. ORA began occupying the laboratory facility in June 2000. The laboratory building is now fully operational.

ARL - Building 50 renovation (Phase III)

Construction on the fit-out of Building 50, floors six and seven (Phase III) was completed and occupied in February 2005. Funding was provided in the FY 2006 appropriation to complete the fit-out of the remaining floors of Building 50 and complete the project.