TITLE VI
RELATED AGENCIES AND FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

For necessary expenses of the Food and Drug Administration, including hire and purchase of passenger motor vehicles; for payment of space rental and related costs pursuant to Public Law 92-313 for programs and activities of the Food and Drug Administration which are included in this Act; for rental of special purpose space in the District of Columbia or elsewhere; and for miscellaneous and emergency expenses of enforcement activities, authorized and approved by the Secretary and to be accounted for solely on the Secretary's certificate, not to exceed $25,000; [$1,217,797,000] $1,335,389,000, of which not to exceed [$149,273,000 in] $161,716,000 to be derived from prescription drug user fees authorized by 21 U.S.C. 379(h) [may], including any such fees assessed prior to the current fiscal year but credited during the current year, in accordance with section 736(g)(4), and shall be credited to this appropriation and remain available until expended: Provided, [That fees derived from applications received during fiscal year 2001 shall be subject to the fiscal year 2001 limitation: Provided further, That none of these funds shall be used to develop, establish, or operate any program of user fees authorized by 31 U.S.C. 9701: Provided further,] That of the total amount appropriated: [(1) $285,269,000 shall be for the Center for Food Safety and Applied Nutrition and related field activities in the Office of Regulatory Affairs; (2) $317,547,000 shall be for the Center for Drug Evaluation and Research and related field activities in the Office of Regulatory Affairs, of which no less than $12,506,000 shall be available for grants and contracts awarded under section 5 of the Orphan Drug Act; (21 U.S.C. 360ee); (3) $140,489,000 shall be for the Center for Biologics Evaluation and Research and for related field activities in the Office of Regulatory Affairs; (4) $64,069,000 shall be for the Center for Veterinary Medicine and for related field activities in the Office of Regulatory Affairs; (5) $165,207,000 shall be for the Center for Devices and Radiological Health and for related field activities in the Office of Regulatory Affairs; (6) $35,568,000 shall be for the National Center for Toxicological Research; (7) $25,855,000 shall be for Rent and Related activities, other than the amounts paid to the General Services Administration; (8) $104,954,000 shall be for payments to the General Services Administration for rent and related costs; and (9) $78,839,000 shall be for other activities, including the Office of the Commissioner; the Office of Management and Systems; the Office of the Senior Associate Commissioner; the Office of International and Constituent Relations; the Office of Policy, Legislation, and Planning; and central services for these offices: Provided further, That funds may be transferred from one specified activity to another with the prior approval of the Committees on Appropriations of both Houses of Congress.] $6,000,000 for costs related to occupancy of new facilities at White Oak, Maryland, to remain available until September 30, 2003. In addition, $2,950,000, solely for carrying out section 804 of the Federal Food, Drug, and Cosmetic Act, to be available only after the requirements of section 804(l) have been satisfied.

In addition, mammography user fees authorized by 42 U.S.C. 263(b) may be credited to this account, to remain available until expended.

In addition, export certification user fees authorized by 21 U.S.C. 381 may be credited to this account, to remain available until expended.

For plans, construction, repair, improvement, extension, alteration, and purchase of fixed equipment or facilities of or used by the Food and Drug Administration, where not otherwise provided, [$31,350,000] $34,281,000, to remain available until expended (7 U.S.C. 2209b).

The Food and Drug Administration (FDA) administers laws concerning misbranded and adulterated foods, drugs, human biologics, medical devices, cosmetics, and human-made sources of radiation. The budget provides a $143.6 million (+ 11.3%) increase over the FY 2001 enacted program level. The budget includes $1,370.9 million for Salaries and Expenses at the program level, which includes funding for the prevention and surveillance of Bovine Spongiform Encephalopathy (BSE); prevention of adverse events related to human drugs, medical devices, and biologic products; protection of human subjects in clinical studies; the food safety initiative; inspections of FDA regulated products and related production processes, as well as funding for the first phase of an integrated financial management system, pay increases for staff, the Los Angeles laboratory, and the first phase of FDA's consolidation into the White Oak, Maryland site. Of the Salaries and Expenses amount, $98.9 million will be used for payments to the General Services Administration for rent and rent related costs (an additional $6.2 million will be derived from fees). In addition, the Budget includes $203.5 million for user fees, an increase of $33.1 million in user fees over FY 2001, which will be used to finance FDA activities. The $203.5 million in user fees includes $20.0 million in new user fees for import program operations and food export certificates. The buildings and facilities appropriation of $34.3 million provides funds for projects related to the repair, construction, alteration, and improvement of buildings and facilities of FDA, including a replacement laboratory in Los Angeles.

Salaries and Expenses
(Legislative Proposal not subject to PAYGO)

Contingent upon the enactment of authorizing legislation, up to $20,000,000 derived from fees assessed for activities related to the issuing of food export certificates, and import program operations consistent with provisions of the World Trade Organization (WTO) agreements may be collected and credited to this appropriation, to remain available until expended for those activities. Any collections in excess of this amount could be credited to this account for use in FY 2003 and subsequent fiscal years.

The budget includes $203,487,000 in user fees, of which $20,000,000 are new user fees to finance FDA activities as reflected in the legislative proposal schedule. Additional appropriation language is being proposed contingent upon the enactment of authorizing legislation. The authorizing language will be proposed to authorize the collection and spending of the fees subject to the appropriations language.

Explanation:
1/ Brackets remove Appropriation language that sets forth specific amounts by program and other areas, and therefore provides some flexibility for FDA resource reallocation. Reprogramming language as contained in the General Provisions, section 724 would still apply.

2/ FDA is proposing additive user fees for the Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Medical Devices Programs to support import program operations. FDA is also proposing the collection of additive user fees under the Foods Program for petitions related to Food Export certificates.

3/ The Appropriation Level of $1,355,389,000 includes a $1,497,000 reduction to a Congressional earmark provided in FY 2001. This level does not include resources for the Medicine Equity and Safety Act of FY 2000 that are not available until requested by the President.

4/ Language is added which provides FDA with the authority for two-year availability of funds for costs specifically related to the occupancy of new facilities at White Oak, Maryland, which may span more than one fiscal year. This authority will provide FDA with greater flexibility in the timing of the contracts. This move is part of a consolidation project for FDA that will replace all the existing fragmented facilities which support the Office of the Commissioner (OC), the Office of Regulatory Affairs (ORA), the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH).

5/ Language is added which provides FDA with the authority to credit to this account fees that may have been collected in excess of amounts appropriated in a previous year, if any such excess collections occurred. This is the intent of section 736(g)(4) of the Food Drug and Cosmetic Act, and it exempts FDA from making small individual refunds of unanticipated excess collections. Excess fees from previous years, if any, would be used to reduce the amount of fees FDA would collect in a subsequent year--in effect lowering the fees that FDA would otherwise assess and collect. This is intended to make appropriation language consistent with authorizing language.

FOOD AND DRUG ADMINISTRATION

Summary of Change -- FY 2002 Justification of Estimates

(Dollars in Thousands)

	Budget Authority	User Fees	Program Level	Program Level FTE
FY 2001 Appropriation	1,099,874	170,393	1,270,267	9,150
.22 percent Rescission	(2,420)	0	(2,420)	0
FY 2001 Current Estimate	1,097,454	170,393	1,267,847	9,150
FY 2002 Budget Estimate	1,207,954	203,487	1,411,441	9,542
Net Increase from Current Estimate	110,500	33,094	143,594	392
Percent Increase from Current Estimate	10.10%	19.40%	11.30%	4.11%
Built in Non-Pay Increases (2.1%)	7,047		7,047	
Absorption of Non Pay Increases	(7,047)		(7,047)	
Program Increases				
Built in Pay Increase				
FY 2002 Pay Raise of 3.6% (75%)	*18,691*		*18,691*	
FY 2001 Pay Raise of 3.7% (25%)	*6,403*		*6,403*	
Within Grade Increases	*12,460*		*12,460*	
One Day More Pay	*2,446*		*2,446*	
Subtotal, Built in Pay Increases	40,000		40,000	
Bovine Spongiform Encephalopathy	15,000	0	15,000	115
Imports and Inspections	10,297	0	10,297	50
Patient Safety / AERS	10,000	0	10,000	43
Human Subject Protection	10,000	0	10,000	47
Food Safety	9,400	0	9,400	44
Management Priorities	8,300	0	8,300	3
Buildings and Facilities - LA Lab	3,000		3,000	0
GSA RENT ($380 increase in PDUFA)	0		0	0
Rent and Rent Related - CDER Lab Move	6,000		6,000	0
Built in Decrease				
Congressional Earmark	(1,497)	0	(1,497)	0
Total Program Changes	110,500	0	110,500	302
User Fees				
Current Law User Fees	*0*	*13,094*	*13,094*	*20*
PDUFA (Includes $380 for GSA Rent)	0	12,443	12,443	20
MQSA	0	462	462	0
Export Certification		189	189	
Proposed User Fees	*0*	*20,000*	*20,000*	*70*
Imports and Inspections	0	14,700	14,700	47
Food Export Certifications	0	5,300	5,300	23
Total, User Fees	0	33,094	33,094	90
Net Change [1/]	110,500	33,094	143,594	392

1/ Does not include offset of $20,000,000 for drug importation, not yet received by the Agency.

Crosswalk for Summary of Change to Budget Authority by Activity 1st page

Crosswalk for Summary of Change to Budget Authority by Activity 2nd page

BUDGET AUTHORITY BY ACTIVITY (EXHIBIT G)–CURRENT LAW PROGRAM LEVEL

BUDGET AUTHORITY BY ACTIVITY (EXHIBIT G)–CURRENT LAW BUDGET AUTHORITY

BUDGET AUTHORITY BY ACTIVITY (EXHIBIT G)–CURRENT LAW USER FEES

BUDGET AUTHORITY BY ACTIVITY (EXHIBIT G)–PROPOSED USER FEES

BUDGET AUTHORITY BY ACTIVITY (EXHIBIT G)–TOTAL PL w PROPOSED USER FEES

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Foods

	FY 2000 Actual	FY 2001 Appropriation	FY 2001 Current Estimate [1/]	FY 2002 Estimate [3/]	FY 2002 +/- FY 2001 Current Estimate [4/]
Total Program Level [2/]	**$279,704,000**	**$285,269,000**	**$284,641,000**	**$319,505,000**	**+ $34,864,000**
Center ($000)	*124,589,000*	*125,118,000*	*124,842,000*	*135,471,000*	*+ 10,629,000*
FTE	*830*	*880*	*875*	*901*	*+ 26*
Field ($000)	*155,115,000*	*160,151,000*	*159,799,000*	*184,034,000*	*+ 24,235,000*
FTE	*1,556*	*1,580*	*1,542*	*1,620*	*+ 78*
Total Budget Authority [2/]	**$279,704,000**	**$285,269,000**	**$284,641,000**	**$306,105,000**	**+ $21,464,000**
Pay Increases					*+ $11,488,000*
BSE			*847,000*	*1,947,000*	*+ $1,100,000*
Imports/Inspections			*157,845,000*	*160,145,000*	*+ $2,297,000*
Patient Safety/AERS			*5,023,000*	*6,023,000*	*+ $1,000,000*
Food Safety			*273,670,000*	*281,070,000*	*+ $7,400,000*
Congressional Earmark			*1,497,000*	*0*	*- $1,497,000*
Total User Fees	**0**	**0**	**0**	**$13,400,000**	**+ $13,400,000**
Proposed User Fees					
Food Export Cert.	*0*	*0*	*0*	*5,300,000*	*5,300,000*
Imports and Inspections	*0*	*0*	*0*	*8,100,000*	*8,100,000*

[1/] Reflects enacted levels adjusted for the 0.22 percent rescission, accounting for $628,000 in the Foods program.
[2/] Reflects decrease in base funding from FY 2001 of $324,000, for Human Subject Protection and Bioterrorism.
[3/] Pay increases shown on separate line, and not reflected in individual increase areas.
[4/] Includes $1,497,000 reduction to a Congressional earmark provided in FY 2001.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
1998 Actuals	$206,249,000	$206,249,000	0	2,239
1999 Actuals	$235,168,000	$235,168,000	0	2,339
2000 Actuals	$279,704,000	$279,704,000	0	2,386
2001 Current Estimate	$284,641,000	$284,641,000	0	2,417
2002 Estimate	$319,505,000	$306,105,000	$13,400,000	2,521

MISSION

- Ensure the food supply is safe, nutritious, wholesome, and honestly labeled and that cosmetics are safe and properly labeled.
- Set standards and develop regulations for the food industry.
- Take timely and appropriate action on new food ingredients before they go on the market to ensure their safety and effectiveness.
- Research ways to provide the necessary basis for regulatory decisions.
- Assure the quality of foods, food ingredients, dietary supplements and cosmetics that are available on the market.
- Identify food-related health hazards.
- Take corrective action to reduce human exposure to these hazards and the possibility of food-related illnesses and injuries.
- Educate and train consumers and industry on food safety.

REQUESTED INCREASES

Pay Increase + $11,488,000

FDA's request for funds to cover pay cost increases is vital to the Agency because personnel are so essential to accomplishing its mission. Pay increases have a major impact on FDA because the Agency is more people-intensive than many other government agencies. Payroll accounts for over 60 percent of the total FDA budget. This has a significant impact on all activities in FDA, particularly the field. The costs of the pay increases are necessary to ensure the integrity of the Agency's work for the Foods Program for review of food additive petitions and other premarket activities including dietary supplements, and the field labor force for inspections and compliance functions for foreign and domestic inspections, and import surveillance.

In order to maintain the level of activities carried out in FY 2001, FDA is requesting $40,000,000 million to cover the cost of the FY 2002 pay raise, annualization of the FY 2001 pay raise, anticipated within grade increases, and one extra day of pay. The Foods Program portion of this increase is $11,488,000.

Bovine Spongiform Encephalopathy (BSE) + $1,100,000 and 5 FTE

Under the Federal Food, Drug, and Cosmetic (FFD&C) Act (Sec. 704), FDA is granted general authority to inspect food establishments, and under FFD&C Act (Sec. 903), the Agency shall be responsible for research relating to foods and cosmetics in carrying out this Act.

BSE, and Chronic Wasting Disease (CWD) both belong to a group of progressive degenerative neurological diseases that are always fatal, known as transmissible spongiform encephalopathies (TSEs). There are several TSE diseases that affect humans: the most well known is Creutzfeldt-Jakob disease (CJD). Potential products regulated by FDA's Foods Program 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. FDA will use the increased resources to:

- Expand work efforts to identify food and cosmetic products containing brain, spinal cord, and other specific risk materials (SRMs); the origin of the animal; and country of origin;

- Research the risk factors and mechanism for CWD which affects elk, deer and other domestic game/pen-reared animals;

- Identify infectious agents in foods; and,

- Participate in international BSE meetings to ensure safety of the U.S. food supply; and provide up-to-date information on the emerging public health issues to the public.

Imports & Inspections + $10,397,000 and 37 FTE (Budget Authority + $2,297,000 and 11 FTE; User Fees + $8,100,000 and 26 FTE)

Under the Federal Food, Drug, and Cosmetic (FFD&C) Act (Sec. 704), FDA is granted general authority to inspect food establishments; under FFD&C Act (Sec. 903), the Agency shall be responsible for research relating to foods and cosmetics in carrying out this Act; and, under FFD&C Act (Sec. 801 and 803), the Agency shall assess potentially violative imports, enhance the safety of imported products through surveillance at the border, and provide that source country quality systems/standards/audits conform to the requirements of the FFD&C Act.

Budget Authority

FDA is responsible for ensuring the safety of products produced and distributed by more than 60,000 domestic establishments. The Agency uses its inspectional authority, as directed by statute, to provide this assurance. FDA is requesting additional resources to:

- Advance FDA's egg safety, as well as compliance and enforcement programs;

- Conduct additional domestic inspections for the Food Safety Initiative (FSI) and increase laboratory samples analyzed by 360 for a total of 6,340; and,

- Increase resources used to support foreign inspections so that the Agency can further assure that products offered for import are safe, effective, and properly labeled.

Proposed User Fees

FDA is also responsible for ensuring the safety of over six million import line entries that cross our borders annually. This will grow to 7 million in FY 2001. The sources of these entries are diversified and include increasingly more products from countries that are typically categorized as emerging economies, with emerging regulatory infrastructures.

FDA proposes to collect $8,100,000 in additive import user fees within the Foods program to fund the Operational and Administrative System for Import Support (OASIS), and other import work. The OASIS system enables FDA to substantially reduce the risk of potentially harmful

foods and other imported products reaching the American marketplace. The importer/broker community benefits through faster turn-around times, elimination of large volumes of paperwork, and reduced costs of doing business. OASIS will give FDA staff access to historical information to better target products and firms at high risk, the ability to plan inspections more effectively, and the ability to share findings from inspection and lab analyses with other offices. With the additional resources, FDA will:

- Modernize the Operational and Administrative System for Import Support (OASIS) import data processing system so that import reviewers will have more rapid and direct access to information necessary for entry decisions about food products, in particular perishable items;

- Implement enforcement strategies for imported foods to improve compliance with and monitoring of Hazard Analysis Critical Control Points (HACCP) Programs and food safety regulations;

- Increase import field exams of imported foods and dietary supplements;

- Expand import entry reviews to keep pace with the increase in import line entries;

- Update on a risk basis the criteria that determines which import line entries are selected for on screen review and increase the frequency of on-screen review;

- Increase FDA data audits, import filer training, and liaison activities to improve the integrity of import data submitted by import filers; and,

- Increase coordination with the U.S. Customs Service to improve the effectiveness of cargo control activities at ports, and monitor food products that have been refused entry pending exportation or destruction (follow-up on refusals).

Patient Safety/AERS + $1,000,000 and 4 FTE

Under the Federal Food, Drug, and Cosmetic (FFD&C) Act (Sec. 903), the Agency shall be responsible for research relating to foods and cosmetics in carrying out this Act, as well as having primary regulatory responsibility for ensuring the safety of ingredients used in dietary supplements.

FDA currently uses several post-marketing surveillance systems for both mandatory and voluntary adverse event reporting associated with foods, cosmetics and dietary supplements. These systems are not optimal because they operate independently and data is not easily shared. Further, the need to share data with other FDA programs is critical for determining if action is needed, particularly with dietary supplements where adverse events are often reported through the Human Drugs Program. FDA will apply the requested funding to:

- Consolidate five existing Adverse Event systems within the Foods Program into one comprehensive, center-wide system to capture and evaluate consumer adverse event reports for foods, food and color additives, cosmetics, and dietary supplements;

- Develop external interfaces with the Agency wide Field Accomplishments Tracking System (FACTS) and AERS to share data; and,

- Supply system users with classification, indexing, research and management tools, and materials for the evaluation of adverse events.

Food Safety + $12,700,000 and 58 FTE (Budget Authority + $7,400,000 and 35 FTE; User Fees + $5,300,000 and 23 FTE)

Under the Federal Food, Drug, and Cosmetic (FFD&C) Act (Sec. 704), FDA is granted general authority to inspect food establishments and under FFD&C Act (Sec. 903), the Agency shall be responsible for research relating to foods and cosmetics in carrying out this Act.

Budget Authority

FY 2002 will mark the fifth year of the highly successful multi-agency Food Safety Initiative (FSI) to control and reduce food borne pathogens in the American food supply. The benefits of this investment are clear: an overall decline of 16 percent in food borne illnesses in America. For certain of the most dangerous pathogens, the reductions are even more pronounced. For example, *E. coli 0157:H7* and Campylobacter fell by 26 percent, Shigella by 44 percent, *Salmonella enteritidis* by 48 percent, and Cyclospora by 70 percent.

The FY 2002 FSI Strategic Plan overall goal is to protect public health by significantly reducing the prevalence of pathogens, and expanding coverage to pesticides and chemical contaminant hazards, thereby reducing acute and chronic illnesses and injuries through science-based and coordinated regulation, inspection, enforcement, research, and education programs. In support of this effort, FDA will devote its increased resources to the following activities:

- Expand current laboratory capacity to increase sample analysis needed for HACCP verification, food sanitation, and food and color additive reviews and audits and other activities;

- Increase activities related to foods using biotechnology;

- Collect and analyze food samples for pesticides, heavy metals and dioxins;

- Evaluate the risks of pesticides and chemical contaminants, and the level of food nutrients in the American diet through a revised FDA Total Diet Program which will provide data on levels of pesticides, industrial chemical, toxic elements, and vitamins and minerals in foods that is more representative of today's consumer eating habits;

- Inspect at least 95 percent of domestic firms annually for high-risk food establishments, currently projected at 7,000 for FY 2002;

- Increase the number of domestic inspections (non-HACCP and Seafood HACCP) by State contract by almost 1,100, for a total of 5,300;

- Expand State audit inspections, enforcement, and data reporting for State inspectional and compliance activities so the States can enter inspection information directly into field data systems; and,

- Expand domestic sample analyses for food borne pathogens and contaminants within the food supply and pathogen tracking (eLexnet).

Proposed User Fee

Food Export Certificates

- Section 801 (e)(4)(B) of the Federal Food, Drug, and Cosmetic Act authorizes user fees for export certificates for drugs, animal drugs, and devices. The requirements for these certificates were amended by the FDA Export Reform and Enhancement Act of 1996, which also established user fees for this service. This section does not cover collection of user fees for export certificates for foods.

- Collection of user fees for food export certificates will enable FDA to fully support this program, and limit the current redirecting of existing monies from other critical food safety programs. Under this provision, FDA expects to issue approximately 30,000 export certificates per year at a cost of $175 per export certificate. Private sector exporters would bear the cost of the program but reap the benefits through the Agency's enhanced ability to facilitate product exports in compliance with the importing countries' requirements. Field staff will continue to prepare export certificates on a timely basis to expedite trade, and in the languages required by current international agreements.

- FDA currently incurs costs in the millions of dollars to support the specific needs of U.S. food exporters. By law, FDA is required to issue certificates to any person wishing to export a drug, animal drug, or device, that the product to be exported meets certain requirements of the law. Food exporters are required to comply with an increasing number of European Union (EU) requirements for certificates attesting to the safety of animal-derived foods. Such certificates attest to product compliance with EU directives and standards, not FDA regulations. If FDA does not receive authority to collect the user fees for export certificates for foods, FDA will continue to spend millions of dollars in food safety resources to support the specific needs of U.S. food exporters instead of supporting food safety activities that benefit the entire population.

JUSTIFICATION OF BASE

Activities Related to Increases for FY 2002

Payroll

- FDA's Foods Program has primary responsibility for assuring that the food supply of the U.S. is safe, sanitary, wholesome, and honestly labeled, and that cosmetic products are safe and properly labeled. Since foods continue to be susceptible to an ever-growing variety of potentially hazardous substances including microbial pathogens, chemical residues, natural toxins, and illegal food additives, FDA has an enormous responsibility that has a direct impact on the health of every man, woman and child in the nation. Base resources will be devoted to meet these responsibilities.

- The field component of Foods inspects regulated industry, and collects and analyzes samples. Other activities that often arise are review and management of enforcement actions, and consumer complaints, trace back efforts to determine the cause of food borne illness outbreaks, and review of import entries for admissibility decisions. These functions are inherently governmental and highly personnel intensive.

Bovine Spongiform Encephalopathy (BSE)

- Study options for addressing the risk posed by BSE for dietary supplements, such as a regulation for certifying source material, an Import Alert for all dietary supplement materials of sheep, goat or bovine origin, and an abbreviated good manufacturing practices (GMP) regulation.

- Revise Import Alert #1704, "Detention without Physical Examination of Bulk Shipments of High-risk Bovine Tissue from BSE Countries" to ensure that all imported products regulated by CFSAN that may contain infective tissues are detained without physical examination until they can be more fully evaluated. This revision is being done in cooperation with other FDA Centers and Department of Agriculture Animal Plant Health Inspection Service to ensure an inclusive import alert.

Imports and Inspections

- Conduct approximately 250 foreign inspections, with top priority to "high-risk" foods.

- Implement the FDA and U.S. Customs Service joint Action Plan to better leverage resources to enhance the safety of imported products through surveillance at the border.

- Fund domestic inspections (Food Safety Initiative) at the following levels:
  –10,900 inspections conducted by FDA;
  – 4,202 inspections conducted by State contracts; and,
  – 1,400 inspections conducted by State partnerships.

- Review more than 4,500,000 import line entries for admissibility into domestic commerce.

Patient Safety/AERS

- Provide training for field staff to improve the information gathered through investigation of consumer complaints.

- Upgrade field data systems to provide improved consumer complaint data.

Food Safety

- Implement our three-year strategy to enhance FDA audit and evaluation of State inspection programs, and increase the rate of State contract audit inspections to ensure consistent application of regulations nationwide by FDA and the States.

- Inspect at least 90 percent of domestic firms annually for high-risk food establishments, currently identified at 6,250, including associated laboratory support for sample analysis. High risk firms include processors of infant formula, ready to eat foods, produce, seafood products, low-acid canned foods, and juice.

- Replace outdated field laboratory equipment to improve the accuracy and timeliness of food product analyses to determine compliance with safety requirements.

- Expand the ability of Federal, State and local partnerships to improve food safety through better data sharing with our partners in the States. The FACTS (Field Accomplishment and Compliance Tracking System) data system was enhanced so that States will enter data directly in the system in FY 2002.

Other Activities Related to Priority Areas

Biotechnology

- Publish biotechnology notification proposal, and draft guidance for voluntary labeling of foods that have or have not been developed using biotechnology.

- Issue guidance to industry on assessing allergenicity in genetically engineered food products.

Dietary Supplements

- Respond to 95 percent of premarket notifications for new dietary ingredients within the statutory time frame (75 days).

- Review the 30-day postmarket notifications for structure/function claims in a timely manner.

- Collaborate across the Agency to publish a proposal for labeling dietary supplements for women who are or may become pregnant.

- Publish dietary supplement GMP proposed rule and conduct an outreach program.

- Collaborate on dietary supplement research with the National Center for Natural Products Research in Oxford, Mississippi as well as with the National Academy of Sciences' Institute of Medicine to review dietary supplement safety.

International Activities

- Participate in and raise visibility in the 17 Codex committees, ad hoc task forces and related drafting and working groups and scientific advisory committees (i.e., Joint Expert Committee on Food Additives (JECFA)) to ensure that source country standards, quality systems, and audits conform to the requirements of the FFD&C Act.

Bioterrorism

- Develop a threat assessment for the food supply. This includes a review of threat agents, targets, federal and state food inspection policies and procedures, and industry practices to prioritize the use of resources to prevent and prepare for terrorist threats against the food supply.

Premarket Activities

- Reduce the possibility of food related deaths or injuries and improve the health and well-being of consumers by ensuring that decisions related to approvals of petitions and notifications are scientifically justified and benefit the public health.

- Develop standards for premarket review of new products and emerging technologies - e.g., genetically modified foods, dietary supplements, infant formulas and medical foods to ensure that foods are properly labeled when there is a significant change in the modified food as compared to the traditional. Examples of significant changes include a nutritional change, compositional change, change in the condition of use, or when an allergenic component has been introduced in a food where it is not present in the traditional food.

- Improve the premarket review process for food and color additives using advanced computer and telecommunications technologies.

- Provide pre-filing assistance to petitioners through the publication of detailed guidance for food contact substances and food color additives.

- Target sampling and analysis of fresh produce through the development of Good Agricultural Practices (GAPs) and Good Manufacturing Practices (GMPs).

- Provide technical assistance and education programs for foreign and domestic producers.

Selected FY 2000 Accomplishments

Imports

- Conducted 160 inspections of foreign food establishments (non-HACCP), almost double the number completed in FY 1999.

- Completed the collection and laboratory analysis of 1,000 samples of high volume imported produce for microbiological pathogens which provided very useful data. Forty-four samples were found to be positive and detained for microbial contamination. Thirty-five samples were positive for Salmonella and nine positive for Shigella. There have been no positive samples for *E. coli 0157:H7*. Twenty-two firms have been placed on Detention Without Physical Examination (DWPE). Subsequently, 11 have been removed from DWPE. Four foreign farm inspections have been conducted as a result of follow-up investigations.

- Began improving OASIS through software modifications which included important new functionality such as supervisory review and proxy functions. The new features enhanced and expedited import review and developed and implemented a new screening process in OASIS which allows for the expedited automated review of FDA regulated import products using more specific criteria then was previously possible under the U.S. Customs Service system.

Domestic Inspections

- Conducted approximately 5,700 "high-risk" food inspections, an increase of 90 percent over the FY 1999 level of 3,000.

- Established DNA finger printing to combat food borne outbreaks using pulsed field gel electrophoresis (PFGE) capability in five field laboratories because it provides timely identification of the source of contamination. This technique has been successfully used in several outbreak situations involving Salmonella and Listeria monocytogenes.

- Established a program to screen Salmonella isolates from foods. In FY 2000, about 250 Salmonella isolates were screened and several multiple-antibiotic resistant strains were found.

- Tracked and investigated 98 pathogen-related incidents. Examples of food borne pathogens tracked which spread across several states include a “salmonella meunchen outbreak” in mangoes that broke out in 13 states; a norwalk-like virus in potato salad that occurred in 11 states; and, a salmonella anatum outbreak which occurred in frozen carrots and peas that occurred in eight states and Canada.

HACCP

- Conducted seafood HACCP inspections and sent 148 seafood HACCP Warning Letters. The Agency pursued the first seafood HACCP injunction against a purveyor of hot and

cold smoked fish because the firm was not controlling the hazard of Clostridium botulinum. The firm entered into a consent decree and agreed to stop processing until this hazard could be controlled.

- Initiated a Dairy Grade A HACCP Pilot Program in collaboration with the National Conference of Interstate Milk Shippers (NCIMS), in six dairy processing plants. The six pilot plants have implemented the voluntary HACCP Pilot and were listed in the Interstate Milk Shippers List under the HACCP alternative to the traditional Pasteurized Milk Ordinance-based program.

Produce

- Worked with USDA's National Agricultural Statistical Service (NASS) to perform an extensive survey of production practices of fresh fruit and vegetable growers and packers in the U.S. to measure adoption of Good Agricultural Practices (GAP)/Good Manufacturing Practices (GMP) guidance. This survey gathered data on the types of practices (e.g., agricultural water source, manure use, employee hygiene and facility sanitation) covered in the guide. A report of the survey results is expected to be available in early 2001.

Food Code Adoption

- Exceeded goal that 35 percent of States would adopt the Food Code. Twenty State agencies having jurisdiction over retail-level establishments have adopted the Food Code. Providing model food codes and model code interpretations and opinions is the mechanism through which FDA, as a lead federal food control agency, promotes uniform implementation of national food regulatory policy.

Harmonize Standards for *E. coli O157: H7*

- Provided funding, in conjunction with USDA, for a pilot project with eight Federal, State and Local laboratories to develop standards for sampling and testing methods for *E. coli 0157:H7*. The pilot is taking *E. coli O157: H7* food sample testing currently being done at the labs and standardizing their methods, as well as working toward accreditation of the procedures used. The pilot will be completed in FY 2001.

Risk Communication Education and Training

- Conducted U.S. - Chile Seminar on Food Safety entitled "An Integrated Food Safety System; Processes and Partnerships". JIFSAN in conjunction with the Government of Chile held a training program on produce safety, emphasizing GAPs. FDA also conducted dairy farm sanitation and milk safety training, emphasizing on-farm practices, in San Salvador, El Salvador. Foreign outreach and education was continued by co-sponsoring a regional food safety meeting in Auckland, New Zealand.

- Funded 19 State Food Safety Task Forces with Small Conference Grants totaling $96,500 and awarded 13 grants totaling $530,000 for Innovative Food Safety Projects to State and local regulatory agencies that were intended to complement, develop and/or improve State and local food safety programs.

- Awarded 39 state food contracts for over 5,100 food inspections for a total of $2,617,000.

Premarket Review of Food and Color Additives and Food Ingredients

- Completed the safety evaluation in less than 360 days for all five food and color additive petitions that qualified for expedited review. This exceeded FDA's goal to complete 80-90 percent of these petitions within 360 days.

- Completed the safety evaluation in less than 360 days for 77 percent (59 of 77) of food and color additive petitions that did not qualify for expedited review. This exceeded FDA's goal to complete 50 - 60 percent of these petitions within 360 days.

- Developed guidance for the industry on preparation of premarket notification for food contact substances.

- Published a final rule on the simultaneous review of food ingredients in meat and poultry.

Nutrition, Health Claims and Labeling

- Received 10 new infant formula notifications, and all were reviewed within the 90-day statutory time frame.

- Published a final rule authorizing a health claim for soy protein and heart disease. FDA completed the evaluation of two additional health claim petitions. One petition was for sterol esters and heart disease. The other was for stanol esters and heart disease. The Agency issued an interim final rule authorizing these health claims.

Dietary Supplements

- Communicated FDA concern about the use and marketing of dietary supplements or other botanical-containing products that may contain aristolochic acid. FDA issued separate letters to address different audiences. The letter to the industry was to deter marketing of aristolochic acid and the one to health care professionals was to deter the issuance of prescription (use) containing aristolochic acid. FDA issued an Import Alert on these products.

- Published three Federal Register notices announcing the availability of new adverse event reports and related information on dietary supplements containing ephedrine alkaloids, as well as announcing withdrawal of the provisions of the ephedrine alkaloids proposed rule relating to the dietary ingredient level and duration of use limit for these products. FDA participated in a public meeting to discuss available information about the safety of dietary supplements containing ephedrine alkaloids.

- Eliminated the Freedom of Information (FOI) backlog that included requests for Special Nutritional/Adverse Events Monitoring System (SN/AEMS) information dating from 1998.

- Published a final rule that defines the types of statements that can be made concerning the effect of a dietary supplement on the structure or function of the body. CFSAN participated in an FDA public meeting addressing pregnancy-related claims under the structure/function rule. Over a ten month period, FDA received approximately 1,400 structure/function notifications. After reviewing the notifications, the Agency sent 102 letters to firms notifying them that the claims for one or more of the products that were the subject of their notifications were not structure/function claims, but were disease claims not permitted for use in the labeling of dietary supplements pursuant to section 403(r)(6) of the FFD&C Act.

- Published a Federal Register notice on the strategy for responding to petitions for health claims for dietary supplements, including the health claims at issue in Shalala v. Pearson. FDA held a public meeting on April 4, 2000 to solicit comments on implementation of the Pearson decision.

- Issued a final determination on the first, second, and third of the four Pearson claims. FDA determined that the proposed claim that stated 0.8 mg of folic acid in a dietary supplement was more effective in reducing the risk of neural tube defects than a lower amount in foods was not authorized; determined that the proposed health claim about dietary fiber and reduced risk of colorectal cancer could not be authorized because the results of studies about dietary fiber consistently showed a lack of relationship between dietary fiber supplements and the risk of colorectal cancer; and determined enforcement discretion to allow a qualified claim about the use of omega-3 fatty acids in dietary supplements and the reduced risk of coronary heart disease. The qualified claim applies to daily intakes that do not exceed three grams per person per day from conventional food and dietary supplement sources.

- Issued the Dietary Supplement Strategy which plans to have, by the year 2010, a science-based regulatory program that fully implements the Dietary Supplement Health and Education Act of 1994, and that provides consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products.

- Initiated recalls of herbal products due to the presence of undeclared prescription diabetic drugs, glycuride, and phenformin. Both drugs are used to lower blood sugar. Recalls of such products involved Sino American Health Products, Inc.; Chinese Angel Health Products, Inc.; and, Diabetic Capital (U.S.) LLC.

Chemical and Other Contaminants

- Published a draft compliance policy guide (CPG) entitled, “Apple Juice, Apple Juice Concentrates, and Apple Juice Products - Adulteration with Patulin”. The purpose of the CPG is to advise FDA's field offices and the industry concerning enforcement actions that may be taken against apple juice products that contain patulin.

- Published a final report on the feasibility of appropriate methods of informing customers of the contents of bottled water, as required by the Safe Drinking Water Act (SDWA) Amendments.

Leveraging Scientific Expertise

- Restructured the Food Advisory Committee to consist of a "parent" Committee and four standing Subcommittees: (1) Additives and Ingredients; (2) Contaminants and Natural Toxicants; (3) Dietary Supplements; and (4) Food Biotechnology.

Codex Committees and Working Groups

- Participated in 18 Codex committees and related meetings to promote development of harmonized food safety and labeling standards. In June 2000, FDA provided a leadership role for the Codex Committee on Nutrition and Foods for Special Dietary Uses in developing international Guidelines for Vitamin and Mineral Supplements. Specifically, FDA participated in the Ad-Hoc Task Force on Foods Derived from Biotechnology in July 2000, and participated in the Task Force's Working and Drafting Groups that are developing draft international Guidelines for the Safety Assessment of Foods Derived from Biotechnology.

Emerging Areas

- Issued a public announcement on plans to strengthen the regulatory approach for bioengineered foods. Three proposals were announced: (1) Development of a proposed rule requiring that developers of bioengineered foods notify the Agency before they market such products; (2) the addition of scientists to the Food Advisory Committee that have expertise in biotechnology; and (3) the development of labeling guidance to assist manufacturers who wish to voluntarily label their foods being made with or without the use of bioengineered ingredients.

- Held 14 public meetings to raise consumer and industry awareness to the presence of allergens in foods and on labeling approaches to identify the presence of allergens.

Foods
Program Activity Data

Program Workload and Outputs	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Food and Color Additives Petitions			
Completed	77.0%	50.0%	65.0%
Percentage of overdue Petitions under review [1/]	N/A	N/A	N/A
Inspections - FSI by FDA [2/]			
Non-HACCP Foreign	160	250	250
Non-HACCP Domestic	3,742	6,200	6,300
Seafood HACCP Domestic	2,362	4,700	4,700
Seafood Importer (HACCP)	529	700	700
Inspections - FSI by State Contract [2/]			
Non-HACCP	3,160	3,660	4,700
Seafood HACCP	546	542	600
Inspections - FSI by State Partnerships [2/]			
Non HACCP	1,956	1,000	1,000
Seafood HACCP	418	400	400
Seafood Importer HACCP	15	10	10
Total FSI Inspections			
Import	689	950	950
Domestic	12,199	16,512	17,710
Field Exams [3/]			
Import - FDA FSI	8,713	3,650	3,650
Domestic - FDA FSI	81	80	100
Import - FDA Non-FSI	4,448	7,200	7,200
Domestic - FDA Non-FSI	1,363	1,720	2,000
Laboratory Samples Analyzed [4/]			
Import - FSI	10,565	12,000	12,000
Domestic - FSI	4,777	5,980	6,340
Import - Non-FSI	4,549	9,200	9,200
Domestic - Non-FSI	4,735	7,750	7,750

[1/] The percentage of Food and Color Additive Petitions Completed is based upon 360 days. The goals for first action for petitions (FY 2000 and FY 2001) are lower than those achieved in FY 1999 due to the conversion of petitions to notifications in FY 2000. FDA will establish new baseline numbers for these goals.

[2/] An inspection is any visit to an establishment during which all or part of one or more phases of that establishment's operation is evaluated against appropriate FDA requirements.

[3/] Field Exams are the on-site examination of a product that is sufficient in itself to determine that the product is in compliance with FDA requirements

[4/] Laboratory samples analyzed are product samples physically analyzed by the laboratory to determine whether or not the product is in compliance with FDA requirements.

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Human Drugs

	FY 2000 Actual	FY 2001 Appropriation	FY 2001 Current Estimate [1/]	FY 2002 Estimate [3/]	FY 2002 +/- FY 2001 Current Estimate
Total Program Level [2/]	**$311,234,000**	**$317,547,000**	**$317,066,000**	**$347,829,000**	**+$30,763,000**
Center ($000)	*$240,381,000*	$244,211,000	*$243,877,000*	*$262,375,000*	*+$18,498,000*
FTE	*1,772*	*1,850*	*1,845*	*1,889*	*+44*
Field ($000)	*$70,853,000*	*$73,336*	*$73,189,000*	*$85,454,000*	*+$12,265,000*
FTE	*737*	*819*	*799*	*836*	*+37*
Total Budget Authority [2/]	**$215,538,000**	**$218,249,000**	**$217,768,000**	**$240,141,000**	**+$22,373,000**
Pay Increases					*+$10,222,000*
Imports/Inspections			*62,113,000*	*66,113,000*	*+4,000,000*
Patient Safety/AERS			*25,940,000*	*30,040,000*	*+4,100,000*
Human Subject Protect.			*14,562,000*	*18,862,000*	*+4,300,000*
Total User Fees	**$95,696,000**	**$99,298,000**	**$99,298,000**	**$107,688,000**	**+$8,390,000**
PDUFA	*95,696,000*	*99,298,000*	*99,298,000*	*106,188,000*	*+6,890,000*
Proposed User Fees					
Imports/Inspections	*0*	*0*	*0*	*1,500,000*	*+1,500,000*

[1/] Reflects enacted levels adjusted for the 0.22 percent rescission, accounting for $530,000 in the Human Drugs program.
[2/] Reflects decrease in base funding from FY 2001 of $249,000, for Human Subject Protection & Bioterrorism.
[3/] Pay increases shown on separate line, and not reflected in individual increase areas.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
1998 Actuals	$262,648,000	$199,579,000	$63,069,000	2,429
1999 Actuals	$278,299,000	$200,423,000	$77,876,000	2,456
2000 Actuals	$311,234,000	$215,538,000	$95,696,000	2,509
2001 Current Estimate	$317,066,000	$217,768,000	$99,298,000	2,644
2002 Estimate	$347,829,000	$240,141,000	$107,688,000	2,725

MISSION

- Ensure the safety and effectiveness of all drug products used for the prevention, diagnosis, and treatment of disease.
- Ensure the prompt approval of safe and effective new drugs so that patients can enjoy the benefits provided by therapies to treat and prevent illness and disease.
- Review premarket applications for new and generic drugs in a timely and quality manner, as well as new and generic drug supplemental applications.
- Monitor adverse drug events to detect safety problems that only become evident after the approval and actual use of a drug.
- Evaluate reports of adverse events, medication errors and product defects associated with drug products.
- Use postmarketing surveillance reporting, and the collection and analysis of drug product samples to evaluate compliance with quality standards and labeling requirements.
- Conduct inspections to determine if fraudulent drugs are marketed in commercial channels, and evaluate foreign and domestic compliance with GMPs.
- Oversee the orphan product program that reviews and approves requests for orphan product designations, which includes granting sponsors seven years of marketing exclusivity. Award grant funding to defray costs of qualified clinical testing incurred in connection with the development of drugs for rare diseases and conditions.

REQUESTED INCREASES

Pay Increase + $10,222,000

FDA's request for funds to cover pay cost increases is vital to the Agency because personnel are so essential to accomplishing its mission. Pay increases have a major impact on FDA because the Agency is more people-intensive than many other government agencies. Payroll accounts for over 60 percent of the total FDA budget. This has a significant impact on all activities in FDA, particularly the field. The costs of the pay increases are necessary to ensure the integrity of the Agency's work in the Human Drugs Program, especially as responsibilities continue to grow with its involvement in the entire life-cycle of a pharmaceutical (pre-clinical studies to postmarket surveillance of medication errors or potential adverse events).

In order to maintain the level of activities carried out in FY 2001, FDA is requesting $40,000,000 million to cover the cost of the FY 2002 pay raise, annualization of the FY 2001 pay raise, anticipated within grade increases, and one extra day of pay. The Human Drugs Program portion of this increase is $10,222,000.

Imports & Inspections + $5,500,000 and 24 FTE (Budget Authority +$4,000,000 and 19 FTE; Proposed User Fees +$1,500,000 and 5 FTE)

Congress mandated bi-annual inspections of drug establishments in Section 510 (h) of the Federal Food, Drug and Cosmetic Act ["...every such establishment engaged in the manufacture, propagation, compounding, or processing of a drug or drugs...shall be inspected ... at least once in the two year period beginning with the date of registration..."].

Budget Authority

FDA needs to improve its regulatory assessment of drugs and drug products manufactured in foreign sites and imported into the United States. Foreign inspections allow FDA to identify and correct problems in the manufacture, distribution, or sale of human drug products. Funding will allow FDA to:

- Evaluate findings and act against violations in an increased numbers of on-site inspections, especially where foreign manufacturing sites have shown evidence of quality problems such as non-uniformity of dosage units, cross-contamination of one drug with another, lack of sterility and mixups in labeling and packaging;

- Negotiate cooperative regulatory agreements with Switzerland, Canada and Mexico;

- Execute existing cooperative agreements regarding foreign drug manufacturing with the European Union, Australia and Japan;

- With new foreign registration authority granted under FDAMA, establish accurate lists of foreign manufacturers exporting to the U.S.;

- Improve existing electronic systems for tracking and evaluating foreign manufacturers by entering all required approval data. Analyze these new data and report requirements; and,

- Write new compliance programs for enhanced monitoring of foreign manufacturers. One such program will be on inspecting the distribution of foreign-source drug chemicals to find counterfeits. Another will be on new inspection approaches.

Domestically, FDA is currently only inspecting 28 percent of human drug establishments and 22 percent of the registered human drug manufacturers, repackers, relabelers, and medical gas repackers. These inspections are necessary to ensure that firms adhere to the terms and conditions of a drug approval described in the application, and that the drug is manufactured in a consistent and controlled manner. Inspections allow FDA to identify and correct problems in the manufacture, distribution, or sale of human drug products. FDA's ability to perform statutory inspections is seriously impeded because the program is not fully funded to meet the statutory schedule of once every two years. There are many other non-statutory human drug inspections that FDA needs to perform that competes with this already under funded area. This includes inspections at excipient manufactures, manufacturers of precursor materials for active pharmaceutical ingredient manufacturers, warehousing and distribution operations, importers and office only locations for record reviews. All of these facilities require coverage in order to ensure overall quality and purity of human drugs. In FY 2002 FDA will:

- Improve collection and analysis of risk data to enhance management decision-making and improve the efficiency and effectiveness of inspections and sample analysis;

- Evaluate findings and act against violators in an increased number of on-site inspections, especially where domestic manufacturing sites have shown evidence of quality problems

such as non-uniformity of dosage units, cross-contamination of one drug with another, lack of sterility and mixups in labeling and packaging;

- Update inspection and sample analysis programs for inspecting domestic manufacturers; and,

- Provide outreach to industry (e.g., facility evaluation, inquiry responses, education leveraging, etc).

Proposed User Fees
FDA proposes to collect $1,500,000 in user fees assessed for activities related to import program operations, including funds for the Operational and Administrative System for Import Support (OASIS), that are consistent with provisions of the World Trade Organization (WTO) agreements. The OASIS system is one of many import services that substantially reduce the risk of potentially harmful imported drug products from reaching the American market place. The importer/broker community benefits through faster turn-around times, elimination of large volumes of paperwork, and reduced costs of doing business. OASIS will give FDA staff access to historical information to better target products and firms at high risk, the ability to plan inspections more effectively, and the ability to share findings from inspection and lab analyses with other offices. In FY 2002 FDA will:

- Increase coordination with the U.S. Customs Service to improve the effectiveness of cargo control activities at ports, and the monitoring of human drug products that have been refused entry pending exportation or destruction (follow-up-to-refusals); and,

- Modernize the Operational and Administrative System for Import Support (OASIS) import data processing system to provide import reviewers with rapid and direct access to information necessary to make entry decisions about human drug products.

Patient Safety/AERS + $4,100,000 and 17 FTE
Under 21 United States Code 355 (the new drug provisions of the Federal Food, Drug, and Cosmetic Act), FDA is granted authority to take action on the sale of pharmaceuticals if the Agency discovers imminent hazard to public health. FDA must collect safety information to determine where the hazards exist.

As reported in the 2000 report "To Err is Human: Building a Safer Health System," it is estimated that over 98,000 Americans die yearly from medical errors. Many of these medical errors are adverse events associated with the use of FDA-regulated products – drugs, biologicals, and medical devices. FDA is committed to conducting additional research on methods of identifying risk and reducing the occurrence of adverse events associated with pharmaceuticals. Increased funding will allow FDA to monitor and respond to an increased number of suspected adverse events associated with the use of FDA's regulated products. During FY 2002 FDA will:

- Complete FDA's new on-line adverse event reporting system (AERS) for drugs and biologics, and provide rapid assessment of injuries and deaths associated with the use of these products;

- Develop links to hospital-based information systems to better support hospital staff working on the "front lines" of patient safety. This includes improving the reporting systems to address under-reporting and incomplete reporting of medical errors, as well as increased use of other electronic systems to monitor problems with use of drug products. Access to drug utilization databases can also provide the Agency with data on patient drug use by individuals in an ambulatory care or inpatient setting;

- Increase FDA's capacity to do the multi-factor analysis necessary to correctly identify the sources of safety problems and potential solutions. This includes establishing links to safety databases maintained within community-level healthcare delivery systems and regional-level safety surveillance systems, and adding to expertise in medical epidemiology and statistical analysis;

- Develop linkages to government and private health care databases. Access to broad-based health information databases will allow for more rapid exploration of potentially serious drug-related problems and more rigorous investigations than currently possible;

- Expand educational and training programs for health care providers and the public to promote the safe use of products;

- Investigate reported errors and develop error reduction strategies with manufacturers and the medical community; and,

- Upgrade field investigational data systems to complement agency error tracking systems, and to provide better information on the incidence of medical errors.

Human Subject Protection + $4,300,000 and 20 FTE

Under Section 505 of the Federal Food, Drug, and Cosmetic Act, the Human Drugs Program is responsible for reviewing data submitted in research and marketing applications for new drug products and determining the safety and effectiveness of these products.

To fulfill this important public health mission, the Human Drugs Program conducts on-site inspections and verifies the quality and integrity of data submitted to the Agency, thereby assuring that drug approval decisions are sound. Another purpose of these inspections is to protect the rights and welfare of the human subjects who participate in clinical trials. To accomplish these goals, the program currently conducts and reviews the reports of approximately 700 bioresearch monitoring (BIMO) inspections of clinical trial study sites, Institutional Review Boards (IRBs), sponsors, and contract research organizations (CROs) annually.

This program is severely stressed due to the increased complexity of the products undergoing testing, the expanded number of clinical trials, and in particular, the high volume of trials performed overseas in countries with less developed standards for the conduct of such studies. Complaints coming in to the Human Drugs Program related to clinical research have skyrocketed: receipt of 9 complaints in 1998, 103 in 1999, and 118 in 2000. Additional staff and resources will ensure that the public health mission of the Human Drugs Program is not

compromised even further. FDA will use these resources for inspections and outreach activities, specifically to:

- Increase the number of Bioresearch Monitoring (BIMO) site inspections by approximately 80 to a total level of approximately 780 BIMO inspections annually;

- Follow-up on complaints related to clinical research, developing and issuing inspection assignments, and completing reviews of inspection reports;

- Enhance Federal coordination of the program by synchronizing operations and increasing communication between FDA's Office of Human Research Trials and the Department of Health and Human Services' Office of Human Research Protection;

- Improve the quality, consistency, and effectiveness of BIMO inspections by developing an investigators' certification program that provides training and practical experience, and an assurance that investigators keep pace with emerging issues in clinical research; and,

- Improve the safety and quality of foreign bioresearch activities by entering into agreements with foreign governments and participating in international regulatory standards organizations.

Current Law User Fees + $6,890,000 and 20 FTE

Prescription Drug User Fee Act II (PDUFA II)
The Prescription Drug User Fee Act of 1992 (PDUFA) authorized the assessment and collection of user fees for drug applications, establishment registrations, and product listings to enhance and expand FDA's existing review process.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) reauthorized the collection of prescription drug user fees (PDUFA II) to enhance the human drug review process, including some biological products, through FY 2002. The Act established fees for applications, establishments, and approved products. The user fees have enabled FDA to improve its performance for drug review and approval times. In FY 1991, the median approval time for human drug applications was 21 months and in FY 1999 the median approval time was 11.9 months. The fees collected in FY 2002 will enable the FDA to continue to meet its PDUFA II performance goals, including:

- Review and act on 90 percent of standard original NDA and PLA/BLA submissions filed during fiscal year 2002 within 10 months of receipt;
- Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 2002 within 6 months of receipt;
- Review and act on 90 percent of standard efficacy supplements filed during fiscal year 2002 within 10 months of receipt;
- Review and act on 90 percent of priority efficacy supplements filed during fiscal year 2002 within 6 months of receipt;

- Review and act on 90 percent of manufacturing supplements filed during fiscal year 2002 within 6 months of receipt and review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt;
- Review and act on 90 percent of Class 1 resubmitted original applications filed during fiscal year 2002 within 2 months of receipt; and,
- Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

JUSTIFICATION OF BASE

Activities Related to Increases for FY 2002

Payroll

- FDA's Human Drugs program ensures the safety and effectiveness of all drug products used for the prevention, diagnosis, and treatment of disease. FDA also ensures the prompt approval of safe and effective new drugs so that patients can enjoy the benefits provided by therapies to treat and prevent illness and disease. The Agency reviews premarket applications for new and generic drugs in a timely and quality manner, as well as new and generic drug supplemental applications.

- The field component of Human Drugs inspects regulated industry, and collects and analyzes samples. Other activities that often arise are review and management of enforcement actions, and consumer complaints, trace back efforts, and review of import entries for admissibility decisions. These functions are inherently governmental and highly personnel intensive.

Patient Safety/AERS

- Maintain the Agency's system of postmarketing surveillance and risk assessment program to identify adverse drug events (ADEs) that did not appear during the drug development process by collecting, evaluating and acting upon information on ADEs associated with marketed products.

- Receive adverse event and medical errors reports via the Adverse Event Reporting System (AERS) database. FDA receives and records over 260,000 individual postmarketing safety reports (ISRs). Adverse event reporting prompts the Agency to conduct around 50 inspections of foreign and domestic firms per year.

- Identify health hazards associated with the manufacturing, labeling, and packaging of pharmaceuticals and remove unsafe and ineffective products from the marketplace. FDA operates the MedWatch Program directed toward health care professionals to voluntary report observed or suspected defects and quality problems associated with marketed drug products. FDA reviews the reports to identify potential health hazards, initiates investigational follow-up and takes appropriate enforcement action. The Agency reviews hundreds of thousands of reports per year and numerous reports result in product recalls and voluntary corrective actions by industry.

- Provide increased health education for U.S. consumers about FDA-regulated products, which may adversely impact their health.

Human Subject Protection

- Conduct inspections of clinical investigators, sponsors, monitors, Investigational Review Boards (IRBs), non-clinical laboratories, and bioequivalence facilities to ensure the protection of the rights and welfare of human subjects who participate in clinical studies.

- Verify the reliability and accuracy of data collected by regulated industry in clinical and non-clinical (animal) studies.

- Review Establishment Inspection Reports (EIRs) pertaining to clinical investigators, sponsors, non-clinical laboratories, and bioequivalence facilities for violations and take corrective actions such as disqualification of clinical investigator ability to receive investigational drugs.

- Conduct inspections and data audits to monitor all aspects of the conduct and reporting of drug product research involving human subjects.

- Conduct inspections to assure the quality and integrity of data submitted to the Agency in support of new drug applications.

Imports and Inspections

- Focus on product quality standards and compliance by manufacturers with standards established in the good manufacturing practices (GMP) regulations to ensure that the highest possible quality products are marketed.

- Conduct field inspections and compliance actions, including postapproval human drug inspections, surveillance GMP inspections for human drugs, as well as compliance actions such as those prompted by complaints or adverse event reports.

- Provide criminal investigation of reported product tampering, counterfeit products and other fraudulent criminal activities involving regulated drug products.

- Perform laboratory validation of analytical methods submitted to support premarket product applications.

- Collaborate with the European Union to assess equivalence of regulatory systems to ensure imported products comply with U.S. standards. FDA will continue equivalence assessments through FY 2002. This agreement will ultimately allow reciprocal reliance on inspections of pharmaceutical manufacturing plants between equivalent regulatory authorities and improve border operations.

Activities Related to Other Priority Areas

New Drug Application Review

- Regulate the testing of investigational new drugs (IND review) and evaluate new drug applications (NDAs) received from sponsors. Over the past several years, FDA approvals for new drug applications (including new molecular entities and priority approvals) have ranged from 71 to over 120 per year.

- Review and act upon standard and priority efficacy supplements -- supplemental applications proposing to add a new use of an approved drug to the product labeling. In the recent past, FDA received between 100 and 150 applications per year for new or expanded uses of an already approved drug.

- Review and act upon manufacturer applications that notify FDA in advance of packaging, location, machinery, processes or supplier changes. In the recent past, FDA received between 1,200 and 1,500 applications per year and approved nearly 90 percent of these.

Pediatric Drug Studies

- Review study requests from industry for manufacturers who conduct and file pediatric studies in response to our written requests. FDA is authorized to grant six months of marketing exclusivity to manufacturers who conduct and file pediatric studies. The six months is a economic incentive so that FDA may gain additional information about a drug's usage in the pediatric population.

Generic Drug Review

- Support an active generic drugs program (Abbreviated New Drug Approvals or ANDA review) with a focus on expanding the availability of high quality generic drug products to the public.

Over-the-Counter Drugs

- Review over-the-counter (OTC) drugs to ensure safety and effectiveness and to help consumers understand how to best use OTC products. There are currently over 100,000 OTC products on the market. FDA published a final rule that will provide new, easy to understand labeling on non-prescription drugs.

Orphan Product Development Program

- Promote the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions through the Office of Orphan Products Development (OOPD). The OOPD administers the major provisions of the Orphan Drug Act (ODA) which provide incentives for sponsors to develop products for rare diseases.

Clinical Pharmacology

- Continue program for research and training for clinical pharmacologists. The Agency awarded a cooperative agreement to the University of Indiana in FY 2000 for one year to

support post-doctoral training and research to study clinical pharmacology and biopharmaceutical issues related to new drug development and review.

Human Drug Related Research

- Leverage scientific capabilities to respond and contribute to major breakthroughs in pharmaceutical research and technology via continued professional development/ training, and continued stakeholder collaborations. In 1999, FDA began a collaborative effort with research scientists from academia and industry to form the Product Quality Research Initiative (PQRI). The PQRI plans to: conduct research in the areas of pharmaceutical chemistry, biopharmaceutics, and science management; identify better test methods for assessing quality of products; and identify optimal manufacturing and management processes.

Outreach with Stakeholders

- Maintain communication lines with stakeholders. Outreach programs include the pharmacist education outreach program to help pharmacists better explain the drug approval process to consumers, and the collaborative efforts between FDA and industry where scientific and regulatory experts discuss electronic submissions, user fees, risk management, product quality, drug safety and other issues on drug development and manufacturing. FDA also updated "From Test Tube to Patient: Improving Health through Human Drugs," a popular FDA publication for consumers which describes new drug development in the United States and highlights the Agency's consumer protection role. This report has been requested by more than 5,000 individuals and can be found at *www.fda.gov/fdac/special/newdrug/ndd_toc.html.*

Selected FY 2000 Accomplishments

Prescription Drug User Fee Act of 1992 (PDUFA)

- In 1997, Congress authorized PDUFA II under the Food and Drug Modernization Act of 1997 (FDAMA) for another five years. The following table illustrates performance for PDUFA/FDAMA for the FY 1999 cohort data.

Fiscal Year 1999 Cohort (as of 12/31/00)

Submission Type	Number of Submissions Filed	Goal (months)	Number of Reviews "On Time"	Percent of Reviews "On Time"
NDAs -				
Priority	31	90% in 6 mo.	31	100%
Standard	95	90% in 12 mo.	95	100%
		30% in 10 mo.	63	66%
NMEs (subset of NDAs) -				
Priority	17	90% in 6 mo.	17	100%
Standard	25	90% in 12 mo.	25	100%
		30% in 10 mo.	14	56%
NDA Resubmissions-				
Class 1	17	90% in 4 mo.	17	100%
		50% in 2 mo.	17	100%
Class 2	47	90% in 6 mo.	47	100%
Efficacy Supplements -				
Priority	15	90% in 6 mo.	13	87%
Standard	122	90% in 12 mo.	122	100%
		30% in 10 mo.	104	85%
Manufacturing Supplements-				
CBE	557	90% in 6 mo.	547	98%
Requiring Prior Approval	902	90% in 6 mo.	889	99%
		30% in 4 mo.	660	73%

Review Performance for the FY 1999 Cohort

- Met or exceeded 14 of the 15 performance review goals for the FY 1999 submission cohort. Only missed the goal for priority efficacy supplements (13 of 15 were reviewed "on time"). In addition to surpassing all goals for NDAs, surpassed all review goals for New Molecular Entities (NME), a subset of the NDA category. The number of original NDAs filed for the FY 1999 submission cohort increased over 10 percent from 1998.

New Drug Evaluations

- Initiated 239 actions on NDAs during FY 2000, 106 of which were approvals. The median approval time was 11.6 months, a three percent decrease in median approval time compared with FY 1999. Sixty-five of these NDAs were approved in 12 months or less. Of the 106 NDA approvals, 39 were for NMEs. Of the 39 NMEs, 12 were drugs given a priority review (products offering notable improvements over currently marketed drugs).

- Approved 23 priority applications (12 NMEs, 11 NDAs that were not NMEs, and 21 priority efficacy supplements) in FY 2000.

- For the FY 2000 submission cohort, FDA received 80 resubmissions for review, 122 NDAs, 175 efficacy supplements and 1,438 manufacturing supplements during the fiscal year. Final on-time performance information for the FY 2000 submission cohort is not yet available. Data will be available mid to late 2001. Drugs approved in FY 2000 under Subpart H (Accelerated Approval) regulations are listed below.

NDAs and Supplemental NDA Approved for Accelerated Approval in FY 2000

Drug	Approval Time	Purpose
Mylotarg (gemtuzumab ozogamicin)	6.6 months	Treatment of patients with CD33 positive acute myeloid leukemia in first relapse who are 60 years of age or older and who are not considered candidates for cytotoxic chemotherapy
Kaletra (lopinavir/ritonavir capsule)	3.5 months	Used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients age six months and older
Kaletra (lopinavir/ritonavir oral solution)	3.5 months	Used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients age six months and older
Celebrex (celecoxib) - *[Supplemental NDA]*	6.0 months	To reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis, as an adjunct to usual care (e.g., endoscopic surveillance, surgery)

Generic Drug Review

- Approved 232 abbreviated new drug applications (ANDAs). This is an increase over the 198 approved last fiscal year. Examples of important first time approvals are as follows:

Drug	Purpose
Paclitaxel (generic for Taxol by Bristol Myers Squibb)	For treatment of breast, ovarian and other types of cancer
Enalapril (generic for Vasotec by Merck)	For treatment of hypertension
Midazolam (generic for Versed by Roche)	For induction of general anesthesia and sedation
Digoxin (generic for Lanoxin by Glaxo Wellcome)	For congestive heart failure
Doxazosin (generic for Cardura by Pfizer)	For use in the treatment of hypertension and benign prostatic hyperplasia

- Made progress in increasing the percent of originals acted upon in less than the statutory 180 days. In the six months from November 1999 to April 2000, FDA acted on 47 percent of original applications in 180 days. This is an increase from the 31 percent acted on in the six months beginning in April 1999.

- Took significant strides in preparation for a paperless review environment with the utilization of $1.5 million provided by Congress for satisfying information technology needs. The funds allowed for the purchase of upgraded hardware, software, and contractual support to allow for the review of electronic submissions and to increase the overall efficiency of the review process.

- Received 101 ANDAs containing at least a portion of the data in electronic format (30 percent of all submissions). This is an increase over last year, when 88 ANDAs were submitted with some portion in electronic format. The increase reflects the commitment of OGD to support the Agency's efforts in this regard.

Generic Approvals by Fiscal Year

Fiscal Year	Number of Approvals	Average Approval Time (months)	Median Approval Time (months)
1993	170	40.4	39.7
1994	168	29.4	24.4
1995	201	35.3	28.2
1996	214	33.2	24.7
1997	256	25.6	19.6
1998	230	22.5	18.7
1999	198	19.9	17.3
2000	232	22.3	18.9

Oncology Programs

- Launched the first regulatory website with a focus on a specific disease. The site, called Oncology Tools (www.fda.gov/cder/cancer), can be searched by specific type of cancer or by approval therapy.

- *Pediatric Oncology Projects.* Prepared a Written Request template that encourages development of oncology drugs in children; wrote guidance entitled, *Pediatric Oncology Studies In Response to a Written Request*; and established an Advisory Committee (Pediatric Oncology Subcommittee).

- Held monthly meetings with the National Cancer Institute (NCI) to discuss clinical trial issues to stress interaction with Department of Health and Human Services (DHHS) agencies. Also worked with Health Care Financing Administration (HCFA), the Agency for Healthcare Research and Quality (AHRQ), the National Cancer Institute (NCI), and other DHHS agencies to develop a plan for Medicare Coverage of Clinical Trials.

Antimicrobial Resistance

- Approved Zyvox, the first of a new class of antibiotics indicated for use against resistant organisms. Labeling encouraged use that would preserve this drug for serious diseases.

- Published a proposed rule, *Labeling Requirements for Systemic Antibacterial Drug Products Intended for Human Use*. Contributed to the drafting of an interagency Public

Health Action Plan to Combat Antimicrobial Resistance and to the publication of the report from the FDA Task Force on Antimicrobial Resistance.

Bioterrorism Activities

- Reviewed and approved an NDA for Ciprofloxacin for post-exposure inhalational anthrax.

- *National Pharmaceutical Stockpile.* Identified drugs that are potentially effective in combating a bioterrorist attack and requested submission of data to support such uses.

- Cooperated with stakeholders on bioterrorism activities, including:
  - Worked with CDC in developing "a streamlined IND" for use in the field during a bioterrorism event;
  - Implemented a shelf-life extension program for drug products contained in the stockpile and worked with NIH to identify the most promising antiviral agent to be used to treat smallpox; and,
  - Provided scientific and regulatory expert consultation to outside groups, including: the Center for Civilian Biodefense at the Johns Hopkins University, the CDC and the Advisory Committee on Immunization Practices (ACIP) on issues related to the use of drug products for prevention and treatment of disease due to biological agents that might be used as weapons.

Pediatric Exclusivity (Section 111 of FDAMA)

- Issued 57 Written Requests with 19 Pediatric Exclusivity determinations. Twelve were active moieties for which pediatric labeling has been approved based on studies conducted to satisfy a written request.

- Maintained and updated a pediatric interactive web page at www.fda.gov/cder/pediatric.

- Assisted in the organization and participated in the Surgeon General's National Conference on Mental Health in Children and co-sponsored the NIMH/FDA workshop on the development of psychotropic agents for young children.

Over-the-Counter (OTC) Drug Products

- Approved twelve new drug products and/or new indications for OTC marketing.

Drug	Purpose
Excedrin Migraine	For the treatment of migraine
Habitrol	A stop smoking aid
Aleve Cold and Sinus	A pain relief/fever reducer/decongestant
Infants' Advil	For use in children 6 months to 23 months of age.
Motrin Migraine Pain	For the pain of migraine headache
Rid Mousse	A topical pediculicide

Advil Migraine Liqui-Gels	For the treatment of migraine
Lamisil AT Spray Pump and Solution Dropper	A topical Antifungal
Trivagizole 3 Vaginal Cream	A vaginal antifungal
ChloraPrep	A topical antimicrobial
Abreva Cream	A cold sore/fever blister treatment
Children's Motrin Cold Suspension	A pain relief/fever reducer/decongestant

Adverse Event Reporting System (AERS)

- Implemented a major release of AERS in May 2000. This release provided new functionality by enhancing searching capability, becoming International Conference on Harmonization (ICH) compliant, and providing better integration for electronic submissions. These enhancements allowed FDA to improve its ability to collect and analyze medical product adverse event data and to ensure timely and appropriate action.

Meeting the Mandates of the Quality Interagency Coordination Task Force (QuIC)

- Participated in the QuIC to address the impact of medical errors on the public health from a federal government perspective, and what can be done to address the problem. Activities include developing standards for drug names and packaging to minimize the potential for confusion leading to medication errors. The QuIC also calls for the Human Drugs program to continue to identify, quantify and address postmarketing safety problems. To this end, FDA increased staffing of safety evaluators and medical epidemiologists and identified data resources (e.g. claims-linked population databases, active surveillance systems, etc.) to meet these needs.

Internet Drug Sales and Promotion

- Issued a total of 60 foreign and domestic cyber letters, 43 warning letters, four untitled letters and accomplished five injunctions, 15 seizures and 18 voluntary destructions. Cyber letters alert the recipients that U.S. citizens are being warned about their products and that copies are being sent to the regulatory drug officials in their country and advising U.S. customs through an Import Alert.

- Seized in June 2000, approximately $1.3 million worth of Street Drug Alternatives at Hit Products a.k.a. Riverdale Organics, in Beltsville, MD. These drugs are marketed as alternatives to illicit street drugs and generally labeled as containing botanicals or other ingredients such as vitamins, minerals or amino acids.

- Foreign Internet sales of unapproved pharmaceuticals: As part of a joint FDA/Customs Service operation several hundred mail entries of unapproved pharmaceuticals ordered over the Internet from pharmacies in Thailand were examined and seized at JFK International Airport.

Foreign Inspections and Pre-Approval

- Reviewed approximately 227 establishment inspection reports of foreign drug establishments. These firms manufacture or test finished drug products or active pharmaceutical ingredients intended for distribution to the U.S.

- Reviewed 1,144 NDA domestic establishment evaluation requests (EERs), 711 NDA international EERs, 1,085 ANDA domestic EERs, and 755 ANDA international EERs.

- In support of applications, 1,855 domestic and international establishments were evaluated for 832 NDA applications and 2,560 domestic and foreign establishments evaluations were conducted for 1,317 ANDA applications.

- Provided joint FDA/Customs Service enforcement instruction on bulk drugs to approximately 200 field personnel. FDA has engaged a private contractor (Battelle) to examine FDA's import strategy/procedures and to develop new Information Technology products to assist in import surveillance.

Good Manufacturing Practices

- Reviewed and concurred with 28 regulatory actions, including 14 seizures and six injunctions. These legal actions were taken due to the seriousness of the Good Manufacturing Practice (GMP) deficiencies observed at the pharmaceutical manufacturers sites and to effect corrections and to prevent adulterated products from being shipped to consumers.

Mutual Recognition Agreements (MRA)

- Established the Recall standard operating procedures in April 2000, which is now operational to facilitate rapid exchange of information on potential drug problems between the U.S. and member states of the European community. Held a public meeting on December 8, 1999 on progress toward implementation of the pharmaceutical annex of the MRA.

Leveraging, Communications and Partnership Programs

- Improved communication with consumers and patients through seminars on risk management, safe use of drugs, new drug therapies and labeling; brochures for consumer and patient use; expanded information available via the Internet; and disseminating information about new and existing products. Expanded the pharmacist education outreach program to help pharmacists better explain the drug approval process to consumers.

- Developed easy to read, user-friendly information for consumers in partnership with the American Pharmaceutical Association, the National Consumers League, and the National Council on Patient Information and Education. Continued to provide consumer-focused information on new and innovative drug approvals via a new drug web page.

Office of Orphan Products Development

During 2000, the Office of Orphan Products Development (OPD) staff reviewed 88 new sponsor requests for designation of drugs as orphan products. As part of the request for designation, sponsors submit data that adequately demonstrate the use of their product for a disease or condition affecting fewer than 200,000 people in the U.S.

Based on OPD reviews, 68 drugs and biological products received designation as orphan products during the year. The following 14 designated orphan products were approved by the FDA in 2000, bringing the total number of orphan products approved to 218 (see chart below). These products potentially treat close to 11 million patients in the United States.

List of Orphan Product Approvals

Generic Name/Trade Name (if present)	*Indication Designated*
Antihemophilic factor (recombinant) ReFacto	For the control and prevention of hemorrhagic episodes and for surgical prophylaxis in patients with hemophilia A (congenital factor VIII deficiency or classic hemophilia).
Antivenin, crotalidae polyvalent immune Fab (ovine) CroFab	Treatment of envenomations inflicted by North American crotalid snakes.
Arsenic trioxide Trisenox	Treatment of acute promyelocytic leukemia.
Botulinum toxin type A Botox	Treatment of cervical dystonia.
Botulinum toxin type B NeuroBloc	Treatment of cervical dystonia.
Epoprostenol Flolan	Treatment of secondary pulmonary hypertension due to intrinsic precapillary pulmonary vascular disease.
Follitropin alfa, recombinant Gonal-F	For the initiation and re-initiation of spermatogenesis in adult males with reproductive failure due to hypothalamic or pituitary dysfunction, hypogonadotropic, hypogonadism. AMENDED indication 6/27/00: For the induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.
Fomepizole Antizole	Treatment of methanol or ethylene glycol poisoning.
Gemtuzumab zogamicin Mylotarg	Treatment of CD33-positive acute myeloid leukemia.
Interferon gamma-1b Actimmune	Delaying time to disease progression in patients with severe, malignant osteopetrosis.
Mitoxantrone Novantrone	Treatment of progressive-relapsing multiple sclerosis.
Somatropin (rDNA orgin) injection Norditropin	Treatment of growth failure in children due to inadequate growth hormone secretion.
Somatropin [rDNA] Genotropin	Treatment of short stature in patients with Prader-Willi syndrome.

Electronic Submissions

- Received 129 original NDA submissions in FY 2000, of which 51 percent were at least partially electronic. Also received 131 NDA supplements and 309 NDA amendments that were at least partially electronic.

Human Drugs
Program Activity Data

Program Workload and Outputs	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Total New Drug Application (NDA) Reviews	239	245	250
NDAs approved	106	96	106
Time from Receipt to Approval (mos.)(mean)	(14.6)	(12.8)	(12.6)
Time from Receipt to Approval (mos.)(median)	(11.6)	(11.5)	(11.2)
NDA Supplemental Reviews	2,836	2,815	2,760
Abbreviated New Drug Application (ANDA) Actions [1/]	1,270	1,333	1,400
ANDA Approvals	232	244	256
Average Review Time from ANDA Receipt to Approval (mos.)	22.3	19.5	19
ANDA Supplemental Actions [2/]	4,376	4,594	4,708
INDs (Active)	12,030	11,900	11,800
Clinical Pharmacology/ Biopharmaceutic Reviews	1,455	1,470	1,470
Inspections (excludes BIMO)	2,255	2,950	2,950
Non-clinical/Clinical Study Investigations	697	700	780
Postmarketing Surveillance Samples Analyzed [3/]	92	84	84
OTC Monographs Under Development	10	10	10
Adverse Reaction Reports	261,000	300,000	345,000
Drug Quality Reporting System Report	2,125	2,200	2,300

[1/] ANDA actions include total of approvals, not approvables,, tentative approvals, and faxed deficiencies.
[2/] CMC and Labeling Supplements. Also includes global supplements.
[3/] Includes postmarket samples analyzed in St. Louis and Laurel, MD only.

Biologics

	FY 2000 Actual	FY 2001 Appropriation	FY 2001 Current Estimate [1/]	FY 2002 Estimate [3/]	FY 2002 +/- FY 2001 Current Estimate
Total Program Level [2/]	**$140,717,000**	**$140,489,000**	**$140,251,000**	**$155,507,000**	**+ $15,256,000**
Center ($000)	*$121,291,000*	*$118,015,000*	*$117,825,000*	*$127,987,000*	*+$ 10,162,000*
FTE	*780*	*861*	*856*	*873*	*+ 17*
Field ($000)	*$19,426,000*	*$22,474,000*	*$22,426,000*	*$27,520,000*	*+ $5,094,000*
FTE	*211*	*238*	*232*	*250*	*+ 18*
Total Budget Authority [2/]	**$106,133,000**	**$108,335,000**	**$108,097,000**	**$119,463,000**	**$11,366,000**
Pay Increases					*+ $4,290,000*
BSE			*2,327,000*	*2,500,000*	*+ $500,000*
Imports/Inspections			*23,321,000*	*23,921,000*	*+$600,000*
Patient Safety/AERS			*2,503,000*	*3,503,000*	*+ $2,200,000*
Human Subject Protect.			*3,505,000*	*7,405,000*	*+ $3,900,000*
Total User Fees	**$34,584,000**	**$32,154,000**	**$32,154,000**	**$35,344,000**	**+ $3,890,000**
PDUFA	$34,584,000	$32,154,000	$32,154,000	$35,344,000	+ $3,190,000
Proposed User Fees					
Imports and Inspections	*0*	*0*	*0*	*$700,000*	*+ $700,000*

[1/] Reflects enacted levels adjusted for the 0.22 percent rescission, accounting for $238,000 in the Biologics program.
[2/] Reflects a decrease in base funding from FY 2001 of $124,000, for Human Subject Protection & Bioterrorism.
[3/] Pay increases shown on separate line, and not reflected in individual increase areas.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
1998 Actuals	$123,012,000	$95,479,000	$27,533,000	1,027
1999 Actuals	$124,368,000	$96,823,000	$29,342,000	989
2000 Actuals	$140,717,000	$106,133,000	$34,584,000	991
2001 Current Estimate	$140,251,000	$108,097,000	$32,154,000	1,088
2002 Estimate	$155,507,000	$119,463,000	$35,344,000	1,123

MISSION

- Ensure the safety, efficacy, potency and purity of biological products including vaccines, therapeutics, and related drugs and devices intended for use in the treatment, prevention or cure of diseases in humans.
- Ensure the safety of the nation's supply of blood and blood products.
- Evaluate the safety and effectiveness of biological products before marketing, and monitors the pre-clinical and clinical testing of new biological products.
- License biological products and manufacturing establishments, including plasmapheresis centers, blood banks, vaccine and biotechnology manufacturers.
- Conduct regulatory research to establish product standards and develop improved testing methods.
- Assure the safety of marketed biological products through monitoring adverse experiences, lot release testing and postmarket surveillance.

REQUESTED INCREASES

Pay Increase + $4,290,000

- FDA's request for funds to cover pay cost increases is vital to the Agency because personnel are so essential to accomplishing its mission. Pay increases have a major impact on FDA because the Agency is more people-intensive than many other government agencies. Payroll accounts for over 60 percent of the total FDA budget. This has a significant impact on all activities in FDA, particularly the field. The costs of the pay increases are necessary to ensure the integrity of the Agency's work to maintain efforts in programs not covered by user fees, such as the review of blood bank and source plasma applications, and the regulation of blood and blood products, biotechnology-derived hematologics, allergenic products, and devices; develop science-based standards and guidance to industry regarding safety issues against novel pathogens in blood and blood products; and continue efforts to detect and remove emerging threats to the blood supply; continue to conduct mission related research activities; and provide professional development for biologics staff is a priority to maintain qualified professionals capable of addressing new technologies.

- In order to maintain the level of activities carried out in FY 2001, FDA is requesting $40,000,000 to cover the cost of the FY 2002 pay raise, annualization of the FY 2001 pay raise, anticipated within grade increases, and one extra day of pay. The Biologics Program portion of this increase is $4,290,000.

Bovine Spongiform Encephalopathy (BSE) + $500,000 and 3 FTE

The authority to operate the program is found under Title 42 CFR Subchapter II Part F Subpart 1.

- Address the potential BSE threat to the safety of biological products. Two biological product areas affected include the safety of the blood supply and the safety of vaccines derived from bovine-sourced material.

Imports and Inspections + $1,300,000 and 5 FTE (Budget Authority $600,000 and 3 FTE; Proposed User Fees + $700,000 and 5 FTE)

The authority to operate the program is found under Title 42 CFR Subchapter II Part G.

- Increase surveillance of imported human tissues and other imported biological products.

- Implement the European Mutual Recognition Agreement and by intensifying biologics inspections in developing countries to improve the confidence that FDA has in the safety of biological products.

Proposed User Fees

FDA proposes to collect $700,000 in user fees assessed for activities related to import program operations, including funds for the Operational and Administrative System for Import Support (OASIS), that are consistent with provisions of the World Trade Organization (WTO) agreements. The OASIS system is one of many import services that substantially reduce the risk of potentially harmful imported drug products from reaching the American market place. The importer/broker community benefits through faster turn-around times, elimination of large volumes of paperwork, and reduced costs of doing business. OASIS will give FDA staff access to historical information to better target products and firms at high risk, the ability to plan inspections more effectively, and the ability to share findings from inspection and lab analyses with other offices. In FY 2002, FDA will:

- Increase coordination with the U.S. Customs Service to improve the effectiveness of cargo control activities at Ports, and the monitoring of biologic products that have been refused entry pending exportation or destruction (follow-up-to-refusals); and,

- Modernize the Operational and Administrative System for Import Support (OASIS) import data processing system to provide import reviewers with rapid and direct access to information necessary to make entry decisions about biologic products.

Patient Safety/AERS + $2,200,000 and 9 FTE

The authority to operate the program is found under Title 42 CFR Subchapter XIX.

- Expand and upgrade the current Biological Product Deviation Reporting System (BPDR). This system contains reports from the product manufacturer of any event associated with the manufacturing of a biological product, including testing, processing, packing, labeling, and storage, or with the holding or distribution of a licensed biological product in which the safety, purity, or potency of a distributed product may be affected.

- Expand the monitoring of reports from the Vaccine Adverse Event Reporting System (VAERS), MEDWatch and hospital fatality reports for biologic related cases. FDA proposes to link to existing external data sources held by both private and government organizations. For example, emergency rooms, poison control centers, health care systems, and the Centers for Disease Control and Prevention, all collect important information on adverse reactions.

- Explore the feasibility of utilizing the Medical Errors Reporting System for Transfusion Medicine (MERS-TM) to perform data aggregation and analysis for AERS. MERS-TM was developed under NIH funding and could serve as the model for the FDA blood error reporting. MERS-TM encourages non-punitive reporting with a well-defined codified method of reporting.

Human Subject Protection + $3,900,000 and 18 FTE

The authority to operate the program is found under Title 42 CFR Subchapter II Part F Subpart 1.

- Perform random inspections of Phase I and II clinical trials for compliance with regulations including human-subject protection considerations. Perform random inspections of Phase I and II clinical trials for compliance with regulations including human-subject protection considerations. This will improve the Agency's ability to monitor clinical trials where a Biologic License Application (BLA)/Product License Application (PLA) has not been submitted. Human subjects are enrolled in clinical trials but historically, no FDA inspection for compliance with regulations, including human-subject protection considerations, takes place until a BLA/PLA is submitted.

- Participate in bioresearch monitoring (BIMO) conferences/workshops to increase sponsor/investigator knowledge of FDA regulatory requirements, especially among developers of new products who have less familiarity with regulations and requirements.

- Review monitoring plans and seek modifications as warranted to improve the quality of monitoring. FDA also proposes to perform surveillance and "for cause" inspections of clinical trials to assess whether the plans are being followed and whether monitoring is sufficiently adequate to identify and correct critical problems.

- Increase by about 50 the number of BIMO oversight inspections.

Current Law User Fees + $3,190,000

Prescription Drug User Fee Act II (PDUFA II)

The Prescription Drug User Fee Act of 1992 (PDUFA) authorized the assessment and collection of user fees for drug applications, establishment registrations, and product listings to enhance and expand FDA's existing review process.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) reauthorized the collection of prescription drug user fees (PDUFA II) to enhance the human drug review process, including some biological products, through FY 2002. The Act established fees for applications, establishments, and approved products. PDUFA is a model for reinventing government with Congress, the Agency, the industry and consumer groups working together to provide necessary resources, to set performance goals, and to hold the Agency accountable. Review performance monitoring is done in terms of fiscal year cohorts, e.g., the FY 1998 cohort includes applications received from October 1, 1997 through September 30, 1998. Fiscal year cohort performance is not immediately measurable at the end of the fiscal year. The measurable outcome will occur

either 6 or 12 months after the last submission received during the fiscal year, depending upon the category of submission. FDA has met or exceeded all its performance goals. The fees collected in FY 2002 will enable the FDA to continue to meet its PDUFA II performance goals including:

- Review and act on 90 percent of standard original NDAs and PLAs/BLAs filed during FY 2002 within 10 months of receipt;

- Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during FY 2002 within 6 months of receipt;

- Review and act on 90 percent of standard efficacy supplements filed during FY 2002 within 10 months of receipt;

- Review and act on 90 percent of priority efficacy supplements filed during FY 2002 within 6 months of receipt;

- Review and act on 90 percent of manufacturing supplements filed during FY 2002 within 6 months of receipt and review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt;

- Review and act on 90 percent of Class 1 resubmitted original applications filed during FY 2002 within 2 months of receipt; and,

- Review and act on 90 percent of Class 2 resubmitted original applications received during FY 2002 within 6 months of receipt.

JUSTIFICATION OF BASE

Activities Related to Increases for FY 2002

Payroll

- FDA's Biologics program ensures the safety, purity, potency and effectiveness of biological products (primarily vaccines, blood and blood products, and therapeutics), most of which represent the leading edge of technology. The Agency also monitors over 5,000 biological firms to ensure they are in compliance with quality and safety regulations.

- The field component of Biologics inspects regulated industry, and collects and analyzes samples. Other activities that often arise are review and management of enforcement actions, and consumer complaints, trace back efforts, and review of import entries for admissibility decisions. These functions are inherently governmental and highly personnel intensive.

Bovine Spongiform Encephalopathy (BSE)

- FDA continues to emphasize the need to protect the nation's blood supply, and minimize any risk to patients of acquiring BSE or Creutzfeldt-Jakob Disease (CJD), and other blood-borne diseases. FDA conducts research of blood and blood products pertinent to FDA's regulatory mission. No tests for the rapid diagnosis of either BSE or CJD or for detection of infected tissue has been validated as either sufficiently specific or sensitive to be used to screen the blood supply. A reliable blood-screening test for BSE is an extremely important goal and is currently the object of considerable research activity.

- BSE issues have featured prominently this past year, following the determination that at least one vaccine manufacturer had not followed FDA guidelines not to use bovine-derived materials from BSE-identified countries. A complete survey of all vaccine manufacturers was conducted and the results discussed at a joint Transmissible Spongiform Encephalopathies (TSE) and Vaccine Related Product Advisory Committee (VRPAC) advisory committee meeting. All manufacturers have agreed to address, in a timely manner, all deviations from FDA policies.

Imports and Inspections

- Provide emergency operation, investigation and response for incidents involving regulated products.

- Coordinate field investigational analytical compliance activities among the five regulatory centers.

Patient Safety/AERS

- Maintain the Agency's system of postmarketing surveillance and risk assessment program to identify adverse event reports (AERS) that did not appear during the product development process by collecting, evaluating and acting on information of AERS associated with marketed products.

- Maintain reporting systems to collect biological product deviation events that occur during manufacturing processes or storage of all biological products, including blood product manufacturers and blood-banking facilities.

Human Subject Protection

- Expedite development and licensing of safe and effective biological products and ensure patient safety through an effective, comprehensive bioresearch monitoring (BIMO) program in the Biologics program. BIMO staff in the Office of Compliance and Biologics Quality (OCBQ) work closely with the review offices to accomplish the Agency's current BIMO program, but recent and highly publicized developments have highlighted the need for several critical changes in the program to address this rapidly changing product development environment.

- Bolster the protection of clinical study participants and the integrity of high risk clinical trials including gene therapy trials.

- Conduct inspections to increase oversight of high risk Investigational New Drug (IND) applications including gene therapy.

- Issue a proposed rule on the public disclosure of information regarding gene therapy and xenotransplantation clinical trials that would provide more information on these trials to the general public, and conduct regulatory research to improve product safety.

- Provide guidance documents to industry and other interested parties on gene therapy products and take action to build upon existing guidance.

- Convene a conference of investigators whereby the most experienced professionals in the field discuss the appropriate monitoring practices.

Activities Related to Other Priority Areas

Regulation of Human Tissue Intended for Transplantation

- Establish comprehensive risk-based oversight of communicable disease transmission from human tissues and cells intended for implantation, transplantation, infusion or transfer. FDA has finalized the proposed rule for tissue establishment registration, listing of human cells, tissues, and cellular and tissue-based products. The Agency needs to move forward on amending the current good manufacturing practice regulations that apply to human cellular and tissue-based products regulated as biological products as well as implementing new donor-suitability procedures. Scientific information gathering, analysis, and policy development is required prior to implementation of the full regulation program. Recent concerns about the safety of human tissues has led the Agency to believe that collection of basic information about the rapidly growing human tissue industry, as well as, proceeding toward implementing regulation of the industry is vital at this time.

Countering Bioterrorism

- Develop safe and effective vaccines and biological products in preparation for defense against biological weapons. The ability of FDA to guide these products through the regulatory process, which includes the manufacturing process, pre-clinical testing, and license application review process determines the speed with which these products will be available for use. Manufacture of biologic products requires intense oversight due to the delicate nature of these products, which are sensitive to heat, light, movement when in liquid form, and are more susceptible to contamination.

- Work with the sponsors of products, as well as contributing and coordinating with other government agencies on the goals of this program. Significant progress is being made. FDA has begun in the last year to focus incremental resources received through the appropriations process as well as funding from the DHHS Public Health and Social Services Emergency Fund on this program.

Xenotransplantation

- Regulate xenotransplantation clinical trials conducted within the United States. The development of xenotransplantation is, in part, driven by the fact that the demand for human organs for clinical transplantation far exceeds the supply. Moreover, recent evidence has suggested that using animal cells and tissues may be therapeutic for certain diseases such as neurodegenerative disorders, liver failure, and diabetes, where, again human materials are not usually available.

- Establish public health policy in xenotransplantation. Although the potential benefits are considerable, the use of live animal materials raises concerns regarding the potential infection of recipients with both recognized and unrecognized infectious agents and the possible subsequent transmission to their close contacts and into the human population. Potential cross-species infection with persistent viruses, such as retroviruses, is of particular public health concern because they may be latent and lead to disease years after infection. Moreover, new or emerging infectious agents may not be readily identifiable with current techniques. As the AIDS epidemic has demonstrated, persistent viral infections may result in person-to-person transmission for many years before clinical disease develops in the index case, thereby allowing an emerging infectious agent to become established in the susceptible population before it is recognized.

Selected FY 2000 Accomplishments

Prescription Drug User Fee Act (PDUFA)

- Review performance monitoring is being done in terms of cohorts, *e.g.*, the FY 2000 cohort includes applications received from October 1, 1999 through September 30, 2000.

- The FY 2000 cohort review performance goals covered under PDUFA for New Drug Applications (NDA), Product License Application (PLA), and Biologics License Application (BLA) are:

    - Reviewed and acted on 90 percent of standard original NDAs/PLAs/BLAs filed during FY 2000 within 12 months of receipt and reviewed and acted on 50 percent within 10 months of receipt in compliance with PDUFA goals; and,

    - Reviewed and acted on 90 percent of priority original NDA and PLA/BLA submissions filed during FY 2000 within 6 months of receipt.

Blood and Blood Products

- Continued to implement the Blood Action Plan to update the blood regulations, reinvent blood regulations, address emerging infectious diseases, ensure compliance of plasma fractionation establishments, blood donor/recipient notification and look back, and FDA emergency and Class I recalls affecting blood safety response procedures. Reduced the number of exemptions to outdated blood regulations and the number of guidance documents lacking enforceability. Increased blood industry's compliance with standards. The Blood Action Plan has greatly enhanced the regulatory oversight and safety of the nation's blood supply.

- Responded to constantly emerging potential threats to the blood supply in a timely and coordinated approach. Examples of the emerging threats include: new HIV variants; new hepatitis agents; human herpes virus-type 8; and Creutzfeldt-Jakob Disease. A specific scientific and regulatory strategy must be developed for each identified threat. The Agency, in collaboration with the CDC and the NIH, engaged in the scientific investigation of the emerging infectious agents. The actions will include an assessment of the risk to the blood supply, diagnostic methods, standards development and regulatory controls.

Vaccines

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

- Approved Diptheria and Tetanus Toxoids and Acellular Pertussis Vaccine, Adsorbed, (trade name Tripedia) for an expanded patient population. The expanded patient population includes a 5th dose at 4-6 years of age after 4 prior doses of Tripedia. Tripedia is a product of Aventis, Pasteur, Incorporated of Swiftwater, PA.

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

- Expedited lot release of influenza virus vaccine through the manufacturing time period. The process of manufacturing the influenza virus vaccine is a very complex one, complicated by the large number of doses administered in a very short time frame. Currently there are three licensed manufacturers of influenza virus vaccine: Medeva Pharmaceuticals. Incorporated manufactures Fluvirin; Aventis-Pasteur, Incorporated (Connaught Laboratories, Incorporated) manufactures Fluzone; and Wyeth Laboratories, Incorporated manufactures Flushield.

- Analyzed patterns of reporting associated with vaccines and vaccine lots. FDA analyzed 6,160 lots in FY 2000. In analyzing patterns of adverse event reporting, the Agency considers more than just the numbers of reports for a lot. More reports will be received for a large lot than a small one, simply because more doses of vaccine from the large lot will be given to more children. Some lots contain as many as 700,000 doses, while others as few as 20,000 doses. Similarly, more reports will be received for a lot that has been in use for a long time than a lot for a short time. When a lot is detected that has received more serious reports than should be expected on the basis of such factors as size, time in use, and chance variation, further investigations are initiated to determine if the lot continues to be safe for use, or if a recall is needed. FDA applies procedures and methods of analysis to help us to understand these complex factors and closely monitor the safety of vaccines. These factors are continually analyzed to ensure that all lots in use are safe.

Therapeutic Products

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

- Published "Suitability Determination for Donors of Human Cellular and Tissue-Based Products" and "Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood Hematopoietic Stem/Progenitor Cell Products" in the Federal Register on April 18, 2000. The comment period for both proposed rules was reopened for 90 days. Through increased tissue regulation, public health will be improved and public confidence will be increased.

Countering Bioterrorism

- Received one-time funding of $7.5 million in FY 2000, from the DHHS Public Health and Social Services Emergency Fund to begin the process of developing the necessary expertise and infrastructure to address regulatory activities for the Countering Bioterrorism activity. The one-time funding was used for activities to expeditiously develop and license new vaccines for anthrax and smallpox and the associated vaccinia immune globulin products used to treat or prevent serious vaccinia infections brought on by the smallpox vaccine.

- Developed regulatory models to accommodate the need for preparedness in the case of an emergency attack. For example, procedures and protocols are being developed to enable the use of investigational new drugs in a highly controlled, safe manner for particular emergency situations, such as responding to a bioterrorist attack that exposed individuals to the agent that causes anthrax.

- Prepared well orchestrated, timely and seamless responses to potential bioterrorist attacks. FDA participates in bioterrorism response interagency working efforts. CBER participated in numerous meetings, briefings, and conferences representing FDA with staff from the Department of Defense, the Office of Management and Budget, the DHHS, as well as, other PHS agencies, including the NIH and the CDC. Coordination with industry and outside organizations.

- Developed and expeditiously licensed products to diagnose, treat, or prevent outbreaks from exposure to the pathogens that have been identified as bioterrorist agents. These products must be reviewed and approved prior to the large-scale productions necessary to create and maintain a stockpile. Staff must guide the products through the regulatory process, including the manufacturing process, pre-clinical testing, clinical trials, and the licensing and approval process. This process is extremely complex and early involvement by staff is crucial to the success of the expedited review process.

Human Subject Protection Program

- Announced, with NIH, two new programs to further strengthen the safeguards for individuals enrolled in clinical studies for gene therapy. FDA's Clinical Trial Monitoring Plan addresses emerging evidence that the monitoring by study sponsors of several recent gene therapy trials has been less than adequate. FDA will require that sponsors of gene therapy trials routinely submit their monitoring plans to the FDA. The Gene Transfer Safety Symposia enhances patient safety by providing critical forums for the sharing and analysis of medical and scientific data from gene transfer research.

- FDA and NIH have taken individual and cooperative actions to achieve greater adherence by researchers to existing requirements and guidance and to bolster the protection of study participants and the integrity of gene therapy trials. These include:

    - Conducted with NIH, more inspections to increase oversight of Investigational New Drug Applications (INDs) in gene therapy;

    - Issued a proposed rule on the public disclosure of information regarding gene therapy clinical trials that would provide more information on these trials to the general public; and,

    - Provided guidance documents to industry and other interested parties on gene therapy products and will take action to build upon existing guidance.

- Biotechnology-produced products have increased dramatically in recent years. The number of INDs received rose from five in FY 1980 to 453 in FY 2000. During FY 2000, FDA received 11,121 investigational amendments for biotechnology INDs. Much of this growth has been in the area of somatic cell/gene therapy and xenotransplantation products for which there were nine INDs in FY 1989 increasing to 146 INDs in FY 2000. Adjunct procedures used in gene therapy, such as stem cell isolation, are also rapidly increasing, leading to a secondary rise in device and biological submissions related to this area.

Biologics
Program Activity Data

Program Workload and Output	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Total Original License Application (PLA/ELA/BLA) Reviews[1/]	98	145	145
PLA/BLA Approval	56	60	65
Mean PLA/BLA Approval Time (months)	6.0	8.0	8.0
Median PLA/BLA Approval Time (months)	1.84	4.0	4.0
License Supplement (PLA/ELA/BLA) Reviews[1/]	2,159	1,950	1,950
NDA & NDA Supplement Approvals	57	40	40
ANDA & ANDA Supplement Approvals	5	5	5
PMA & PMA Supplement Reviews[1/]	17	30	30
510(k) Reviews[1/]	30	110	160
Commercial IND/IDE Receipts	303	300	300
IND/IDE Amendments Receipts[2/]	14,914	15,000	15,000
Active INDs/IDEs[2/]	3,565	3,600	3,600
Bioresearch Monitoring (BIMO) Inspections	167	120	170
Inspections	1,802	2,130	2,140
Adverse Reaction Report Reviews[3/]	31,853	22,300	22,300
Biologic Product Deviation Report Received	23,528	25,000	27,000

[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 files receipts.
[3/] Includes MedWatch, Foreign reports and VAERS reports.

Animal Drugs and Feeds

	FY 2000 Actual	FY 2001 Appropriation	FY 2001 Current Estimate [1/]	FY 2002 Estimate [3/]	FY 2002 +/- FY 2001 Current Estimate
Total Program Level [2/]	**$49,593,000**	**$64,069,000**	**$63,928,000**	**$81,809,000**	**+ $17,881,000**
Center ($000)	*$36,471,000*	*$49,025,000*	*$48,917,000*	*$54,323,000*	*+ $ 5,406,000*
FTE	*271*	*311*	*306*	*320*	*+14*
Field ($000)	*$13,122,000*	*$15,044,000*	*$15,011,000*	*$27,486,000*	*+$ 12,475,000*
FTE	*135*	*158*	*154*	*255*	*+101*
Total Budget Authority [2/]	**$49,593,000**	**$64,069,000**	**$63,928,000**	**$81,109,000**	***+$17,181,000***
Pay Increases					*+ 2,354,000*
BSE			*1,100,000*	*14,200,000*	*+13,100,000*
Imports/Inspections			*17,393,000*	*17,693,000*	*+ 300,000*
~~Food Safety~~			*39,134,000*	*40,634,000*	*+ 1,500,000*
Total User Fees	**$0**	**$0**	**$0**	**$700,000**	**+ $700,000**
Proposed User Fees					
Imports and Inspections	*$0*	*$0*	*$0*	*$700,000*	*+ $700,000*

[1/] Reflects the enacted levels adjusted for the 0.22 percent rescission, which accounts for $141,000 in the Animal Drugs & Feed program.
[2/] Reflects a decrease in base funding from FY 2001 of $73,000, for Human Subject Protection & Bioterrorism.
[3/] Pay increases shown on separate line, and not reflected in individual increase areas.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
1998 Actuals	$41,354,000	$41,354,000	$0	391
1999 Actuals	$43,253,000	$43,253,000	$0	393
2000 Actuals	$49,593,000	$49,593,000	$0	406
2001 Current Estimate	$63,928,000	$63,928,000	$0	460
2002 Estimate	$81,809,000	$81,109,000	$700,000	575

MISSION

- Protect the health and safety of all animals that serve either as companions or food sources for mankind.
- 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 the resulting products are safe, wholesome, and free of drug residue when they reach the consumer.
- Surveillance of marketed products for all animal drugs and feeds to minimize harm to humans or animals which might arise from the use of these products. This is accomplished through science-based review of drug experience reports, nationwide monitoring systems, and compliance programs implemented by the FDA field offices through inspections, sample collections and analysis, and investigations.

REQUESTED INCREASES

Pay Increase + $2,354,000

FDA's request for funds to cover pay cost increases is vital to the Agency because personnel are so essential to accomplishing its mission. Pay increases have a major impact on FDA because the Agency is more people-intensive than many other government agencies. Payroll accounts for over 60 percent of the total FDA budget. This has a significant impact on all activities in FDA, particularly the field. In order to maintain the level of activities carried out in FY 2001, FDA is requesting $40,000,000 to cover the cost of the FY 2002 pay raise, annualization of the FY 2001 pay raise, anticipated within grade increases, and one extra day of pay. The Animal Drugs and Feeds Program portion of this increase is $2,354,000.

Funding of the pay increase is necessary to ensure the integrity of the Agency's work in the field labor force for inspections, compliance, and for the Center for Veterinary Medicine (CVM) to sustain recent progress made toward meeting the core statutory requirements of the program. Specifically, this increase will position the program to maintain the FY 2001 levels of 75 percent of new animal drug applications (NADAs) and Abbreviated New Animal Drug Applications (ANADAs) reviewed and acted on within 180 days, conduct biennial inspections of 50 percent of animal drug and feed manufacturers, and continue to provide, through NARMS an early warning system for identifying emerging resistance in food borne pathogens.

Bovine Spongiform Encephalopathy (BSE) + $13,100,000 and 105 FTE

Bovine Spongiform Encephalopathy (BSE), widely known as "Mad cow disease" is a deadly chronic, degenerative disorder affecting the central nervous system of cattle. The first case was diagnosed in 1986 in Great Britain, and is spread via meat-and-bone meal fed to cattle. Some of the feed given to cattle includes remnants of the slaughtering process, such as the brain and spinal cord, which may harbor the agent that causes BSE. BSE belongs to a group of progressive degenerative neurological diseases known as transmissible spongiform encephalopathies (TSEs). There is strong epidemiologic and laboratory evidence suggesting that the human disease of new variant Creutzfeldt-Jakob disease (vCJD) and BSE are caused by the same infectious agent. The goal of FDA is to prevent the introduction of BSE in U.S. cattle.

On August 4, 1997, FDA's Regulation, entitled "Animal Proteins Prohibited From use in Animal Feed" was finalized. The purpose of the rule is to prevent the establishment and amplification of BSE through animal feed. The regulation prohibits the use of certain proteins derived from mammalian tissue in feeding ruminant animals. Active surveillance efforts have yet to detect BSE in the U.S. If BSE were to enter the U.S., it would pose a serious health risk to humans, and be financially devastating to the U.S. beef industry. FDA's goal is to assure 100 percent compliance with the BSE feed regulation through inspections and compliance actions. With this increase, FDA will:

- Modernize the existing information technology infrastructure to facilitate electronic inspection reporting and information collection and distribution;

- Develop and validate detection methods for BSE collaborating with experts and foreign scientists to assist in developing BSE methods;

- Educate industry and the general public on BSE through public meetings, publications, and FDA's website;

- Review and evaluate field inspection data and take enforcement action when necessary;

- Train Federal and state inspectors on the BSE feed regulation, update them on the current European Union situation, Animal Plant and Health Inspection Service (APHIS) authority and approach, and what to look for and how and when to sample;

- Develop a domestic sampling plan, collecting and analyzing 600 domestic feed, and feed component samples for BSE related contaminants. In addition, the Animal Drugs and Feeds Program will increase the number of import samples by 600. This sampling plan will ensure proper labeling of animal feeds and feed components;

- Conduct targeted BSE inspections of all renderers and licensed and non-FDA licensed feed mills handling prohibited material, such as meat and bone meal on a yearly basis;

- Leverage with State agencies by funding approximately 4,000 contract inspections of feed mills and renderers, and conduct compliance, follow-up, and audit inspections to state contracts; and,

- Provide intensive line entry and label review of an anticipated 175,000 import line entries for use in domestic commerce for the Animal Drugs and Feeds Program by expanding import staff by 17 FTE.

Imports and Inspections + $1,000,000 and 4 FTE (Budget Authority +$300,000 and 2 FTE; User Fees +$700,000 and 2 FTE)

Budget Authority

Surveillance of the animal drug industry and the marketplace for imports is necessary to assure that animal drugs are available and that they are manufactured according to Good Manufacturing Practices (GMPs). This is necessary to ensure that companion and other non-food animals are

treated with safe imported products. The importation of food and animal feed from other countries with facilities that lack proper food safety process controls is growing. For imports the Animal Drugs and Feeds Program collects samples and conducts a laboratory analysis on about 0.3 percent of animal drug and feed products. The ability to protect consumers will be compromised without additional inspectors and updated review criteria to examine imports. With this increase FDA will:

- Increase domestic inspection and take appropriate regulatory action when necessary;
- Ensure current information is available to import examiners to ensure well founded regulatory decisions; and,
- Conduct 30 inspections for illegal residue and contaminants in domestic animal feed.

Proposed User Fees

FDA proposes to collect $700,000 in additive import user fees to fund the Operational and Administrative System for Import Support (OASIS), and other import operations. The OASIS system enables FDA to substantially reduce the risk of potentially harmful foods and other imported products reaching the American market place. The importer/broker community benefits through faster turn-around times, elimination of large volumes of paperwork, and reduced costs of doing business. OASIS will give FDA staff access to historical information to better target products and firms at high risk, the ability to plan inspections more effectively, and the ability to share findings from inspection and lab analyses with other offices. With this increase FDA will:

- Modernize the Operational and Administrative System for Import Support (OASIS) to allow import reviewers to have rapid and direct access to information necessary for entry decisions; and,
- Increase data audits, import filer training, and liaison activities to ensure the integrity of import data submitted by import filers.

Food Safety + $1,500,000 and 6 FTE

The Animal Drugs and Feeds Program is requesting food safety increases in four areas: Antimicrobial Resistance, Hazard Analysis and Critical Control Point (HACCP), aquaculture, and animal biotechnology. The first area, antimicrobial resistance is a top priority for the Center and is important because several bacterial species have developed strains that are resistant to multiple antimicrobial drugs. We need to take steps to minimize food borne disease outbreaks and identify emerging health problems from non-human use os antibiotics. The next increase, HACCP is a systematic approach for assuring food safety, and is employed by segments of the food industry and federal regulatory agencies to control and prevent hazards, most notably those of microbiological origin. The third increase, aquaculture, is a rapidly growing industry abroad, and discussions with foreign governments reveal that there are many animal drugs used in the production of imported aquaculture products which are not approved, and are even banned in the U.S. Ingestion of animal drug residues and contaminants that may be contained in imported food products could potentially cause unsafe conditions for humans, ranging from drug allergies

to cancer. The fourth area is Biotechnology, or genetically engineered animals. This industry is characterized by entrepreneurs and small companies due to the relatively low startup costs for production. Since the science is only now emerging we must conduct research, develop testing methods and build the regulatory system for these products. With this increase, FDA will:

- Conduct research to identify food animal species causing human drug resistance;

- Develop educational devices, such as interactive CD-ROMS, to describe the issue of antimicrobial resistance and government and industry efforts taken to reduce or eliminate risks to consumers from the use of antimicrobials in food-producing animals;

- Propose HACCP regulations for the animal and vegetable rendering (processing) industry by September, 2002, and organize a pilot program with one or two manufacturing plants. FDA regulation 21 CFR 500.35 declares certain feed ingredients to be adulterated under 402(a) of the Federal Food Drug and Cosmetic Act if they contain Salmonella;

- Develop training programs for federal and state inspectors to conduct HACCP audit inspections and co-sponsor workshops with the field to gather information and support from the feed industry;

- Compile a list of animal drugs that are used in foreign aquaculture and develop risk assessment priorities by importance to human health, through literature searches and equivalence discussions with other nations;

- Prepare guidances to the industry explaining that animal biotechnology products are subject to premarket approval as new animal drugs and the information required to show safety and effectiveness for this class of products; and,

- Develop an inventory of firms that are developing products derived from bioengineered animals. If animals are milked or they produce offspring, the planning should address their safe disposition because they may not be suitable for use as a human food source or to be rendered and processed into an animal feed component.

JUSTIFICATION OF BASE

Activities Related to Increases for FY 2002

Payroll

- FDA's Animal Drugs and Feeds program protects the health and safety of all animals that serve either as companions or food sources for mankind. This is accomplished through processing premarket applications to increase the availability and diversity of safe and effective veterinary products that relieve animal pain and suffering, while ensuring the resulting products are safe, wholesome, and free of drug residue when they reach the consumer; and through the surveillance of marketed products for all animal drugs and

feeds to minimize harm to humans or animals which might arise from the use of these products.

- The field component of Animal Drugs and Feeds inspects regulated industry, and collects and analyzes samples. Other activities that often arise are review and management of enforcement actions, and consumer complaints, trace back efforts, and review of import entries for admissibility decisions. These functions are inherently governmental and highly personnel intensive.

Bovine Spongiform Encephalopathy (BSE)

- Enforce the rule "Animal Proteins Prohibited From Use in Animal Feed". Prevent the establishment and amplification of BSE through animal feed. The regulation prohibits the use of certain proteins derived from mammalian tissue in feeding ruminant animals. In addition update compliance guidance regulations, when necessary, and work with state counterparts on the coordination and inspection of all renderers, protein blenders, and feed mills, as well as some of the ruminant feeders.

- Maintain relationship with industry using telecommunication and conferences to provide information on regulation compliance and share inspection data.

Food Safety

- Leverage with the USDA Agriculture Residue Violation Information System and the FDA Tissue Residue Information Management System.

- Participate on a Joint Subcommittee on Aquaculture of the National Science and Technology Council of the Office of Science and Technology Policy in the Office of the Science Advisor to the President to encourage the development of safe and effective aquaculture in the United States. Assist in the development of approved aquaculture drugs through participation in the National Research Support Project #7 (NRSP #7).

- Identify emerging resistance in food borne pathogens through an early warning system, the National Antimicrobial Resistance Monitoring System (NARMS). This has improved our ability to detect emerging resistance among food borne pathogens.

- Reduce the transfer of resistant animal pathogens to humans by conducting research studies and risk assessments that will yield future benefits, and begin to reverse the trend of food borne pathogen antibiotic resistance development.

- Deliver the food safety message to livestock producers and veterinarians at trade shows to educate them on the risk of antimicrobial resistance of bacteria following the use of antimicrobial drugs in food animals.

- Work with the public on the education of biotechnology products and assist developers through the regulatory process, while continuing research on challenging biotechnology issues.

Imports and Inspections

- Inspect 50 percent of statutory biennial inspections, which include registered animal drug and feed establishments and FDA licensed feed mills, and provide postmarket inspectional coverage and investigations for domestic establishments. In addition continue sampling program for animal feeds detained at U.S. ports of entry in the U.S. that contained ingredients possibly derived from contaminated animals.

- Develop laboratory analytical methods to permit the analyses of products for chemical and microbiological hazards, and performed laboratory validation of analytical methods submitted to support pre-market product applications.

Activities Related to Other Priority Areas

Premarket Activities

- Increase availability of safe and effective animal products, by reviewing animal drug applications in a timely manner for safety and effectiveness, and continue to work with regulated industry to minimize drug development time.

- Continue pre-submission conferences, meeting, and workshops with industry, and support electronic submission of applications.

- Conduct method validation studies required before applications for new drugs for food producing animals can be approved.

- Continue to expand inspectional expertise emerging technologies and increase quality assurance to monitor the inspection process to improve the quality and timeliness of product reviews.

Bioterrorism

- Collaborate with state diagnostic laboratories to ensure they are aware of the potential for a terrorist attack against food-producing animals, and begin to develop a secure communication network in order to share intelligence information, and continue to participate in the planning for and coordination of exercises simulating responses to bioterrorist attacks.

- Develop an internet feed contaminants web-site to share information with federal and state governments, academia and industry.

Postmarket Activities

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

Selected FY 2000 Accomplishments

Premarket Review

New Product Applications – During FY 2000, the Office of New Animal Drug Evaluation (ONADE) processed 5,497 submissions for new animal drug applications (NADAs), abbreviated new animal drug applications (ANADAs), investigational new animal drug files (INADs), generic investigational new animal drug (JINADs) files and master files.

- Approximately 74 percent of the submissions for NADAs, ANADAs and supplements were processed within the applicable statutory time frame of 180 days;
- 72 submissions were for original NADAs and ANADAs, and 977 were for supplements to previously approved NADAs and ANADAs;
- FDA reviewed 367 phased data submissions under INADs and JINADs to support approvals; and,
- FDA published 53 documents in the Federal Register relating significant NADA and ANADA approvals. Significant approvals included: 3 new chemical entities, 8 products for use in new animal species, 1 new dosage form of a previously approved product and 4 products available in new dosages.

Antibiotic Resistance

Augmentations of NARMS during FY 2000 included:

- Testing non-typhoid Salmonella, Campylobacter, Enterococcus and E.coli isolates collected from animal sources; and, non-typhoid Salmonella, Campylobacter, Enterococcus, Shigella, Salmonella typhi and E. coli isolates from human clinical samples;
- Incorporated isolate collection from two additional state veterinary diagnostic laboratories;
- Began limited retail food testing in conjunction with the CDC; and,
- Continued studies with the University of California (Davis) and Michigan State University examining antimicrobial use on the farm.

International Expansion of NARMS:

- Conducted a pilot study with medical microbiologists from Mexican hospitals in close proximity to significant animal agriculture;
- Provided initial training for Mexican investigators in standardized laboratory methodologies for the isolation, identification, and antimicrobial susceptibility testing of food borne Salmonella; and,

- Sample collection and isolation of Salmonella from clinically ill humans in Mexican hospitals and from healthy children in community daycare centers.

Continued finalizing framework document describing FDA's regulatory approach:

- Obtained input through avenues such as public meetings, workshops, and federal register notices;

- Examined the objectives of pre-approvals studies and their role in making microbial safety determinations;

- Prepared and released a discussion paper for public comment, outlining a proposed approach for applying the threshold concept;

- Conducted and finalized risk assessment study on Campylobacter;

- Initiated risk assessment feasibility study on Enterococcus; and,

- Developed Antibiotics Sensitivity Screening of Salmonella, to detect Salmonella with resistant genes to multiple antibiotics.

Bovine Spongiform Encephalopathy (BSE)

- Continued work to prevent the introduction and spread of BSE in the United States.

- Issued an interactive CD-ROM that provides training on the BSE feed regulation for use by FDA, state regulatory authorities, and the regulated industry.

- Continued enforcement strategy to conduct inspections of 100 percent of renderers, protein blenders and feed mills, and a sampling of ruminant feeders to assure compliance with BSE regulation.

- Began an evaluation of the inspectional information on the BSE feed regulation to begin developing a strategy for the future.

- FDA provided technical expertise and assistance to the Department of Agriculture (USDA) in identifying entry criteria for import examination. FDA provided early information to its field offices in the identification of products susceptible to BSE contamination, and instructions regarding forwarding of this information to local USDA, Animal Plant Health Inspection Service (APHIS) offices.

- USDA/APHIS enacted an immediate prohibition on the importation of all meat and bone meal (MBM), bone/meat/blood meals, tankage, offal or any product containing such, which originates directly from Europe or was rendered/processed in European plants processing animal materials, regardless of the species of origin, including poultry and fish meal FDA issued an import bulletin to disseminate information to field import offices and to provide guidance to districts when they encounter any of these products.

Dioxin Contamination

FDA continued to follow through on earlier findings of animal feed contaminated with dioxins:

- Issued revised guidance to industry and the general public cautioning users of anti-caking products to check for dioxin;

- Coordinated an overall government response to the Environmental Protection Agency's (EPA) dioxin risk assessment report as a member of the Inter-Agency Working Group, and developed an extensive question and answer document made available to the public through agency web-sites; and,

- Issued a sampling assignment to determine dioxin-like compounds in animal fats, animal meals, oilseed meal, deodorizer distillates, and molasses.

Animal Drug Availability Act (ADAA)

The primary effect of the ADAA, enacted in 1996, was to modify the effectiveness standard for new animal drugs. The following steps have been taken to implement the ADAA:

- The final rule on Medicated Feed Mill Licensing was published in the Federal Register;

- Issued a proposed regulation to implement the Veterinary Feed Directive Drugs provision of the ADAA and, a proposed regulation describing the procedures for requesting, conducting, and documenting a pre-submission conference published; and,

- Provided technical assistance on legislation to implement FDA's proposal, the "Minor Animal Species Health and Welfare Act" (HR 4780), which was introduced in Congress.

Food and Drug Administration Modernization Act (FDAMA)

During FY 2000, Section 116 of FDAMA (section 506A of the act) has been implemented as follows:

- A proposed rule amending 21 CFR 514.8 supplemental new animal drug applications was published; and,

- A notice of availability of the draft companion guidance document to the above proposed rule entitled #83 Guidance for Industry: Chemistry, Manufacturing and Controls Changes to an Approved NADA or ANADA was announced.

Generic Animal Drug and Patent Term Restoration Act (GADPTA)

Generic animal drugs are approved under the Abbreviated New Animal Drug Application (ANADA) review process. FDA publishes a bimonthly listing of all approved new animal drug applications in the FDA Veterinarian. In FY 2000, the Office of New Animal Drug Evaluation (ONADE): approved ten ANADAs; received approximately a two-fold increase in JINADs (compared to FY 1999); and received 12 Suitability Petitions--six were approved, three were denied, one was not required, and two are currently under review.

Minor Use and Minor Species

Published a final rule to reclassify sheep as a minor species for all data collection purposes. This reclassification allows sponsors of new animal drug applications to extrapolate human food safety data from a major species such as cattle. This rule will allow the extrapolation of the tolerances for residues of new animal drugs in cattle to sheep.

Biotechnology

- CVM is working on a case study on genetically engineered salmon in an Office of Science and Technology Policy/Council on Environmental Quality (OST/CEQ) Interagency Working Group examining the regulatory framework for products of animal and plant biotechnology.

- CVM is contracting with the National Academy of Sciences/National Research Council (NAS/NRC) to examine risks and risk assessment methods for animal biotechnology products. An ad hoc steering committee of the National Research Council's Standing Committee on Biotechnology, Food and Fiber Production and the Environment will prepare a brief consensus report identifying risk issues concerning products of animal biotechnology.

Aquaculture

In support of Congressionally mandated aquaculture drug review in FY 2000:

- Hired two aquaculture drug reviewers and created the Aquaculture Drugs Team to perform review of aquaculture investigational new animal drug (INAD) files;

- Eliminated the backlog of aquaculture submissions awaiting review; and,

- Upgraded the aquaculture INAD database, and worked with INAD sponsors to generate the data necessary for aquaculture drug approvals.

Inspections and Recalls

- Provided audits of 1,000 feed mills, of which 350 were tissue residue domestic inspections completed by the states under contract to FDA.

- Awarded 19 state contracts for inspection of medicated feeds, 453 Good Manufacturing Practices (GMP)/BSE inspections and 96 BSE-only inspections for a total of $330,000 and 15 state tissue residue contracts for 548 inspections for a total of $260,000.

- In October 1999, Pet Valu International Inc. of Wayne, Pennsylvania recalled certain dog chew products manufactured by Farm Meats Canada Ltd. because of possible Salmonella contamination. Following notification from the Canadian Food Inspection Agency, FDA initiated inspections and sample collections that resulted in several nation-wide recalls and a seizure action.

- Non-pathogen related incidents were investigated by FDA, including: adverse reactions; chemical contaminants; recalls; and drug residues.

Animal Drugs and Feeds
Program Activity Data

Program Workload and Output	FY 2000 Actuals [1/]	FY 2001 Estimate	FY 2002 Estimate
New Animal Drug Applications Processed Originals: [2/]			
Received	28	57	57
Completed	30	53	53
Approved	23	22	22
Pending [3/]	23	27	31
Average (median) months from receipt to approval, original NADAs and reactivations	(14)	(12)	(12)
New Animal Drug Application Supplements: [4/]			
Received	1,286	1,276	1,276
Completed	854	848	848
Approved	279	550	550
Pending	662	1,090	1,518
Original Abbreviated New Animal Drug Applications:			
Received	55	63	63
Completed	42	53	53
Approved	7	22	22
Pending	35	45	
Average (median) months from receipt to approval, original ANADAs	(20)	(16)	(16)
Abbreviated New Animal Drug Application Supplements:			
Received	195	81	81
Completed	126	93	93
Approved	35	42	42
Pending	109	97	85

[1/] The Center has experienced an increase in the receipt of applications from FY 1999 to FY 2001. Companion animal drug applications received have increased by three-fold.
[2/] Includes originals and reactivations. If application is not approvable, the sponsor may submit additional information until the Agency is able to approve the application.
[3/] All applications received during a fiscal year are not reviewed during the same fiscal year. Pending applications indicates the number of applications in our backlog.
[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).

Animal Drugs and Feeds
Program Activity Data

Program Workload and Output	FY 2000 Actuals	FY 2001 Estimate	FY 2002 Estimate
Investigational New Animal Drug (INAD) Files:			
Received	3,422	5,000	5,000
Completed	3,072	4,318	4,318
Pending	1,200	1,882	2,564
Generic Investigational New Animal Drug Files:			
New Receipts	194	430	430
Final Actions	180	157	157
Pending	67	340	613
Plant Biotech Notification Processed	5	10	15
GRAS (Generally Recognized as Safe) Notifications/Petitions	3	10	20
Feed Mill License Applications Processed	64	60	60
Investigational Food Additive Petitions	27	50	50
Food (Animal) Additive Petitions [5/]	5	30	20
Domestic Inspections			
By FDA	981	1,440	2,470
By State Contract	1,313	790	4,790
By State Partnership	130	120	120
Field Exams/Tests by FDA			
Domestic	4	0	0
Import	199	100	100
Laboratory Sample Analyses by FDA			
Domestic	2,320	4,200	4,800
Import	277	170	770
Foreign Inspections by FDA			
All Other (including Feed Contaminant)	2	50	50
BIMO/Pre-Approval	30	40	40

[5/] Applications for non-drug substances added to animal feed are considered Food Additive Petitions, which require review and approval.

Animal Drugs and Feeds
Program Activity Data

Program Workload and Output	FY 2000 Actuals	FY 2001 Estimate	FY 2002 Estimate
Manufacturers' Drug Experience Reports (DERs) [6/]	4,800	4,800	4,800
Received	3,500	4,000	4,800
Reviewed			
Adverse Experience Reports (AERs)			
Received	18,000	24,000	30,000
Reviewed	12,000	18,000	24,000
Tissue Residue Program/Investigations	650	500	600
Animal/Medicated Feed Partnership Agreements	26	26	26

[6/] DERs contain AERs. Due to an increased number of AERs within the submitted DERs, the number of DERs completed is not as great as in the past (4,400 in FY 1998).

Devices and Radiological Health

	FY 2000 Actual	FY 2001 Appropriation	FY 2001 Current Estimate [1/]	FY 2002 Estimate [3/]	FY 2002 +/- FY 2001 Current Estimate
Total Program Level [2/]	**$170,257,000**	**$180,154,000**	**$179,791,000**	**$197,676,000**	**+ $17,885,000**
Center ($000)	*$120,493,000*	*$127,113,000*	*$126,844,000*	*$135,295,000*	*+ $8,451,000*
FTE	*1,018*	*1,009*	*1,009*	*1,022*	*+ 13*
Field ($000)	*$49,764,000*	*$53,041,000*	*$52,947,000*	*$62,381,000*	*+ $9,434,000*
FTE	*454*	*488*	*477*	*506*	*+ 29*
Total Budget Authority [2/]	**$157,656,000**	**$165,207,000**	**$164,844,000**	**$178,572,000**	**+ $13,728,000**
Pay Increases					*+7,317,000*
Imports/Inspections			*60,533,000*	*63,333,000*	*+2,800,000*
Patient Safety/AERS			*9,950,000*	*12,250,000*	*+2,300,000*
~~Human Subject Protec.~~			*4,897,000*	*6,397,000*	*+1,500,000*
Total User Fees	**$12,601,000**	**$14,947,000**	**$14,947,000**	**$19,104,000**	**+ $ 4,157,000**
MQSA	*12,601,000*	*14,947,000*	*14,947,000*	*15,404,000*	*+ 457,000*
Proposed User Fees					
Imports/Inspections	*0*	*0*	*0*	*3,700,000*	*+ 3,700,000*

[1/] Reflects enacted levels adjusted for the 0.22 percent rescission, accounting for $363,000 in the Devices program.
[2/] Reflects a decrease in base funding from FY 2001 of $189,000, for Human Subject Protection & Bioterrorism.
[3/] Pay increases shown on separate line, and not reflected in individual increase.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
1998 Actuals	$155,705,000	$144,329,000	$11,376,000	1,555
1999 Actuals	159,008,000	145,790,000	13,218,000	1,480
2000 Actuals	170,257,000	157,656,000	12,601,000	1,472
2001 Current Estimate	179,791,000	164,844,000	14,947,000	1,486
2002 Estimate	197,676,000	178,572,000	19,104,000	1,528

MISSION

- Meet all statutory responsibilities.
- Apply the Total Product Life Cycle model across the range of Devices and Radiological Health activities, by covering products from concept to obsolescence.
- Connect to the global public health community.
- Partner with stakeholders.
- Use science in the regulatory process to the maximum extent.
- Set and maintain standards for quality.
- Attract and retain people who want to help us fulfill our public health mission.
- Measure and set targets to assess our continuing impact on public health.

REQUESTED INCREASES

Pay Increase + $7,317,000

FDA's request for funds to cover pay cost increases is vital to the Agency because personnel are so essential to accomplishing its mission. Pay increases have a major impact on FDA because the Agency is more people-intensive than many other government agencies. Payroll accounts for over 60 percent of the total FDA budget. This has a significant impact on all activities in FDA, particularly the field. The costs of the pay increases are necessary to ensure the integrity of the Agency's work in the medical devices area for review of device applications, and the field labor force for inspections, compliance, and research functions.

In order to maintain the level of activities carried out in FY 2001, FDA is requesting $40,000,000 million to cover the cost of the FY 2002 pay raise, annualization of the FY 2001 pay raise, anticipated within grade increases, and one extra day of pay. The Medical Devices and Radiological Health Program portion of this increase is $7,317,000.

Imports and Inspections + $6,500,000 and 25 FTE (Budget Authority $2,800,000 and 13 FTE and Proposed User Fees $3,700,000 and 12 FTE)

Statutory authority/requirement for conducting biennial inspections of Class II and III device manufacturers is in Section 510(h) of the FFD&C Act and general statutory authority for conducting inspections is found in Section 704 of the Act.

Budget Authority

The device and radiological health industry is growing, and products are growing in clinical impact and technological complexity. FDA's inspection coverage is decreasing, and domestic recall rates are increasing. FDA does not conduct pre-clearance for lower risk Class I products, nor does the Agency routinely inspect the manufacturers of those products. In 2002, FDA anticipates a total inventory of 5,000 domestic and 2,600 foreign Class II and Class III firms. FDA estimates that the domestic inventory will include approximately 400–600 hospitals that will be registered as reprocessors of Class II or Class III devices that are designed and labeled for single use. Quality System Inspection Technique (QSIT)/Good Manufacturing Practices (GMP) inspections monitor the extent to which manufacturers conform to the Quality System requirements and provide educational feedback to manufacturers to help them make voluntary corrections or improvements to their quality systems and medical device reporting procedures.

By concentrating inspection resources on higher-risk manufacturers, FDA will still not be able to conduct routine inspections of Class I manufacturers. With increased funding, FDA will:

- Increase inspection coverage of domestic Class II and Class III manufacturers from 17 percent to 20 percent. FDA's statutory authority requirement is a 50 percent annual coverage rate;

- Maintain coverage of foreign Class II and Class III manufacturers at nine percent. The inventory of foreign manufacturers continues to increase each year;

- Conduct audits of the approximately 6,000 U.S. hospitals to determine which ones are reprocessing single use devices. The audits will validate whether the hospitals that continue to reprocess devices have registered and listed their products with FDA. The audits will be conducted through a survey mechanism;

- Improve the confidence that FDA has in the safety of foreign device products by implementing the European Mutual Recognition Agreement; and,

- Improve imported medical device compliance by increasing surveillance and product testing of these products.

Proposed User Fees

FDA proposes to collect $3,700,000 in additive import user fees to fund the Operational and Administrative System for Import Support (OASIS), and other import operations. The OASIS system enables FDA to substantially reduce the risk of potentially harmful foods and other imported products reaching the American market place. The importer/broker community benefits through faster turn-around times, elimination of large volumes of paperwork, and reduced costs of doing business. OASIS will give FDA staff access to historical information to better target products and firms at high risk, the ability to plan inspections more effectively, and the ability to share findings from inspection and lab analyses with other offices. In addition FDA will:

- Increase coordination with the U.S. Customs Service and improve the effectiveness of cargo control activities at Ports, and the monitoring of products that have been refused entry pending exportation or destruction (follow-up-to-refusals);

- Expand import entry review resources to keep pace with the increase in line entries. By FY 2002 Devices import line entries may reach 1.7 million;

- Update the criterion that determines which import line entries are selected for on screen review on a risk basis and the frequency of on-screen review will be increased; and,

- Increase data audits, import filer training and liaison activities and improve data submitted by import filers.

Adverse Event Reporting + $2,300,000 and 10 FTE

FDA's Medical Device Reporting authority is Section 519(b) of the FFD&C Act.

FDA estimates that there may be as many as 300,000 injuries and deaths annually associated with device use. FDA currently receives about 90,000 adverse event reports every year, with only five percent coming from user facilities. This severe under reporting is attributed to a lack of recognition of device events, concerns over liability, lack of feedback from FDA, and the reporting burden.

In FY 2002, FDA will continue to build the Medical Product Surveillance Network (MeDSuN) program. The MeDSuN approach is designed to correct these problems and improve the quality and quantity of the data received from the user facility community. As the MeDSuN network grows, FDA's ability to detect and analyze medical device problems in the user community will improve, allowing FDA to be more proactive in preventing injuries and deaths. With the increase, FDA will:

- Maintain the existing 100 facilities in the program, which includes both hospitals and nursing homes;

- Recruit between 75-100 new user facilities and expand the program to include other types of user facilities such as ambulatory care surgical centers; and,

- Expand data analytic capability, and outreach and feedback opportunities to the medical community, industry, and other stakeholders.

Human Subject Protection + $1,500,000 and 7 FTE

The authority to operate the program is found under 21 CFR Part 50.

The protection of human subjects who participate in research is fundamental. Research study volunteers, who may or may not even benefit from participating in a clinical trial, and who accept some degree of risk in doing so, deserve the assurance that their protection is a top priority. Currently, human subject protection in device clinical trials is fragmentary. The program is correcting big problems, but there are many more research problems that we are not able to detect and address.

FDA's Bioresearch Monitoring (BIMO) Program inspects sponsors, contract research organizations, monitors, and institutional review boards (IRB) to ensure that the rights and welfare of human subjects who participate in device research are protected, and to verify that data collected by the regulated industry are accurate and reliable. An IRB is a group formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, modify, or disapprove research.

FDA would use the increase in funding to:

- Increase by 30 percent the annual number of FDA onsite inspections of the device

research community, focusing on increased IRB and Sponsor/Monitor inspections. Domestic inspections would grow from 250 in FY 2001 to 325 in FY 2002;

- Work more effectively with non-compliant firms and IRBs to develop and implement corrective and preventive actions to their human subject protection and research integrity systems;

- Follow-up on complaints of research misconduct that may place research subjects' welfare at risk;

- Recruit and train additional staff with expertise in legal, ethical and/or clinical research areas associated with medical device research. This expertise will strengthen FDA's ability to address policy matters and develop guidance that are important and meaningful to our stakeholders;

- Increase FDA's voluntary compliance efforts by educating those involved in critical areas of human subject protection and device research;

- Maintain and update the knowledge, skills, and abilities of existing staff in the areas of evolving and breakthrough device technologies and their related regulatory issues;

- Establish a bioresearch monitoring investigators certification program that through training and practical experience will improve the quality, consistency, and effectiveness of inspection and assure that investigators keep pace with emerging issues in clinical research;

- Improve the timeliness of the Clinical Investigator Disqualification Process and improve the consistency of these actions in the device program;

- Conduct a requirement's analysis to determine the cost and features of an information system that will track and coordinate the many FDA bioresearch monitoring activities; and,

- Leverage agency resources through interagency cooperation and international resources to increase awareness and understanding of the Bioresearch Monitoring Program by pre-clearance review scientists.

Current Law User Fees

Mammography Quality Standards Act + $457,000

The Mammography Quality Standards Act of 1992 was reauthorized in 1998 for an additional five years (P.L. 105-298).

MQSA required that mammography facilities be certified by October 1, 1994, to remain in operation and inspected annually to ensure compliance with national quality and safety

standards. FDA requests an increase of $ 457,000 for the medical devices program in MQSA authorized inspection user fees to cover inflation, for a total of $15,404,000 and 48 FTE in FY 2002. The fees collected will pay for the costs of inspections.

JUSTIFICATION OF BASE

Activities Related to Increases for FY 2002

Payroll

- FDA's Devices and Radiological Products program ensures the safety and effectiveness of regulated medical devices by applying a total product life cycle model across the range of Center activities, by covering products from concept to obsolescence.

- The field component of Devices and Radiological Products inspects regulated industry, and collects and analyzes samples. Other activities that often arise are review and management of enforcement actions, and consumer complaints, trace back efforts, and review of import entries for admissibility decisions. These functions are inherently governmental and highly personnel intensive.

Imports and Inspections

- Provide criminal investigation of reported product tampering, counterfeit products and other fraudulent criminal activities involving regulated products.

- Provide emergency operation, investigation and response for incidents involving regulated products.

- Coordinate field investigational, analytical, activities among the five regulatory centers.

- Perform laboratory validation of analytical methods submitted to support pre-market product applications.

- Fund about 8,900 state contract device inspections.

- Review about 1.5 million devices import lines for admissibility into domestic commerce.

- The field was unable to meet its inspection obligation. In the Device inspection program FDA will inspect only 17 percent of its statutory requirement of 50 percent.

Adverse Event Reporting

- Continue implementing the FDA Medical Surveillance Network (MeDSuN). In FY 2001, we will recruit and train 75-100 health care facilities. The long-term goal is to expand the program to include different types of health care facilities and to include drug and biologic products. The timing and specifics of the expansion will depend on funding. In the field, FDA:

- Provide training for field staff to improve the information gathered through investigation of consumer complaints;

- Utilize upgraded field data systems to provide improved consumer complaint data; and,

- Provide increased health education for U.S. consumers about FDA-regulated products, which may adversely impact their health.

Human Subject Protection

- Conduct human subject protection onsite inspections and data audits as part of our Bioresearch Monitoring activities (BIMO) to ensure that the rights and welfare of human subjects participating in medical device research are protected, and to verify that clinical data (human subjects) and non-clinical data (animals and others) submitted to FDA, in support of research or marketing applications, are accurate and reliable.

Activities Related to Other Priority Areas

Premarket Activities

Statutory Review Times

- Continue on-time, high quality device review with no overdue device applications. FDA must regulate both medical devices and radiation-emitting products consistent with the provision of the Federal Food Drug & Cosmetic (FFD&C) Act.

- Premarket Approval Applications (PMAs) are high-risk devices with the highest likelihood of significantly improving the treatment of patients. The FDAMA statutory requirement is to review 100 percent PMA first actions within 180 days. FDA's FY 2002 performance target is to meet the requirement 90 percent of the time.

- Another Device Program objective is to review and complete 90 percent of PMA supplement final actions within 180 days. For FY 2002, the FDAMA requirement is to review and complete 100 percent of PMA supplements within 180 days. Supplemental applications are generally submitted for changes in already approved applications. Such changes might include technology changes or the addition of a new indication.

Third Party Review

- To expand industry's use of the FDAMA Third Party ("Accredited Persons") program, FDA initiated an expansion pilot that will allow third party review of 510(k)s for Class II devices for which there are no device-specific guidance documents. The list of eligible Class II devices was expanded to include approximately 460 device types lacking such guidance. As a result, all 674 Class I and Class II devices regulated by FDA that meet the statutory criteria for third-party review will be included in the program.

FDAMA

- FDA will continue to implement the Least Burdensome FDAMA provision through training, meetings with sponsors, and guidance development. FDA works with industry representatives to develop a common approach to the interpretation and implementation of the Least Burdensome Provisions.

Radiation Safety

- The Radiation Control for Health and Safety Act of 1968 requires FDA to reduce exposure to unnecessary man-made radiation from medical and non-medical electronic products. Most modern products used in homes, businesses, and hospitals are electrically powered and produce some radiation. Examples of products that require radiation to perform their intended function are fluoroscopic x-ray imaging and laser industrial welders. As a result of the use of these products, there is a resurgence of previously solved radiation issues such as skin burns from fluoroscopic procedures. FDA will continue to prioritize and leverage its radiation protection efforts with state governments, professional societies, and other federal agencies.

Outreach

- FDA will continue to provide technical assistance to small medical device manufacturers and accessible, timely feedback to industry, health professionals, and consumers. FDA's information technology infrastructure will take full advantage of the Internet by providing industry, health professionals, and consumers with feedback via: (1) Device Advice comment line: dsma@cdrh.fda.gov; (2) E-mail: Director@cdrh.fda.gov; (3) Internet Comments and Feedback; (4) links for submitting comments on proposed regulations; and (5) use of automation to provide the public with the latest information.

Device Reuse

- FDA will continue implementing policy on the reprocessing and reuse of single-use devices. The practice of reusing medical devices designed and labeled for single use has dramatically increased in the past two decades and is surrounded by controversy. FDA will develop a training program for FDA investigators who will be conducting inspections of hospital reprocessing facilities. The program is expected to train approximately 30 to 50 field investigators. In addition, FDA will inspect hospital reprocessors beginning in fall 2001, when all hospital reprocessors are required to have registered their facilities with the Agency. FDA anticipates that it may need to inspect several hundred hospitals within the next year. At this time, the Agency anticipates that FDA's field staff will perform all the inspections.

Genetic Testing

- FDA will continue to develop scientific expertise and regulatory strategies for evolving medical device areas such as genetic testing. We will collaborate with other DHHS agencies as part of an inter-agency working group and as a participant in the CDC CLIAC subcommittee on genetics testing and the CDC genetics forum. We will continue with internal training efforts and informal outreach efforts to address issues dealing with reviews and the development of guidance and standards.

Bioterrorism

- FDA will continue to monitor, evaluate, and follow up on the public health needs of new medical devices for use in bioterrorism preparedness and response, in order to regulate them in a manner that best serves the public health. A key element of FDA's approach is to strengthen its scientific expertise to respond knowledgeably to this threat. This involves preparing expert reviewers to review new submissions and developing standards for devices needed for bioterrorism response, such as diagnostic products.

Clinical Laboratory Improvement Amendments (CLIA)

- In FY 2000, FDA assumed responsibility from the Center for Disease Control and Prevention (CDC) for making complexity determination decisions on in vitro diagnostic (IVD) products. This activity is funded by a portion of the CLIA user fees collected by the Health Care Financing Administration. Manufacturers can now obtain a complexity determination from one agency (FDA) and not two (FDA and CDC), as was previously the case. FDA has interacted with stakeholders throughout the transition of this program from CDC to FDA. FDA expects the steady volume of applications requesting waived status to continue in FY 2002.

International Activities

- Implementation of the U.S.-European Union (EU) Mutual Recognition Agreement (MRA) is intended to develop information about EU based medical device manufacturers, to provide more information about the status of those manufacturers and speed product approval. This involves training, assessing the work performance of third-party, Conformance Assessment Bodies (CABs) for inspections of medical device manufacturers. Provisions for making a determination about the pre-market status of some medical device products are included in the MRA. The Office of Regulatory Affairs (ORA) is heavily involved in all aspects of implementation. Eventually, both the U.S. and the EU may be able to save resources by relying on evaluations of manufacturers and products conducted by the other country. The first on-site assessment visit by the EU of the U.S. will be in March 2001.

- FDA's international inspection program continues to be one of the Agency's top priorities as more FDA regulated products originate from foreign sources. The Agency's international inspection program is paramount in attaining confidence that all imported FDA regulated products meet the same standards as domestic goods. While FDA is working to foster effective international inspection cooperation agreements, the primary tool for this assurance is for FDA to conduct international inspections.

Selected FY 2000 Accomplishments

Premarket

The Medical Device and Radiological Health Program is responsible for review the of device premarket approval applications (PMAs), premarket notification 510(k)s, and investigational device exemptions (IDEs).

- Received 9,753 major submissions. The number of major submissions for medical devices has been level for the past few years—9,824 in FY 1997, 10,016 in FY 1998 and 9,792 in FY 1999;

- Approved six humanitarian device exemptions (HDE). These devices are used in the treatment or diagnosis of rare conditions or diseases affecting fewer than 4,000 individuals in the United States per year. An HDE application is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA;

- Approved the start and design of 213 new studies to test the safety and effectiveness of a variety of experimental devices in humans; and,

- Maintained high quality, timely reviews despite increasingly complex device technology. There were no overdue submissions for the fourth consecutive year.

Significant Medical Device Approvals/Clearances

The evolution of medical and scientific technology resulted in the approval/clearance of many novel and medical breakthrough devices that will provide significant improvements in patient care. Some examples are listed below:

- Robotic Device: The Da Vinci Surgical System is a first of its kind device that enables a surgeon to perform laparoscopic gall bladder and reflux disease surgery while seated at a console with a computer and video monitor.

- Digital Mammography System: The Senographe 2000D, the first mammography system to produce digital images on a solid state receptor instead of analog images on a radiographic film, was approved on the basis of clinical data showing its safety and effectiveness and on the recommendation of FDA's Radiological Devices Panel.. Film/screen (analog) mammography along with physical examination and breast self-examination is the standard method for breast cancer screening in women.

- Surgically Implanted Hearing Device: This new, first of its kind, type of surgically implanted hearing device helps adults with moderate to severe nerve hearing loss. The device, made by Symphonix Inc, provides an alternative to traditional hearing aids. The Symphonix implant should not be confused with cochlear implants that are intended as a surgical treatment for the profoundly deaf.

- Surgical Sealant for Lung Cancer: FDA expedited the review of a new type of surgical sealant made by Focal Inc. for use in lungs to seal air leaks following removal of cancerous lung tumors because of its potential benefit in reducing the number of patients who experience such air leaks.

- Colon cancer device: The Optical Biopsy System laser system, using laser light energy, is used to improve a physician's ability to distinguish small harmless growths from pre-cancerous growths in the colon.

Genetic Testing

- Completed appointments to its Molecular and Clinical Genetics panel, which was an addition to the Medical Devices Advisory Committee. In addition, we participated actively in three DHHS groups working on the regulation of genetic tests. FDA and professional groups are actively involved in developing guidance and templates to support future regulatory activity.

Reuse of Single Use Devices

- Developed a regulatory strategy for the practice of reusing single use devices (SUDs) and issued a final guidance. This guidance finalizes FDA's policy on how it intends to regulate entities that reprocess single-use devices for reuse and sets forth the Agency's priorities for enforcing these requirements. The guidance is designed to protect the public health by assuring that the practice of reprocessing and reusing "single use" medical devices is based on good science, while ensuring that regulatory requirements are equitable to all parties.

Human Subjects Protection

FDA inspects sponsors, contract research organizations, monitors, and institutional review boards to ensure that the rights and welfare of human subjects who participate in research or clinical trials are protected, and to verify that data collected by the regulated industry are accurate and reliable.

- Conducted 250 inspections under the bioresearch monitoring program. FDA relies heavily on the integrity of data generated from clinical trials in making many of its review decisions.

FDAMA Update

- Third Party Reviews. In March 2000, FDA issued "Use of Standards in Substantial Equivalence Determinations" (see http://www.fda.gov/cdrh/ode/guidance/1131.pdf), a guidance document clarifying how information on conformity with standards may be used to support 510(k) substantial equivalence determinations. As a result, the combined receipts of abbreviated and special 510(k)s, plus third party-reviewed 510(k)s, rose from 513 in fiscal year 1999 to 778 this year, a 52-percent increase.

- Real Time PMA Review. In the PMA process, real time PMA supplements (designated types of PMA supplements with selected, non-data intense device changes that are reviewed during a meeting, teleconference, or video conference with the firm) account for more than one-fourth of all PMA supplements received.

- Least Burdensome Provisions. FDA has been working with the industry representatives to develop a common approach to the interpretation and implementation of the Least Burdensome Provisions. We developed training classes for review staff and Advisory Committee Panels, incorporated language in correspondence with industry to raise least burdensome concerns and added least burdensome considerations to the Good Manufacturing Practices (GMPs). A Least Burdensome web site was created at

http://www.fda.gov/cdrh/modact/leastburdensome.html to update interested parties on FDA's progress in interpreting and implementing the Least Burdensome provisions.

- International Harmonization. FDA and others participating in the Global Harmonization Task Force Study Group 2 (SG2) (Medical Device Vigilance and Postmarket Surveillance) developed a process for the global exchange of vigilance reports between National Competent Authorities (NCAs). Most of the postmarket vigilance reports exchanged thus far involve recalled devices with a potential for adverse events in countries where the product is distributed. The pilot portion of the program was recently concluded. The program is now fully operational with expansion to other NCAs planned.

Science and Standards Activities

FDA uses high scientific standards to promote and protect the public health and to expedite premarket reviews. The Agency issued several standards for industry use.

- In March 2000, "Use of Standards in Substantial Equivalence Determinations" (see http://www.fda.gov/cdrh/ode/guidance/1131.pdf),a guidance document clarifying how information on conformity with standards may be used to support 510(k) substantial equivalence determinations. This document, along the FDA June 2000 expansion of the 510(k) third-party review program (see http://www.fda.gov/cdrh/thirdparty), were aimed at stimulating greater industry use of streamlined submission/review procedures;

- Completed implementing, in May 2000, "Electrode Lead Wires and Patient Cables", in response to reports of patient deaths caused when the cables were accidentally plugged into 110-volt wall circuits. The standard requires electrically protected connectors for electrode lead wires and patient cables to improve patient safety;

- Issued in September 2000, "Wireless Medical Telemetry Risks and Recommendations" (see http://www.fda.gov/cdrh/comp/guidance/1173.html) asking all wireless medical telemetry manufacturers to analyze and reduce the risk in their equipment; and,

- Clinical Laboratory Improvement Amendments (CLIA): In FY 2000, FDA assumed responsibility from the Center for Disease Control and Prevention (CDC) for making complexity determination decisions on in vitro diagnostic (IVD) products. FDA finalized a regulation for waived tests. The CLIA program is user fee funded; therefore, all costs of administering the program must be covered by the regulated industry.

- Completed a combined CLIA/premarket review of the first product successfully. The AvoSure point-of-care monitoring device for anticoagulant therapy from Avocet Medical received both a CLIA waived status and premarket clearance from FDA; and,

- Held a Public Workshop in August 2000, to solicit comments on the criteria and process that the Agency should use to determine when a particular test should be waived. FDA will develop guidance for manufacturers of IVD devices seeking waived status, and re-propose a regulation for waived tests or finalize the one proposed earlier by CDC.

Bioterrorism

- Initiated rulemaking specific to the bioterrorism program, held an advisory panel meeting to discuss data requirements for approval of devices intended to detect exposure to biothreat agents, and engaged with CDC and the Department of Defense (DOD) on premarket and postmarket regulations affecting these products.

Medical Error Reduction Activities

- FDA continues to look for ways to reduce preventable deaths and injuries associated with the use of medical device products. To be effective, it is essential that FDA have access to a sufficient amount of quality information regarding device events. In FY 2000, FDA began Phase II of the MeDSuN pilot which will cover 25 hospital facilities.

Mammography

Congress enacted MQSA to ensure that all women have access to quality mammography for the detection of breast cancer in its earliest, most treatable stages. In the fall of 1998, Congress reauthorized MQSA, extending the program to 2002. During FY 2000, FDA:

- Trained 16 new inspectors on the requirements of the MQSA regulations, and performed 200 audit inspections under the Inspector Quality Assurance program;

- Developed a continuing education video on phantom image scoring and distributed it to each state and district office; and,

- Drafted final regulations for "States as Certifiers," which will transfer certification authority from FDA to applicant States, as provided for by MQSA. Final regulations will become effective some time in April 2001.

Outreach Activities and Leveraging

- FDA initiated, and is an active member of, the Hospital Bed Safety Work Group. The work group has focused on raising awareness of the entrapment hazard and educating care givers and family members on the problems associated with bed rail use. The work group recently issued an educational brochure, *A Guide to Bed Safety,* that highlights the benefits and risks of bed rails, ways to meet a patient's need for safety, and patient or family concerns about bed rail use.

- FDA continued a Site Visit Program, to enhance reviewer knowledge of how specific medical devices are designed, manufactured, and tested. The program include visits to medical device manufacturing firms and hospitals to observe devices in use.

- FDA hosted several Vendor Days throughout the year covering various medical device-related topics, to help FDA reviewers better understand medical technology, improve communications between industry and FDA, and provide a better understanding of health issues involved with medical technology. For example a Vendor Day was held that featured the major manufacturers of single-use reprocessed devices from all product areas, including catheters, blood pressure cuff, and pulse oximeter sensors.

Devices and Radiological Health
Program Activity Data

Program Workload and Outputs	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
PMAs Received (includes PDPs)	67	73	75
PMAs Approved	43	40	40
Average Elapsed Time (FDA days-approval)	244	255	255
Total PMA Actions [1/]	321	350	375
HDEs Received	11	12	12
HDEs Completed	6	12	12
Average FDA Review Time	112	75	75
PMA Supplements Received	545	588	588
PMA Supplements Approved	474	548	548
Average Elapsed Time (FDA days-approval)	95	95	95
PMA Supplement Panel Tracks [2/]	12	14	16
510 (k)s Received (Includes Traditional, Special, Abbreviated, 3rd Party)	4,202	4,500	4,500
510 (k)s Completed	4,397	4,500	4,500
Average Elapsed Time (FDA days-decision)	77	75	75
IDEs Received	311	330	330
IDEs Approved/Total	320	330	330
Average Elapsed Time (FDA days-approval)	28	30	30
IDEs Supplements Received	4,388	4,450	4,450
IDEs Supplements Completed	4,335	4,450	4,450
Average Elapsed Time (FDA days-approval)	20	20	20
MDR Initial Reports Received (FDA 3500A mandatory)	49,312	53,000	53,000
MDR Line Item Summary Reporting [3/]	42,387	40,000	40,000
Total MDR Incidents (mandatory)	91,699	93,000	93,000
MDR Voluntary Reports Received	3,012	3,000	3,000
Export Certificates and Permits	2,821	3,000	3,000
Devices/Radiological Inspections (domestic) [4/]	1,294	1,660	1,810
MQSA Annual Inspections (94% State, 6% Federal)	9,484	9,590	9,590
MQSA Facility Certifications [5/]	3,812	3,179	3,009
BIMO Inspections [6/] (Domestic & Foreign)	249	260	335

[1/] Includes filing decisions, review determinations, and approval decisions.

[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 (no 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 alternative reporting program, effective January 2,000 where certain firms are authorized to send FDA abbreviated reports on a quarterly basis.

[4/] Data Source: ORA Field Accomplishment and Compliance Tracking System (FACTS).

[5/] FY 2000 certifications were lower than anticipated because originally the majority of certificates were renewed every third year but now one third of the certificates are renewed every year.

[6/] Bioresearch Monitoring inspections involve the inspection of sponsors of premarket applications (PMAs), clinical investigations, Institutional Review Boards (IRBs), and non-clinical laboratories.