

**ANIMAL DRUGS AND FEEDS
CENTER FOR VETERINARY MEDICINE (CVM)**

	FY 2004 Actual	FY 2005 Enacted ^{1/}	FY 2006 Estimate	Increase or Decrease
Program Level	\$67,656,000	\$75,658,000	\$78,338,000	+\$2,680,000
<i>Total FTE</i>	<i>349</i>	<i>373</i>	<i>385</i>	<i>+12</i>
Budget Authority	\$66,573,000	\$67,551,000	\$67,769,000	+\$218,000
<i>GSA Rent & Rent Related</i>	<i>\$12,043,000</i>	<i>\$12,259,000</i>	<i>\$12,477,000</i>	<i>+\$218,000</i>
<i>Total FTE</i>	<i>346</i>	<i>315</i>	<i>309</i>	<i>-6</i>
User Fee	\$1,083,000	\$8,107,000	\$10,569,000	+\$2,462,000
<i>ADUFA</i>	<i>\$1,083,000</i>	<i>\$8,107,000</i>	<i>\$10,569,000</i>	<i>+\$2,462,000</i>
<i>FTE</i>	<i>3</i>	<i>58</i>	<i>76</i>	<i>+18</i>

ORA Estimate				
<i>Budget Authority</i>	<i>\$33,080,000</i>	<i>\$39,383,000</i>	<i>\$39,519,000</i>	<i>+\$136</i>
<i>FTE</i>	<i>246</i>	<i>240</i>	<i>228</i>	<i>-12</i>

Includes structure changes to FDA's budget, which displays GSA and Other Rent and Rent Related Activities in the Program line, and the Office of Regulatory Affairs as its own program. ORA estimates are for information purposes only and are not included in the Center program level total.

^{1/}*Contains budget authority rescission of 0.8 percent.*

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2002 Actual ^{1/}	\$55,727,000	\$55,727,000	\$0	323
2003 Actual	\$57,115,000	\$57,115,000	\$0	341
2004 Actual	\$67,656,000	\$66,573,000	\$1,083,000	349
2005 Enacted	\$75,658,000	\$67,551,000	\$8,107,000	373
2006 Estimate	\$78,338,000	\$67,769,000	\$10,569,000	385

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

^{1/}*Includes FDA's FY 2002 Appropriation and the Counterterrorism Supplemental.*

STATEMENT OF BUDGET REQUEST

The Animal Drugs and Feeds Program is requesting \$78,338,000 in program level resources to accomplish its mission activities including:

- Foster public and animal health by approving safe and effective products for animals and by enforcing applicable provisions of the Federal Food, Drug, and Cosmetic Act, and other authorities;
- Process premarket applications as quickly as possible to increase the availability and diversity of safe and effective veterinary products that relieve animal pain and suffering while ensuring the resulting products are safe, wholesome, and free of drug residue when they reach the consumer; and,
- Monitor marketed products for all animal drugs and feeds to minimize harm to humans or animals that might arise from the use of these products. This is accomplished through science-based review of drug experience reports, nationwide monitoring systems, compliance programs conducted by FDA field offices through inspections, sample collections, analysis, investigations, and appropriate regulatory actions to control violative goods and firms.

PROGRAM DESCRIPTION

The Animal Drugs and Feeds Program (Program) is administered by FDA's Center for Veterinary Medicine (CVM) and supported by the Office of Regulatory Affairs' (ORA) field force. The authority to regulate animal drugs and medicated feeds is derived from the Food, Drug, and Cosmetic Act, which in 1968 was amended to include sections specifically addressing animal drugs. These amendments were designed to ensure that animal drugs are safe and effective for their intended uses and that the drugs do not result in unsafe residues in foods. In November 2003, the Animal Drug User Fee Act was enacted that provided the authority for FDA to collect user fees for its animal drug review work. The new law is intended to supplement the appropriated resources for conducting the animal drug review program. These resources provided by the law will help the Animal Drugs and Feeds Program's scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for animals.

The Animal Drugs and Feeds' Program scope is far-reaching. The program's customers include:

- *115 million dogs and cats*
- *6.9 million horses*
- *7.5 billion chickens*
- *292 million turkeys*
- *109 million cattle*
- *92 million pigs*
- *7 million sheep*
- *293 million humans in the U.S.*

The safety of the food supply is a paramount concern for the Program, as the average American consumes nearly 200 pounds of meat and fish, 30 pounds of eggs, and 600 pounds of dairy products each year. While most of these food products are regulated by the USDA FDA plays a key role in ensuring that animal drugs and feeds used in the care of these animals do not result in unsafe residues in food products that are harvested or produced (e.g., eggs) from these animals.

ORA supports the CVM, by conducting preapproval inspections of both domestic and foreign establishments and other premarket-related activities such as: bioresearch monitoring of clinical research and laboratory method validations needed for premarket application decisions, and inspections of manufacturing facilities to determine if the factory is able to manufacture the product to the specifications stated in the application. In addition to overseeing regulated products on a surveillance or "for cause" basis, ORA staff also responds to emergencies and investigates incidents of product tampering and terrorist events or natural disasters. To complement the regular field force, the Office of Criminal Investigations investigates instances of criminal activity in FDA regulated industries. In FY 2006, ORA will expend an estimated \$39,519,000 in support of the Animal Drugs and Feed Program.

The Program's other priorities are animal drug review, antibiotic resistance, prevention of Bovine Spongiform Encephalopathy (BSE) or "mad cow disease," and the safety of food derived from genetically modified animals. Of these priorities, efforts have sought to limit the exposure of BSE in the food and feed supply began in 1997 when FDA issued a regulation prohibiting the use of most animal proteins in feeds for cattle and other ruminants. In its enforcement strategy, FDA initiated a comprehensive inspectional program using the Field and its state partners covering 100 percent of the affected industry. With its educational emphasis and other outreach efforts, the result has been that more than 99 percent of all renderers and feed mills in the U.S. who process prohibited material now comply with this regulation. Concurrent with this approach was the development of a response planning mechanism coordinated by FDA's Office of Crisis Management that would be used when a BSE-positive animal was discovered. In addition, FDA began to monitor imports through entry review of all feed and feed ingredient commodities and sampling for the presence of processed animal protein. In late December 2003, a BSE-positive animal was identified and the response plan went into action. A series of inspections and trace-back procedures were instituted which determined that all of the BSE-infected materials were recovered. In mid-January 2004,

FDA announced additional safeguards to protect the public from becoming exposed to infected BSE material in the food supply.

PERFORMANCE ANALYSIS

During the latest completed performance period, (FY 2004), CVM achieved the targets for two of its three performance goals, and expects to meet the other one when data becomes available in October 2005. For more detailed explanation of these goals and results, please see their respective section contained in the Detail of Performance Analysis under the Supporting Information tab.



With the passage of the Animal Drug User Fee Act (ADUFA) of 2003 and the resulting availability of user fees, the Program changed its new animal drug review performance goals to reflect the more ambitious performance target plans under ADUFA. Since the ADUFA fee structure is predicated on supplementing existing appropriated funding, the request must be designed to ensure that budgetary authority and user fees are adequate. The performance goal and target below is dependent upon a sustained level of base and user fee resources.

Performance Highlight:

Goal Target	Context	Results
Complete review and action on 90% of original NADAs & reactivations of such applications received in FY 2006 within 230 days.	The user fee program reflects the implementation of a five (5) year plan to improve the performance for animal drug review.	The benefits provided by the user fee program include: shorter review times; a more predictable and stable review process; and overall reduction in drug development times.

RATIONALE FOR BUDGET REQUEST

This request for Budget Authority and User Fees supports various activities that contribute to the accomplishment of program outputs and performance goals, and presents FDA's justification of base resources and selected FY 2004 accomplishments by strategic goal.

PROGRAM RESOURCE CHANGES

Program Account Restructuring

GSA Rent and Other Rent Activities Structure Change

To provide increased flexibility and accountability, eliminate the need for the many reprogramming requests to Congress, place accountability for rental costs within the

operating program, would better reflect the total cost of each program. This budget changes the way the GSA Rent and Other Rent-Related Activities budget lines are displayed by incorporating these resources into the Animal Drugs and Feed program level requests.

Office of Regulatory Affairs (ORA) Estimate and Structure Change

This budget also establishes a single budget line item for the ORA. To help the field program provide services more effectively, especially by providing much needed flexibility to respond to shifting program priorities. This additional flexibility is essential to allow FDA to respond to emerging situations without being hindered in performing its mission critical activities. These activities have been removed from each program line and the Field estimates will be provided under the Office of Regulatory Affairs to reflect the planned spending for each program area.

Budget Authority

GSA Rent + \$218,000

To help meet the rising costs of GSA rent, a total increase of \$4,100,000 is requested, of which \$218,000 is for the Center for Veterinary Medicine. This increase will help cover inflation on FDA's current GSA leased facilities.

User Fee

Animal Drug User Fee Act (ADUFA): + \$2,462,000 and + 18 FTE

ADUFA enacted in November 2003, contained a required appropriations action enabling FDA's implementation of ADUFA. ADUFA helps the FDA, through a strengthened animal drug pre-market review program, to provide greater public health protection by ensuring that animal drug products that are approved to be safe and effective are readily available for both companion animals and animals intended for food consumption. Additional resources provided by ADUFA will also help FDA scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for our animals. ADUFA, which requires new animal drug applicants, sponsors, and establishments to incur a fee to expedite their respective applications, will help provide a cost-efficient, high quality animal drug review process that is predictable and performance driven. This increase of \$2,462,000 will cover inflationary costs, as well as overhead and rent costs, for additional staff associated with the Act.

JUSTIFICATION OF BASE

USING RISK-BASED MANAGEMENT PRACTICES

Base resources will be used to conduct science-based risk management in all agency regulatory activities; so that the agency's limited resources can provide the most health promotion and protection at the least cost for the public. These activities include premarket review compliance activities related to the BSE regulation and imports and inspections.

Bovine Spongiform Encephalopathy (BSE)

BSE or “Mad Cow Disease” is a deadly chronic, degenerative disorder affecting the central nervous system. Feed containing remnants of the slaughtering process, such as the brain and spinal cord, may harbor the agent that causes BSE. To ensure such substances are not contained in animal feed, and to prevent the establishment and amplification of BSE through animal feed, the FDA finalized a regulation on August 4, 1997 entitled “Animal Proteins Prohibited from use in Animal Feed”. FDA will:

- Conduct annual, targeted BSE inspections of all known renderers and feed mills processing products containing prohibited material, such as meat and bone meal;
- Conduct selected inspections of animal feed industry firms subject to the animal protein prohibition, including renderers, feed mills, feed distributors, feed retailers, transporters, on-farm mixers, and ruminant feeders;
- Issue and coordinate assignment for directing identification and inspections of firms engaged in animal feed salvaging and feed transportation;
- Implement enforcement actions and conduct re-inspections involving firms found to be in violation of the regulation;
- Issue and implement import alerts and bulletins regarding animal feed, animal feed ingredients and other products for animal use consisting of or containing ingredients of animal origin from both countries at-risk and not at-risk for BSE;
- Collect and analyze samples of domestic and imported feeds and feed ingredients to monitor for the presence of prohibited animal proteins;
- Maintain relationships with industry using telecommunication and conferences to provide information on regulatory compliance and share inspection data;
- Develop and validate an improved method for detecting prohibited animal proteins in feed using Real Time PCR (Polymerase Chain Reaction) that will allow for the identification of up to four different prohibited species in a single reaction;
- Adapt the Real Time PCR methodology to identify prohibited animal proteins in rendered materials from the European Union as well as materials rendered in the United States;
- Continue to evaluate commercially available rapid tests for prohibited proteins in animal feeds;
- Maintain the database and data entry procedures for BSE inspections, and new BSE inspection checklist to target firms for re-inspections and to collect high quality data from both FDA and state inspectors;

- Maintain a web-based, dynamic report available to the public and other health related agencies that summarizes the most current information concerning the results of inspections involving all firms subject to BSE inspections;
- Test proposed risk management proposals in terms of the effects on the spread and the rate of elimination of BSE, if introduced into the U.S., with the help of the Harvard BSE Risk Assessment simulation;
- Leverage with state agencies by funding contract inspections of feed mills and renderers, and conduct compliance, follow-up, and audit inspections to state contracts;
- Provide education to state feed control officials and FDA investigators on policies and inspectional procedures concerning the animal protein prohibition through training seminars, courses and feed safety meetings; and,
- Provide intensive line entry and label review of Animal Drug and Feed product import line entries for use in domestic commerce.

Premarket Review

The availability of safe and effective animal drugs allows food animal producers to maintain healthy animals with assurance that products will be safe, wholesome, and free of harmful drug residues when they reach the consumer. FDA strives to improve product review performance and meet the increasing complexity of review workload. Keeping pace with technological advances will contribute to the efficiency of agency reviews, and decrease review time. FDA will:

- Continue to increase the 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;
- Conduct pre-submission conferences, meetings, and workshops with industry and develop policy and practical guidance documents as necessary to industry;
- Continue implementation of the ADUFA;
- Continue the enhanced review performance achieved in FY 2004;
- Improve the quality and timeliness of product reviews by monitoring pre-approval inspections and expanding inspectional expertise in emerging technologies;
- Review previously approved new animal antimicrobial drug submissions with respect to antimicrobial resistance and human food safety;

- Conduct method validation studies for the approval of applications for new drugs for food producing animals;
- Continue development and validation of multi-residue drug screening methods;
- Resolve new and emerging scientific issues that impact on the CVM's ability to make approval decisions; and,
- Prepare implementation regulations for the Minor Use and Minor Species Animal Health Act of 2004 (MUMSAHA) to help make more medications legally available to veterinarians and animal owners to treat minor animal species and also uncommon diseases in the major animal species.

EMPOWERING CONSUMERS FOR BETTER HEALTH

Base resources will be used to better enable consumers to make informed decisions weighing benefits and risks of FDA-regulated products. These activities include:

- Delivering food safety and veterinary health messages to livestock producers, veterinarians, industry and consumers via trade shows, videotapes, and pamphlets to educate them on safe drug use, including prudent use of antibiotics in food animals to minimize the risk of antimicrobial resistance; and,
- Enhancing the transparency of the National Antimicrobial Resistance Monitoring System (NARMS) program to stakeholders, the public and other interested parties by increased reporting and communications of NARMS results and program information by: publishing annual reports of animal, human and retail meat data; posting NARMS publication references on the web, and presenting NARMS susceptibility testing results at scientific meetings via poster or oral presentations.

PATIENT AND CONSUMER PROTECTION

Base resources will be used to promote improved patient and consumer safety by reducing risks associated with FDA-regulated products.

Food Safety

Millions of people get sick annually from food they eat. Some foodborne illnesses are due to harmful or illegal residues in animal products while other illness is due to microbiological infection. In order to safely manage animal drug use at home and abroad, we must have the knowledge to make proactive, sound science based decisions. In pursuit of these objections the Agency will:

- Continue the retail meat arm of NARMS by monitoring changes in antimicrobial drug susceptibilities of selected enteric bacterial organisms in retail meats to a panel of antimicrobial drugs important in human and animal medicine;
- Continue research to identify food animal species causing human drug resistance;

- Provide educational information on biotechnology products and assist developers through the regulatory process;
- Continue to support the World Health Organization's Global Salmonella Surveillance;
- Continue leveraging FDA's Tissue Residue Information Management System (RVIS) with the USDA's Residue Violation Information System to Maintain Tissue Residue and Feed contaminants compliance programs;
- Continue FDA field inspections and take appropriate regulatory and enforcement action against firms illegally compounding animal drugs;
- Develop intervention measures to establish additional controls over the shipment, receipt, and use of bulk active pharmaceutical ingredients in compounding animal drugs; and,
- Maintain early warning systems by collecting information from Drug Experience Reports and Adverse Event Reports.

PROTECTING THE HOMELAND -- COUNTERTERRORISM

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

- Sample domestic animal feeds and those detained at U.S. ports of entry that contain ingredients possibly derived from prohibited animal material;
- Strengthen relationships with state partners and solicit interest in the expansion of contracting efforts with state laboratories to provide surveillance and surge capacity related to counter terrorism activities;
- Work with Iowa State University on a database that assists "first responders" by providing quick identification of qualified labs that have the capability to analyze feed and/or animal tissues for the presence of a chemical or biological agent, immediate contact with national experts on the disease or toxicant to obtain help in diagnosis and appropriate follow-up, and information on how to take, preserve, and ship an appropriate feed or animal sample to the laboratory for analysis;
- Continue developing more efficient rapid analytical methods for screening imports at the border;

- Develop a list of high priority products for countermeasures and periodically review and update list;
- Assist state diagnostic laboratories in acquiring the scientific expertise, analytical expertise and capability to handle a feed contamination incident;
- Maintain a comprehensive inventory of registered animal drug establishments and listed animal drug products and use the database to assess the availability or anticipated shortage of animal drug products that would be needed to deal with terrorist attacks;
- Continue to develop analytical methods to detect the presence of prohibited toxic substances that could be introduced into U.S. animal feed supplies. Once developed and optimized, these methods would be used by FDA laboratories to test prohibited substances in routine animal feed surveys;
- Work with CDC on a bioterrorism surveillance system for companion animals that can be used as an early detection mechanism; and,
- Intensify the review of products offered for import and collaborate with the Custom Service on safety and security issues at ports of entry.

SELECTED FY 2004 ACCOMPLISHMENTS

USING RISK-BASED MANAGEMENT PRACTICES

Bovine Spongiform Encephalopathy (BSE)

- For fiscal year 2004, inspected over 6,806 renderers, feed mills, and other firms, including on-farm mixers and ruminant feeders, to determine compliance with the BSE feed regulations. At the end of the FY 2004, 17 firms were classified as being out of compliance at the time of their last inspection. Re-inspections of these facilities determined to be out of compliance with the BSE regulation are still ongoing;
- FDA and state investigators specifically inspected a high-interest subset of 645 firms as part of our annual BSE performance goal feed inspections obligation. This subset represented 100 percent of all known renderers and feed mills processing products containing prohibited material;
- In July 2004, co-published with USDA an advanced notice of proposed rulemaking (ANPRM) requesting comments and scientific information on several additional regulatory measures that would strengthen the feed regulation;

- Developed a real-time Polymerase Chain Reaction (PCR) based method capable of detecting cattle, swine, sheep, goats, horses, or deer material along with poultry, goose, and turkey for use in analyzing samples of animal feeds and feed ingredients in support of the animal protein prohibition;
- Evaluated two commercially available diagnostic test marketed to detect mammalian proteins in animal feed and feed ingredients;
- Issued 10 Warning Letters for animal proteins prohibited in ruminant feed, and 15 class II recalls involving 15 firms and 25 products in response to violations of the BSE rule;
- Issued assignments for collection of 600 samples from domestic animal feeds, 300 samples of animal feeds imported from countries not considered at risk for BSE, and 300 samples of animal feeds imported from countries considered at risk for BSE for subsequent feed analysis to determine possible non-compliance with the ruminant feed ban regulation and the import alert prohibiting importation of feeds containing animal tissues;
- Provided separate formal ruminant feed ban inspection training seminars to feed safety officials in the states of Montana, Washington, Oregon, New York, Wisconsin, Oklahoma, and Idaho;
- Participated in BSE working groups at three separate meetings of the Association of American Feed Control Officials;
- Provided staffing to the FDA and USDA/APHIS emergency operation centers, tracking the distribution and disposition of suspect material, communicating with state authorities, and overseeing the final disposition of destruction of suspect material after discovery of a BSE-infected cow in the U.S.; and,
- Issued Guidance for Industry (GFI #174) for the disposition of material from BSE positive cattle in animal feed.

Premarket Review

- Approved the following noteworthy medicines.
 - **SIMPLICEF (cefpodoxime proxetil)** new chemical entity to treat skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus intermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.
 - **EXCEDE for Swine (ceftiofur crystalline free acid) sterile suspension** - EXCEDE for Swine is an antimicrobial indicated for the treatment of swine

respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*.

- **METACAM Injectable Solution (meloxicam)** original approval for the control of pain and inflammation associated with osteoarthritis in dogs.
- **NAVIGATOR Oral Paste (nitazoxanide)** new chemical entity for the treatment of equine protozoal myeloencephalitis (EPM).
- **ULCERGARD (omeprazole) Oral Paste** original OTC approval for the prevention of gastric ulcers in horses.
- **VETSULIN (insulin)** new chemical entity and the first veterinary insulin approval. The product is approved to treat hyperglycemia and hyperglycemia-associated with diabetes mellitus in dogs.
- **BUSCOPAN Injectable Solution (N butylscopolammonium bromide)** new chemical entity for the control of pain associated with spasmodic colic, flatulent colic and simple impactions in horses.
- **SURPASS Topical Anti-inflammatory Cream (diclofenac)** new chemical entity for the control of pain and inflammation associated with osteoarthritis in horses.
- **SEDIVET Injectable Solution (romifidine hydrochloride)** new chemical entity for use as a sedative and analgesic for the facilitation of handling, examination, and minor surgical manipulations in horses.
- **PREVICOX Tablets (firocoxib)** new chemical entity for the control of pain and inflammation associated with osteoarthritis in dogs.

CVM Approves First 4-Way Combination Drug

CVM recently approved the first four-way drug combination product under the Animal Drug Availability Act of 1996 (ADAA) that eased the requirements for combination approvals.

Before ADAA, a drug sponsor had to prove the effectiveness of each drug in the combination drug. Under ADAA, the sponsor faces no additional requirements to prove effectiveness of combinations made up of previously approved drugs. The sponsor needs only to show that each drug brings an additional claim to the combination and the drug's safety is not diminished. For combination drugs, ADAA "streamlined the process" and removed certain regulatory hurdles.

The recently approved four-way combination product is an over-the-counter Type A medicated feed article approved for use in heifers fed in confinement for slaughter. The product is made up of four previously approved products—Optaflexx (ractopamine hydro-chloride), Rumensin (monensin sodium), Tylan (tylosin phosphate) and MGA (melengestrol acetate). The sponsor is Elanco Animal Health.

This combination product is approved for increased rate of weight gain, improved feed efficiency, increased carcass leanness, the prevention and control of coccidiosis due to Eimeria bovis and E. zuernii, reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes and suppression of estrus.

- Issued a regulation describing the procedures for requesting, conducting and documenting presubmission conferences;
- Issued draft Guidance for Industry (GFI #169) on the chemistry, manufacturing and controls information to be submitted for certain drug substances to ensure continued drug substance and drug product quality;
- Issued draft Guidance for Industry (GFI #162) for preparing and using comparability protocols for changes in chemistry, manufacturing and controls of protein drug products;
- Issued draft Guidance for Industry (GFI #135) for validation of analytical procedures for Type C medicated feeds;
- Issued draft Guidance for Industry (GFI #171) for waiver of in vivo demonstration of bioequivalence of animal drugs in soluble powder oral dosage form products and Type A medicated articles;

- Issued draft and final guidance documents resulting from collaborative efforts with industry and international regulatory partners within VICH to harmonize preapproval guidance;
- Completed a Public Master File for tylosin through the National Research Support Project #7 (NRSP-7) initiative for the control of American Foulbrood Disease in honeybees. An announcement of the availability of these data was published in the Federal Register. These data may now be used by reference to support a New Animal Drug Application for this claim; and,
- Held a NSRP-7 meeting with stakeholders in the spring to improve the communication between producer groups, the regulated industry, and government.

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

- On August 2, 2004, President signed The Minor Use and Minor Species Animal Health Act of 2004 (MUMSAHA) to help make more medications legally available to veterinarians and animal owners to treat minor animal species and also uncommon diseases in the major animal species; and,
- Established the new Office of Minor Use and Minor Species Animal Drug Development, as mandated by MUMSAHA.

New “MUMS” Legislation to Help Make Animal Drugs Available for Limited Uses, Minor Species

President Bush has signed legislation that will help make more medications legally available to veterinarians and animal owners to treat minor animal species and uncommon diseases in the major animal species.

The goal of this legislation is to provide incentives to pharmaceutical companies to develop drugs for limited uses and to provide some alternative approaches to the usual drug approval process for limited-use animal drugs, thus changing the economic outlook for the drug approval process.

In addition, the measure is expected to benefit people who own small or unusual pets such as guinea pigs or ornamental fish, and will likely aid zoo veterinarians. Before this, pharmaceutical companies could rarely afford to bring to market drugs for novel pets and zoo animals. The markets were just too small to generate an adequate financial return.

Minor use drugs are drugs for use in major species (cattle, horses, swine, chickens, turkeys, dogs and cats) that are needed for diseases that have a limited geographic range or affect a small number of animals. Minor species includes all animals other than the major species, which includes zoo animals, ornamental fish, parrots, ferrets and guinea pigs. Some animals of agricultural importance are also minor species. These include sheep, goats, catfish and honeybees.

Animal Drug User Fee Act (ADUFA)

- Implemented ADUFA by hiring reviewers, developing procedures for applying the new law, and establishing fee rates and payment procedures;
- FDA met or exceeded all review times defined under ADUFA for FY 2004 for applications and submissions that have been acted on as of September 30, 2004. Additional applications and submissions received in FY 2004 are pending review and action, but are still within ADUFA time frames;
- The 833 submissions not associated with abbreviated new animal drug applications (ANADAs) that were pending before September 30, 2003, have been reviewed and acted upon. FDA was required to review and act on pending NADAs, supplemental NADAs, and INAD submissions within 24 months after user fee payments were initiated;
- FDA has made substantial progress in recruiting for its review staff and will meet its goal of having 50 percent of additional FDA review staff recruited and on-board by the first quarter of FY 2006;
- On March 15, 2004, FDA published Guidance for Industry (GFI #170) “Animal Drug User Fees and Fee Waivers and Reductions” to help industry understand the ADUFA fee structure and the options available to individuals who qualify for a fee waiver or reduction;
- On September 28, 2004, FDA published draft Guidance for Industry (GFI #173) “Animal Drug Sponsor Fees under the Animal Drug User Fee Act”;
- The implementation included developing and publishing in the Federal Register the fees for FY 2004 and 2005, as follows: *Establishment of Animal Drug User Fee Rates for Applications for FY 2004 and Payment Procedures* on February 18, 2004; *Establishment of Animal Drug User Fee Rates and Payment Procedures for Product, Establishment, and Sponsor Fees for FY 2004* on April 27, 2004; and, *Establishment of Animal Drug User Fee Rates and Payment Procedures for FY 2005* On August 2, 2004; and,
- The financial implementation also included an electronic prototype for FDA that fully automated the application fee collection and billing process using a web based front-end tool called the *IStore*. The ADUFA implementation highlights FDA progress in improving financial management, budget and performance integration, and in expanding E-government in strategic alignment with the President’s Management Agenda.

Biotechnology

- The Animal Biotechnology Working Group made progress concentrating its effort on ensuring personnel are aware of the critical issues in biotechnology, possess the scientific skills necessary to address the rapidly evolving and highly technical issues associated with animal biotechnology, and are familiar with the regulatory environment surrounding those issues;
- As part of staff development program, instituted a rotating detail program for reviewers with senior staff to acquaint them with policy development and potential implementation in animal biotechnology;
- Continued to develop a transgenic animal policy. Participated in White House-level deliberations to evaluate the role of genetically engineered animals in the Coordinated Framework for the Regulation of Biotechnology. Prepared case studies on animal biotechnology products to serve as a basis for legal and policy deliberations. Participated in listening sessions sponsored by the Office of Science and Technology Policy with stakeholders from industry, the research community, and non-government organizations;
- Continuing to work with sponsors of animal biotechnology products to ensure that their progress is responsible but not duly burdened as the Federal government prepares a policy on transgenic animals; and,
- Completed draft Risk Assessment on Animal Clones and their Progeny; prepared a Proposed Risk Management Plan and a draft Guidance for Industry on the use of cloning technology in animal breeding and release of clones and their progeny into the food supply; briefed the Secretary's staff on the cloning package.

Aquaculture

- Determined the effectiveness of formalin treatments to reduce mortality associated with fungal infections in rainbow trout. The data was submitted to a public master file for use in possible approvals for drugs for fish under the Minor Use Minor Species program;
- Continued to standardize methods for antimicrobial susceptibility testing (AST) of microorganisms in aquatic species by developing a broth micro dilution AST method. Standardized methods are necessary for monitoring antimicrobial resistance in aquaculture;
- Developed a relational database of information on pharmacokinetic parameters in fish that provides a rapid access to data about the metabolism, accumulation, and elimination of drugs or chemicals in fish tissues;
- Conducted a number of studies to provide incurred residues of drugs in fish tissues to support the development of methods for detecting drug residues in fish tissues. One

such study provided incurred tissues for development of a single method for detecting multiple drug residues in fish;

- Coordinated and collaborated in a study to compare a chemical method and a microbiological method for detecting erythromycin in fish tissues;
- Developed an internal parasite infection model in largemouth bass. These fish containing the internal parasite will be used to test the effectiveness of various drugs for the treatment of the infection; and,
- Developed a Risk Assessment Tool to evaluate data collected on the risk of drugs used in foreign aquaculture that will help assess possible hazardous drug residues in food and prioritize them for analytical method development and drug residue monitoring.

Imports, Inspections, and Surveillance

- Issued a guidance describing the four conditions veal producers needed to meet to be able to sell their calves for veal that were illegally implanted with hormone implants;
- Issued a Guidance For Industry (GFI #122) “Manufacture and Labeling of Raw Meat Foods for Companion and Captive Non-companion Carnivores and Omnivores” which contains specific recommendations manufacturers can take to decrease the health risks to the public from handling and feeding raw meat diets to their animals;
- Issued a notice in July 2004 reminding dairy producers and others that they should not feed milk replacer products that contain neomycin to calves that could go to slaughter as veal;
- Investigated 743 tissue residue violations via our compliance program resulting in issuing 105 tissue residue-related Warning Letters, and 3 injunctions against dairy farms that had marketed cows and calves whose edible tissues contained illegal drug residues;
- Initiated use of a drug inventory survey form by investigators who make on-farm visits to help establish priorities for drugs to be included in the USDA National Residue Plan;
- Met with various trade associations and issued an assignment to FDA District Offices to inspect 20 compounding pharmacies to reduce the risk from use of compounded veterinary drug products in food-producing and non-food-producing animals;
- Completed inspections of more than half of the approximately 1141 FDA-licensed medicated feed mills in the United States;
- Completed 50 feed recall events. Thirty-three of the 50 recall events were feed related. Fifteen of the 33 recalls were related to BSE feed regulation;

- Assisted the states in reviewing feed labeling and pursued regulatory action if necessary. Completed 131 label reviews;
- Per FDA's request, the manufacturer of the heartworm medication ProHeart6 agreed in September 2004 to cease production immediately and recall the drug from the market until FDA's concern about adverse reaction reports associated with the product could be resolved;
- Reviewed and summarized comments received from a two-day public meeting in September 2003, with industry, government and public consumers, to discuss the potential development of a comprehensive, risk-based Animal Feed Safety System. Prepared a report identifying the strengths and weaknesses of current U.S. and international programs. Made available the draft definitions for comprehensive and risk-based, and the basic elements of process control for public review. All were placed in the AFSS docket to allow for public comment;
- Issued FACTS Assignment #539994 entitled "Dioxins in Fish Meals, Fish Oils, Deodorizer Distillates and Filtering/Bleaching Clays – Nationwide Survey." on June 16, 2004;
- Summarized the results to date on dioxin levels in grains, grain by-products, fish meal, fish oil, and forages. Also summarized the dioxin results from 14 follow-up investigations in cattle that the FDA conducted as a result of a recent USDA survey;
- Received 28,424 adverse experience reports, over 5,000 more than FY 2003, and reviewed 18,625 of these complaints. Because of the severity of this year's complaints, we spent considerably more review time than in previous years reviewing individual adverse drug event (ADE) submissions involving heartworm drug safety and lack of effectiveness; and,
- Finalized a curriculum for cGMP training and initiation of the Pharmaceutical Inspectorate Training Course in August 2004. This supports the FDA's priority of modernizing the health care system through improved cGMPs.

Emerging Issue – Monkey-Pox

- On November 4, 2003, in collaboration with CDC, issued an interim final rule for Monkey-Pox, a zoonotic disease that spread from imported African rodents to prairie dogs to humans. The interim final rule is to establish new restrictions and modify existing restrictions on the original FDA/CDC Joint Order adopted on June 11, 2003 under the Public Health Service Act; and,
- Assured affected parties were notified of the Interim Final Rule, coordinated the follow-up to possible violations of the Rule, and evaluated requests for permits to allow movement of animals for reasons other than those identified in the Rule.

During FY 2004, FDA responded to approximately 125 requests for a permit, mostly dealing with the capture and transport of wild prairie dogs, to transport these animals.

PATIENT AND CONSUMER PROTECTION

Antimicrobial Resistance

- Published the final Guidance for Industry #152 document on antimicrobial resistance on October 23, 2003. This guidance was developed with public input and is significant because it provides a scientific, risk-based approach to preventing antimicrobial resistance that may result from the use of antimicrobial drugs in food-producing animals;
- Developed a database that will be searchable from the web containing a listing of all antimicrobials approved for use in food animals;
- Prepared a draft risk assessment to assess the link between the use of Virginiamycin in animals and Synercid resistance in humans and released it for public comment due back by February 23, 2005;
- Created animated video that depicts the ways bacteria typically acquire resistance to antimicrobial drugs to advance understanding to key audiences, particularly veterinary students and livestock producers;
- Continued to review previously approved new animal antimicrobial drug submissions with respect to antimicrobial resistance and human food safety;
- Completed the review of the penicillin approvals for microbiological food safety concerns and discussed findings and recommended actions with the drug sponsors;
- Supported an advanced WHO training course on the surveillance of Salmonella and antimicrobial resistance in food borne pathogens; and,
- Participated in the cooperative agreement with four sites in Mexico to determine the prevalence of Salmonella species and quinolone-resistant E.coli from symptomatic and asymptomatic humans.

National Antimicrobial Resistance Monitoring System (NARMS)

- Continued expanding the retail meat arm of NARMS at FDA/CVM/Office of Research by having 10 FoodNet sites collect samples from local grocery stores and submit the isolates to the CVM/OR for antimicrobial susceptibility testing to obtain a more representative picture of the contribution of the food supply to antimicrobial resistance and helps sponsor with their submissions to CVM under GFI #152;

- Continued to improve NARMS methods including development of a Campylobacter broth microdilution method approved by the National Committee for Clinical Laboratory Standards Veterinary Antimicrobial Susceptibility Testing;
- Completed the first annual NARMS retail meat report on September 30, 2004, which can be found on CVM's website. This report provides data on the prevalence of antimicrobial resistant foodborne pathogens and commensal bacterial among retail meat and poultry samples;
- Enhanced the robustness of the NARMS retail meat arm by training personnel in state public health labs in isolation and testing methodologies. The retail meat arm was expanded from 6 labs in FY 2002 to 10 in FY 2004;
- Screened animal feeds and animal feed components for the presences of resistant pathogens including Salmonella, E. coli and Enterococcus;
- Conducted numerous presentations on NARMS at national and international scientific meetings; and,
- Completed total revision of the NARMS web page with the addition of NARMS peer-reviewed publications and FDA Veterinarian articles.

PROTECTING THE HOMELAND -- COUNTERTERRORISM

Counterterrorism

- Participated with Agencies and other sectors in coordinating:
 - Food and Agriculture, Critical Infrastructure Protection Sector –Wide Meetings;
 - Foot and Mouth Disease Dairy Research Working Group;
 - White House Agroterrorism Blue Ribbon Panel;
 - Development and testing of emergency response plans for chemical, biological, and radiological incidents;
- Assisted in publication and education outreach efforts for the Bioterrorism Act of 1992 covering Registration, Prior Notice, Automatic Detention, and Record Keeping Rules;
- Evaluated rapid laboratory methods to permit analysis of feedstuffs for microbiological hazards, and comparing these methods to existing cultural methods;
- Collaborated with other government agencies on the development of a list of priority products for countermeasures which will be used in assembling a National Strategic Veterinary Stockpile;
- Responded to Homeland Security Presidential Directives (HSPD)-7 and -9 by drafting and submitting the Animal Feeds portion of the National Infrastructure Protection Plan which is a part of DHS National Critical Infrastructure Protection Program, as

well as, working on methods that will integrate surveillance systems to quickly detect emerging diseases, pests, toxic substances, and radioactive agents that threaten agriculture and the food supply; and,

- Performed initial vulnerability assessments of animal feeds.

IMPROVING FDA'S BUSINESS PRACTICES

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

- Implemented CVM's Activity Time Reporting System center-wide with the 1st pay period of FY 2004. The system was developed and designed to be a user friendly integrated system dedicated to supporting the Center's Activity Based Management goals and contributing to improved program planning/prioritization, and budget and performance integration and management. Data from the system was utilized to support ADUFA financial implementation and supports the tracking of allowable ADUFA costs by activity. The Agency is developing a plan to leverage these activities agency-wide;
- Implemented Strategic Human Capital Management – Used the Staff College Competency Model in the recruiting and interview process to ensure identification and selection of the best-qualified candidates for the hiring of the new animal drug reviewers to meet the workload increase with the initiation of the ADUFA;
- Continued to develop and expand the CVM Staff College that was established in FY 2002 through a state-of-the-art Knowledge Management Center providing the framework to support the development and delivery of a robust scientific, management, leadership, and team building curriculum based upon researched and established core competencies necessary for high performance in specific positions and functional areas;
- Implemented the mandatory EEO and Diversity Management Training Program for all managers and supervisors;
- Continued to enhance IT management consistent with the President's expanded E-government initiative;
- Supported the implementation of the FDA IT Director's Migration Plan that moved the Agency IT managers and staff into the Agency's Office of the Chief Information Officer; and,
- Reduced and redistributed the administrative workload and consolidated functions and tasks that are required in the organizational area to exceed its 2004 targeted administrative position reductions as directed by the Agency.

**Animal Drugs and Feeds
Program Activity Data**

PROGRAM WORKLOAD AND OUTPUTS ¹	FY 2004 Actuals	FY 2005 Estimates	FY 2006 Estimates
New Animal Drug Applications (NADAs): ²			
Received	15	23	23
Completed	23	23	23
Approved	18	18	18
Pending ³	3	3	3
New Animal Drug Application Supplements: 2 ⁴			
Received	408	408	408
Completed	476	476	476
Approved	356	356	356
Pending 3	156	88	20
Abbreviated New Animal Drug Applications (ANADAs): ²			
Received	61	61	61
Completed	55	61	61
Approved	19	19	19
Pending 3	47	47	47
Abbreviated New Animal Drug Application Supplements: 2 4			
Received	211	241	241
Completed	195	220	220
Approved	163	183	183
Pending 3	78	99	120
Investigational New Animal Drug (INAD) Files: ⁵			
Received	2,138	2,138	2,138
Completed	2,200	2,200	2,200
Pending 3	264	202	140

¹ CVM has implemented a user fee program in FY 2004. Outputs are not expected to increase substantially until new reviewers are hired and fully trained. Performance estimates are dependent upon a sustained level of base and user fee resources. The FY 2005-2006 estimates do not include invited labeling change supplement applications because it is not possible to accurately project sponsor or CVM requests for this type of application.

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

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

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

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

Animal Drugs and Feeds Program Activity Data

ADUFA Performance Cohort*	FY 2004		
Application/Submission Type:	Goal: Review & Act On	# Reviewed & Acted On	Perf. As of 9/30/04
<i>New Animal Drug Applications (NADAs)</i>			
NADAs & reactivations	90% w/in 295 days	5	100%
Administrative NADAs & reactivations**	90% w/in 90 days	8	100%
<i>New Animal Drug Application Supplements & Reactivations***</i>			
Non-manufacturing**** (Safety & Efficacy)	90% w/in 320 days	8	100%
Manufacturing	90% w/in 225 days	230	100%
<i>Investigational New Animal Drug (INAD) File Submissions</i>			
Data (Studies)	90% w/in 320 days	107	100%
Protocols	90% w/in 125 days	147	100%

This chart reflects information provided in the FY 2004 ADUFA Performance Report.

*All FDA review performance statistics are based on fiscal year receipt cohort. This methodology calculates performance statistics for submissions for the fiscal year FDA received them, regardless of when FDA ultimately acted on or approved the submissions. A consequence of this approach is that the statistics shown for a particular year may change from one report to the next. This is because as time passes, FDA completes work on more and more submissions in a receipt cohort. As more submissions are completed, the statistics for that year of receipt must be adjusted to reflect the new completions. Until all submissions in a cohort are completed, only a preliminary performance assessment can be provided for that cohort. With the exception of this report, where only information for the first reporting year (FY 2004) is available, FDA will report, in subsequent years on two performance years for ADUFA performance. Starting with the FY 2005 report, the status of the current year and an update on the previous year will be included.

**Administrative includes both original and supplemental applications, including their reactivations.

***Certain supplements are excluded, such as sponsor changes, minor changes to labeling, requests to withdraw and trade name changes, not involving safety and/or effectiveness data.

****Non-Manufacturing hybrids are included. A "supplemental animal drug application" is: a supplement, manufacturing or non-manufacturing, to an application approved under section 512(c)(1) of the act (21 U.S.C. 360b(c)(1)) (i.e., a supplement to an NADA), regardless of whether data with respect to safety or effectiveness are required for approval; *or* a supplement, manufacturing or non-manufacturing, to an application approved under section 512(c)(2) of the act (21 U.S.C. 360b(c)(2)) (i.e., a supplement to an ANADA), provided that data with respect to safety or effectiveness are required for the supplement to be approved.

PERFORMANCE GOAL AND TARGET

The following table of performance goal and FY 2006 target is presented to compliment the sequential display of this program’s “outputs” by more closely linking the traditional budget presentation of base and increased activities and workload outputs contained in the Program Activity Data (PAD) charts. Activities discussed throughout this narrative support the accomplishment of outputs (PAD and performance goals) which in turn contribute to the accomplishment of long term outcome and strategic goals. Full cost information for these goals as well as other historical information has been provided in their respective sections in the Detail of Performance Analysis contained in the supporting information tab.

Performance Goal	Target
<p>Promote safe and effective animal drug availability ensuring public and animal health by meeting ADUFA Performance goals.</p> <p>This goal is dependent upon a sustained level of base and user fee resources. (14020)</p>	<p>FY 06: Complete review and action on 90% of original NADAs & reactivations of such applications received in FY 2006 within 230 days.</p>

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