FISCAL YEAR 2006 - OCTOBER 1, 2005 - SEPTEMBER 30, 2006

ANNUAL REPORT

CENTER FOR VETERINARY MEDICINE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES - Food and Drug Administration

USING SCIENCE AND LAW TO PROTECT PUBLIC AND ANIMAL HEALTH

THE CENTER FOR VETERINARY MEDICINE

ANNUAL REPORT

Fiscal Year 2006: October 1, 2005–September 30, 2006

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CELEBRATING THE CENTENNIAL YEAR

FDA's Centennial Bike Ride

The year 2006 was FDA's Centennial year, celebrating the anniversary of the Food and Drug Act of 1906. The 1906 law transformed FDA into a scientific regulatory agency, making it the oldest consumer protection agency in the United States. Throughout the year, FDA worked with stakeholder organizations that represent the interests of FDA employees, consumers, professional societies, public health organizations, and industry to celebrate the Centennial. These organizations played important roles in changing mandates and in increasing the Agency's capacity to carry out its mission over the last century.

A few of the many participants in the FDA Centennial Bike Ride: (Front row, left to right) Dr. Bernadette Dunham, CVM; Dr. Ann Stohlman, CVM; Dr. Elizabeth Luddy, CVM; Dr. Susan Storey, CVM. (Back row, left to right) Dr. Heather Case, American Veterinary Medical Association 2006-2007 Congressional Fellow; Dr. Raymond Petryshyn, National Institutes of Health; Dr. Bonnie Buntain, U.S. Department of Agriculture.

GOALS OF FDA'S CENTENNIAL EVENTS

- Commemorate the first 100 years of contributions to Americans' public health and the world community with a focus on the future.
- Observe FDA's role – past, present, and future – in protecting and promoting the health of the public.
- Inspire the next generation of science, innovation, and public health through partnerships and alliances with key stakeholders.
- Salute the contributions of dedicated FDA employees, alumni, legislators, academicians, industry, advocacy groups, and public health leaders who support the consumer protection mission of the Agency.

As a means of educating the public about FDA's history and mission, the Center for Veterinary Medicine (CVM) partnered with the Potomac Pedalers Touring Club in its annual Historic Back Roads Bicycle Tour held in September 2006 in Berryville, VA. More than 1,200 riders celebrated FDA's Centennial by participating in cycling tours of up to 100 miles, providing an opportunity for FDA to lead by example through FDA employee participation in activities that encourage exercise, fitness, and overall personal health. The Potomac Pedalers Touring Club provided well-planned and marked cycling routes, great food, and plenty of friendly volunteers for the event.

A Health Fair provided a venue for FDA, along with numerous community and public health groups, to communicate health information to the public. Groups working with diseases such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), hemophilia, and kidney disease, and organizations such as the American Lung Association and VA-MD Regional College of Veterinary Medicine, were represented. The FDA Office of Women's Health, FDA History Office, and CVM brought exhibit displays. CVM gave riders informational fliers about companion animals, such as: *"Taking Care of Pets During a Disaster or Emergency," "Caution to Pet Owners – Pet Treats and Toys May Cause Problems for Your Pet,"* and *"Selecting Nutritious Pet Foods."*

The event brought together volunteers from across FDA and the local community to provide health information, encourage fitness, and share FDA's history of public health protection with the public. Riders and their families enjoyed the day and left with a deeper appreciation of FDA's rich history and mission.

RECOGNIZING EFFORTS BY TEAMS DRAWN FROM ACROSS THE CENTER AND THROUGHOUT FDA

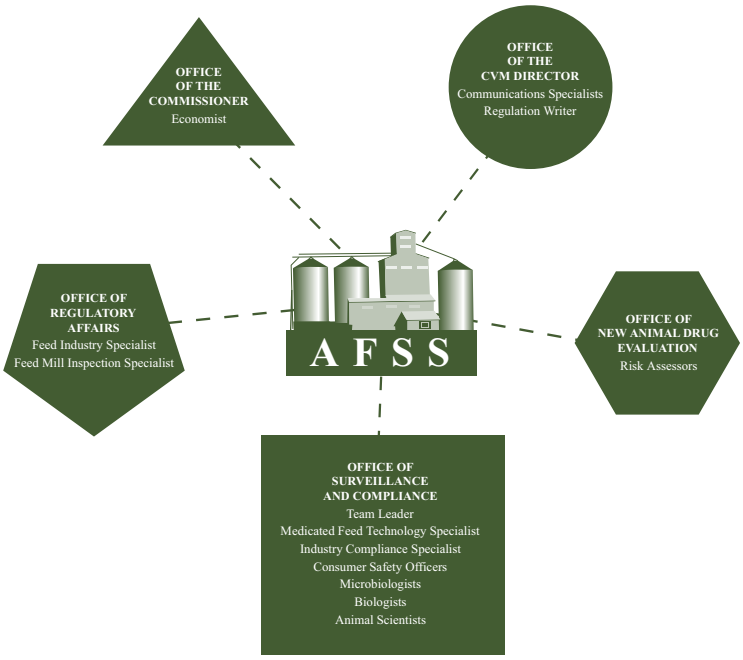
Feed Safety Team Shows Center's Ability to Assemble Best Team

CVM is not known for its size, but is recognized for its ability to reach out and find the expertise it needs to tackle scientifically and logistically complex issues. This ability was evident in the way CVM approached the task of developing the Animal Feed Safety System (AFSS).

The Center undertook the AFSS initiative in 2003 to bring together all aspects of its feed safety responsibilities under one unified program. The initiative is "an umbrella regulatory program aimed at protecting human and animal health. The AFSS covers regulation of the labeling, production, and distribution of all feed ingredients and mixed feeds, at all stages of manufacture, distribution, and use," according to the draft framework the AFSS Team issued in 2005.

To get the job done, CVM drew team members from across the Center and from other parts of the Food and Drug Administration (FDA). Dr. George Graber, Deputy Director of the Office of Surveillance and Compliance, leads the AFSS Team. The Team includes experts from within the Center: a microbiologist, a biologist, chemists, animal scientists, a medicated feed technology specialist, risk assessors, an industry compliance specialist, and several consumer safety officers with expertise in feed manufacturing and regulatory issues.

In addition, the Team has a communications specialist and a regulation writer from the Center Director's Office, an economist from the Commissioner's Office, and representatives of FDA's Office of Regulatory Affairs.



CVM's Animal Feed Safety System Team uses experts from across the Center and FDA to develop the initiative.

Early in its work, the AFSS Team decided to take a risk-based approach in developing the feed safety system. This approach would allow the greatest attention to be focused on the greatest risks in the manufacturing, distribution, and use of animal feed.

CVM had already assembled a risk assessment team, which resides in CVM's Office of New Animal Drug Evaluation (ONADE). A previous risk assessment initiative, addressing antimicrobial resistance, had coincided with the development and use of risk assessment methodology to address microbial risks in the food industry. Dr. Barry Hooberman, the member of the CVM risk assessment team who joined the AFSS Team, said, "The CVM risk assessment team has

generally viewed one of its goals to be 'spreading the gospel' about how the tools of risk assessment can be used to aid decisionmaking in much of what CVM does, whether the issue pertains to new drug approval, surveillance, compliance, or addressing emerging public health issues. Although the risk assessment team is officially housed in ONADE, we have been given a great deal of support in reaching across office boundaries."

Dr. Hooberman said, "The risk assessment process is a very fluid process, in that it can be adapted to fit a wide range of problems and issues. However, the basic tenets remain constant, and it provides a structure to organize and analyze the relevant data to support decision-making by the risk managers."

To implement a risk-based system, the AFSS Team needed to develop a risk-ranking tool that incorporates a three-step process. The first step is identifying specific hazards. A hazard can be chemical, physical, or biological contamination (for instance, dioxin or aflatoxins). The second step is determining the likelihood of animal exposure to the contaminant, and the third-step is determining what the consequences of that exposure would be (which could range from reduced productivity in animals to illness or death in animals or humans, for example). Once all three steps have been taken, the feed safety system can be utilized to rank the relative risks of all hazards. The AFSS Team will use the information to develop an approach for determining which feed contaminants present the greatest risk to animal and human health, and for deciding how such risks can be prevented or controlled.

Dr. Hooberman added, "What is particularly challenging about the risk assessment component of the AFSS is that the AFSS Team is developing a risk-ranking scheme that attempts to combine both chemical and biological risks. One other feature that is of particular concern is the need to address data gaps and the resulting uncertainties associated with the risk ranking results."

After creating the framework document and a concept paper, the AFSS Team sponsored three public meetings to discuss initial concepts for AFSS, the framework, and the first part of the risk assessments. The AFSS Team's work on the initiative is scheduled to conclude in FY 2007 with recommendations on how to implement the AFSS concepts. This report has highlighted specific FY 2006 accomplishments in the section on "Ensuring Feed Safety."

Even though its work is not yet completed, the AFSS Team provides an example of the Center's flexible nature. The Team can draw on expertise from across the Center and even across the Agency to address a complex task such as this one.

Innovative Work of a Multi-Office, Multidisciplinary Inspection Team Receives FDA Recognition

This past year, FDA recognized members of a multi-office, multidisciplinary team that collaborated to conduct a pre-approval Good Laboratory Practices (GLP) inspection of a pharmaceutical company that manufactures several generic animal drugs.[1] This was a complex inspection of four different facilities, and it included an audit of data from five bioequivalence studies that impacted four separate generic animal drug applications.

The inspection was "for cause," conducted because of possible data inconsistencies found in bioequivalence studies that had been submitted to support a generic new animal drug application. Such studies are crucial in generic applications, because the drug must be shown to be bioequivalent to a pioneer drug before CVM can approve the generic drug.

[1] The team consisted of members of CVM's Offices of Surveillance and Compliance and New Animal Drug Evaluation: Jean E. Bowman, D.V.M., John K. Harshman, D.V.M., Zollie A. Perry, Ph.D., George A. Prager, Sharon L. Ricciardo, Vernon D. Toelle, Ph.D. and Fredda Shere-Valenti; and the Denver District Office, FDA's Office of Regulatory Affairs: Teena H. Aiken, Kent C. Faul, and Eric R. Smith.

This collaborative effort featured several innovations, including a user-friendly, efficient, technology-driven format the team developed for electronic exchange of data and information submitted by the sponsor, as well as exchange of comments from team members in different locations. In the past, FDA District Offices – which conduct facility inspections for all FDA Centers – had received thousands of pages of documents for use in inspections, with no convenient way to cross-reference studies. In this inspection, FDA's Denver District Office received two password-protected CDs with all documents in .pdf format. This novel approach allowed detailed explanations of reviewer or inspector concerns to be placed electronically on a page with an embedded link to other examples of similar concerns. This inspection was the first time a District Office had received information from any FDA Center in this format.

In preparation for the inspection, members of the Bioresearch Monitoring and Administrative Actions Teams (from CVM's Office of Surveillance and Compliance) and the primary reviewer on the Generic Animal Drug Team (from CVM's Office of New Animal Drug Evaluation) carefully reviewed volumes of study data to categorize possible inconsistencies that the District Office investigators would use to plan the inspection and determine the best utilization of resources.

The actual inspection of the pharmaceutical company involved two inspectors from the Denver District Office and a representative from the Generic Animal Drug Team. Each individual represented unique expertise: a chemist, an experienced field investigator, and a Consumer Safety Officer with a clinical veterinary medicine background. The inspection took place at all four sponsor sites and included employee interviews and review of all clinical data.

The team members collaborated on the Establishment Inspection Report, decisions on final disposition, and further review of data. This inspection was a model of thorough, efficient, cohesive regulatory action. The unique presentation of data will be used as a possible prototype for all FDA Centers involved with pre- and post-regulatory inspections. The professional respect for individual and group expertise and efficient use of resources shown in this joint effort represent an outstanding example of what is being done to fulfill the CVM Mission.

The Generic Animal Drugs GLP Inspection Team received an FDA Group Recognition Award "for exceptional performance and outstanding innovation by CVM and the Office of Regulatory Affairs in coordinating and executing a complex GLP inspection."

RECOGNIZING INDIVIDUAL ACHIEVEMENT

Award Winner Recognized for Creating a High-Performance Division at CVM

Director's Award to William Marnane: *"For providing exceptional leadership in the management of personnel and critical manufacturing initiatives important to the mission and goals of the Center."*

William Marnane, Director of CVM's Division of Manufacturing Technologies (center) was presented a leadership award for his work to develop the division. On the left is Dr. Dennis Bensley, Jr., Division Deputy, and on the right is Dr. Julie Conwell, a supervisory team leader in the division.

The FY 2006 "Director's Award," the highest award the Center presents, went to William Marnane, who, a decade ago, took on the job of developing the Center's Division of Manufacturing Technologies. Through innovation, enhanced communications with the FDA field staff, and development of a highly productive staff, Mr. Marnane succeeded in developing a Division that offers drug sponsors a more efficient review process.

CVM created the Division in 1996 as part of the Center's Strategic Plan to centralize all aspects of the chemistry, manufacturing, and control portion of animal drug application review and approval. Mr. Marnane has developed the Division's organization over the years by creating the Feed/Topical Team, the Biotherapeutics Team, and the Generic Review Team. (The previously existing Chemotherapeutics and Antimicrobial Teams remain in the Division.) The Division is involved with a drug "from birth to death," Mr. Marnane says. The Division conducts pre-approval reviews of the drug applications to make sure the proposed manufacturing standards are adequate to produce safe and effective drugs. The Division coordinates with FDA field investigators, who inspect the actual manufacturing sites to make sure they can continuously manufacture high-quality drugs, both pioneer and generic. And it reviews supplemental applications and annual reports for changes to approved applications, in addition to carrying out other post-approval responsibilities.

Under Mr. Marnane's leadership, the Division introduced concepts such as "Quality by Design." This concept allows a sponsor to demonstrate process knowledge, apply risk assessment and quality system techniques, and significantly improve the quality of the submission. High-quality submissions ease the regulatory burden and can lead to shorter review times, which is consistent with the Division's efforts to move toward One-Cycle Review. Quality by Design is an example of CVM's efforts to facilitate drug approval review by improving the Center's relationship with the animal drug industry. Further improvement will be "the result of more and better communication between a well-organized Division and its customers," Mr. Marnane said.

Mr. Marnane has also focused attention on coordination with the FDA field staff. "The Division's organizational structure facilitates frequent interactions between pre-market review staff and FDA field investigators. To further enhance communication with the FDA field, reviewers from the Division participate in on-site pre-approval inspections with field investigators to provide technical support when necessary," he said.

Undoubtedly, an important part of Mr. Marnane's success is his development of the Division's staff. He relied on the management strategy called "High Performance Organization" (HPO), introduced in the Center at about the same time the Center created the Division. "Building the concepts of the HPO into the Division made sense, because the vision and values (contained in HPO) are consistent with the kind of Division that we wanted to build," Mr. Marnane said. "Quality of life, alignment with Division, Office, and Center goals and objectives, transparency, empowerment, stewardship, metrics, and business plan objectives being sought by the Division were all key components of HPO."

Mr. Marnane gave the Division staff as much direct involvement and responsibility as possible to achieve the goals. "We have empowered staff through a participative process in which staff members make recommendations on bonus award allocations based on individual performance, participate in the process of interviewing and recommending candidates to be offered a position in the division, and tackle longstanding issues pertinent to consistent review quality across the Division," he said.

According to Mr. Marnane, "Transparency, coupled with development of a bottom-up philosophy and alignment, were probably the most important building blocks needed for empowerment. The greatest contributors to the success of HPO implementation within the Division of Manufacturing Technologies are the people themselves and their willingness to embrace the concepts of the HPO model."

INNOVATING FOR MANAGEMENT EFFICIENCY AND SUCCESS

Project Management Employed in Several Areas at CVM

Several years ago, the CVM adopted a strategic plan that called for the Center to "improve, and bring discipline to and through, our business practices." To give that statement weight, the Center implemented project management, applying it initially to four pilot projects and later to other priority projects. CVM's project management strategy is designed to help the Center become more effective and efficient in carrying out its core and supporting functions.

Project management specialists at CVM: (From left) Madeline Vanhoose, Project Management Professional (PMP), Director of CVM's Project Management Staff; Susan Dewitt, Project Manager; Petra Kotek, PMP, head of the Project Management Team in CVM's Office of New Animal Drug Evaluation; and Kim Sanders, PMP, head of the Information Technology Project Management Office at CVM.

In simplest terms, project management is a methodical approach to planning and guiding a project from start to finish. At CVM, project management tools, techniques, and processes are flexible, depending on the size, duration, and complexity of the project. We initiate small or simple projects with a brief project definition and timelines monitored using an Excel spreadsheet. On the other end of the spectrum, for large or complex projects, we define fully the goal, objectives, implementation strategies, deliverables, assumptions, and risks, and monitor progress using Microsoft Project software.

CVM's senior project management official and Director of the CVM Project Management Staff is Madeline Vanhoose, M.S., who recently received certification as a Project Management Professional (PMP) from the Project Management Institute. Madeline works with Susan Dewitt, Project Manager for the CVM Project Management Staff, to implement and support project management throughout the Center. Susan is also the administrator for Enterprise Microsoft Project, CVM's standard project management software.

We applied project management to the following four high-priority crosscutting projects in 2006:

CVM Communications Clearance Project. Before the communications clearance policy development team completed its work, different offices within the Center had different publication clearance procedures. For example, scientists within the Center who wanted to publish a report or release other information did not have a clear path to follow to obtain appropriate authorization. Collaborating authors in different offices had different and sometimes conflicting publication clearance procedures to follow.

CVM had attempted several times to develop a Center-wide policy, but only with limited success. It decided to apply project management to the goal of drafting a Center-wide policy for staff and management to use in seeking clearance of various publications, such as articles, speeches, and other documents, for release to the general public.

To accomplish this task, the Center formed the Communications Clearance Policy team that included representatives of each office that clears publications, and a project manager. By applying project management principles, the team was to develop a unified policy that, with Center Leadership Team approval, was implemented Center-wide early in FY 2006.

"Lessons Learned" sessions revealed that the team was successful because it used a variety of project management principles, tools, and techniques, including: use of a Project Definition document that defined the goal, objectives, scope, deliverables, risks, assumptions, and project environment impacts; a Team Charter that defined the roles for team members and ground rules for meeting conduct; and a project plan that served as a roadmap and checklist for the efforts of the team and to avoid "scope creep."

Office of New Animal Drug Evaluation (ONADE) Office-Wide Project Management Pilot Project. The ONADE Project Management Team (PMT), headed by Petra Kotek, M.S., PMP, arose out of the Animal Drug User Fee Act (ADUFA) and the need for the organization to manage animal drug reviews at the application level. The ONADE PMT has two primary focuses.

First, the team brings the tools of project management to bear on submissions to Investigational New Animal Drug files and New Animal Drug Applications, enhancing the abilities of the team leaders and review staff to manage those applications. The team ensures that ONADE is meeting ADUFA timeframes, thus promoting efficiency in the drug approval process in order to get safe and effective drugs to market faster. The team is also developing procedures to facilitate periodic project meetings with drug sponsors, which will allow ONADE to project workload and better manage its human capital.

Second, the team is enhancing the project management of internal ONADE projects, such as development of guidance documents and standard operating procedures. The team works closely with ONADE's Management Team to ensure that these systems effectively support the new animal drug review process and mission of the Office.

With the incorporation of project management into the drug development process, the ONADE PMT has begun to schedule and manage post-approval meetings for all significant approvals. The goal of the meetings is for CVM and the drug sponsor to document "lessons learned" so future projects run more smoothly and efficiently. Drug sponsors are encouraged to contact the PMT to schedule these meetings.

Document Control Unit Upgrade. CVM has applied project management to the design and development of physical space for housing the Center's drug application records. The challenge had two parts: to expand the space for documents, and to ensure either that all the documents were properly "backed-up" or that copies were stored in case of damage to the original documents. A special team completed this project near the end of the fiscal year and was conducting closeout evaluation and "lessons learned" sessions at that time.

Animal Feed Safety System Project. Described elsewhere in this annual report, the AFSS is a longer-term project management pilot. The project has successfully achieved its early milestones, including several public meetings.

Other projects initiated this past year to which the Center applied project management include:

- The development and proposal of "index" rules under the Minor Use and Minor Species Animal Health Act of 2004, a priority project that had high visibility outside the Center.

- The development of import tolerance regulations and guidance that will enable stakeholders to know the process and data requirements needed to apply for a tolerance for drug residues in imported animal food products.
- The development of project management templates for some of CVM's ongoing internal processes with deadline commitments, to help manage these processes more efficiently and achieve their deadlines. Some of these processes include the CVM Annual Report (including this one!), the *FDA Veterinarian*, and the National Antimicrobial Resistance Monitoring System Retail Meat Annual Study Report.

Project management at CVM continues to evolve and improve, with more resources becoming available to support an increasing number of project managers and projects, and to improve CVM's business practices. For example, the Center is applying project management to its Information Technology (IT) initiatives. Specifically, it is applying a project management technique called Earned Value Management (EVM), which objectively measures the technical, schedule, and cost performance of an IT project. EVM provides early warnings of performance problems, enabling project managers to take timely corrective action. Kim Sanders, PMP, leads the Office of Information Technology Project Management Office that supports CVM and oversees the planning, execution, and management of all CVM-approved IT projects.

A MESSAGE FROM THE DIRECTOR

CVM Director, Dr. Stephen F. Sundlof

Many of the accomplishments we report this year are the result of multidisciplinary and multiorganizational efforts. Teamwork is one of our guiding principles. The initiatives we describe reach across the offices within the Center for Veterinary Medicine (CVM) and outside the Center – throughout the Food and Drug Administration (FDA), to other government agencies (international, Federal, and State), to colleges and universities, and into the private sector. Some of the vignettes contained in the preface describe these sorts of cooperative efforts, and a number of CVM-related FDA awards given this year included recipients who have partnered with us.

We value these alliances, for they bring the best possible combination of skills and experience to bear on problems that are within our mandate, doing so with the minimum expenditure of valuable resources. Virtually all of the accomplishments cited in this annual report involve cooperative efforts, and all of CVM's offices contributed to the achievement. I would like to highlight some of the successes.

Progress in New Animal Drug Approvals

The major part of the work in this area comes from our Office of New Animal Drug Evaluation, and our Office of Minor Use and Minor Species Animal Drug Development (OMUMS). But other offices contribute much – for example, the Office of Management in the planning and expenditure of funds under the Animal Drug User Fee Act (ADUFA), and the Office of Research in conducting work that supports drug approvals both for major and minor species and uses.

ADUFA. CVM met all of its performance and financial goals under ADUFA during fiscal year 2005, the second year of the program. We worked diligently to accomplish the ADUFA goals for FY 2006. We are using the increased resources from user fees to bolster our ability to review animal drug applications in a timely fashion. We are working against tighter deadlines each year; for example, 230 days to complete reviews of 90 percent of new animal drug applications in FY 2006, compared with 270 days in FY 2005 and 295 days in FY 2004. ADUFA requires recruitment of significant numbers of new staff. We met our FY 2006 goals for hiring new professional staff to review new animal drug applications under ADUFA, and we were pleased with the high caliber of those we were able to employ.

2006 New Animal Drug Approvals. This year, we approved a number of new animal drug applications. EQUIOXX (Firocoxib) oral paste for control of pain and inflammation associated with osteoarthritis in horses – the first nonsteroidal anti-inflammatory drug approved for horses in over a decade – is an example of an approval for nonfood animals. For food animals, we approved ZILMAX (zilpaterol hydrochloride), a nonhormonal, nonantimicrobial new chemical entity for improved production efficiency and increased carcass leanness in cattle. And we approved CYDECTIN (moxidectin) oral drench for treating parasites in sheep, a minor species.

Drugs for minor uses and minor species. We made steady progress during the past year in implementing the Minor Use and Minor Species (MUMS) Animal Health Act of 2004, which will significantly expand the availability of drugs for minor species, as well as minor uses in major species of animals. The Agency proposed regulations in August 2006

that will implement a MUMS provision under which FDA may add a minor species drug to an "index" of unapproved new animal drugs that may be legally marketed when the potential market for the drug is too small to support the costs of the drug approval process. We also took major steps toward implementing the "designation" provisions of the Act, which provide incentives to drug sponsors for gaining approval for MUMS drugs.

Achievements in this area resulted from leadership by OMUMS. Other CVM offices contributed, including the Office of Research, which conducted efficacy studies and published an online database for use by researchers. The U.S. Department of Agriculture (USDA), along with scientists in a number of universities, continued to facilitate MUMS approvals through National Research Support Project #7 (NRSP-7).

Attacking Public Health Issues – Ongoing and New

Antimicrobial Resistance. This past year, we took strides in several areas to minimize antibiotic resistance resulting from the use of antimicrobial drugs in animal medicine. Along with our partners – USDA and the Centers for Disease Control and Prevention – we continued to expand monitoring for antimicrobial resistance under the National Antimicrobial Resistance Monitoring System (NARMS). The three agencies strengthened data reporting and began implementing other recommendations made by an outside review panel convened during FY 2005. To provide leadership for all three arms of NARMS (animal, retail meat, and human), Dr. David White of CVM's Office of Research was named during the year as NARMS director.

We continued to develop the utility of NARMS to facilitate the pre-approval review of new animal drugs, through the efforts of people from several offices within CVM. NARMS data on the susceptibility of *Salmonella* spp. and *E. coli* to cefquinome were presented in the September 2006 Veterinary Medicine Advisory Committee meeting that addressed the microbial food safety of an antimicrobial drug application currently under review for use in food-producing animals.

A booklet published during the year, "Judicious Use of Antimicrobials for Aquatic Veterinarians," resulted from a joint effort of the Aquatic Veterinary Medicine Committee of the American Veterinary Medical Association and CVM's Aquaculture Working Group. The booklet helps aquatic veterinarians treat animals in a way that minimizes the development of resistance in human and animal pathogens.

Bovine Spongiform Encephalopathy (BSE). The Office of Research during the year completed the development of a real-time polymerase chain reaction method for the identification of bovine, sheep/goat, and deer/elk material in animal feeds. This is a major step that will permit identification of material that is prohibited from use in ruminant feed by our BSE feed regulation. After validation, the method will be ready for regulatory use.

The Office of Surveillance and Compliance is working with the FDA Office of Regulatory Affairs (ORA) to develop a risk-based plan for inspection of facilities that process prohibited material; this plan will result in improved product quality and safety through prioritization of facilities inspections based on risk. In FY 2006, investigators exceeded their goals for BSE-related inspections of feed manufacturers and animal product renderers – the result of cooperative efforts involving CVM, ORA, and State agencies.

Animal Drug Residues. Regulatory activity designed to reduce illegal drug residues in domestic meat products continued throughout the year. In addition, we are challenged by the need for safety oversight to catch up with the growth in the volume of imported products, especially seafood, that are under FDA's jurisdiction, as emphasized in FDA's strategic plan. Most of the U.S. seafood imports are products of aquaculture; drugs may be used for treatment or production in aquacultured species, both imported and domestically raised. This year, CVM researchers completed

the validation of a multi-residue method to detect drug residues in tilapia and trout. This accomplishment means that a multi-residue, multi-class method for drug residue analysis that provides great flexibility for laboratories testing imported and domestic aquacultured products is now available for a total of four of the most commonly aquacultured finfish species.

With the assistance of USDA, CVM researchers developed a provisional method for detecting 17 drugs in honey. This development is significant because the United States imports nearly 100,000 metric tons of honey each year, dwarfing our domestic production, and illegal drug residues have been found in some imported honey.

Avian Flu. In May 2006, we issued a final rule prohibiting the extralabel use in animals of two human drugs approved for prevention of influenza A, adamantane and neuraminidase inhibitor. The rule, which prohibits use of the drugs in chickens, turkeys, and ducks, is based on evidence that such use could lead to the emergence of resistant strains of influenza A virus, causing the anti-influenza drugs to be ineffective in humans.

Side Effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). When we learned that some dog owners were not being informed about the potential for serious adverse reactions of NSAIDs and had not received Client Information Sheets concerning these drugs from their veterinarians, we launched an extensive education program. We had considerable assistance in this effort – which was directed both to veterinarians and pet owners – from the American Animal Health Association and the American Veterinary Medical Association. Our Communications Staff, part of the Office of the Director, took the lead for CVM in designing and conducting the program.

Bioterrorism Vulnerability Assessments. During the year, we participated with other Federal agencies, State agencies, and industry volunteers, in conducting vulnerability assessments for grain elevators and cattle feedlots. These initiatives were carried out under the auspices of the Strategic Partnership Program-Agroterrorism (SPPA), created in FY 2005, to assess the potential risk from terrorist attacks against sectors of the agriculture and food industry.

Innovation – Critical Path to Drug Approvals

FDA has undertaken an initiative that addresses the recent slowdown in innovative medical therapies reaching patients. This high-priority area focuses on the urgent need to improve predictability and efficiency along the critical path from laboratory concept to commercial product. The Agency is addressing its role in advancing development science by working to make sure that its standard-setting process is informed by the best science.

CVM is a participant in this effort. For example, Dr. Raafat Fahmy of our Division of Manufacturing Technologies is conducting critical path research that supports innovation and efficiency in pharmaceutical development, manufacturing, and quality control. His work, done in collaboration with the University of Maryland School of Pharmacy, involves ground-breaking research in chemometric modeling – the application of mathematical and statistical models to predict physical and chemical properties of the active pharmaceutical ingredient and finished drug product – and near infra-red sampling technique.

Implementing Risk Management and Resource Management

We made progress during the year in developing a method for ranking feed contaminants according to the relative risks they pose to animal and public health. In doing so, we have had the assistance of representatives from other FDA offices, State regulatory officials, and feed industry representatives. This effort is a vital part of the Animal Feed Safety System (AFSS).

AFSS is just one of several CVM initiatives to use science-based risk management to obtain maximum public protection with limited resources. Similarly, we are using new management techniques to maximize the use of limited resources. For example, during the year, we utilized the Activity-Based Costing (ABC) System in conjunction with data from the associated Activity Time Reporting (ATR) System to develop management reports that have enabled us to better understand, manage, define, and assign the true costs of doing business.

Organizational Management and Change

The Center Leadership Team collaborates on day-to-day management and policy decisions facing the Center, as well as long-range planning, budgeting, and policy development.[2] In making its decisions, the Team considers scientific, economic, international, and environmental issues and their impact on the Center. Through its leadership, the Team continues to develop a work culture in CVM that fosters high performance and reinforces the Center's vision, values, and behaviors.

CVM's Center Management Team discussing issues during one of its regular meetings.

Appointments of individuals to serve in key positions are essential to the success of any organization. We made one such selection during the year, the appointment of Dr. Bernadette Dunham as Director, Office of Minor Use and Minor Species Animal Drug Development. Before coming to CVM in 2002 as ONADE Deputy Director, Dr. Dunham was Acting Director of the American Veterinary Medical Association's Government Relations Division. In that role, she was an effective part of a coalition that helped with the passage of the MUMS legislation.

Providing Leadership Within FDA

CVM continued to provide leadership on an Agency-wide basis during the past year. The Center's leadership role on the Agency-wide Bioinformatics Board, established in February 2006, is an example. The Board was created to achieve the FDA goal for a modern, well-integrated, efficient, and affordable infrastructure to support FDA administrative and regulatory business operations. CVM also served as the FDA pilot for the development of a marginal cost analysis requested by the President's Office of Management and Budget. Using ADUFA as an example, the analysis assessed how the impact of a change in funding on performance will help to improve budgetary and policy decisionmaking.

[2] CVM's Center Leadership Team members are as follows:
Dr. Stephen F. Sundlof, Director, Center for Veterinary Medicine
Dr. Andrew J. Beaulieu, Special Assistant to the Director, Center for Veterinary Medicine
Ms. Catherine Beck, Associate Director for Policy and Executive Programs
Dr. Bernadette Dunham, Acting Deputy Director, Center for Veterinary Medicine and Director, Office of Minor Use & Minor Species Animal Drug Development
Dr. David Grau, Senior Management Consultant
Dr. Daniel G. McChesney, Director, Office of Surveillance and Compliance
Mr. David E. Wardrop, Jr., Director, Office of Management
Dr. Marleen Wekell, Acting Director, Office of Research
Dr. Steven D. Vaughn, Director, Office of New Animal Drug Evaluation

Achieving on an Individual and Group Basis

The accomplishments of an organization are often reflected in the public recognition of its people. FDA and CVM management during the year recognized the outstanding work of our Center employees through the presentation of a large number of group and individual awards. In addition to numerous scientific, technical, and administrative awards this year, CVM honored several individuals for excellence in mentoring fellow employees. We recognized Dr. Andrew Beaulieu, Dr. Dennis Bensley, Mr. David Wardrop, and Dr. Haile Yancy for their extraordinary contributions to the lives and careers of numerous CVM staff as dedicated mentors and teachers. Full details for all the awards are in Appendix C.

The large number of articles published by CVM scientists during the year is evidence of their professional productivity. The article topics included antimicrobial resistance, drug metabolism and residues, drug effectiveness, pharmaceutical analysis, methods for detection of unsafe feed ingredients, biotechnology, and more. We have included a complete publications list in Appendix D.

The achievements we report resulted from the hard work of a competent and dedicated staff. As I have noted, this report also documents continued expansion of collaborative activities with many of our stakeholders and partners. These arrangements provide mutual benefit and allow us to fulfill our role in protecting the public health more effectively and efficiently. We are grateful for the support of our stakeholders and partners as we work together for the public good.

Reaching Performance Goals

We present more details on the Center's many accomplishments in this annual report. The following pages set out the challenges we face and our accomplishments during the past year. As highlighted throughout this report, our performance goals are aligned with the President's Management Agenda, the Department of Health and Human Service Secretary's 500-Day Plan and Department-Wide Objectives, and the FDA Strategic Goals. Where we reached our performance goals for FY 2006, we have so indicated. Where we fell short of the goals, we have indicated this also. We believe we best serve the public by reporting our shortcomings along with our accomplishments.

We believe that the reader can best appreciate the Center's FY 2006 accomplishments by understanding what CVM is all about, including our mission, plans, organization, and sphere of influence. Thus, the first major section of our annual report is "About CVM."

Our Mission and Guiding Principles

OUR MISSION…

The Center for Veterinary Medicine (CVM) is a consumer protection organization. We foster public and animal health by approving safe and effective products for animals and by enforcing other applicable provisions of the Federal Food, Drug, and Cosmetic Act and other authorities.

OUR GUIDING PRINCIPLES…

We are committed to:

Health Protection. We honor our role in protecting the health of people and animals, and value the principles and spirit of the supporting laws and regulations.

Integrity. We conduct ourselves with honesty and integrity, recognizing that upholding the public trust requires the highest standards of moral and ethical conduct.

Quality. We achieve excellence through the ongoing development of our competencies and continuous quality improvement in all our processes. In particular, we recognize the value and importance of science and law in reaching quality and timely regulatory decisions.

Teamwork. Everyone's contribution is important. Working together, we place the mission of the Center first and align our contributions, whether individual or in teams, toward that end. We conduct ourselves in accordance with the principles of consultative and participative decisionmaking.

Communication. We communicate information, ideas, decisions, and provide feedback, internally and externally to the organization, in a candid, timely, constructive, and clear manner.

Equity. We treat our customers and each other with fairness, courtesy, respect, and compassion, while fostering an atmosphere of mutual trust.

Diversity. We promote workforce diversity to strengthen and enrich the Center.

Innovation. We apply new concepts, ideas, and creative approaches to improve current operations and to meet the challenges of the future.

Safety and Health. We seek to ensure a safe and healthful workplace.

Quality of Worklife. We create and use programs that enhance our quality of worklife to improve our ability to carry out the mission of the organization.

Our Strategic Plan

CVM's strategic plan reflects the principles set forth in the President's Management Agenda, the 500-Day Plan initiative of the Secretary of Health and Human Services, and the Food and Drug Administration's Strategic Goals.

Our plan, "CVM's Back to Basics Approach for Carrying Out Our Public and Animal Health Mission," commits us to focus on our *core functions* of:

- Animal drug review (pre-market activities)
- Compliance-related actions
- Post-approval monitoring
- Animal feed safety

To help us focus on the basics, our plan establishes the following goals. We will:

- Set priorities (reviewed annually) and say "no" to lower priority items
- Improve, and bring discipline to and through, our business practices
- Support and use good science in establishing solid regulatory policy
- Improve the capacity of the organization to meet current and future demands on the Center
- Develop revenue enhancing strategies for core programs

Our Organization and Responsibilities

We carry out our mission through the efforts of people who are organized into six offices: the Office of the Director, the Office of Minor Use and Minor Species Animal Drug Development, the Office of Management, the Office of New Animal Drug Evaluation, the Office of Surveillance and Compliance; and the Office of Research. All of our offices are located in Rockville, MD, except the Office of Research, which is located in Laurel, MD.

OFFICE OF THE DIRECTOR (OD)

OD directs overall Center activities, coordinates and establishes Centerwide policy, and provides guidance for the implementation of the Center's "Back to Basics" strategic plan. The Center Director serves as CVM's representative and spokesperson concerning our activities, interacting with the general public, industry, the media, other government agencies, and national and international organizations.

The Director approves new animal drug applications and exercises other statutory authority that has been delegated to him. Other functions are performed through a Deputy Director and Associate Director for Policy and Executive Programs. The Office conducts communication and education programs, coordinates policy development and implementation, provides project management support for the Center, offers the services of the CVM Ombudsman, manages the Veterinary Medicine Advisory Committee, and coordinates the Center's international activities. The Office of Animal Care and Use coordinates accreditation and compliance with regulatory requirements of the Agency's animal care and use programs, and provides consultation on these issues.

OM Director David E. Wardrop, Jr., and Deputy Director Barbara Leach.

OFFICE OF MANAGEMENT (OM)

OM provides executive leadership and direction for management and administrative programs, policies, and issues at Center and Agency levels. OM management serves in strategic leadership positions on CVM and FDA councils and committees. The Office provides the Center's liaison services to the

Agency's Office of Shared Services, the Rockville Human Resources Center, and the Office of the Chief Information Officer to ensure efficient administrative services, as well as the effective delivery of information resources management services to CVM employees.

OM leads and directs the planning, development, and execution of the CVM budget, including the oversight of the Animal Drug User Fee Act (ADUFA) of 2003. It also serves as the Center liaison with the Agency concerning Government Accountability Office and Inspector General studies/inquiries. OM provides leadership for the Center's Activity-Based Costing/Activity Time Reporting System and integrates it into the business culture of the Center's operation.

OM directs the interaction with the CVM program offices and other FDA offices to assist with the efficient delivery of such services as property management, space and workplace planning, facilities management/operations, and workplace safety. In addition, OM represents management on issues regarding the FDA and National Treasury Employees' Union Collective Bargaining Agreement.

The CVM Staff College directs the development and implementation of the competency-based management, leadership, team-building curriculum, and an extensive scientific/technical curriculum. The College sets the Center's expectations with regard to required competencies through the Staff College Knowledge Center.

OM supports the vital information resources management function to enhance employees' abilities to efficiently work with the integrated Information Technology (IT) systems to reach CVM goals.

OFFICE OF MUMS ANIMAL DRUG DEVELOPMENT (OMUMS)

The Minor Use and Minor Species Animal Health Act of 2004 provided for the establishment of OMUMS. The Office reports directly to the CVM Director and is responsible for overseeing the development and legal marketing of new animal drugs for minor uses in major species (disease conditions that are rare) and minor species (including, for example, pet animals – except dogs, cats, and horses; many animals of agricultural importance, such as sheep, goats, catfish, honey bees; and zoo animals).

OMUMS Staff: New Director, Dr. Bernadette Dunham; previous Director, Dr. Andy Beaulieu; Dr. Meg Oeller.

OMUMS is responsible for writing the implementing regulations for those provisions of the MUMS Act relating to Designation and Indexing and is assisting in the drafting of the implementing regulations for Conditional Approval. The Office is currently responsible for designating new animal drugs. This responsibility may involve a determination of whether the intended use of a new animal drug qualifies as a minor use in a major species. Once implementing regulations are finalized, OMUMS will also be responsible for all aspects of animal drug indexing.

OFFICE OF NEW ANIMAL DRUG EVALUATION (ONADE)

ONADE's mission is to protect the public health by ensuring the availability of an adequate number of safe and effective animal drugs to meet the therapeutic and production needs of animals. ONADE administers the core function of drug review, which involves directing the approval process for animal drugs. FDA must review an animal drug for safety, effectiveness, and quality before the drug can be legally marketed in interstate commerce. CVM approves drugs intended to benefit the health and productivity of food animals and the health of companion animals.

ONADE Director, Dr. Steven Vaughn; Deputy Director for Administration, Dr. David Newkirk.

Drug sponsors must submit clinical tests to establish drug safety and effectiveness. Sponsors of drugs intended for food animals must also prove that food products derived from treated animals do not contain unsafe drug residues and that the food products are safe with respect to microbial safety. The sponsors must develop analytical methods to detect and measure drug residues in edible animal products. The Federal Food, Drug, and Cosmetic Act provides for approval of both pioneer and generic animal drugs and for FDA-granted authority to use investigational animal drugs. CVM classifies the animal drugs it approves, for distribution and use purposes, as over-the-counter, prescription, or veterinary feed directive.

ONADE administers the ADUFA, which authorizes FDA to collect fees in support of the review of new animal drugs. Under ADUFA, CVM agreed to pursue a comprehensive set of review performance goals to improve the timeliness and predictability of the review of new animal drug applications and investigational new animal drug submissions.

OFFICE OF SURVEILLANCE AND COMPLIANCE (OS&C)

OS&C has primary responsibility for three of CVM's four core functions: compliance-related actions, post-approval monitoring, and animal feed safety. OS&C monitors the safety and effectiveness of approved drugs after they enter the market. Working with the U.S. Department of Agriculture and State agencies, OS&C monitors the occurrence of unsafe drug residues in meat and poultry products, and guides efforts to protect consumers through educational and enforcement activities related to drug residues. The Office coordinates enforcement actions against unapproved drugs that are on the market and that threaten public and animal health. Working with epidemiologists in CVM's Office of Research, OS&C utilizes epidemiological skills to protect public and animal health.

OS&C Director, Dr. Dan McChesney.

OS&C conducts surveillance and compliance programs to protect animal feed from contamination by toxic materials such as mycotoxins, pesticides, heavy metals, and industrial chemicals, and to prevent the establishment and amplification of bovine spongiform encephalopathy through feed. The Office administers the feed mill licensing program and coordinates biennial inspections of medicated feed manufacturers. It approves food additives for use in animal feed and reviews genetically modified plant varieties for safety. OS&C coordinates the Center's counterterrorism efforts. The Office's Bioresearch Monitoring Team oversees inspections of both nonclinical (laboratory) and clinical studies to provide assurance of the integrity of data submitted in support of animal drug applications. OS&C also coordinates the Center's administrative actions involving approved drugs, such as actions to withdraw drug approvals.

OS&C Deputy Director, Dr. George Graber.

OFFICE OF RESEARCH (OR)

OR Acting Director, Dr. Marleen Wekell; Deputy Director, Dr. David Batson.

OR conducts applied research in support of regulatory decision-making related to each of CVM's core functions. The Office is located in a state-of-the-art research complex containing offices, laboratories, animal buildings, and pastures.

In support of the drug review function, OR conducts studies in animal drug safety and efficacy, antimicrobial resistance mechanisms, metabolism, standardization of test methods, and pharmacokinetics/pharmacodynamics. The goal of these efforts is to provide a science base for guideline development. OR supports the compliance program of the Center through the development of analytical methods and evaluation of screening tests for detection of drug residues in imported and domestic food products. The position of Director of the National Antimicrobial Resistance Monitoring System (NARMS) resides within OR, and OR is responsible for the monitoring of retail meats for antimicrobial resistant foodborne bacterial pathogens under NARMS. These pathogens are also subjected to molecular typing as part of the national PulseNet program. OR conducts research to understand the microbiology of animal feeds and the dissemination of resistant bacteria via livestock feeds. The Office is also developing methods to detect material prohibited by the BSE feed regulation that could compromise animal feed safety.

OR prepares a detailed annual report. For a copy, write to: Center for Veterinary Medicine, Office of Research, 8401 Muirkirk Road, Laurel, MD 20708, attention Ms. Katie Orr.

Our Sphere of Influence

CVM's efforts to help ensure that domestic and imported animal food products are safe affect millions of consumers. On the average, American consumers eat 110 pounds of meat, 70 pounds of poultry, 15 pounds of fish, 590 pounds of dairy products, and 30 pounds of eggs each year. Besides protecting the health of consumers in a population that has now passed 300 million, CVM works to safeguard the health of food-producing animals in the United States: 8.8 billion chickens, 264 million turkeys, 96 million cattle, 60 million pigs, and 6.1 million sheep are produced each year. The United States produces more than $100 billion worth of livestock and livestock products each year.

CVM approvals are now in effect for several hundred animal drug applications, including generics, for use in food-producing animals. We have approved many of these drugs for administration through animal feed. Under a law passed by Congress in 1996, CVM began licensing firms that manufacture certain medicated feeds; presently, there are 1,070 licensed feed mills. In addition, we have published regulations that authorize use of more than 50 food (feed) additives. Several hundred more approved drug applications, including generics, are available to maintain the health of our Nation's increasing pet population, which now includes 65 million dogs and 75 million cats, in addition to 11 million birds and 6 million horses.

FDA is responsible for ensuring the safety of all animal feed and feed ingredients mixed by commercial and noncommercial feed manufacturers. We estimate the number of firms, including livestock and poultry producers and firms in a variety of specialized industry groups, to be at least 90,000. We also regulate nearly 400 animal drug manufacturers and other sponsors of animal drug applications and Type A medicated articles (new animal drugs intended for use in the manufacture of medicated animal feed).

The drugs we approve help the Nation's 69,000 veterinarians accomplish their task of maintaining the health of the Nation's animals.

Our Stakeholders and Partners

OUR STAKEHOLDERS

Many organizations and millions of individuals have a stake in the outcome of CVM's work, including consumers, animal owners, veterinarians, and firms in the regulated industries – companies that market the drugs, feeds, and other products that we regulate. Our stakeholders also include trade associations; consumer organizations; State, Federal and foreign regulatory agencies; and international standard-setting organizations.

We use a variety of methods to keep stakeholders informed and to seek their advice and opinions about our policies and programs. These methods include public meetings; requests for comment on proposed regulations and guidance documents; the CVM Web site; and a variety of informal means, such as letters, phone calls, and e-mails.

OUR PARTNERS

Our success in promoting and protecting the public health depends not only on the active involvement of our stakeholders, but also on the formation of partnerships with those whose goals align with ours. Government downsizing, a changing economy, technical advances, and other factors have prompted FDA and CVM increasingly to seek out partnering opportunities to maximize the use of our resources.

The concept of collaboration and partnership is generally known as leveraging, and we are working to make it one of the foundations of our day-to-day operations. Our partners include:

- Other Federal agencies with whom we share related regulatory responsibilities, such as the U.S. Department of Agriculture's (USDA) Food Safety and Inspection Service (e.g., surveillance for animal drug residue and antimicrobial resistance) and Animal and Plant Health Inspection Service (e.g., BSE) and the U.S. Environmental Protection Agency (EPA) (e.g., pesticides). For example, the Interagency Residue Control Group, with members from FDA, USDA, and EPA, coordinates information on residues of animal drugs, pesticides, and environmental contaminants in animal food products.
- Centers for Disease Control and Prevention, National Center for Infectious Diseases (e.g., surveillance for antimicrobial resistance).
- USDA's Agricultural Research Service and Cooperative State Research, Education, and Extension Service.
- State agencies, especially through the Association of American Feed Control Officials, which partner with us to conduct inspections for compliance with the BSE feed regulation and other feed inspections and to carry out other regulatory and surveillance functions.
- Veterinarians, who share with us numerous public and animal health goals, such as testing and surveillance of animal drugs for safety and effectiveness, avoiding drug residues in food products, minimizing the development of antimicrobial resistance through prudent drug use practices, and educating producers and related industries as to their public health responsibilities.
- Foreign regulatory agencies that have responsibility and authority for controlling animal drugs and feeds in their countries; we leverage such international work through our participation and leadership in the International Cooperation on Harmonisation of Technical Requirements for the Registration of Veterinary Medicinal Products, the CODEX Committee on Residues of Veterinary Drugs in Foods, and other multilateral organizations.

We partner through cooperative agreements, cost-sharing contracts, cooperative research and development agreements, interagency agreements, cosponsorship agreements, and informal agreements. We hold joint workshops, cosponsor training sessions, work with scientists on mission-related research, and cooperate with others in many ways.

We include a number of examples of current partnership arrangements in this annual report.

FISCAL YEAR 2006 CHALLENGES AND ACCOMPLISHMENTS

Introduction

Although the Center for Veterinary Medicine (CVM) is organized into six separate offices, our Guiding Principles call for the staff to work together, placing the mission of the Center first. In fact, most of our significant accomplishments involve the efforts of people from two or more offices, through teams, committees, and day-to-day coordination.

Thus, the presentation of FY 2006 accomplishments is not organized according to office structure, but according to crosscutting topics. These topics reflect issues of significant public interest. The report introduces each of these areas of concern with a statement of the challenges that CVM faced as it attempts to meet its "Back to Basics" goals.

To help us achieve our strategic goals in FY 2006, CVM established targets for the year – a number of specific *performance goals* (the performance goals may be either program goals or management goals). Individual offices have primary responsibility for achieving some of the performance goals, but two or more offices share many of the performance goals because they relate to activities that require collaborative efforts.

The report highlights our performance goals in the appropriate sections below and indicates (with a or ) whether we accomplished the goals.

We have worked during the past year to focus on the priorities in the President's Management Agenda and the HHS-wide program and management objectives. We also focused on achieving FDA's Strategic Goals:

1. Enhance protection for patients and consumers and empower them with better information about regulated products
2. Increase access to innovative products and technologies to improve health
3. Improve product quality, safety, and availability through better manufacturing and product oversight
4. Transform administrative systems and infrastructure to support FDA operations

Throughout this report, we give examples of how our FY 2006 accomplishments responded to the targets set by the President, the Department, and the Agency, including the long-term goals established by the Agency to support achievement of its strategic goals.

Increasing the Availability of Safe and Effective Animal Drugs

THE CHALLENGE

Statutory standards and the needs of CVM's stakeholders – and especially the needs of the billions of animals whose health CVM seeks to protect – require that the center make the right pre-approval decisions and do so efficiently and expeditiously. CVM's challenge is to protect public and animal health by ensuring that there is an adequate supply of animal drugs to meet therapeutic and production needs of animals. The Animal Drug User Fee Act (ADUFA) of 2003 challenges CVM to expedite and improve the review of new animal drug applications so as to increase the availability and diversity of safe and effective drugs.

FY 2006 ACCOMPLISHMENTS

The Center responded to the pre-approval challenges in a number of ways, as described below. In general, CVM directed these actions toward achieving the FDA's long-term goal of increasing access to safe and effective veterinary products.

This report lists significant FY 2006 new animal drug approvals in Appendix B. During the year, CVM issued five original new animal drug application approvals, 16 significant supplemental application approvals, and 17 significant generic animal drug application approvals.

ADUFA

Implementing ADUFA was a major CVM emphasis during FY 2006. ADUFA authorizes the collection of fees totaling $43 million over 5 years to enable FDA to hire and train additional scientific reviewers and implement enhanced processes to accelerate and improve the new animal drug review process.

This legislation is helping make safe and effective new animal drug products available more quickly. Specifically, the law establishes performance goals, including 5-year goals to be implemented by the end of FY 2008. CVM has made steady progress in implementing ADUFA; the Center can report the following:

- **CVM met or exceeded all FY 2004 and FY 2005 ADUFA performance goals.** All applications and submissions received in FY 2004 have been completed, and CVM met or exceeded each of the FY 2004 ADUFA review performance goals. As of September 30, 2005, CVM was meeting or exceeding all the ADUFA review timeframe goals for applications and submissions for FY 2005.

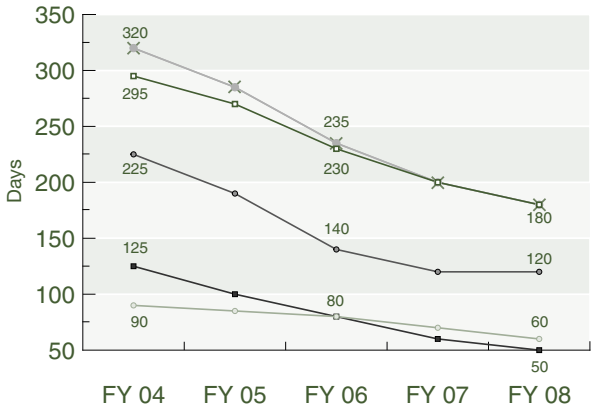
- **CVM continued to make substantial progress in recruiting additional personnel for its review staff.** CVM met its goal of having 50 percent of additional CVM review staff recruited and on-board by the first quarter of FY 2006.
- **CVM published policy and procedure documents to improve the new animal drug review process.** The Center is committed to improving the efficiency, quality, and predictability of the new animal drug review process. In keeping with this commitment, CVM published four policy and procedure documents that were adopted in FY 2005. These are available on the CVM homepage on the FDA Web site at http://www.fda.gov/cvm.

The FY 2005 ADUFA Financial Report shows that CVM met the legal conditions that must be satisfied before the Agency can collect and spend user fees. During FY 2006, CVM worked to achieve goals set for the year. Performance and financial reports for FY 2006 will be published separately.

ADUFA Goals for Reduction in Review Time

NADAs, Supplemental NADAs and Reactivations INADS

(Review time goal, in days)



Goal: Complete reviews of 90 percent of applications within these time limits.

Submission Type

- × - Non-manufacturing supplemental applications and reactivations
- ● - Investigational animal drug study submissions
- ▫ - Original New Animal Drug Applications (NADAs) and reactivations
- ◦ - Manufacturing supplemental animal drug applications
- ▪ - Investigational animal drug submissions consisting of protocols, essential to decision on drug approval
- ◦ - Administrative NADAs and reactivations

FY 2006 Performance Goals

Continue implementation of the Animal Drug User Fee Act of 2003 (ADUFA).

Meeting this goal accomplishes the Department-wide objective of increasing access to high quality, effective health care that is predictably safe.

Build enhancements into the review process by defining and completing critical Standard Operating Procedures (SOPs) and Guidances for Industry (GFIs), interim performance measures, and outcome measures to standardize processes to be efficient, consistent, and clear.

Implement a Performance Management System using the Submission Tracking and Reporting System (STARS), Activity Time Reporting, Activity-Based Costing and Project Management systems, limiting resource expenditures on work outside of our core business.

Develop improved SOPs for review processes and develop scientific policies for review staff.

Direct and target training and educational opportunities for staff and management to improve the knowledge base of the review organization.

ENHANCING THE REVIEW PROCESS BY DEFINING AND COMPLETING CRITICAL REGULATIONS AND GUIDANCE DOCUMENTS

Regulations and guidance documents are important mechanisms for implementing improvements in the animal drug approval process. During FY 2006, CVM completed work on important revisions to CVM regulations on supplemental applications and other changes to approved applications to implement the manufacturing changes provisions of the Food and Drug Administration Modernization Act of 1997. The final rule will require manufacturers to assess the effect of a manufacturing change on the identity, strength, quality, purity, and potency of a drug as those factors relate to safety and effectiveness, along with other changes. This initiative responds to the Agency's strategic goal of improving product quality, safety, and availability through better manufacturing and product oversight.

CVM issued a number of draft and final guidance documents during the year. These included:

- Draft guidance for industry #183, "Animal Drug User Fees: Fees Exceed Costs Waivers and Reductions," which explains the procedures FDA expects to use to evaluate waiver requests under the "fees exceed costs" waiver provision of ADUFA.
- Documents prepared under the auspices of the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). VICH is a trilateral (European Union-Japan-United States) program aimed at harmonizing technical requirements for veterinary product registration. An example is a guideline, "Environmental Impact Assessments for Veterinary Medicinal Products, Phase II-Final" (GL-38). The document provides guidance for the use of a single set of environmental fate and toxicity data to be used by applicants/sponsors to obtain marketing approval in all VICH regions for those veterinary medicinal products identified as recommending data during the Phase I process.
- Guidance # 171: "Waivers of *In Vivo* Demonstration of Bioequivalence of Animal Drugs in Soluble Powder Oral Dosage Form Products and Type A Medicated Articles."

Additional guidance documents published during FY 2006 are listed in Appendix A (Significant Regulations, Guidances and Other Documents).

ACTIONS TO INCREASE THE EFFICIENCY OF THE REVIEW PROCESS

The Center took a number of actions during FY 2006 to improve the efficiency, quality, and predictability of the animal drug review process. For example, Office of New Animal Drug Evaluation (ONADE) divisions continued to work with animal drug industry representatives to reduce the number of drug application review cycles. Presented here are other actions the Center has taken.

Development of Standard Operating Procedures. The Center continued to develop standard operating procedures (SOPs) for review processes, scientific policies for review staff, and procedures for expedient resolution of scientific issues. For example, ONADE completed work on SOPs for refusal to file, refusal to review applications, and for scheduling and holding meetings with outside parties.

Implementation of a Performance Management System. CVM continued during FY 2006 to implement a quality business system using an activity-based model to demonstrate better performance-to-budget efficiency. ONADE is working with a consultant to merge Activity-Based Costing (ABC) and Activity Time Reporting (ATR) data with project management and application review. Using the ATR system that has been in place since October 2003, the Office Management Team (OMT) members planned their resource availability for various performance goals so that resources can be balanced between animal drug review work and other essential non-review work. This balance facilitates

the maximum utilization of available assets. The OMT has begun implementing after-action reviews on a quarterly basis, responding to the President's Management Reform Agenda initiative for Budget and Performance Integration.

As an example of ONADE's performance management initiatives, the Division of Manufacturing Technologies has effectively utilized available information from CVM's Corporate Database Portal to evaluate core business activities, specifically to assess past performances/work-flow, predict incoming submissions, determine resource allocations, and propose process improvements. This initiative is the first attempt to use both the Submission Tracking and Reporting System (STARS) and ATR data to make business decisions regarding workload and resource allocations at a Division level.

In 2006, the Center used this analysis to place new hires in teams with the highest potential workload and to reallocate review responsibilities within the Division for increased efficiency. For instance, the responsibility for the review of drug substance information has been reassigned within the Division to only two teams: the Chemotherapeutics Team for synthetic drug substances and the Biotherapeutics Team for fermentation drug substances. A trend analysis also revealed that the Center needs to focus more on review activities and building efficiencies into the review process if it is to meet the ONADE goal of doing better than ADUFA timeframes for FY 2007. The Center will continue to use this type of analysis to make effective business decisions at the Division level.

Providing Training and Educational Opportunities. CVM continued to direct and target training and educational opportunities for staff and management to improve reviewers' knowledge base. This training includes core curricula for new reviewers, policy and procedure competency, and expansion of the scientific knowledge base. CVM also offered training to review scientists to help them maintain and develop the cutting-edge knowledge required for reviewing applications that contain information on emerging technologies.

As an example of training opportunities during FY 2006, some of CVM's reviewers visited a large, integrated swine operation to familiarize themselves with current production practices. The staff toured the feed mill, farrow-to-finish facilities, and packing plant. The experience will enable reviewers to discuss more accurately protocol development, label language, data sets, and drug usage issues with drug sponsors.

RESEARCH TO SUPPORT ANIMAL DRUG REVIEW

Drug sponsors are responsible for submitting studies to prove that their drugs are safe and effective. Complementary work – accomplished by CVM, its contractors, and collaborators – may alter the type and number of studies required for approvals, thus improving the efficiency of the drug approval process. An example of this is a pharmacokinetics/pharmacodynamics (PK/PD) program to assess the effects of drugs in diseased animals, an important contribution because most data submitted to CVM are generated in healthy animals.

In a follow-up to a previous PK/PD study of enrofloxacin in beef steers, preliminary analysis of data from a recent study has demonstrated that the instillation of sterile saline or culture medium (the "carrier" used to introduce the bacteria into the lung in the infection model) had no effect on plasma or bronchial fluid pharmacokinetics of the drug in beef steers. CVM scientists could conclude, therefore, that the PK effects observed were due to the bacterial infection and not the carrier.

Karyn Howard is evaluating milk samples for florfenicol.

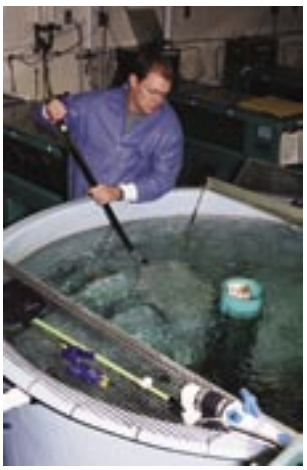
Data from this study will be combined with some of the data from the earlier enrofloxacin study, which utilized the infection model, to document the bronchial fluid levels of the drug and the impact of infection on PK parameters. At the end of the year, these results are being prepared for publication.

CVM scientists also completed the animal phase of an investigation into determining the levels of endotoxin/pyrogens that can be present in veterinary pharmaceuticals without causing a safety concern to the animals. Results from this pilot study, which were undergoing analysis at the close of the fiscal year, will determine the parameters to be used and the physiological biomarkers to measure during a larger study. Data from the larger study will help reviewers determine safe limits for these compounds.

Increasing Drug Availability for Aquaculture and Other Minor Uses/Minor Species

THE CHALLENGE

The Minor Use and Minor Species Animal Health Act of 2004 (MUMS) challenges CVM to implement measures that will significantly expand the availability of drugs for minor uses and minor species. Because the potential sales volume is low, animal drug manufacturers lack economic incentive to seek animal drug approvals for minor uses (diseases that are rare) or minor species (animal species other than cattle, horses, pigs, chickens, turkeys, dogs, or cats). The need in aquaculture is a good example. The U.S. aquaculture industry is expanding, and the need for therapeutic and production drugs is growing as well.



Microbiologist Ron Miller removing a trout from a tank at CVM's aquaculture research facility at OR.

IMPLEMENTATION OF MUMS LEGISLATION

Overview of MUMS Law Implementation

DESIGNATION: Provides incentives for approvals.
FY 2006 action: *Designations granted under interim processes and progress made in preparing final regulations.*

CONDITIONAL APPROVAL: Provides for marketing of safe drugs while effectiveness studies are underway.
FY 2006 action: *Development of policies and procedures for interim conditional approval and preparation of proposed regulations.*

INDEXING: Permits marketing of unapproved drugs under certain circumstances.
FY 2006 action: *Proposed regulations published.*

The Law's Major Provisions

This MUMS legislation provides innovative, flexible ways to provide drugs to treat minor animal species as well as uncommon diseases in the major animal species. The new law modifies provisions of the Federal Food, Drug, and Cosmetic Act in three key ways, providing for:

Indexing–In August 2006, FDA issued proposed regulations that, when finalized, would provide administrative procedures and criteria for Index listing a new animal drug for use in a minor species. The new law provides that FDA may add a minor species drug to an Index of unapproved new animal drugs that may be legally marketed when the potential market for the drug is too small to support the costs of the drug approval process, even under a conditional approval. The Index is limited to nonfood-producing minor species with a limited exception for some early life stages of food animals, such as certain fish eggs. The proposed regulations describe a process under which the Agency would make determinations regarding the eligibility of a new animal drug for Indexing, the selection of a qualified expert panel, and the findings of the qualified expert panel.

Work is ongoing to develop the administrative document control and electronic tracking processes needed to support the Indexing system described in the proposed Indexing regulations.

FY 2006 Performance Goals

- Review comments received on the proposed Designation regulations to implement the Minor Use and Minor Species (MUMS) Animal Health Act of 2004.
- Draft proposed regulations to implement section 572 (Indexing) of the MUMS Animal Health Act of 2004.
- Publish MUMS drug designations on the MUMS Web page.
- Develop procedures and policies in cooperation with the Office of New Animal Drug Evaluation to implement conditional approval prior to finalization of regulations.

Meeting these goals accomplishes FDA's long-term goal of increasing access to safe and effective veterinary products.

Designation–This aspect of the legislation provides incentives for minor use/minor species approvals. For example, at the time that a designated drug gains approval or conditional approval, it is awarded 7 years of exclusive marketing rights. FDA published proposed implementing regulations in September 2005. The proposed regulations describe the criteria CVM would use for granting or denying the requests, define content and format requirements for Designations, and specify other implementing procedures. CVM completed its review of comments on the proposed regulations and drafted final regulations during FY 2006.

During the fiscal year, CVM processed 63 submissions relating to Designation, and the Office of Minor Use and Minor Species Animal Drug Development (OMUMS) granted 31 requests for Designation. Designations have been listed on the MUMS Web page, (http://www.fda.gov/cvm/MUMSDrugDesg.htm), each within a few weeks of being granted.

Conditional Approval–The sponsor of a minor use/minor species veterinary drug can ask CVM for Conditional Approval, which allows the sponsor to market the drug for up to 5 years after proving the drug is safe and establishing a reasonable expectation of effectiveness, but before collecting all of the effectiveness data needed to support a full approval. During FY 2006, CVM developed procedures and policies to implement Conditional Approval prior to finalization of regulations, and worked on drafting the proposed regulations for Conditional Approval.

Communication with Stakeholders

OMUMS has reached out to stakeholders to update them on the status of MUMS Act implementation. During the year, OMUMS met with numerous potential new animal drug sponsors interested in utilizing the Designation and/or Conditional Approval provisions of the MUMS Act. OMUMS staff members have given general presentations about MUMS to a number of groups, and have also answered numerous telephone and e-mail inquiries about various aspects of the MUMS legislation and its implementation.

RESEARCH TO SUPPORT DRUG APPROVALS (MUMS)

Trout held in a tank at CVM's OR aquaculture facility.

Food Safety Database. CVM has published an on-line database of literature (designated the PhishPharm Database) detailing drug metabolism, residues, and pharmacokinetics in multiple fish species. This database includes information from more than 450 articles, including not only the pharmacokinetic data, but also specific information regarding the holding conditions, i.e., the water temperature, salinity, size of the animals, drug dosage, and methods of administration. The database is a valuable tool for researchers and regulators and can be accessed by going to http://www.aapsj.org/view.asp?art=aapsj070230 and scrolling down to the zip links.

Efficacy studies. CVM researchers have developed a reproducible model for infecting channel catfish with a fungus (*Saprolegnia parasitica*) for testing the efficacy of potential therapeutic agents. This model will be used in future studies supporting a publicly held Investigational New Animal Drug (INAD) application.

Antimicrobial Susceptibility Testing Standards. During FY 2006, CVM researchers provided data to support the development of two international antimicrobial susceptibility testing (AST) standards for aquatic bacteria. These tests have been accepted as Official Methods by the Clinical and Laboratory Standards Institute (CLSI, formerly the National Committee for Clinical Laboratory Standards). The standards (M-42-A and M-49-A), published in July 2006, provide the first internationally recognized standards for AST of aquatic bacteria.

National Research Support Project #7 (NRSP-7). NRSP-7 is a national agricultural research program sponsored by the U.S. Department of Agriculture, in collaboration with CVM and others, to obtain clearances for drugs for minor species and minor uses. The program had a very active year in FY 2006. Its Public Master File (PMF) for the use of oxytetracycline immersion for otolith marking of finfish was used by a fourth sponsor to support an approved new animal drug application. A new PMF for the use of tylosin for the control of American foulbrood in honeybees was used to support the first new approval in decades for a drug for use in honeybees. Significant studies were submitted and accepted to support projects for the use of a progesterone intravaginal device for sheep, erythromycin for salmonids, and crude carp pituitary for finfish. New projects are in development for drugs for fish, deer, goats, and pheasants.

At fiscal year end, NRSP-7 had 20 active projects for rabbits, various fish species, sheep, goats, game birds, deer, and honeybees. To date, NRSP-7 files have supported 26 unique minor species drug approvals, and PMFs are available to support additional approvals.

Reducing Risk From Antimicrobial Resistance

THE CHALLENGE

Scientific evidence demonstrates that the use of antimicrobial drugs in food-producing animals can result in the selection for resistant bacteria. Resistant foodborne bacteria can then be transferred to humans, resulting in illness. If the patient needs antimicrobial drug treatment, that therapy may be compromised because the drugs of choice may be ineffective. CVM is challenged to develop policies and programs that reduce this risk to human health.

FY 2006 ACCOMPLISHMENTS

In cooperation with other agencies, CVM has undertaken proactive surveillance, research, education, risk assessment, and risk management programs to reduce the risk to human health that can result from the use of antimicrobials in food-producing animals. The Center achieved significant progress in these efforts during the past year, responding to the FDA strategic goal of enhancing patient and consumer protection.

MONITORING FOR THE DEVELOPMENT OF RESISTANCE

CVM plays an active leadership role in the National Antimicrobial Resistance Monitoring System (NARMS), established a decade ago as a collaborative effort between CVM, the U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC). The NARMS program monitors changes in antimicrobial drug susceptibilities of selected enteric bacterial organisms in humans, animals, and retail meats to a panel of antimicrobial drugs important in human and animal medicine. The ultimate goal of these activities is to prolong the lifespan of approved drugs by promoting prudent and judicious use in animals of antimicrobial drugs and to identify areas for more detailed investigation. FY 2006 achievements include the following.

Implementing Recommendations of Expert Panel. During the fiscal year, CVM started implementation of several recommendations of a panel of outside experts, convened during FY 2005 for a review of all three arms of the NARMS program. These changes included enhanced sampling strategies in the retail meat program and human component, application of NARMS data in CVM's drug pre-approval process, and other modifications, all of which are described in the following subsections.

Althea Glenn, working in the laboratory at CVM's OR, serotypes *Salmonella* strains to identify them.

Appointment of NARMS Director. To lead the NARMS program, CVM named Dr. David White of CVM's Office of Research (OR) as NARMS director, with oversight responsibilities for all three arms of the NARMS program.

Expansion of Web site and Data Reporting. NARMS' expansion continued in FY 2006, including progress in the development of a uniform Web site and reporting scheme for all three components of NARMS: the human isolates (conducted by CDC), animal isolates (directed by USDA), and retail meat (administered by CVM). The Web site, which incorporates annual reports, is on line at http://www.cdc.gov/drugresistance/actionplan/aractionplan.pdf. The three agencies strengthened data reporting during FY 2006 by developing complementary databases, improving timeliness of reporting, and harmonizing data presentation between the three agencies.

Growth of DNA Fingerprinting. CDC coordinates PulseNet, a national network of laboratories (including CVM's) that perform molecular subtyping (or "fingerprinting") of foodborne disease-causing bacteria by pulsed-field gel electrophoresis (PFGE). PFGE can be used to distinguish strains of organisms at the DNA level. Participants submit data electronically to CDC; the databases are available on-demand, allowing for rapid comparisons and early identification of common source outbreaks.

OR does PFGE analysis on all retail meat isolates, and submits them to the PulseNet database. OR also performs analysis on isolates from food-producing animals and humans. During FY 2006, OR performed PFGE analysis on more than 1,000 isolates of *Salmonella*, *E. coli*, and *Campylobacter* recovered from food animals, retail meats, and humans. Multi-drug resistant (MDR) *Salmonella* serotypes and clones have been included in CVM's submissions. This database will assist CDC and CVM in monitoring the emergence of multi-drug resistant foodborne bacterial pathogens in the United States in an effort to better understand how antimicrobial resistance develops, spreads, and persists in animal production environments and retail meats.

FY 2006 Performance Goals

- Develop the detection capability of multi-drug resistant foodborne bacterial pathogens through participation in national surveillance programs including FoodNet and PulseNet.
- Food Safety-Antimicrobial Resistance: Continue research to identify food animal species causing human drug resistance.
- National Antimicrobial Resistance Monitoring System (NARMS): Continue efforts to maximize cooperation and communication between FDA, USDA, and CDC to increase efficient use of limited resources in addressing problems of mutual interest.
- Implement recommendations from external review of all three arms of the NARMS program.

Meeting these goals accomplishes the Department-wide objective of achieving continuous improvement in the safety of food and drugs.

Ensuring Data Accuracy. During the year, NARMS microbiologists teamed with FoodNet epidemiologists on two visits to participating State public health laboratories, with a goal of ensuring continued accuracy of generated data. These visits were part of the NARMS program's continued partnering with other active and passive surveillance systems to help public health officials better understand the dynamics of foodborne illness in the United States.

Publication of Retail Meat Annual Report. Sites in 10 States that are part of the FoodNet system collect and culture samples of ground beef, pork chops, chicken breast, and ground turkey for the presence of *Salmonella*, *Campylobacter*, *E. coli*, and *Enterococcus* organisms. The isolates are sent to OR for identity confirmation, serotyping of the *Salmonella* isolates, antimicrobial susceptibility testing, and molecular characterization. CVM published the 2004 retail meat annual report during the past year. The report provides data on the prevalence of antimicrobial resistance in nearly 4,700 samples of foodborne bacteria in retail meats. The report is accessible at http://www.fda.gov/cvm/NARMSReport2004.htm.

[3] The Foodborne Diseases Active Surveillance Network (FoodNet) is the principal foodborne disease component of CDC's Emerging Infections Program (EIP). FoodNet is a collaborative project of CDC, EIP sites in 10 States, USDA, and FDA.

Human Arm Expansion. The human arm of NARMS has expanded to include all 50 States plus three local health departments. CDC has developed a new *Campylobacter* sampling scheme, which took effect on January 1, 2005, with continued revision in 2006. The new strategy is being implemented in three stages to ensure a more robust, nationwide system.

Improvement in Testing Methods. The agencies involved in NARMS continued during FY 2006 to improve their testing methods. These improvements included development and implementation of a *Campylobacter* broth microdilution method approved by the Clinical and Laboratory Standards Institute. This method is being incorporated into public health systems in Canada, Europe, Central and South America, and is being used in World Health Organization (WHO) training laboratories worldwide. The method enhances the quality of data and ensures intra- and inter-laboratory reproducibility among the three arms of NARMS and other surveillance systems worldwide. NARMS also continued to participate in the External Quality Assurance System (EQAS) of the WHO Global *Salmonella* Surveillance and Laboratory Support Project (Global Salm-Surv). The EQAS supports the assessment of the quality of serotyping and antimicrobial susceptibility testing of *Salmonella* in all participating laboratories.

Continued Outreach. During FY 2006, CVM published NARMS information on CVM's Internet site, in peer-reviewed publications, in the *FDA Veterinarian*, in scientific meeting proceedings and abstract books, and on posters presented at scientific meetings. The Center also presented NARMS results at a number of major scientific meetings.

UTILIZATION OF NARMS DATA AND RISK ASSESSMENT IN THE PRE-APPROVAL PROCESS

NARMS has traditionally been more involved in the post-approval aspects of CVM's mission, but during FY 2006, the Center continued to develop pre-approval aspects of NARMS and NARMS data. For example, the NARMS retail component tested *Salmonella* and *E. coli* isolates from the past several years against cefquinome (not yet approved in the United States) and showed a highly susceptible population. However, *Salmonella* isolates displaying resistance to ceftiofur did possess increased minimum inhibitory concentrations (MICs) to cefquinome, suggesting that resistance may develop in several steps, beginning with ceftiofur resistance.

These and other NARMS data were presented in the September 2006 Veterinary Medicine Advisory Committee (VMAC) meeting that addressed the microbial food safety of an antimicrobial drug application currently under review for use in food-producing animals in accordance with CVM's Guidance for Industry #152, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbial Effects on Bacteria of Human Health Concern." Among other documents, VMAC reviewed "Cefquinome Formulations for Parenteral Injection for the Treatment of Bovine Respiratory Disease," prepared by the drug sponsor and available on the CVM Web site.

RESEARCH TO SUPPORT ANTIMICROBIAL RESISTANCE SURVEILLANCE AND REGULATION

The overarching goal of antimicrobial resistance research at CVM is to identify and implement methods to reduce microbial hazards associated with antimicrobial drug use in food-producing animals. This effort includes basic and applied research focusing on the prevalence, propagation, and persistence of antimicrobial resistant bacteria in the animal production environment and on foods of animal origin. A comprehensive research effort will help ensure that any regulatory actions taken to control antimicrobial resistance

Veterinary Medicine Advisory Committee members.

will be based on sound science. CVM's FY 2006 research included accomplishments within several broad objectives, including the following:

Use Existing Microbiological Collections to Examine Historical Susceptibility of Foodborne Bacterial Pathogens to Antimicrobial Agents. To better interpret the public health threat represented by current antimicrobial resistance levels, CVM contracted with the American Type Culture Collection (ATCC) to measure resistance among banked historical collections of *Salmonella*, *Campylobacter*, and *E. coli*. The Center has completed antimicrobial susceptibility testing of these isolates and has begun studies to examine the genetic bases of resistance, including the distribution of plasmid types in different isolates. Data from this study will help the Center better assess the impact over the past 6 decades of antimicrobial use in veterinary and human medicine.

Panelists at the Veterinary Medicine Advisory Committee meeting in September 2006, (from left) CVM Director Dr. Stephen Sundlof; ONADE Director Dr. Steve Vaughn; Dr. John Powers, Lead Medical Officer with FDA's Center for Drug Evaluation and Research; and Dr. Kelly Lechtenberg of Midwest Veterinary Services, Inc.

In 2006, CVM evaluated the isolates collected from 1950 to 1999 for their evolutionary development and changes in their antimicrobial resistance profiles. Preliminary data, presented in two scientific meetings during FY 2006, indicate that increasing resistance to antimicrobials is related to more recently evolved complexes.

Identify the Food-Producing Animal Species That Contribute to Antimicrobial Resistance in Foodborne Pathogens. CVM's ongoing Bacterial Source Tracking project investigates the animal origin of *Salmonella* and *Campylobacter* isolates associated with foodborne-related bacterial infections in humans. OR scientists are using a variety of phenotyping and genotyping techniques to determine if a human *Salmonella* infection can be traced to a specific food-producing animal species. Results obtained during FY 2006 reveal that serotyping, antibiograms, multilocus sequence typing, and PFGE can show some host-specific clustering for specific *Salmonella* serotypes. Other *Salmonella* serotypes may require a combination of phenotypic and genotypic methods to identify the animal source of a human infection. However, definitive answers may not be possible even with these tools.

Sharon Friedman working with a Pulse Field Electrophoresis equipment at CVM's OR lab.

In addition, preliminary data obtained using a subset of *Salmonella* isolates suggests that a combination of serotyping, antibiograms, PFGE, and multi-locus sequence typing may be required to fully characterize the strains. These data also show that multi-drug resistant strains from all animal origins are evolving to less susceptible phenotypes. Other genetic techniques are being explored for their capacity to compare distinct bacterial isolates.

Controlling Risk From Bovine Spongiform Encephalopathy (BSE)

THE CHALLENGE

The discovery of a third BSE-infected cow in the United States during FY 2006 added to CVM's challenge to strengthen controls that will prevent the spread of BSE through feed. (The first infected cow was discovered in December 2003, the second in June 2005, and the third in March 2006. The first cow had been imported from Canada, and the other two were more than 10 years old.) BSE is a chronic, degenerative, always fatal neurological disease affecting the central nervous system of cattle. BSE belongs to a family of diseases known as transmissible spongiform encephalopathies (TSEs) that includes several ruminant and nonruminant animal diseases. Laboratory and epidemiological evidence strongly suggests that people can contract a human TSE, variant Creuzfeldt-Jakob Disease (vCJD), by consuming food from BSE-infected cattle. In the absence of adequate controls, BSE could spread among the cattle population through feed ingredients derived from infected cattle.

Christine Deaver, in the Office of Research, performing a real-time polymerase chain reaction assay, which is a method to identify bovine, sheep/goat, and deer/elk material in animal feeds.

FY 2006 ACCOMPLISHMENTS

CVM continued to provide the expert scientific knowledge and review on BSE for the Agency. Much of the Center's effort during the year focused on enforcing and strengthening FDA's BSE feed regulation. CVM made significant progress in developing analytical methods that will enhance efficient, effective compliance with the regulation. Following are highlights of some of the Center's achievements during the fiscal year, as the Center focused on:

- The FDA strategic goal of consumer protection, and
- The Department-wide objective of achieving the safety of food for animals and humans.

STRENGTHENING THE BSE REGULATION AND CVM'S INSPECTIONAL EFFORTS

Strengthening the BSE Feed Regulation. CVM analyzed and addressed all comments submitted to FDA's FY 2005 proposal to amend the BSE feed regulation to prohibit from use in the food or feed of all animals certain cattle materials that have the highest risk of carrying the BSE-infectious agent and drafted the final rule. The BSE feed regulation currently prohibits the use of certain mammalian-origin proteins – known as "prohibited material" – in ruminant feed (e.g., for cattle and sheep). Its purpose is to prevent the establishment and amplification of BSE in the United States through feed.

BSE-Infected Cow. Following the March 2006 confirmation by the USDA of a 10-plus-year-old cow found positive for BSE, FDA worked with Federal and State authorities to investigate the origin of the feed consumed by the cow. USDA confirmed that the cow did not enter the animal feed or human food supply. FDA investigators visited feed mills in the vicinity and reviewed their inspection history to evaluate compliance with the FDA feed regulation.

Risk-Based Inspectional Planning. CVM's Office of Surveillance and Compliance is working closely with FDA's Office of Regulatory Affairs (ORA) to develop new and/or revised performance goals for CVM programs. As part of this effort, the Center is reviewing the BSE compliance program and has proposed a risk-based approach to the frequency of inspections. CVM completed a risk-based work-planning module for the BSE compliance program that will help prioritize future investigational efforts. CVM is developing inspection/compliance performance goals, based on a risk-based evaluation of the Feeds Manufacturing Program, to be implemented in FY 2008.

The ultimate outcome of the risk-based approach to inspections, which is being implemented throughout FDA, is improved product quality and safety through better oversight of the manufacturing facilities, such as rendering plants and feed mills. CVM will prioritize BSE-related inspections based on risk, helping to target firms or facilities that engage in riskier practices. This prioritization will result in more efficient use of the limited resources that are available for inspectional purposes, while maintaining a high level of compliance.

The process involves setting compliance priorities by conducting a series of annual assessments that identify the internal and external hazards a regulated firm faces; addressing risk estimate and characterization of the hazard; and determining the consequences to the public health as a result of Agency action versus inaction. The risk-based approach will also include a procedure for conducting statistically based audits of areas not identified as high risk.

Inspections and Recalls. Through the FY 2006 work-planning process, CVM allocated adequate field resources to allow for selected inspections of animal feed industry firms subject to the animal protein prohibition in the BSE feed rule. These firms include renderers, feed mills, feed distributors, feed retailers, transporters, on-farm mixers, and ruminant feeders. For the fiscal year, CVM collaborated with ORA to conduct a total of 472 directed BSE inspections, including all renderers, protein blenders, and feed mills known to process products containing prohibited material. These inspections included the 310 targeted BSE inspections listed as one of the performance goals

FY 2006 Performance Goals

- ✓ Ensure the safety of marketed animal feeds by conducting 310 targeted BSE inspections of all known renderers, protein blenders, and feed mills processing products containing prohibited material (in conjunction with the Office of Regulatory Affairs [ORA]).
- ✓ In conjunction with ORA, provide educational training seminars, courses, and feed safety meetings to State feed control officials and FDA investigators on policies and inspectional procedures concerning the animal protein prohibition.
- ✓ Test proposed risk management proposals in terms of the effects on the spread and the rate of elimination of BSE if introduced into the United States, with the help of the Harvard BSE Risk Assessment simulation.
- ✓ Develop a new or revised inspection/compliance performance goal that is more risk-based and outcome-oriented.
- ✓ In the FY 2006 work plan, allocate resources to be able to conduct annual, targeted BSE inspections of all known renderers and feed mills processing products containing prohibited material.
- ✓ In the FY 2006 work plan, allocate resources to be able to 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.
- ✗ Finalize a proposed rule that revises the existing feed ban rule. Carefully analyze comments received on the October 2005 proposed rule.

Work on the rule was ongoing at the end of the fiscal year.

Following discovery during FY 2006 of possible contamination of animal feeds in violation of the BSE feed regulation, 40 recalls of product were made; 38 of those involved a single feed manufacturer.

Training and Outreach. CVM continued to provide BSE inspection training to FDA investigators and State inspectors during the fiscal year. Included in this training were inspectors from more than 10 States and investigators from as many FDA District Offices. CVM also explained its BSE inspectional checklist revision to State officials at the Feed Administrator's Seminar held by the Association of American Feed Control Officials.

FY 2006 Performance Goals

- ✓ 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.
- ✗ Issue draft Guidance for Industry explaining what commercial test kit manufacturers should do to verify that their kits meet label claims for detecting prohibited proteins (in conjunction with the Office of Chief Counsel).

Work on the guidance document was ongoing at the end of the fiscal year.

DEVELOPING ANALYTICAL METHODS FOR DETECTING PROHIBITED PROTEINS

The availability of practical, validated methods to detect protein from different animal species could improve effectiveness and efficiency in the enforcement of the BSE feed regulation. Methods to detect mammalian protein have been available for some time, but because not all mammalian proteins are prohibited from ruminant feed, methods are needed to identify protein from prohibited species, such as cattle.

Real-Time PCR Methods

CVM completed the development of a real-time polymerase chain reaction (rtPCR) method for the identification of bovine, sheep/goat, and deer/elk in animal feeds. ("Real-time" means that the technicians detect the presence of prohibited material as the reaction is taking place, so they do not have to further process the sample.) The method is capable of detecting such materials at levels at least as low as 0.1 percent in feed. It can detect bovine or ovine (sheep/goat) materials produced according to the requirements of the European Union as well as those processing conditions used in the United States.

CVM completed a thorough in-house evaluation of the method, using the same acceptance criteria used for our evaluation of commercial diagnostic test kits. CVM also demonstrated this method to representatives of 10 laboratories that will be participating in the validation trial.

Once validated, this method will be available to ORA and any State laboratories that want to use it. Feed microscopy remains the official regulatory method. However, the new rapid test could be used to screen more samples prior to using feed microscopy, saving time and effort in the laboratories. It could also be used to confirm positives found by feed microscopy.

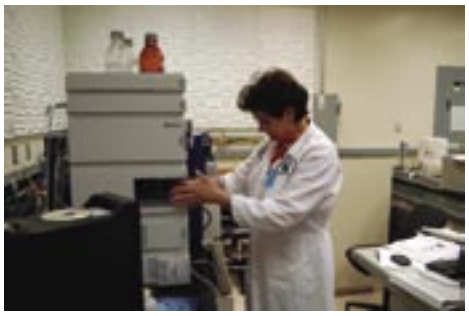
Commercial Diagnostic Kits

Commercially available diagnostic test kits marketed for the detection of ruminant proteins in animal feed could be important tools for surveillance and quality assurance. FDA does not have preclearance authority over such kits, but does have authority over labeling claims; CVM undertook evaluation of these kits to assess their usefulness and accuracy of claims made. The Center has now completed the evaluation of four commercially available test kits using criteria developed by CVM. Three of the four tests were unable to detect bovine meat and bone meal in animal feed at a level of 0.1 percent, the level that is detectable using feed microscopy (the current regulatory method), and therefore are not useful tools from a regulatory standpoint. However, two of the test kits have been shown to have the capability of detecting bovine meat and bone meal at the 1 percent level.

Avoiding Unsafe Drug Residues in Human Food

THE CHALLENGE

Improper use of approved drugs or use of unapproved drugs in domestic animals can result in unsafe residues in meat, poultry, seafood, and milk. Firms or individuals who repeatedly present animals for slaughter that are adulterated with illegal drug residues may represent a significant public health risk. In fact, investigation of repeat violators is a top priority. In addition, investigating first-time violations of residues from drugs prohibited from extralabel use in food-producing animals, residues of drugs not approved for food animal use, and very high-level drug residues are high priorities for investigation.



Dr. Mayda Lopez working with one of the mass spectrometers in the Division of Residue Chemistry in CVM's OR.

Also, CVM is challenged by the need for safety oversight to catch up with the rapid growth in the volume of imported products, especially seafood, that are under FDA's jurisdiction. Meeting this challenge requires CVM to implement compliance and research initiatives directed toward regulating drug residues in aquacultured species, which account for a high proportion of all U.S. seafood imports.

FY 2006 ACCOMPLISHMENTS

The following summarizes CVM's FY 2006 efforts to avoid unsafe residues in meat, milk, and seafood.

ENFORCEMENT TO CONTROL DRUG RESIDUES IN MEAT

Under CVM's direction, FDA's Office of Regulatory Affairs (ORA) and State agencies working on the Agency's behalf under contracts or cooperative agreements investigated 493 firms under the Tissue Residue Program. FDA issued 45 tissue residue-related Warning Letters. CVM's Division of Compliance also reviewed and approved three tissue residue-related injunction actions in FY 2006. Two injunctions were filed in court during the year.

Enforcement actions resulted in consent decrees of injunction entered against several firms whose actions resulted in illegal drug residues in edible tissues. Two examples follow.

In February 2006, a U.S. District Court entered a Consent Decree of Permanent Injunction against a Kentucky cattle company that buys and sells cattle and delivers cattle for slaughter as human food. The firm does not medicate animals, but due to inadequate recordkeeping practices, the firm has been responsible for delivering for slaughter numerous cattle containing illegal drug residues. The residues, found over a 10-year period, included gentamicin, penicillin, tilmicosin, and sulfadimethazine. Under the terms of the Consent Decree, the defendants must develop and implement a residue avoidance plan for the cattle that they handle.

FY 2006 Performance Goal

Continue developing more efficient rapid analytical methods for screening imports at the border.

In June 2006, a Consent Decree of Permanent Injunction was filed in another U.S. District Court against individuals responsible for the operations of an Indiana family-owned livestock grower/dealer and dairy farm. The injunction action was based on 23 illegal residues in the edible tissue of 10 bovine animals sampled by the U.S. Department of Agriculture between 1999 and 2005. The drug residues included antibiotics such as streptomycin, neomycin, gentamicin, oxytetracyline, flunixin, and sulfadimethoxine. Under the terms of the Consent Decree, the defendants must implement systems for identifying animals, recordkeeping, drug control, drug accountability, and drug residue withdrawal control.

IMPORT TOLERANCES

CVM currently is drafting a proposed rule and draft guidance for industry on procedures for establishing and revoking import tolerances. FDA plans to publish a proposed rule relating to the implementation of the import tolerances provision of the Animal Drug Availability Act of 1996 (ADAA). The ADAA authorizes FDA to establish tolerances (import tolerances) for drug residues in imported food products of animal origin for drugs that are used in other countries but are unapproved new animal drugs in the United States. The Center is currently reviewing and considering requests for import tolerances. Without a tolerance, any amount of residue from a drug not approved in the United States causes the food to be adulterated under the Federal Food, Drug and Cosmetic Act. The United States imports nearly $15 billion worth of animal products, including nearly $3 billion in aquaculture products, underscoring the importance of regulation in this area.

CONTROLLING DRUG RESIDUES IN AQUACULTURE PRODUCTS

Imported seafood products account for an increasingly higher percentage of U.S. seafood consumption, and a major proportion of the imported seafood is a product of aquaculture. For example, most of the imported Atlantic salmon and tilapia (importation of the latter has more than doubled in the past 5 years), and approximately half of the 500-million- pounds or more of imported shrimp comes from aquacultural operations. In addition, the U.S. domestic aquaculture industry produces nearly $1 billion worth of product each year.

CVM works closely with FDA's Center for Food Safety and Applied Nutrition (CFSAN) and ORA to assist in prioritizing analytical method development for drug residues in imported and domestic aquaculture seafood. CVM also works closely with CFSAN on the prioritization of sampling for CFSAN's Compliance Program, Chemotherapeutics in Aquaculture Seafood, and provides technical support for drug residue compliance actions as well as other drug use issues. As new analytical methods become available and validated, they are incorporated into CFSAN's sampling program as resources allow.

In FY 2001, CVM awarded a 5-year contract for data collection on aquaculture drug use in countries that exported seafood to the United States. The contract has been completed, and CVM now has a user-friendly database with foreign drug use information. The Center also has a risk assessment tool that the Center can use to create different scenarios in determining risk to U.S. consumers from foreign drug use in aquaculture. This information will be used in the Center's collaborative efforts with CFSAN and ORA.

RESEARCH TO SUPPORT SAFETY OF IMPORTED AND DOMESTIC FOOD PRODUCTS

CVM scientists, in collaboration with scientists in FDA district laboratories, have continued to develop improved methods to detect veterinary drug residues in food products, many of which are imported. Much of the effort in FY 2006 was focused on the development of methods for drug residues in honey and in fish.

Drug Residues in Imported Honey. Illegal drug residues continue to be found in imported honey. Honey is different than most food products that may contain animal drug residues. Seafood, meat, and milk contain large amounts of protein and fats, while honey contains primarily sugars. Because of these significant differences, the traditional approaches used to isolate drug residues do not work for honey.

CVM researchers during FY 2006 developed a provisional multi-residue method for 17 drugs in honey. The method uses liquid chromatography-tandem mass spectrometry (LC-MS/MS), both to confirm the identity of the drug and determine the amount of drug residue present. The USDA Beltsville Bee Laboratory, in an ongoing collaboration with CVM, is generating needed biologically incurred residue samples for the drugs in the multi-residue method.

A method for detecting nitrofurans in honey, which was developed during FY 2005, is being transferred to ORA for use in regulatory testing. Additionally, CVM scientists are providing guidance and recommendations to the Florida Department of Agriculture and Consumer Services (FDACS) in developing a method for detecting fluoroquinolones in honey. Because of the assistance provided by CVM, the data generated by the FDACS method meet FDA requirements for confirming the identity of a drug residue. This has allowed FDA to take regulatory actions based on positive results from testing conducted by the State of Florida.

Drug Residues in Fish. This year, CVM researchers completed the validation of a multi-residue method for drug residues in tilapia and trout. The method has now been validated for use in four of the most commonly aquacultured finfish species, since the method has previously been validated in salmon and catfish. The availability of a multi-residue, multi-class, multi-species method for drug residue analysis provides great flexibility for laboratories testing imported aquaculture products.

CVM researchers during FY 2006 tentatively identified 3-O-desmethyl-ivermectin as the major ivermectin metabolite present in rainbow trout. The identification of this metabolite is a key step in development of methods for the detection of ivermectin residues. Previous published methods for ivermectin in fish have used parent ivermectin, the major residue found in terrestrial animals, as the marker residue for unapproved use. The identification of the metabolite will facilitate the development of better methods to detect the unapproved use of ivermectin in imported aquaculture products.

Ensuring Feed Safety

THE CHALLENGE

Threats to the safety of the Nation's animal feed supply could come from several sources, including bioterrorism. Contaminants and unsafe additives in animal feed can harm the animals, as well as humans who consume animal products, and can adversely affect the Nation's food and feed supplies. Improper manufacture of animal feeds can also result in health problems for animals and humans.

FY 2006 ACCOMPLISHMENTS

Following are highlights of CVM's FY 2006 accomplishments with regard to feed safety. In addition to the actions described below, CVM completed a variety of ongoing assignments, including processing several medicated feed mill licensing applications during the year. Firms that manufacture certain medicated feeds are required to be licensed.

CVM is working to protect the animal feed supply.

RISK-BASED SYSTEM – ANIMAL FEED SAFETY SYSTEM (AFSS)

CVM is developing a nationwide, comprehensive risk-based system that would be preventive. The Center is designing the AFSS to detect hazards before feed products are distributed, and thus minimize detrimental animal and human health effects. The AFSS incorporates FDA's historic feed safety role. It is focused on making the Agency's feed safety program more comprehensive, preventive, and effective in addressing feed hazards that present the greatest risks to animal and human health, with risk considerations made open to public review and comment. Additional background on AFSS is available on the AFSS page that was added to CVM's Web site during FY 2006, http://www.fda.gov/CVM/AFSS.htm. The report describes some of the AFSS accomplishments during the year in the following paragraphs.

The AFSS Team continued exploring systems approach options for ensuring that all feed manufacturers use adequate control steps throughout the animal feed production process to ensure the safety of the products they produce, distribute, and use.

The Team also drafted a standard operating procedure describing the process for development of analytical methods when the Agency decides to establish a regulatory limit for a feed contaminant, such as a mycotoxin or heavy metal.

CVM held a public meeting in September 2006 to present work in progress on a method for ranking feed contaminants according to the relative risks they pose to animal and public health. Contaminants are potentially toxic or deleterious biological, chemical, or physical hazards that are inadvertently present in animal feeds and feed ingredients. The relative risk posed by a feed contaminant to animal and human health consists of two components – health consequence scoring and exposure scoring. At this meeting, the Center described the methods it plans to use to develop animal and human health consequence scoring for chemical, physical, and biological feed contaminants. At one or more subsequent public meetings, FDA will present information about the exposure of animals and humans to contaminants in feed.

COMPLIANCE CHALLENGES IN ANIMAL FEED SAFETY

Review of Data from Dioxin Surveys

Dioxin in Animal Fat. In a survey of more than 500 animal fat samples, USDA found elevated dioxin levels of 2.0 parts per trillion (ppt) toxic equivalents (TEQ) or greater in 16 samples from slaughtered steers, heifers, and barrows. As a follow-up to the discovery of these elevated levels, FDA conducted on-farm investigations in an attempt to determine the source of the dioxin. Based on these investigations, a panel of experts from USDA, FDA, and EPA reviewed the data, discussed the most likely source of the dioxin contamination, and developed recommendations on how to remove the dioxin source. In January 2006, FDA mailed letters to the 16 affected animal producers summarizing the committee findings and making recommendations to several of these producers.

Dioxin in Feed Samples. CVM is reviewing the results from all feed samples collected by FDA over the past 6 years that were analyzed for dioxin contamination, and the Center's researchers are working on a manuscript for publication. Much of the data on dioxin presence in animal feeds that will likely be included in the manuscript have previously been summarized in presentations to two scientific and professional organizations.

Dioxin in Rendered Products. CVM presented summary data from the survey (FACTS Assignment #585971) of dioxins in rendered mammalian/poultry fats, in yellow grease, and in filtering/bleaching agents during the October 2005 FDA-AAFCO Annual Briefing and Planning Conference. The data on dioxin levels in rendered animal fats showed levels similar to the levels found by USDA in individual animal fat samples collected at slaughter.

FY 2006 Performance Goals

- ✓ Work with FDA, USDA, and EPA scientists to complete a report on the follow-up investigations that FDA conducted as a result of a USDA survey on dioxin levels in barrow, gilts, heifers, steers, broilers, and young turkeys.
- ✗ Summarize dioxin results from all feed samples collected by FDA over the past 6 years and prepare a manuscript for publication.

The report was being prepared for publication at the end of the year.

- ✓ Review available results from the survey of dioxin levels in rendered fats, yellow grease, and filtering/bleaching agents (FACTS Assignment #585971).
- ✓ Perform prior notice import security reviews on 35,000 food and animal feed line entries considered to be at high risk for bioterrorism and/or present the potential of a significant health risk (in conjunction with the FDA Office of Regulatory Affairs [ORA]).
- ✓ Develop a new or revised inspection/compliance performance goal that is more risk-based and outcome-oriented.
- ✓ Complete at least 80 percent or better each year of Food Additive Petitions (FAPs), Adverse Event Reports (AERs) evaluations, GRAS/GRAE Petitions, Warning Letters, Untitled Letters, Compliance Programs, Compliance Policy Guides, responses to Field inquiries and recommendations, general correspondence, and Congressional correspondence input to the Office of Executive Programs. *(Note: this goal applies also to the section on Additional Surveillance and Compliance Actions to Protect Public and Animal Health.)*

Import Alerts

As part of the Center's efforts (with ORA) to review animal feed imports considered to present the potential of a significant health risk, CVM issued two import alerts: "Detention Without Physical Examination Of Medicated Feeds Containing Monensin For Failing To Meet Assay Specifications" and "Detention Without Physical Examination Of Animal Feeds, Other Than Pet Treats, Due To The Presence Of *Salmonella*."

Injunction Against Feed Manufacturer

As a result of investigations following the death of livestock fed suspect feed, a Federal court entered a Consent Decree of Permanent Injunction against a Kansas firm that produces medicated and non-medicated feed for consignees in Kansas, Oklahoma, and Colorado. The August 2006 injunction was based on multiple consecutive inspections that documented significant violations of FDA's current Good Manufacturing Practice (cGMP) requirements for feed manufacturers.

Voluntary Self Inspection by Feed Manufacturers

During the year, CVM prepared a Voluntary Self Inspection of Medicated Feed Manufacturing Facilities Draft Compliance Policy Guide, which was expected to be published during FY 2007.

METHOD DEVELOPMENT FOR CHEMICAL CONTAMINANTS IN ANIMAL FEEDS

During FY 2005, CVM developed and validated a screen for detecting 27 drug compounds from 9 chemical classes in animal feed. During FY 2006, CVM applied the method by testing commercially available feed used as control feed in aquaculture studies at the Office of Research (OR). The control feed is required to be drug-free, for accurate comparison with results in fish dosed with medicated feed. As a result of this work, CVM disqualified several samples of control feed because drug levels of about 0.1 percent of the levels were found in the medicated feed.

During FY 2006, CVM developed a second screening method, complementary to the method developed and validated during FY 2005. The method, used for analyzing additional drugs as well as pesticides in animal feed, was based on consultations with analysts from ORA and EPA. This method required the submission of samples both to gas chromatography (GC) and liquid chromatography because some of the compounds are amenable only to one of the methods. This dual testing provides complete coverage for pesticides that are used in pest control in feed mills, in addition to having the potential for use in deliberate contamination. This method will also be validated with the standardized set of model feeds developed during FY 2005 to represent the wide range of protein, carbohydrate, fiber, oil, and moisture content that is typical of animal feed nationwide. Testing with the model feeds is necessary to determine if some feed ingredients affect or interfere with the method's performance.

Feed mixing equipment at CVM's research farm.

Also during FY 2006, CVM developed a novel chromatographic system for analysis of a small group of drugs that are not amenable to conventional liquid chromatography. Work is underway to develop a method for extracting these drugs from feed, to be applied in combination with the new chromatographic system.

CVM plans to start method development for screening of fungal and other toxins in feeds during FY 2007. To date, most regulatory feed methods have aimed to verify the drug concentration of one or only a few approved products used at therapeutic levels. The new methods being developed at the OR will meet a need for efficient screening for the presence at low levels of a wide range of possible contaminants and unapproved or misused products. In addition, this initiative addresses a gap identified by FDA's Animal Feed Safety System: feed safety and security requires additional surveillance methods for animal feeds.

Microbiologist Dotty Farrell, conducting PCR analysis on feed samples in CVM's OR laboratories.

Protecting Against Bioterrorism

THE CHALLENGE

There is widespread concern that microbial and/or other toxic agents could be used in the food chain as weapons to harm human and animal health. Bioterrorism against the human food and animal feed supplies would also harm the U.S. economy. FDA-regulated products, including animal drugs, would play a central role in countering the effects of such terrorism. FDA is responsible for implementing provisions of the Bioterrorist Act relating to protection of the Nation's food and drug supplies. CVM is working with other Federal agencies to help the country prepare for a biological emergency, natural disaster, or terrorist attack by making sure there is a safe and adequate supply of animal drug products and a safe animal feed supply system.

FY 2006 ACCOMPLISHMENTS

As CVM continues to clarify its role and goals with respect to bioterrorism, it has been active during the past year with respect to several initiatives that are in line with Agency, Department, and government-wide priorities.

BIOTERRORISM VULNERABILITY ASSESSMENTS

Four Federal Government agencies, including FDA, during FY 2005 launched the Strategic Partnership Program–Agroterrorism (SPPA) initiative. Under this program, the agencies work with industry volunteers and State agricultural and health counterparts to assess the potential risk from terrorist attacks against sectors of the agriculture and food industries. FDA participants include CVM and the Center for Food Safety and Applied Nutrition (CFSAN). The other participating Federal agencies are the Department of Homeland Security, the U.S. Department of Agriculture, and the Federal Bureau of Investigation.

The SPPA initiative has several technical goals, but the overall aim is for private industry participants and Federal and State government officials to understand better the vulnerabilities and to identify mitigation steps for industry subsectors. Government specialists use the findings to improve the National Infrastructure Protection Plan, which is a blueprint of ways to protect critical infrastructures and key resources against terrorism.

Export Grain Elevators

The Federal agencies examined the vulnerability of export grain elevators in the first joint SPPA initiative exercise, held in December 2005. The exercise was conducted at an export grain elevator outside of New Orleans, LA. The Port of New Orleans handles a significant amount of exported product that is used for human and animal consumption. A harmful agent placed in the processing system where the maximum amount of damage can occur could cause harm to animal and public health as well as to U.S. export markets.

The agenda for the visit included a review of the design flow diagram of the production process at the site, a CARVER+Shock analysis, and an assessment of the site's vulnerabilities. After completing the analysis, the exercise team identified mitigation steps and information gaps that need more research.

Information developed from the exercise will be distributed to other members of the grain industry to allow the firms to protect themselves from a potential terrorism attack. Government officials plan to provide periodic classified briefings for industry, State, and Federal partners who have the necessary security clearances, and to produce unclassified summary reports that will highlight cross-sector lessons learned and best practices.

FY 2006 Performance Goals

- Perform a risk analysis in cooperation with the FDA Center for Food Safety and Applied Nutrition, USDA, FBI, and Department of Homeland Security on exporting grain elevators in New Orleans, LA, and Galveston, TX.
- Seek further industry input and continue training industry in the CARVER risk analysis tool of vulnerability of livestock and poultry feed.
- Develop analytical methods to detect the presence of prohibited animal substances that could be introduced into U.S. animal feed supplies by bioterrorists.

Meeting these goals responds to FDA's high-priority area of food defense, including targeted food defense research, and to the Department-wide objective of increasing the capacity of the health care system to respond to public health threats from bioterrorism.

Beef Cattle Feedlots

CVM participated with other agencies in a July 2006 CARVER + Shock assessment and training that included volunteers from the cattle feedlot industry. The exercise evaluated the vulnerability of beef production in Nebraska and elsewhere in the heartland of the United States. The focus was on gaining information that would help protect the industry from exotic animal diseases and chemicals that may be used to undermine the beef industry.

THE CARVER+Shock Analysis

The "CARVER+Shock" analysis is a tool that analysts use to determine the desirability of a target to terrorists. CARVER is an acronym for:

- Criticality – what effect would the attack have on public health or the economy?
- Accessibility – can a potential terrorist get to and from the target easily?
- Recuperability – does the target have the ability to recover from the attack?
- Vulnerability – how easily can a terrorist attack the facility?
- Effect – what would be the direct loss from an attack, measured in terms of lost production?
- Recognizability – how easily would a terrorist recognize that a facility would make a good target?

The "shock" part of the evaluation is a combination of health, economic, and psychological effects of an attack. In other words, this part of the review is an analysis of how much of a psychological jolt an attack would cause.

FDA and USDA have used the CARVER+Shock assessment tool to evaluate the potential vulnerabilities of farm-to-table supply chains for various food commodities. Under SPPA, the tool is adapted to individual companies or industry groups.

Additional Vulnerability Assessments

The SPPA assessments at the export elevator and feedlots were two of many evaluations that the Federal agencies intend to accomplish. For example, USDA in March 2006 conducted an assessment on swine operations with the Iowa Department of Agriculture and the national and Iowa pork producers associations. The four cooperating government agencies have identified more than 60 other types of food and agriculture facilities for analysis under SPPA, including animal feed manufacturers, animal byproduct manufacturers, corn refiners, poultry farms, cereal manufacturers, fluid milk and infant formula manufacturers, and produce processors.

Cattle in a feedlot.

Industry participants in SPPA initiative evaluations are volunteers. Companies that volunteer to participate in an SPPA review are provided training in conducting a CARVER+Shock Analysis. Firms volunteer by contacting their representative trade association, or they can obtain more information on the SPPA page of CFSAN's Web site, http://www.cfsan.fda.gov/~dms/agroterr.html.

The responsibility for a safe animal feed supply belongs to the feed industry, but to help achieve this goal, government agencies such as FDA are responsible for establishing standards, providing education, conducting outreach, and performing oversight.

FDA Veterinarian Article on Vulnerability Assessments

The November/December 2005 *FDA Veterinarian* contained an article entitled, "Federal Agencies Partner with Private Industry for Bioterrorism Vulnerability Assessment," that describes in more detail the SPPA initiative.

RESEARCH RELATED TO BIOTERRORISM

CVM made considerable progress during the year in developing analytical methods to detect the presence of toxins, drugs, pesticides, and other substances that could be introduced into U.S. animal feed supplies by bioterrorists. Intentional contamination of feed with animal pathogens is also a significant concern with regard to agroterrorism.

Some pathogens are present in the environment as part of the normal ecosystem but not at population densities that would allow infection. To make decisions about the potential cases of intentional contamination with naturally occurring pathogens, officials need to know the normal background levels of these organisms. Office of Research scientists during FY 2006 continued survey programs to assess background levels of the animal pathogen *Bacillus anthracis* (anthrax) that can routinely be recovered from animal feeds. These data will provide a baseline for comparison against levels in feed where intentional contamination has occurred.

These FEDERAL AGENCIES

FDA CFSAN

USDA FBI

created the
STRATEGIC PARTNERSHIP PROGRAM AGROTERRORISM (SPPA)
to perform with the help of
STATE GOVERNMENT AGENCIES & INDUSTRY

BIOTERRORISM VULNERABILITY ASSESSMENTS

FY 2006
Export Grain Elevators
Beef Cattle Feedlots

to help protect
AGRICULTURE AND FOOD INDUSTRIES

A second phase of this work involves testing the performance of rapid methods to identify accurately suspect anthrax isolates recovered from feed samples. Animal feed commodities are often retained for a very short period of time at feed manufacturing facilities and, thus, rapid detection methods are essential for timely decisionmaking with regard to the ultimate disposition of these materials. The results of these tests will be compared with the results of reference identification methods used for *Bacillus anthracis*.

In FY 2006, we examined a number of feed samples for the presence of mesophilic[4] organisms using a spore-counts methodology. This method is designed to detect bacteria belonging to the *Bacillus cereus* group of which *Bacillus anthracis* is one of the members. CVM researchers found *Bacillus* spores in all of the samples. Isolates that are suspected of being *Bacillus anthracis* are undergoing further testing to confirm the identity of the organisms. At fiscal year's end, none of the organisms identified as being part of the *Bacillus cereus* group had been identified as *Bacillus anthracis*. These data will nevertheless provide baseline information on the prevalence of mesophilic spores in animal feeds, which will be important in detecting intentional contamination of animal feeds with *Bacillus anthracis*.

[4] Mesophilic bacteria develop and grow best at moderate temperatures, i.e., temperatures between 20 and 45 degrees Centigrade.

Ensuring the Safety of Animal Biotechnology

THE CHALLENGE

The application of biotechnology to the production of animals and products derived from animals continues to grow in diverse directions. Animal biotechnology includes both genetic engineering and cloning. Animal cloning is seen as a means of expanding populations of cattle, swine, and goats with desired phenotypes. Genetic engineers are investigating broader ranges of applications in animals, from BSE-resistant cattle, to production of biomedical products secreted into transgenic chicken eggs and transgenic goats, to pigs as sources of organ transplants. Producing animals through biotechnology raises potential food and animal safety issues, and CVM needs to have a thorough understanding of the scientific and risk issues that the two kinds of animal biotechnology present.

FY 2006 ACCOMPLISHMENTS

In addition to working on continuing activities, such as reviewing products of plant biotechnology used as animal feeds, CVM's biotechnology-related activities during FY 2006 involved participation in international efforts to develop innovative resource documents.

EDUCATIONAL INFORMATION ON ANIMAL BIOTECHNOLOGY

CVM scientists during FY 2006 provided educational information on biotechnology products in a wide range of settings, including book chapters and other publications; meetings of international forums, such as the Organization for Economic Cooperation and Development (OECD); the Codex Alimentarius Commission (CODEX); committees of Congress; and the USDA Agricultural Outlook Conference.

ANIMAL CLONING

FDA has prepared a draft risk assessment and proposed risk management plan for animal clones, their offspring, and meat and milk derived from these animals. FDA evaluated the data from several hundred scientific studies, including those from peer-reviewed scientific publications. Those data that have not yet been published in scientific journals are presented in the draft risk assessment.

The risk assessment concludes that the meat and milk from cattle and goat clones and their offspring, and the meat from swine clones and their offspring, are as safe as that from conventionally bred animals.

The draft risk assessment was peer reviewed, in accordance with the Office of Management and Budget requirements. The peer reviewers concurred with FDA's conclusions and offered only minor recommendations, which have been incorporated into the draft document.

The documents will be released upon completion of the clearance process within the U.S. Government.

FDA will request public comment on the draft documents and, after the comment period has closed, the Agency will release a final risk assessment and risk management plan.

FDA has also prepared communication materials that should help the public understand the issue better, including a primer on cloning, myths about cloning, and frequently asked questions for consumers and producers.

COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY

During the year, CVM officials had regular contact with USDA Biotechnology Regulatory Service to discuss progress in developing a coordinated policy for the regulation of biotechnology.

CVM scientists, including John Matheson and Dr. Larisa Rudenko, provided leadership within international organizations that addressed biotechnology issues during the year. The organizations included the OECD, CODEX, the World Organization for Animal Health, and the International Embryo Transplant Society.

GENETICALLY ENGINEERED ANIMAL POLICY IMPLEMENTATION

While the U.S. Government continues to discuss the Coordinated Framework for Genetically Engineered Animals, CVM is tasked to continue to work with companies developing this technology and to control introductions of food derived from these animals into the animal and human food supply. CVM scientists conducted a number of sessions during the year with prospective and current sponsors of Investigational New Animal Drugs, and persons interested in the establishment of import tolerances, for animal biotechnology products.

CVM scientists are also working to develop a new paradigm for the review of submissions to demonstrate the safety and effectiveness of constructs used to produce genetically engineered animals, and they have assembled a team to work through the paradigm on a pilot basis using an animal biotechnology product under consideration at CVM.

FY 2006 Performance Goals

✓ Provide educational information on biotechnology products and assist developers through the regulatory process.

✗ Complete draft Risk Assessment on Animal Clones and their Progeny, Proposed Risk Management Plan (related to the risk[s] identified in the risk assessment); and a draft Guidance for Industry for public comments (which reflects the Agency's current thinking on recommendations on the use of animal clones and their progeny as food) after obtaining the necessary Department clearances; review the public comments in preparing the final documents.

CVM completed updating the Draft Risk Assessment in late spring 2006, submitted it to external peer review as required by the Office of Management and Budget, addressed the minor concerns raised by the review, and at the end of FY 2006, was in the process of obtaining clearance from relevant Federal departments prior to release.

✓ Participate with other members of the U.S. Government in the recently reconvened Office of Science and Technology Policy (OSTP)-led activities to update the Coordinated Framework for the Regulation of Biotechnology to include genetically engineered animals.

Meeting these goals accomplishes the Department-wide objective of achieving continuous improvement in the safety of food and drugs.

Additional Surveillance and Compliance Actions To Protect Public and Animal Health

THE CHALLENGE

Surveillance and compliance activities are key parts of CVM's efforts with regard to antimicrobial resistance, BSE, drug residues, feed safety, and other crosscutting issues described above. CVM has had challenges in additional areas that are related to CVM's core functions of compliance-related actions and post-approval monitoring. These challenges include acting against specific threats to public and animal health, monitoring to assess post-approval drug safety, taking steps to ensure proper manufacture of approved drugs, and regulating animal drug compounding and the marketing of unapproved drugs.

FY 2006 ACCOMPLISHMENTS

Following are highlights of CVM's accomplishments during the past fiscal year.

PUBLIC HEALTH ACTION – AVIAN INFLUENZA

In May 2006, CVM issued a final rule prohibiting the extralabel use of anti-influenza adamantane and neuraminidase inhibitor drugs in chickens, turkeys, and ducks based on evidence that such use could lead to the emergence of resistant strains of influenza A virus. These drugs are approved for human use and could be used in animals under a veterinarian's supervision unless the use is prohibited. If drug-resistant strains develop in animals and then infect humans, it is possible that the approved anti-influenza drugs would no longer be effective for treating or preventing disease in the human patients.

CVM also collaborated with FDA's Center for Food Safety and Applied Nutrition in leading the Food and Feed Safety Subgroup of the Pandemic Task Force in support of the FDA Pandemic Influenza Preparedness Strategic Plan.

> CVM's work in this area responds to the Agency's high-priority area of pandemic preparedness, and the Department-wide objective of increasing the Nation's preparedness for a potential disease pandemic.

ANIMAL HEALTH ACTIONS

Aflatoxin-Contaminated Pet Food

Following discovery of death and illness in a number of dogs due to contamination of pet food with a potent toxin called aflatoxin, FDA, working closely with the State feed regulatory agencies in the affected States, issued alerts and conducted follow-up investigations. FDA advised customers who had purchased the dog food to stop using it immediately, return any remaining product to their retailer, and contact their veterinarian if their pets exhibit certain symptoms. Aflatoxin comes from a fungus found on corn and other crops and can cause severe liver damage in pets.

FDA also has discovered that some of the product, which was recalled by the manufacturer, had been exported to at least 29 countries; FDA's Office of International Programs notified those countries.

Use of Unapproved Formaldehyde in Aquaculture

CVM issued an UPDATE in June 2006 to remind aquaculture producers to use an approved formaldehyde product rather than chemical grade formaldehyde. The Center had received reports that some aquaculture producers had been using unapproved chemical grade formaldehyde as a parasiticide for their fish. Using an unapproved product can be unsafe for fish, and the effectiveness of an unapproved compound is questionable.

Three firms are sponsors of approved new animal drug applications for use of formaldehyde for a variety of therapeutic purposes. The sponsors have demonstrated that their products are safe and effective for the approved uses. Approved formaldehyde products are manufactured under strict good manufacturing practice standards to ensure quality, purity, and strength. The standards by which chemical grade formaldehyde is manufactured are different, and the products are not appropriate for aquaculture use.

INNOVATIONS IN ADVERSE DRUG EXPERIENCE REPORTING AND REVIEW

One of FDA's high-priority areas is medical product safety, and accelerating the adoption and use of an electronic health information infrastructure is a Department-wide objective. CVM worked to achieve these purposes during FY 2006 in several ways, as follows.

FY 2006 Performance Goals

- ✓ Pilot PV-Works (Vet) in order to reduce the amount of data entry time in order to review all pending Adverse Event Reports (AERs).
- ✓ Examine the potential use of certain veterinary antimicrobials for human use in a worst-case emergency, at the request of the National Security Council.
- ✓ Ensure the safety of animal drugs and animal feeds by conducting appropriate and effective surveillance and monitoring activities by inspecting 390 registered animal drug and feed establishments.
- ✗ Animal Drug Compounding: Complete the inspections of the two remaining compounding firms (18 finished, 20 total) and release a summary detailing the findings and conclusions derived from the March 2004 inspection assignment.

The two remaining inspections were completed near the end of the fiscal year. The summary was to be drafted during the early part of FY 2007.

- ✓ Develop intervention measures to establish additional controls over the shipment, receipt, and use of bulk active pharmaceutical ingredients in compounding animal drugs.
- ✓ Complete at least 80 percent or better each year Food Additive Petitions (FAPs), Adverse Event Reports (AERs) evaluations, GRAS/GRAE Petitions, Warning Letters, Untitled Letters, Compliance Programs, Compliance Policy Guides, responses to Field inquiries and recommendations, general correspondence, and Congressional correspondence input to the Office of Executive Programs. *(Note: this goal also applies to the section on Ensuring Feed Safety).*

Pilot Effort to Expedite Adverse Drug Experience (ADE) Review

CVM has integrated PV Works (a commercially available, off-the-shelf product that provides an animal health drug safety system designed for both animal and human reactions to veterinary pharmaceuticals) with other CVM applications including the Drug Experience Reporting System. This change is part of an effort to develop a streamlined, fully automated ADE review process in which reviewers can monitor, track, and assess ADEs, and coordinate, share, and communicate information.

CVM selected PV Works for its enhanced analysis and reporting capabilities. As part of this integration, CVM built the capability to collect, store, and process the electronic reports by building an Information Exchange Repository Service (IERS). This integration provides a more efficient system to support pharmacovigilance business processes and regulatory reporting requirements worldwide and has integrated workflow to provide accurate performance metrics to users.

The pilot of this integrated system, which includes testing the exchange and reporting capabilities with data sent in XML format from industry sponsors on CD ROM, continued during FY 2006. The Center is moving toward full deployment of this integrated Adverse Event Reporting System with FDA's electronic gateway. This system will allow electronic submissions directly from industry sponsors and will be fully functional in late 2007.

Improved Public Access to ADE Summaries

During the year, CVM changed the way the summaries of ADE reports are presented, and the report is now posted at: http://www.fda.gov/cvm/ade_cum.htm. CVM several years ago posted the Cumulative Adverse Drug Experiences Summaries Report so that veterinarians and animal owners could have easy access to information about signs in treated animals that have been associated with the use of the active ingredient. The Internet site information allows a search for the active ingredient of a drug to determine if particular signs associated with adverse reactions have been reported with the drug's use. The adjustments made during the fiscal year were directed at reducing possible confusion and misinterpretation on the part of those who access the summaries on the Web site.

Publication of ADE Guidelines

CVM published the following ADE-related guidelines during the fiscal year:

VICH GL-42: Pharmacovigilance of Veterinary Medicinal Products; Data Elements for Submission of Adverse Event Reports - notice of availability of draft guidance published in May 2006 (Guidance for Industry #182)

VICH GL-24: Pharmacovigilance of Veterinary Medicinal Products: Management of Adverse Event Reports - notice of availability of draft guidance published in May 2006 (Guidance for Industry #117)

COMPLIANCE ACTIONS TO ENSURE DRUG AND FEED SAFETY

Inspections of Registered Establishments

CVM collaborated with ORA to complete the inspection of 433 registered animal drug and 577 feed establishments to ensure the safety of marketed animal drugs and animal feeds, thus surpassing CVM's FY 2006 Performance Goals in this area.

Compounding

In September 2006, a U.S. District Court entered a consent decree between the United States and a Kentucky firm, resolving a dispute over compounded drug products for use in horses. The Government had seized the compounded drug products in 2004 on the grounds that the drugs were unapproved and failed to bear adequate directions for use. The consent decree requires the firm to pay costs and to destroy the seized compounded drug products.

CVM during the year issued industry letters to two compounding pharmacies concerning the compounding of recently approved animal drugs. In addition, the Center began to focus during the year on firms identified by the compounding inspection assignment as being responsible for the majority of the active pharmaceutical ingredient (APIs) used in compounding, with the intent of reducing the illegal importation of veterinary APIs. The initiative involved cooperation with FDA's Center for Drug Evaluation and Research, and ORA. It included development of enforcement actions focused on, among other things, the practice of importation of animal drugs and subsequent resale of relabeled drugs to various firms that specialize in veterinary compounding.

Two drug compounding inspections remaining from a 2004 compounding inspection assignment were completed near the end of FY 2006. CVM was in the process of summarizing the inspectional findings from all of the assignments at the end of the year, and expected to have a draft summary completed early in FY 2007.

Compliance Action Processing

CVM received 88 requests for regulatory actions (Warning Letters, injunctions, and seizures) and processed the requests in an average time of 29 days.

RECALLS OF UNSAFE PRODUCTS

In 2006, FDA processed 136 recalls, involving 47 firms, including 37 Class I Recalls, 89 Class II, and 10 Class III Recalls. (Class I Recalls involve the highest degree of health hazard). The Class I Recalls involved a product that had its approval withdrawn by FDA; monensin in horse feed (three horses died); aflatoxin in various pet foods (many dogs died, 31 products recalled); excessive salt in chicken feed (numerous chicken deaths); and monensin in lamb feed (five lambs died). Class II Recalls (all pet food) included excessive levels of Vitamin D3 (six products); and contamination by metal substances (one product) and enamel (15 products).

IMPROVING THE EFFICIENCY AND EFFECTIVENESS OF DRUG REGISTRATION AND LISTING

FDA in August 2006 issued a proposed rule to make managing drug information more efficient and effective through automating the process by which drug firms register and list their products with the Agency. The proposed rule, which includes animal drugs, is part of a broader Federal effort to modernize the management of health information. The Electronic Drug Registration and Listing System would make the complete list of drug products marketed in the United States readily accessible electronically. Currently, part of the list is kept on paper. The proposal would improve the quality and completeness of the drug product information that FDA receives and manages.

Enhancing Productivity Through Achievement of Management Goals

THE CHALLENGE

The challenge for the Office of Management (OM) was to provide the essential executive leadership and knowledgeable support necessary for CVM to successfully meet the 2006 goals as outlined in the President's Management Agenda and the Agency's Strategic Plan. The organization's challenge also includes continued implementation and guidance of the improved management systems and business practices, as outlined by the Department of Health and Human Service and FDA.

FY 2006 ACCOMPLISHMENTS

Through the leadership and active guidance of OM, the Center successfully met specific performance goals for 2006, as described in the following significant outcomes and achievements.

The implementation of the Animal Drug User Fee Act (ADUFA) has been particularly successful and on track, and CVM has met or exceeded each of the prescribed ADUFA performance goals to date. OM has facilitated the industry fee collection activities in a citizen-centered manner. Revenue goals have been achieved with precision, including the timely publication of fee adjustments required by the Act. OM has ensured that industry revenues are appropriately utilized to help CVM reach the Department/Agency goal to provide safe and effective animal drug products to ensure public health.

CVM fully participated in the Agency's budget and strategic performance planning efforts again in 2006. As a result, the Center's FY 2007 President's Budget Request reflected a significant increase of 8.14 percent over the 2006 enacted budget level (not including ORA funding). Such effort to obtain maximum resource funding allows for full program support that is essential for the Center to meet the Department-wide objectives.

OM, with support from the Office of New Animal Drug Evaluation, has undertaken a leadership role on the Agency-wide Bioinformatics Board that was established in February 2006 to achieve the FDA goal for a modern, well-integrated, efficient and affordable infrastructure to support FDA administrative and regulatory business operations. The Board's approach is based upon the premise that oversight of the design, building, and maintenance of such an infrastructure must be both business-driven and business-owned. The Board provides oversight for planning and control of bioinformatics activities and ensures that such activities are communicated to all levels of the Agency. The Board also addresses a growing number of business automation challenges to ensure that the Agency's plans for future business automation meet the needs of FDA programs and, at the same time, satisfy external demands.

STRATEGICALLY MANAGE HUMAN CAPITAL

Implementation of the New, Department-Wide Performance Management Appraisal Program (PMAP)

OM promoted and ensured that CVM fully supported the Department's objective to implement a new, single PMAP, by December 31, 2006. PMAP is part of the President's Management Agenda. The Center's senior management worked with special subject matter experts to review the requirements for the new performance system, developed a series of templates for position descriptions, and initiated an efficient process to produce the 2007 employee PMAP plans. Through this proactive process, the Center was in a position to accurately align each employee's functions and responsibilities with the goals of the Department, put the plans in place as scheduled, and begin the calendar year fully compliant with the requirements of the PMAP initiative.

FY 2006 Performance Management Goals:

- Strategically Manage Human Capital
- Complete the 2006 Competitive Sourcing Program
- Improve Financial Performance
- Expand Electronic Government
- Improve Budget and Performance Integration
- Consolidate Management Functions and Streamline Administrative Operations

Delivery of Diversity Initiatives – Section 508 of the Rehabilitation Act

Under Section 508 of the Rehabilitation Act of 1973, amended in 1998, Congress requires all Federal agencies to provide electronic and information technology formats to be in accessible formats to persons with disabilities. Section 508 was enacted to eliminate barriers to this information technology. CVM is committed to complying with this mandate. Employees are required to take the on-line Phase I training and to attend Phase II training. CVM signed a Memorandum of Agreement with the HHS Office of Disability to bring on-site training to the Center's Staff College early in FY 2007. CVM is the first center to bring the face-to-face training to employees.

OM Demonstrated Commitment to CVM Vision and Values Through the High Performance Initiative

OM continued to demonstrate the organization's commitment to the Center's vision, values, and behaviors through initiatives and programs that assisted CVM employees in reaching the highest performance level possible. CVM has emphasized the vital importance of actively empowering each of CVM's employees to participate and feel full ownership of the initiatives and programs of OM and the Center. To better prepare and encourage such participation in 2006, the CVM Staff College coordinated Basic Feedback Workshops, 360 Degree Feedback Programs, training in Myers-Briggs, and Conflict Resolution. It introduced new offerings, including Interview Architect and Introduction to Emotional Intelligence, as well as other on-site management, leadership, and team building training for all employees. These efforts have resulted in positive employee response, such as increased productivity and morale, and assisted CVM in attracting and keeping the best and brightest employees for the Center/Agency.

Graduate Credit Courses Offered to Eligible CVM Employees

In March 2006, CVM's Staff College offered a graduate level course, "Statistics for Veterinarians and Animal Scientists." Students who enrolled and completed course requirements were eligible to receive graduate credit hours that would fulfill core curriculum requirements towards the Master's in Public Health (MPH) degree. The graduate level

course, "Principles of Epidemiology," started in September 2006. The Staff College, in collaboration with the University of Maryland, designed the course in a "blended-learning" format. Blended-learning is a combination of Web-based technology, through which students are able to access course lectures and materials via the Internet, and traditional classroom settings for interactive class discussion. This method of course delivery allows flexibility and accessibility for CVM employees while still allowing maximum class interactions.

New Scientific Seminars Presented in 2006

CVM's Staff College offered new seminars that presented information on cutting-edge technology in diagnostic methods, analysis, and manufacturing of drugs, animal feed, and other products regulated by CVM. The seminar series, "Emerging Technology," included topics such as "Process Monitoring of Pilot-Scale Pharmaceutical Blends by Infrared Techniques" and "Ornamental Fish Diseases and Commercial Ornamental Fish Husbandry."

Migration to the Department-Wide Learning Management System (LMS)

OM actively represented the Center's Staff College in leadership roles on the FDA Lead Migration Team to assist in bringing about the successful migration to a single, Department-wide, HHS University LMS. Three OM Staff College representatives served on the Team, with one representing the Agency on all continuing education unit issues. The others reviewed the candidate LMS systems to select one as the Department-wide LMS. This major effort responds to the President's Management Agenda by consolidating employee training initiatives and development experiences and thereby reduces redundancies in training expenditures and programs.

COMPLETE THE FY 2006 COMPETITIVE SOURCING PROGRAM

CVM updated all data for the Federal Activities Inventory Reform Act inventory and accurately changed all clerical positions to the correct Reason Code to reflect the end of the clerical study effort. The material was provided to the Agency ahead of deadline in early April 2006 to fully support the Competitive Sourcing Program.

IMPROVE FINANCIAL PERFORMANCE

Addition of Audits to Provide Improved Process Oversight

OM prepared the FY 2006 Federal Manager's Financial Integrity Act (FMFIA) report and proactively launched two new audit programs that include (1) quarterly IMPAC purchase card audits (IMPAC is the International Merchant Purchase Authorization Card), and (2) bi-monthly travel audits. This work provided further assurance to CVM and the Agency that both systems use appropriated funds properly and are accompanied by the essential, required paperwork.

Early 2006 Closeout by the OM Budget and Finance Staff

CVM conducted early closeout for FY 2006. This action ensured that all procurements were conducted on schedule to ensure adequate time for adjustments in the United Financial Management System. Furthermore and most importantly, it guaranteed the appropriate use of the Center's end-of-year budget funds.

NEW COST AND TIME REPORTING

During the year, CVM utilized the Activity-Based Costing (ABC) System in conjunction with data from the associated Activity Time Reporting (ATR) System to develop management reports that have enabled CVM management to better understand, manage, define, and assign the true costs of doing business. CVM has developed new reports and written new processes to identify discrepancies and validate the data.

EXPAND ELECTRONIC GOVERNMENT

Collaboration With Other FDA/Center Information Technology (IT) Organizations

Office of Information Technology, CVM (OIT/CVM), has implemented two new electronic tools (Web services) that can be used by any custom application. This new approach to developing applications eliminates the need for this functionality of these services to be built into each application independently or to develop complex inter-relationships between systems. As a result, the effort required to update and change custom applications has been reduced, freeing up resources to work on new electronic functionality to support employees. In addition, two common services – Documentum Web Services/Mediator (which allows applications to use the document management functionality contained in Documentum from any custom application), and Information Exchange Repository Service (which allows import and export services for exchanging electronic information) – have been built so they can be used throughout FDA and not just in support of CVM.

Improved Process for Adverse Drug Event (ADE) Reports

OIT/CVM built the capability to collect, store, and process ADE reports electronically, which allows for the ADE electronic submissions to be received directly from sponsors and be imported into the Veterinary Information Exchange Repository Service (VIERS) using the Import Services as the unaltered, official copy of the submission, significantly improving the electronic health information infrastructure.

Integration of the VIERS, DERS, and PV Works Systems

VIERS, Drug Experience Report System (DERS), and PV Works (Pharmacovigilence Works) were integrated into one system to provide a complete ADE receipt and review system for compliance safety reviewers. Compliance safety reviewers and industry will begin fully utilizing this system in 2007. This integration provides a more efficient system to support pharmacovigilance business processes, regulatory reporting requirements worldwide, and has integrated workflow to provide accurate performance metrics to users.

Automation of the CVM Annual Report Review Process

OIT/CVM automated the CVM annual report review process in which reviewers monitor, track, and access annual reports submitted by sponsors of approved New Animal Drug Applications, and coordinate, share, and communicate information both internally and externally. In doing so, OIT/CVM took software that it had built for another purpose – the Outlook Notification Form Integration project (an automated engine for receiving, storing, and tracking electronic submissions) – and used it for this project. The automation has significantly improved the drug review process in this functional area, particularly IT communication and tracking, by expanding the functionality of the electronic systems.

Support of the New eTravel/GovTrip System

OM played a key role in communicating information to travelers about the new eTravel/GovTrip system. (GovTrip is a travel management system that allows users to log into a single Web-based system to create authorizations, vouchers, and local vouchers end-to-end. GovTrip interfaces with the Unified Financial Management System (UFMS) to obligate and de-obligate real-time funds and payments electronically. OM developed a list of questions and answers for CVM employees about the new travel system that is now used by the Agency for all FDA travelers. Prior to implementation, OM ensured that all travel preparers took training, and all travelers were provided the opportunity to take Web-based training. This effort helped to ensure that all travelers would receive payment promptly and that the required processes and procedures were followed properly.

IMPROVE BUDGET AND PERFORMANCE INTEGRATION

Develop Methodology for the Agency's Marginal Cost Analysis

OM served as the FDA pilot for the development of a marginal cost analysis methodology requested by the Office of Management and Budget to achieve a milestone on the President's Management Agenda. This analysis assessed how the impact of a change in funding on performance will help to improve budgetary and policy decisionmaking. The pilot also outlined the impact and outcomes of a marginal investment on CVM's long-term performance goals for the ADUFA.

CONSOLIDATE MANAGEMENT FUNCTIONS AND STREAMLINE ADMINISTRATIVE OPERATIONS

OM management officials continued to serve in key Agency council and committee leadership roles in 2006 to guide the business re-engineering process, update consolidated service agreements, review proposed budgets, and transfer additional consolidated services, all of which effectively supported the streamlining of administrative operations. OM's leadership provided assurance that the mission of the Agency continues to be efficiently met through these successful consolidated efforts, while maintaining the high level of service necessary to meet FDA's vital public health mission.

Leveraging Productivity Through Partnerships

THE CHALLENGE

Budget tightening and other factors have prompted FDA and CVM continuously to seek out partnering opportunities to maximize the use of resources. CVM's success in promoting and protecting the public health depends in large part not only on active involvement by stakeholders, but also partnerships with those whose goals align with the Center's.

FY 2006 ACCOMPLISHMENTS

CVM continued work under a number of partnering arrangements during the year. These mutual-benefit arrangements have influenced CVM policies and practices and have enhanced its research and epidemiological efforts. Seventeen CVM staff members (along with many more individuals from other parts of FDA, other government agencies, academic institutions, and industry) received leveraging/collaboration awards during FY 2006 awards ceremonies. This is a powerful illustration of CVM's extensive involvement in leveraging and collaboration arrangements.

FDA Recognizes Industry Leader

Cooperation and support of industry groups is often critical in the passage of legislation, and the adoption of regulations, that further FDA's mission of protecting the public health. A significant example occurred in the adoption of the Agency's BSE feed regulation. Initially, FDA, with the voluntary participation of key industry segments, planned only to prohibit use of sheep byproducts in cattle feed. Then, following discovery in the United Kingdom of human deaths that could be linked to BSE, the Agency decided to broaden the scope of its regulation to prohibit the feeding to ruminants of virtually all ruminant-derived feed material.

Support of the affected industries – rendering, feed, and ruminant producers – that would need to make major changes was essential. The leadership of one individual, Dr. Gary Weber, overcame initial opposition from some industry groups. Dr. Weber, who was Executive Director, Regulatory Affairs, for the National Cattleman's Beef Association,[5] articulated a position in support of the proposed regulation that eventually was adopted by other industry groups. "A careful interpretation of the data that were available, and risk analysis, indicated that a BSE outbreak in the United States cattle industry would be inevitable if nothing was done," Dr. Weber said. "By the time cases

Dr, Gary Weber, who provided key leadership in developing BSE policy when he was with the National Cattleman's Beef Association.

[5] As of September 1, 2006, Dr. Weber became the CEO of Harrison Ethanol, an integrated dairy and beef cattle operation located in Southern Ohio.

of BSE were discovered, we would be at the beginning of an epidemic curve that could involve human exposure and would mean disaster for the beef industry," he said. Thus, Dr. Weber advocated a preemptive approach that required action even though BSE had not at that time been found in the United States.

Dr. Weber continued to be a forward-looking advocate in the area of BSE regulation, following promulgation of the feed regulation. "The regulation has been effective," he said. "It was the right thing to do." In recognition of his effort, Dr. Weber was awarded the Commissioner's Special Citation during the 2006 FDA Awards Program.

The report highlights a number of partnership agreements and informal arrangements in this report. Examples of these and other initiatives include:

- Participation with regulatory agencies in other countries through the International Cooperation on Harmonisation of Technical Requirements for the Registration of Veterinary Medicinal Products (VICH). For example, CVM participated in a March 2006 meeting of the VICH Metabolism and Residues Working Group to agree on topics that would become the focus of guidelines. Based on the meeting's outcome, the VICH Steering Committee in July 2006 officially directed the Metabolism and Residues Working Group to begin work on new residue chemistry guidelines. In addition, CVM's Dr. Gregg Claycamp served as FDA lead and Rapporteur for the internationally harmonized guideline, Q9 Quality Risk Management, published during FY 2006. The guideline applies both to human and animal drugs, and is utilized by CVM's Division of Manufacturing Technologies.
- Participation in the Joint Subcommittee on Aquaculture's (JSA) working group "National Aquatic Drug Research Forum," held in August 2006, to help provide researchers involved in drug approval studies with a mechanism by which to obtain information from other researchers in the field. The goal of this working group is to disseminate information about issues that arise when researchers are developing animal disease models and study protocols, and while they are conducting animal studies. The Forum is composed of participants from U.S. Geological Survey, U.S. Fish and Wildlife Service, U.S. Department of Agriculture, and FDA/CVM. CVM has participated for a number of years in the JSA, which is a statutory committee – including representatives of a number of Federal agencies – that operates under the auspices of the Office of the Science Advisor to the President. The JSA's goal is to increase the overall effectiveness and productivity of Federal aquaculture research, transfer, and assistance programs.
- Participation in bioterrorism vulnerability assessments, described in the section on Protecting Against Bioterrorism, has a broad goal of the establishment or strengthening of working relationships that include Federal, State, and local governments, and private sector companies.
- Collaborative effort with USDA and CDC in the National Antimicrobial Resistance Monitoring System.
- Arrangements with state regulatory agencies to conduct BSE feed rule and medicated feed current Good Manufacturing Practice inspections. State inspectors accomplished more than half of these inspections during FY 2006. (FDA investigators conducted the remaining inspections.)
- Cooperation with USDA and a number of universities in the National Research Support Project #7 (NRSP-7). Public master files created with NRSP-7 support have aided in new animal drug application approvals for 26 unique minor species over the years.

FDA Recognizes Innovative Work by USDA Scientist

Dr. Mark Feldlaufer of the USDA Bee Laboratory received the Commissioner's Special Citation in 2006 for working with FDA and NRSP-7 in conducting the studies that led to approval of Tylosin for American foulbrood in honeybees. He proposed the project based on his realization that the foulbrood organism was becoming resistant to the only approved treatment and worked with CVM's Dr. Meg Oeller on protocol development before conducting the studies.

- Collaborative efforts with universities and industry to provide up-to-date information on scientific issues and research progress through courses offered by the CVM Staff College. During FY 2006, subject matter experts from the academic community and industry presented information on cutting-edge technology in diagnostic methods, analysis, and manufacture of drugs, animal feeds, and other products regulated by CVM. In addition, the Staff College and the University of Maryland's School of Public Health are collaborating on a Master of Public Health (MPH) program that offers CVM employees an opportunity to pursue an MPH with concentration in veterinary public health.
- Development of the Animal Feed Safety System with the assistance of representatives from State regulatory agencies, the animal feed industry, and several FDA components.
- Coordination with the USDA Biotechnology Regulatory Service and leadership in international organizations with respect to policy development for the regulation of biotechnology products.

Communicating With Stakeholders

CHALLENGES

To do the best job it can, CVM must communicate with its stakeholders. Animal drug and feed companies, veterinarians, and livestock producers must know about new policies and regulations as soon as possible, particularly because this information helps stakeholders comply with FDA regulations. Consumers, often reached through reporters and TV producers, need to know what steps CVM has taken to protect the food supply and keep our pets safe. CVM must present information to these diverse audiences about programs and initiatives that are sometimes technical and usually quite complex. CVM has the challenge of presenting scientific information and regulatory changes to these varied audiences in ways that will be fully understood by each of the audiences. When done successfully, proper communication will help ensure that regulations dealing with human and animal health are correctly followed and that consumers are well informed and capable of understanding the issues.

CVM issued a brochure as part of its educational outreach campaign concerning NSAIDs for dogs.

FY 2006 ACCOMPLISHMENTS

CVM undertook a broad range of initiatives to provide important information on public health issues, as well as on CVM programs and accomplishments during the year. Among other things, the Center provided responses to queries on a range of issues from its stakeholders. The Communications Staff provides leadership in many of the Center's outreach initiatives, but all of its offices also take leadership and play active roles in the Center's effort to communicate with constituents. The following highlights illustrate the range of Center-wide participation in communications efforts.

SPECIAL INITIATIVES TO RESPOND TO SPECIFIC PUBLIC HEALTH ISSUES

Educational Outreach Campaign - NSAIDS for Dogs

During the fiscal year, CVM received information indicating that some dog owners had not been informed about the potential side effects of using non-steroidal anti-inflammatory drugs (NSAIDs), nor had they received Client Information Sheets (CIS) concerning these drugs from their veterinarians. Veterinary NSAIDs are commonly prescribed and extremely effective pain control drugs for dogs, but many adverse reactions occur. Most adverse reactions are mild, but some result in permanent impairment or even death.

Based on this information, CVM launched an educational outreach campaign to remind veterinarians that there is information about NSAIDs that is written specifically for pet owners and to urge veterinarians to inform dog owners of the risks and benefits of these drugs so that they can make informed decisions.

CVM partnered with veterinary associations to get the word out to their members. As a result of this collaboration, both the American Animal Health Association and the American Veterinary Medical Association (AVMA) published information about NSAIDs in their publications and plan to publish additional information.

CVM has published articles in the *FDA Veterinarian* http://www.fda.gov/cvm/FdaVetFirst2006.htm#6059 (advice to dog owners) and http://www.fda.gov/cvm/FdaVetFirst2006.htm#6058 (advice to veterinarians). Also, an article on the subject, directed to pet owners, appeared in the September/October *FDA Consumer* magazine http://www.fda.gov/fdac/features/2006/506_nsaid.html.

CVM has provided information to television reporters on this subject, and stories about NSAIDs have appeared on news programs in several large cities. In addition, CVM has supplied information on NSAIDs to listserv (electronic newsletters) that reach pet owners, dog rescue groups, and news organizations.

FY 2006 Performance Management Goals:

- Communicate with livestock producers, veterinarians, industry, and the public to ensure a clear understanding and acceptance of FDA veterinary programs and policies. Post critical animal and public health information for CVM stakeholders on the CVM Web site.
- Provide timely information to stakeholders on the safety of products for food and companion animals.
- Expand the use of electronic communication and information dissemination to provide important public health information to CVM stakeholders.

Work is ongoing to provide interviews to trade press reporters, create brochures, submit journal articles, arrange audio-visual presentations for CVM staff scientists, and gather information on training programs that drug sponsors are now offering on NSAIDs use.

Use of Antimicrobials in Aquaculture

A collaborative effort during the year resulted in a booklet titled, "Judicious Use of Antimicrobials for Aquatic Veterinarians." The booklet helps veterinarians who treat food-producing aquatic animals with their efforts to use antimicrobials judiciously so that the effectiveness of these drugs in the treatment and prevention of bacterial diseases would be maintained, while the development of resistance in human and animal pathogens would be minimized. The AVMA's Aquatic Veterinary Medicine Committee and CVM's Aquaculture Working Group joined together to produce the publication, which is available on CVM's Web site at http://www.fda.gov/cvm/JUAQUATIC.htm.

Pet Treats

After learning that some pets were suffering from choking or blockages from pet treats and toys including chew toys, CVM wrote and posted useful consumer-oriented information on the CVM Web site, at http://www.fda.gov/cvm/consumerpettreat.htm.

WEB SITE INNOVATIONS

CVMWeek-L

CVM created a listserv (CVMWeek-L) in March 2006 to make its outreach efforts more effective. Members of the listserv receive weekly e-mail notices of additions to the CVM Web site. The Center sent out 27 e-mails as of the end of the fiscal year, and ended the year with approximately 290 subscribers. Sign-up is at http://www.fda.gov/cvm/CVMeList.htm.

Web Site Improvement

Recognizing that information on the Center's Web site was sometimes difficult to find, primarily due to the wealth of available information, the Center's Communications Staff has made revisions to the content and format of the Web site. The changes make the task of finding important information easier for CVM stakeholders. Among other things, the comminucations staff has created subject-specific pages for consumers (especially pet owners), veterinarians, and animal health and animal feed companies. Here are some examples of the changes:

- Revisions to the Adverse Drug Experience page (http://www.fda.gov/cvm/adetoc.htm) to help clarify what information is posted and how it could be used by veterinarians and the general public.
- Posting a new Animal Drug Safety page on the CVM Web site at http://www.fda.gov/cvm/AnimalDrugSafety.htm. CVM established the page to help interested individuals more easily locate safety information on drug products regulated by CVM. Those individuals can go to CVM's new Animal Drug Safety page to find links to various pages that provide information they need. The Animal Drug Safety page also links to a new Animal Drug Safety Frequently Asked Questions (FAQ) page (http://www.fda.gov/cvm/AnimalDrugSafetyFAQ.htm.)
- Posting a new Animal Feed Safety System (AFSS) page on the Center's Web site, at http://www.fda.gov/CVM/AFSS.htm. This page includes links to information on AFSS, including CVM UPDATES, *Federal Register* notices, meetings, and other information.
- Posting a new NSAIDs page, which has links to CVM UPDATES, guidance documents, current labels, *FDA Veterinarian* articles, and other information on these products at www.fda.gov/cvm/nsaids.htm.

EDUCATION THROUGH THE *FDA VETERINARIAN*

Issues of the *FDA Veterinarian*, CVM's bimonthly magazine, published in FY 2006 contained information about a variety of topics, including: actions taken against livestock producers for selling animals containing illegal drug residues; warnings and cautions for livestock producers about the use of certain drugs; description of the drug review process used by the Center, including an explanation of how production drugs are reviewed; international activities to harmonize drug registration requirements; developments concerning user fees under ADUFA; and BSE feed rule inspections.

STAFFING, SPACE, AND BUDGET

STAFF, BUDGET

Budgeted staffing levels for CVM and CVM-related field activities and budget details, including the ADUFA-related funding are in Appendix E.

SPACE

With the passage of the Animal Drug User Fee Act (ADUFA), CVM required new space to house approximately 80 additional personnel over the first 3 years of ADUFA. To meet this requirement, CVM secured 18,156 square feet of office space on the second floor of Metro Park North IV. To facilitate the ADUFA-related growth in ONADE offices in Metro Park North II, CVM consolidated its Office of Surveillance and Compliance (OS&C) into offices in Metro Park North IV. The OS&C consolidation was completed during the spring 2005.

To better support CVM business processes in both ONADE and OS&C, CVM acquired an additional 3,500 square feet of space in Metro Park IV to house a Satellite Document Control Unit (DCU). Construction of the Satellite DCU began in 2005 and was completed in early 2006. Work continued throughout 2006 on the remaining renovation phases of the multi-phased ADUFA-driven space plan for ONADE offices in Metro Park North II.

CVM now has offices in Metro Park North II, Metro Park North IV, and Metro Park North V in Rockville, MD, in addition to the Office of Research facilities in Laurel, MD.

APPENDIX A

Significant Regulations, Guidances, and Other Documents

THE DOCUMENT DEVELOPMENT PROCESS

The preparation of regulations, guidances, and other documents intended for the public is a Center-wide responsibility. However, much of the effort is carried out by the Policy and Regulations Staff (PRS) within the Office of the Director. For example, PRS is primarily responsible for coordinating *regulation* development for CVM. In doing so, PRS works with CVM subject matter experts and with FDA technical and legal experts in developing the regulations. This responsibility includes ensuring that the rule complies with Federal laws. PRS is also the focal point for development, clearance, and issuance of *guidance documents* in CVM. PRS ensures that all guidance documents are issued in accordance with 21 CFR 10.115, the Good Guidance Practices regulation. The staff shepherds the documents through the clearance process, which involves cooperation with subject matter, legal, and paperwork reduction staff.

SIGNIFICANT REGULATIONS, GUIDANCES, AND OTHER DOCUMENTS

Regulations

Final Rule - New Animal Drugs; Adamantane and Neuraminidase Inhibitor Anti-influenza Drugs; Extralabel Animal Drug Use; Order of Prohibition. March 22, 2006.

Proposed Rule - Index of Legally Marketed Unapproved New Animal Drugs for Minor Species. Docket No. 2006N-0067. August 22, 2006.

Guidances

Guidance for Industry #73 - Stability Testing of New Veterinary Drug Substances and Medicinal Products (Revision) (VICH GL-3 [R], Draft Revised Guidance). April 13, 2006.

Guidance for Industry #92 - Impurities in New Veterinary Drug Substances (Revision) (VICH GL10 [R], Draft Revised Guidance). January 5, 2006.

Guidance for Industry #93 - Impurities in New Veterinary Medicinal Products (Revised) (VICH GL- 11 [R], Draft Revised Guidance). January 10, 2006.

Guidance for Industry #123 - Development of Target Animal Safety and Effectiveness Data to Support Approval of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for Use in Animals. January 5, 2006.

Guidance for Industry #135 - Validation of Analytical Procedures for Type C Medicated Feeds. November 7, 2005.

Guidance for Industry #137 - Analytical Methods Description for Type C Medicated Feeds, Draft Guidance. June 28, 2006.

Guidance for Industry #166 - Environmental Impact Assessments (EIAs) for Veterinary Medicinal Products (VMPs), Phase II (VICH GL-38). January 9, 2006.

Guidance for Industry #171 - Waivers of *In Vivo* Demonstration of Bioequivalence of Animal Drugs in Soluble Powder Oral Dosage Form Products and Type A Medicated Articles. February 16, 2006.

Guidance for Industry #176 - Specifications: Test Procedures and Acceptance Criteria for New Veterinary Drug Substances and New Medicinal Products: Chemical Substances (VICH GL-39). June 14, 2006.

Guidance for Industry #177 - Specifications: Test Procedures and Acceptance Criteria for New Biotechnological/Biological Veterinary Medicinal Products (VICH GL-40). June 14, 2006.

Guidance for Industry #178 - Recommended Study Design and Evaluation of Effectiveness Studies for Swine Respiratory Disease Claims, Draft Guidance. April 13, 2006.

Guidance for Industry #182 - Pharmacovigilance of Veterinary Medicinal Products: Data Elements for Submission of Adverse Event Reports-2 (VICH GL-42, Draft Guidance). May 2, 2006.

Guidance for Industry #183 - Animal Drug User Fees: Fees Exceed Costs Waivers and Reductions, Draft Guidance. August 17, 2006.

Compliance Program

Feed Contaminants Program, Compliance Program 7371.003. Revised December 13, 2005.

Animal Drug Manufacturing Inspections, Compliance Program 7371.001. Revised August 4, 2006.

Other Documents

Animal Drug User Fee Rates and Payment Procedures for Fiscal Year 2007. August 2, 2006.

APPENDIX B

Significant New Animal Drug Approvals

ORIGINAL APPROVALS

EQUIOXX (Firocoxib) Oral Paste for Horses

A non-steroidal anti-inflammatory drug administered for up to 14 days for the control of pain and inflammation associated with osteoarthritis.

ZILMAX (zilpaterol hydrochloride)

For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in cattle feed in confinement for slaughter during the last 20-40 days on feed.

CYDECTIN (moxidectin) Oral Drench for Sheep

For the treatment and control of various internal parasites.

AQUAFLOR (florfenicol) Type A medicated article

For the control of mortality due to enteric septicemia of catfish.

Animal Drug Availability Act combination of AUREOMYCIN (chlortetracycline) and BOVATEC (lasalocid)

For multiple claims in cattle.

SUPPLEMENTAL APPROVALS

BANAMINE-S (flunixin meglumine) Injectable Solution

For the control of pyrexia associated with Swine Respiratory Disease.

CYDECTIN (moxidectin) Injectable Solution for Beef and Nonlactating Dairy Cattle

For additional claims for the treatment and control of internal parasites.

EXCEDE (ceftiofur crystalline free acid) Sterile Suspension

To add a new route of administration for injection in the posterior aspect of the ear where it attaches to the head (base of ear); to add a new indication, "For the treatment of bovine respiratory disease (BRD, shipping fever, pneumonia) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* in lactating dairy cattle"; and to establish a 13-day pre-slaughter withdrawal period for cattle.

DRAXXIN (tulathromycin) Injectable Solution

To add *Mycoplasma bovis* to the list of target pathogens for the bovine respiratory disease (BRD) treatment indication.

EXCENEL RTU (ceftiofur hydrochloride) Sterile Suspension

To establish a 3-day pre-slaughter withdrawal period for cattle.

NAXCEL (ceftiofur sodium) Sterile Solution

To establish a 4-day pre-slaughter withdrawal period for cattle.

SPECTRAMAST LC (ceftiofur hydrochloride) Sterile Suspension

To establish a 2-day pre-slaughter withdrawal period for cattle.

SPECTRAMAST DC (ceftiofur hydrochloride) Sterile Suspension

To establish a 16-day pre-slaughter withdrawal period for cattle.

MICOTIL 300 (tilmicosin phosphate)

To provide user safety information on the product labeling related to the mechanism of toxicity and medical intervention.

TYLAN (tylosin tartrate) Soluble

For the control of American foulbrood (*Paenibacillus larvae*) in honeybees.

TERRAMYCIN 200 FOR FISH (oxytetracycline dihydrate) Type A medicated article

For the change of the active ingredient from the mono-alkyl trimethylammonium oxytetracycline to the oxytetracycline dihydrate, the change of the oxytetracycline concentration from 100 g/lb. to 200 g/lb.; for the change of the product name to reflect the change in the oxytetracycline concentration; and for the addition of the approved lobster indication to the label for the control of gaffkemia caused by *Aerococcus viridans*.

PENNCHLOR (chlortetracycline) Type A medicated article

To change the withdrawal time for cattle from 1 day to 0 days.

RUMENSIN

To allow feeding to dairy cattle as a top-dress or as a component, and to allow feeding monensin to replacement beef and dairy heifers in drylot/not on pasture.

PAYLEAN (ractopamine hydrochloride)

Added for use in swine with no weight restriction.

Hyaluronate sodium

To add a new multi-dose formulation for intravenous administration for horses.

Moxidectin and Moxidectin praziquantel

To add 6 additional endoparasite species to the labeled indications for horses.

GENERIC APPROVALS

Melengestrol acetate, monensin sodium

An original Abbreviated New Animal Drug Application (ANADA) for the use of two single-ingredient Type A medicated articles containing HEIFERMAX 500 (melengestrol acetate) and RUMENSIN (monensin sodium) for the manufacture of two-way combination Type C medicated feeds. This product is a generic copy of MGA 500 (melengestrol acetate) plus RUMENSIN.

Melengestrol acetate, monensin sodium, ractopamine hydrochloride, tylosin phosphate

An original ANADA for the use of single-ingredient Type A medicated articles containing HEIFERMAX 500 (melengestrol acetate), OPTAFLEXX (ractopamine hydrochloride), RUMENSIN (monensin sodium), and TYLAN (tylosin phosphate) for the manufacture of four-way combination Type C medicated feeds. This product is a generic copy of MGA 500 (melengestrol acetate) plus OPTAFLEXX, RUMENSIN, and TYLAN.

Melengestrol acetate, tylosin phosphate

An original ANADA for the use of two single-ingredient Type A medicated articles containing HEIFERMAX 500 (melengestrol acetate) and TYLAN (tylosin phosphate) for the manufacture of two-way combination Type C medicated feeds. This product is a generic copy of MGA 500 (melengestrol acetate) plus TYLAN.

Lasalocid sodium, melengestrol acetate, tylosin phosphate

An original ANADA for the use of three single-ingredient Type A medicated articles containing HEIFERMAX 500 (melengestrol acetate), BOVATEC (lasalocid), and TYLAN (tylosin phosphate) for the manufacture of three-way combination Type C medicated feeds. This product is a generic copy of MGA 500 (melengestrol acetate) plus BOVATEC and TYLAN.

VETRO-MAX Ointment (betamethasone valerate, clotrimazole, gentamicin sulfate)

An original ANADA for the treatment of canine acute and chronic otitis externa associated with yeast (*Malassezia pachydermatis* formerly *Pityrosporum canis*) and/or bacteria susceptible to gentamicin. This product is a generic copy of OTOMAX Ointment.

Oxytetracycline hydrochloride

An original ANADA for treatment of bacterial disease in chickens, turkeys, and swine. This product is a generic copy of OXYTET Soluble (oxytetracycline hydrochloride).

EQUIZONE 100 Powder (phenylbutazone)

An original ANADA for oral use in horses for the relief of inflammatory conditions associated with the musculoskeletal system. This generic product is a copy of Phenylbutazone Tablets, USP.

PRICONAZOLE Lotion and Spray 1% (miconazole nitrate)

An original ANADA for the topical treatment of fungal infections caused by *Microsporum canis*, *Microsporum gypseum*, and *Trichophyton mentagrophytes* in dogs and cats. This product is a generic copy of CONOFITE Lotion and Spray 1%.

LINCOMED 100 and LINCOMED 300 (lincomycin hydrochloride)

An original ANADA for the treatment of infectious forms of arthritis caused by organisms sensitive to its activity. This includes most of the organisms responsible for the various infectious arthritides in swine, such as *staphylococci*, *streptococci*, *Erysipelothrix* and *Mycoplasma* spp. It is also indicated for the treatment of mycoplasma pneumonia in swine. LINCOMED 100 and LINCOMED 300 are generic copies of LINCOMIX 100 Injectable and LINCOMIX 300 Injectable (lincomycin hydrochloride).

Furosemide 1% Syrup

An original ANADA for use as a diuretic-saluretic for oral use in the treatment of edema associated with cardiac insufficiency and acute non-inflammatory tissue edema in dogs. This product is a generic copy of LASIX Syrup 1% (furosemide).

SULFAMED-G Soluble Powder (sodium sulfadimethoxine)

An original ANADA for oral use in the drinking water of chickens, turkeys, and cattle for the treatment of coccidiosis or various bacterial diseases. This is a generic copy of ALBON (sodium sulfadimethoxine) soluble powder.

Neomycin Sulfate 325 Soluble Powder

An original ANADA for the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* in cattle, swine, sheep, and goats; and the control of mortality associated with *Escherichia coli* organisms susceptible to neomycin sulfate in growing turkeys. This product is a generic copy of NEOMIX 325 (neomycin sulfate) Soluble Powder.

FLUNAZINE (flunixin meglumine) injectable solution

An original ANADA for the alleviation of inflammation and pain associated with musculoskeletal disorders in horses. It is also recommended for the alleviation of visceral pain associated with colic in horses. In cattle, flunixin meglumine is indicated for the control of pyrexia associated with bovine respiratory disease and endotoxemia and also indicated for the control of inflammation in endotoxemia. This generic product is a copy of BANAMINE (flunixin meglumine) Injectable Solution.

Amprolium 9.6% Oral Solution

An original ANADA as an aid in the treatment and prevention of coccidiosis caused by *Eimeria bovis* and *E. zurnii* in calves. This product is a generic copy of CORID (amprolium) 9.6% Oral Solution.

Ivermectin Paste 1.87%

An original ANADA for the treatment and control of large strongyles, small strongyles, pinworms, roundworms (ascarids), hairworms, new threadworms, large-mouth stomach worms, and bots in horses. This product is a generic copy of EQVALAN (ivermectin) Paste 1.87%.

Griseofulvin Powder Microsize

An original ANADA for the treatment of equine ringworm infection caused by *Trichophyton equinum* or *Microsporum gypseum*. This product is a generic copy of FULVICIN U/F (Griseofulvin microsize) Powder.

Gentamicin sulfate solution

An original ANADA for the control of bacterial infections of the uterus (metritis) in horses and as an aid in improving conception in mares with uterine infections caused by bacteria sensitive to gentamicin. This product is a generic copy of GENTOCIN Solution Veterinary.

APPENDIX C

Awards

CENTER FOR VETERINARY MEDICINE* 2006 HONOR AWARD RECIPIENTS

*In cases in which the award recipients included individuals from CVM and other organizations, only the CVM staff members are mentioned.

2006 SECRETARY'S AWARD FOR DISTINGUISHED SERVICE

BSE Animal Feed Rule Team

For outstanding performance in developing a regulatory strategy to protect consumers against the amplification and spread of bovine spongiform encephalopathy (BSE) through animal feed.

Neal Bataller, D.V.M.
Margaret Bowman, D.V.M.
George Graber, Ph.D.
Dragan Momcilovic, D.V.M., Ph.D.
Burt Pritchett, D.V.M.
Ronald R. Scherzberg
Raanan A. Bloom, Ph.D.
William T. Flynn, D.V.M.
Shannon T. Jordre
Judith M. Oharo
Jeffrey L. Punderson, D.V.M.

AWARD OF MERIT

William T. Flynn, D.V.M.
For outstanding leadership and performance supporting the development and clearance of policy and regulations of critical importance to the Center for Veterinary Medicine, FDA.

Russell A. Frobish, Ph.D.
For sustained and exemplary leadership and devotion to CVM's Animal Research Program in support of pre-market and post-market regulatory programs.

OUTSTANDING SERVICE AWARD

William L. Bargo
For exceptional and outstanding performance in the management of complex cases involving animal drug compounding.

Edward H. Hudson
For sustained, outstanding, information technology work performance in support of the Center for Veterinary Medicine, FDA.

Randall A. Lovell, D.V.M., Ph.D.
For outstanding service to the Food and Drug Administration, Center for Veterinary Medicine for his leadership role in the Feed Contaminants Program.

Dianne T. McRae, D.V.M.
For sustained superior performance and perseverance in finalizing the Drug Efficacy Study Implementation Program of the Center for Veterinary Medicine, FDA.

Renate Reimschuessel, V.M.D., Ph.D.
For dedication and outstanding effort in developing a database of pharmacokinetic parameters of drugs in fish to support the aquaculture regulatory and scientific communities.

Sharon L. Ricciardo
For emergency response to catastrophic events, in a manner consistent with FDA's and CVM's mission to safeguard and protect public and animal health.

Arleen G. Wang
For outstanding contributions to the Food and Drug Administration, Center for Veterinary Medicine's Human Resources Program.

Sherri Stephenson-Washington
For outstanding service in support of the CVM Staff College and the development and implementation of the Center's Core Curriculum.

S. Steve Yan, Ph.D.
For contributions as an exceptional Agency expert reference on current issues in microbiology and microbial food safety, and for continued excellence in scientific review.

GROUP RECOGNITION AWARD

AMDUCA/Compounding Training Team

For outstanding initiative in the development of a new training course designed to educate ORA field personnel about appropriate compounding policies and AMDUCA regulations.

William L. Bargo
Deborah A. Cera
Douglass S. Oeller, D.V.M.
Frances M. Pell
Neal Bataller, D.V.M.
Lynn G. Friedlander, Ph.D.
Julia A. Oriani, Ph.D.
Michael R. Talley, D.V.M.

CVM's International Outreach BSE Technical Experts

For meeting with foreign government officials to diplomatically describe FDA's requirements and compliance activities that are designed to prevent the spread of BSE through animal feed.

Neal Bataller, D.V.M.
Dragan Momcilovic, D.V.M., Ph.D.
Shannon T. Jordre
Burt A. Pritchett, D.V.M.

CVM UFMS and iProcurement Transition Team

For outstanding contributions to the development, implementation, and transition of CVM to the Agency's Unified Financial Management System (UFMS) and iProcurement.

Sonia C. Gallagher
Anita L. Heinrich
Ann M. Norris

Generic Animal Drugs GLP Inspection Team

For exceptional performance and outstanding innovation by CVM and ORA in the coordination and execution of a complex GLP inspection.

Jean E. Bowman, D.V.M.
John K. Harshman, D.V.M.
Zollie A. Perry, Ph.D.
George A. Prager
Sharon L. Ricciardo
Vernon D. Toelle, Ph.D.
Fredda Shere-Valenti

LEVERAGING/COLLABORATION AWARD

Meg R. Oeller, D.V.M.
For prolonged, outstanding contribution to the development of drugs for minor species while working in collaboration with USDA's National Research Support Project #7 (NRSP-7).

Aquaculture Working Group/Drug Approval Coordination Workshop

For outstanding collaboration with State and Federal agency partners developing data to support aquaculture drug approvals.

Charles E. Eirkson, III.
Kevin J. Greenlees, Ph.D.
Donald A. Prater, D.V.M.
Eric M. Silberhorn, Ph.D.
Susan Storey, D.V.M.
S. Steve Yan, Ph.D.

Monensin Contaminated Feed Recall Team

For excellence in the detection, investigation, and recall efforts associated with a widespread toxicological problem of monensin contamination in equine feed.

Henry E. Ekperigin, D.V.M., Ph.D.
Randall A. Lovell, D.V.M., Ph.D.
Barbara A. Rodgers
Michael R. Talley, D.V.M.

Pet Turtle-Associated Salmonella Enforcement Team

For providing exceptional scientific expertise, policy clarification, and coordination which furthered the protection of public health and led to precedent-setting Agency enforcement actions.

Gloria J. Dunnavan
Linda A. Grassie
Joseph C. Paige, D.V.M., M.P.H.

QUALITY OF WORK LIFE AWARD

Zoe A. Gill
For her outstanding level of commitment and service to improving the morale and quality of life for the Division of Animal Feeds, OSC, and CVM.

CVM DIRECTOR'S HONOR AWARD

William G. Marnane
First place recipient
For providing exceptional leadership in the management of personnel and critical manufacturing initiatives important to the mission and goals of the Center.

Elaine A. Johanson
Second place recipient
For exemplary performance, outstanding leadership, dedication, and commitment to the Center for Veterinary Medicine's IT activities.

CVM ADMINISTRATIVE EXCELLENCE AWARD

Susan M. Banks
For providing extraordinary administrative management support to the supervisors, management officers, and employees of the Center for Veterinary Medicine.

Vivian G. Vontress
For her outstanding performance in the management and oversight of the administrative systems of the CVM Office of Research.

CVM COMMUNICATIONS EXCELLENCE AWARD

Elizabeth Canter
For outstanding service in overseeing CVM's Records Management.

Vashti D. Klein
For her superior efforts in producing a video for FDA field offices and other regulatory agencies demonstrating CVM's method for detecting nitrofuran residues in shrimp.

CVM SUPPORT STAFF EXCELLENCE AWARD

Kendra A. Biddick
For the independent, industrious, and consistently excellent final human food safety reviews that improve review efficacy of the Division.

Irma M. Carpenter
For diligent and consistent service in providing application examiner, timekeeping, travel management, and additional administrative support for multiple divisions and groups within ONADE.

CVM EXCELLENCE IN MENTORING AWARD

Andrew J. Beaulieu, D.V.M.
For appreciation of the extraordinary contributions Dr. Beaulieu has made to the work, career, and lives of innumerable CVM employees through his role as a dedicated mentor and teacher.

Dennis M. Bensley, Jr., Ph.D.
For sustained leadership, significant contributions, and exemplary commitment to CVM's mission through the mentoring of CVM scientists involved in ensuring product quality.

David E. Wardrop, Jr.
For his ability to encourage others to grow and succeed by mentoring their talents and enabling them to acquire the skills necessary to be successful.

Haile Yancy, Ph.D.
For his outstanding efforts in mentoring young scientists in CVM's Summer Intern Program and in tutoring fellow scientists within the Office of Research.

CVM TEAM EXCELLENCE AWARD

2005 New Reviewer Orientation Training Group

For delivery of a CVM New Reviewer Orientation training program to aid new and existing reviewers in the performance of the review function.

Charles J. Andres, Ph.D.
Dennis M. Bensley, Jr., Ph.D.
Melanie R. Berson, D.V.M.
H. Gregg Claycamp, Ph.D.
Bernadette M. Dunham, D.V.M., Ph.D.
Charles E. Eirkson, III
Joan C. Gotthardt, D.V.M.
Norman R. Gregory
John K. Harshman, D.V.M.
Mai X. Huynh
Woodrow M. Knight, Ph.D.
William G. Marnane
Daniel G. McChesney, Ph.D.
Dragan Momcilovic, D.V.M., Ph.D.
David R. Newkirk, Ph.D.
Meg R. Oeller, D.V.M.
Mark M. Robinson, Ph.D., D.V.M.
Nadine R. Steinberg, J.D.
Fredda C. Shere-Valenti
Vitolis E. Vengris, D.V.M., Ph.D.
Katherine P. Weld, Ph.D.
Kim R. Young
Andrew J. Beaulieu, D.V.M.
Daniel A. Benz, Ph.D.
Elizabeth Canter
Eric S. Dubbin, D.V.M.
Gloria J. Dunnavan
Lynn G. Friedlander, Ph.D.
George Graber, Ph.D.
Sam L. Hansard II, Ph.D.
Barry H. Hooberman, Ph.D.
Jeffery S. Jones, D.V.M., Ph.D.
Elizabeth A. Luddy, D.V.M.
Marilyn N. Martinez Pelsor, Ph.D.
Janis R. Messenheimer, D.V.M.
Anna B. Nevius, Ph.D.
Douglass S. Oeller, D.V.M.
Donald A. Prater, D.V.M.
Patricia A. Ryan
Vernon D. Toelle, Ph.D.
Steven D. Vaughn, D.V.M.
Marleen M. Wekell, Ph.D.
Linda M. Wilmot, D.V.M.
Margaret A. Zabriski, Ph.D.

PHS Unit Commendation

CDR Charlotte A. Spires, D.V.M. *CAPT Norman J. Turner, R.Ph., P.D., M.P.H*

CVM Server Relocation Team

For the efficient and successful server relocation effort resulting in cost savings for the Center for Veterinary Medicine, FDA.

Karen S. Alder *Stephanie W. Dove*
Edward H. Hudson *Kimberly A. Sanders*
Michelle D. Talley

DHFS Pre-Approval Microbial Food Safety Review Team

For setting a standard in the pre-approval microbial food safety review process in conjunction with CVM's Veterinary Medicine Advisory Committee consultation.

Jeffrey M. Gilbert, Ph.D. *Karen E. R. Lampe, Ph.D.*
Mark M. Robinson, Ph.D., D.V.M.

STARS Formulation Database Team

For exceptional teamwork in the design and implementation of the STARS formulation database at CVM.

Karen S. Alder *Kristen L. Anderson, Ph.D.*
Matt D. Anderson, Ph.D. *Dennis M. Bensley, Jr., Ph.D.*
Renee S. Blosser *Jean-Michael Campagne, Ph.D.*
Xikui Chen, Ph.D. *Julie V. Conwell, Ph.D.*
Elizabeth P. Cormier, Ph.D. *Joseph W. Cormier, Ph.D.*
Bharati R. Dhruva, Ph.D. *Anne D. Edelson*
Raafat M. Fahmy, Ph.D. *Scott M. Fontana, Ph.D.*
Alem Ghiorghis, Ph.D. *Charles W. Gray, Jr., Ph.D.*
Norman R. Gregory *Laura S. Huffman*
Gregory W. Hunter, Ph.D. *Mai X. Huynh*
Kalatu S. Kamara *Jessica R. Lawrence*
June Liang, Ph.D. *William G. Marnane*
James K. Nitao, Ph.D. *Charles P. O'Brien, Ph.D.*
Michael E. Oehlsen, Ph.D. *Rebecca L. Owen, Ph.D.*
Michael J. Popek *Anthony M. Stone*
Robin M. Stone *Michelle M. Timmerman, Ph.D.*
Faye Y. Wei, Ph.D. *Geoffrey K. Wong*
Margaret A. Zabriski, Ph.D.

PHS Unit Commendation

LCDR Wei Guo, Ph.D. *CDR Minnis T. Hendricks, Jr., Ph.D.*

FDA SCIENTIFIC ACHIEVEMENT AWARD

EXCELLENCE IN ANALYTICAL SCIENCE
CVM ANALYTICAL SCIENCE EXCELLENCE AWARD

David N. Heller

For developing more efficient multi-class analysis of animal drug residues via LC/MS/MS, and for harmonizing and substantiating the use of mass spectral data in regulatory actions.

EXCELLENCE IN LABORATORY SCIENCE
CVM LABORATORY RESEARCH EXCELLENCE AWARD

David D. Wagner, Ph.D.

For demonstrating the impact that the use of streptogramins in chickens has on the selection for antimicrobial resistant *Enterococcus*.

EXCELLENCE IN REVIEW SCIENCE
CVM EXCELLENCE IN REVIEW SCIENCE

Michele J. Sharkey, D.V.M.

For sustained excellence reviewing new animal drug applications and for significant contributions to companion animal NSAID and antimicrobial policy development.

OUTSTANDING NEW REVIEWER
CVM OUTSTANDING NEW REVIEWER AWARD

Adele M. Turzillo, Ph.D.

For providing critical scientific review and analysis of the European Commission's beef hormone ban in support of the Office of the U.S. Trade Representative.

OUTSTANDING SUPPORT SCIENTIST
CVM OUTSTANDING SUPPORT SCIENTIST AWARD

Sherry L. Ayers

For providing outstanding support and a high degree of dedication in coordinating intramural and extramural laboratory research programs, in particular NARMS.

PHS COMMISSIONED CORPS HONOR AWARDS
PHS COMMENDATION MEDAL

For demonstrating leadership initiative and innovative problem solving by creating ONADE/CVM drug process overviews in IGRAFX that are vital for standardizing processes and orienting new reviewers.

CDR Charlotte D. Spires, D.V.M.

OTHER AGENCY AWARDS

(CVM employees included in individual or group recognition awards from other Centers.)

COMMISSIONER'S SPECIAL CITATION

FDA Hurricane Katrina/Rita Response Team

(nominated by the Office of Regulatory Affairs)

For outstanding service in assisting the State, the FDA/FEMA mission assignments and FDA's responsibilities in response to the devastation and adverse working conditions as a result of Hurricanes Katrina and Rita.

Gloria J. Dunnavan
Joanne M. Kla
Francis R. Pelsor, Ph.D.
Linda A. Grassie
Mary C. Masser, D.V.M.
Kim R. Young

FDA TOPOFF 3 Exercise Group

(nominated by the Office of the Commissioner)

For significant contributions to the Nation's preparedness goals through planning and participation in the TOPOFF 3 Terrorism Exercise series.

Neal Bataller, D.V.M.
Jack Geltman
Christopher Melluso, Ph.D.
Julia W. Punderson, D.V.M.
Vernon D. Toelle, Ph.D.
Lowell P. Fried
Randall A. Lovell, D.V.M., Ph.D.
Francis R. Pelsor, Ph.D.
Jon F. Scheid

PHS Unit Commendation

CDR Alfred W. Montgomery, D.V.M.
CAPT Lynn O. Post, D.V.M.

Salmonella Contamination in Pet Treats Emergency Response Group

(nominated by the Office of the Commissioner)

For exceptional group performance in responding to a public health incident which resulted in a voluntary recall of pet treats due to salmonella contamination.

Deborah A. Cera
Henry E. Ekperigin, D.V.M., Ph.D.
Randall A. Lovell, D.V.M., Ph.D.
Gloria J. Dunnavan
Jack Geltman
Barbara A. Rodgers

OUTSTANDING SERVICE AWARD

2005 FDA Science Forum Organizing Committee

(nominated by the Center for Drug Evaluation and Research)

For their extraordinary efforts and focused commitment in planning the successful and world class 2005 FDA Science Forum that had FDA and nationwide impact.

Linda A. Benjamin, Ph.D.
Tomislav Modrick, D.V.M., Ph.D.

GROUP RECOGNITION AWARD

Clinical Trials Course Team

(nominated by the Center for Biologics Evaluation and Research)

For development and delivery of an updated clinical trials course focused on current regulatory issues and on the current portfolio of CBER-regulated products.

Kathy A. Eberhart

FDA Import Strategy and International Legal Services Working Group

(nominated by the Office of the Commissioner)

For exceptional achievement developing FDA's Import Strategy for a stronger, risk-targeted import safety system and providing legal service on significant international import and export issues.

Catherine P. Beck
Deborah A. Cera
Gloria J. Dunnavan
Jack Geltman
Ann M. Norris
Kim R. Young

FDA Performance Budget Improvement Work Group

(nominated by the Office of the Commissioner)

For outstanding achievement to improve the planning and formulation process for FDA's $1.9 billion annual performance budget.

Heidi M. Jackson
David E. Wardrop, Jr.
Roxanne K. Schweitzer

Laboratory Support Services Group

(nominated by the Center for Food Safety and Applied Nutrition)

For developing and implementing the consolidated chemical, biological, and radiological laboratory waste contract for FDA Headquarters and CFSAN field activities.

Bruce D. Bradley

QUALITY OF WORK LIFE

Parklawn Chapter of FEW (Federally Employed Women)

(nominated by the Center for Devices and Radiological Health)

For exemplary initiative in promoting outstanding programs to foster and improve the quality of work life for HHS/FDA employees.

Lesley J. Groves
Fredda C. Shere-Valenti
Vivian G. Vontress

LEVERAGING/COLLABORATION AWARD

U.S.-Canada-Mexico Security & Prosperity Initiatives

(nominated by the Office of the Commissioner)

For sustained outstanding teamwork throughout prolonged and complex trilateral, and intergovernmental negotiations, that successfully represent and advance FDA's position and interests.

David B. Batson, Ph.D.
Elaine A. Johanson
Merton V. Smith II, Ph.D., J.D.
Bernadette M. Dunham, D.V.M., Ph.D.
CAPT Lynn O. Post, D.V.M.

FDA – Swissmedic Bilateral Collaboration

(nominated by the Office of the Commissioner)

For sustained outstanding contributions to foster and advance shared public health goals under the Memorandum of Understanding between FDA and Swissmedic.

Kim E. Bell
William G. Marnane
Merton V. Smith II, Ph.D., J.D.
Steven D. Vaughn, D.V.M.
Bernadette M. Dunham, D.V.M., Ph.D.
Daniel G. McChesney, Ph.D.
Robin M. Stone

PLAIN LANGUAGE AWARD

FDA User Fee Working Group

(nominated by the Office of the Commissioner)

For exceptional work in successfully producing the FY 2005 User Fee Performance Reports for PDUFA, MDUFMA, ADUFA and OCP.

A. Robert Miller
Jacquelyn L. Pace
Karen L. Tracey
David R. Newkirk, Ph.D.
Roxanne K. Schweitzer

OUTSTANDING INTERCENTER

The FDA GeneTox Network

(nominated by the Center for Drug Evaluation and Research)

For facilitation of harmonized genotoxicity standards for carcinogenicity assessment FDA-wide, and creation of an expertise resource for the Centers.

Devaraya Jagannath, Ph.D.

Working Group on Accumulation of Toxins in Pufferfish from Dietary Sources

(nominated by the Center for Food Safety and Applied Nutrition)

For establishing and maintaining a productive collaboration between CVM and CFSAN that has produced key information to address important issues regarding seafood safety.

Charles M. Gieseker *Renate Reimschuessel, V.M.D., Ph.D.*

CLEAR SCIENCE COMMUNICATION POSTER AWARD

Title: Determination of Nitrofuran Residues in Honey

Pak S. Chu, Ph.D. *Mayda Lopez, Ph.D.*

SIGMA XI OUTSTANDING POSTER AWARD

Title: Antimicrobial Resistance among *E.coli* Isolates Recovered from Retail Foods of Animal Origin, NARMS 2004

Sherry L. Ayers
Althea Glenn
LCDR Elvira Hall-Robinson, D.V.M.
David G. White, Ph.D.
CDR Tom M. Chiller
Patrick F. McDermott, Ph.D.
Robert D. Walker, Ph.D.

APPENDIX D

Publications

(CVM employees are shown in **boldface**.)

Anderson, K., R. Lyman, **S. Bodeis-Jones**, and **D. G. White**. 2006. Genetic diversity and antimicrobial susceptibility profiles among *Staphylococcus aureus* isolated from bovine mastitis. *American Journal of Veterinary Research*. 67:1185-91.

Arlet, G., T. J. Barrett, P. Butaye, A. Cloeckaert, M. R. Mulvey, and **D. G. White**. 2006. *Salmonella* resistant to extended-spectrum cephalosporins: prevalence and epidemiology. *Microbes and Infection*. 8:1945-54.

Beilie, G., W. Girard, **S. Zhao**, **S. Gaines**, **S. Friedman**, J. Meng. 2006. Genotypying of *Campylobacter* spp. from Retail Meats by Pulsed-Field Gel Electrophoresis and Ribotyping. *Journal of Applied Microbiology*. 100:175-84.

Butaye, P., G. B. Michael, S. Schwarz, T. J. Barrett, A. Brisabois, and **D. G. White**. 2006. The clonal spread of multidrug-resistant non-typhi *Salmonella* serotypes. *Microbes and Infection*. 8:1891-7.

Carson, M. C., and **V. B. Reeves**. 2006. Veterinary Drug Residues: Analytical Methods for Residue Analysis. *Journal of AOAC International*. 89:566.

Chen, S., S. Cui, **P. F. McDermott**, **S. Zhao**, **D. G. White**, I. Paulsen, and J. Meng. 2006. Contribution of target gene mutations and efflux to decreased susceptibility of *Salmonella* Typhimurium to fluoroquinolones and other antimicrobials. *Antimicrobial Agents and Chemotherapy*, Oct. 16. (E-pub ahead of print.)

Chiesa, A. O., **J. von Bredow**, **M. L. Smith**, **D. N. Heller**, and **M. H. Thomas**. 2006. Use of tissue-fluid correlation to estimate Gentamicin residues in Holstein Steers. *Journal of Veterinary Pharmacology and Therapeutics*. 29:99-106.

Chiesa, O. A., **R. Cullison**, D. E. Anderson, K. Moulton, L. D. Galuppo, and **J. von Bredow**. 2006. Development of a technique for serial bilateral renal biopsy in steers. *Canadian Journal of Veterinary Research*. 70:87-93.

Chu, P. S., and **M. I. Lopez**. 2005. Liquid chromatography-tandem mass spectrometry for the determination of protein-bound residues in shrimp dosed with nitrofurans. *Journal of Agricultural and Food Chemistry*. 53:8934-39.

Chu, P.-S., **M. I. Lopez**, S. Serfling, **C. Gieseker**, and **R. Reimschuessel**. 2006. Determination of 17α-methyltestosterone in muscle tissues of tilapia, rainbow trout, and salmon using liquid chromatography-tandem mass spectrometry. *Journal of Agricultural and Food Chemistry*. 54:3193-8.

Crowe, L., L. Chui, D. Everett, S. Brisdon, L. Gustafson, E. Galanis, L. McIntyre, L. MacDougall, L. Wilcott, A. Paccagnella, D. MacDonald, A. Ellis, A. Drake, J. Koepsell, C. Debolt, S. McKeirnan, J. Duchin, R. Baer, M. Leslie, M. L. Collins, J. M. Johnson, D. E. Farmer, C. E. Keys, **H. Ekperigin**, F. Angulo, and R. E. Colindres. 2006. Human salmonellosis associated with animal-derived pet treats – United States and Canada, 2005. *Morbidity and Mortality Weekly Report* 55 (25):702-705.

Deeds, J., **R. Reimschuessel**, and A. Place. 2006. Histopathological effects in fish exposed to the toxins from *Karlodinium micrum* (Dinophyceae). *Journal of Aquatic Animal Health*. 18:136–48.

Fahmy, R., and S. W. Hoag. 2006. Excipient Development for Pharmaceutical, Biotechnology, and Drug Delivery System Book. Chapter 22. *Excipient Quality Assurance: Handling, Sampling, and Regulatory Issues*. (Ashok Katdare and Mahesh V. Chaubal, eds.) *Informa Healthcare*.

Fahmy, R., and S. W. Hoag. 2006. Collaborative Research Project between the University of Maryland and Center for Veterinary Medicine at FDA. N.I.R News; *The Newsletter of the International Council for Near Infrared Spectroscopy*. Vol. 17 No. 5 July/August.

Fahmy, R., A. S. Tatavarti, **W. Marnane**, **D. Bensley**, G. Hollenbeck, and S. W. Hoag. (In press.) Effects of Preprocessing of Near Infrared Spectral Data on the Chemometric Analysis of Chemical and Physical Properties of Intact Pharmaceutical Tablets. *Journal of Pharmaceutical and Biomedical Analysis*.

Foley, S. J., **D. G. White**, **P. F. McDermott**, **R. D. Walker**, B. Rhodes, P. J. Fedorka-Cray, S. Simjee, and **S. Zhao**. 2006. Comparison of subtyping methods for differentiating *Salmonella enterica* serovar Typhimurium isolates obtained from food animal sources. *Journal of Clinical Microbiology*. 44 3569-77.

Gieseker, C., S. Serfling, and **R. Reimschuessel**. 2006. Evaluation of formalin to control mortality associated with *Saprolegnia parasitica* on rainbow trout, *Oncorhynchus mykiss*. *Aquaculture*. 253:120-9.

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APPENDIX E

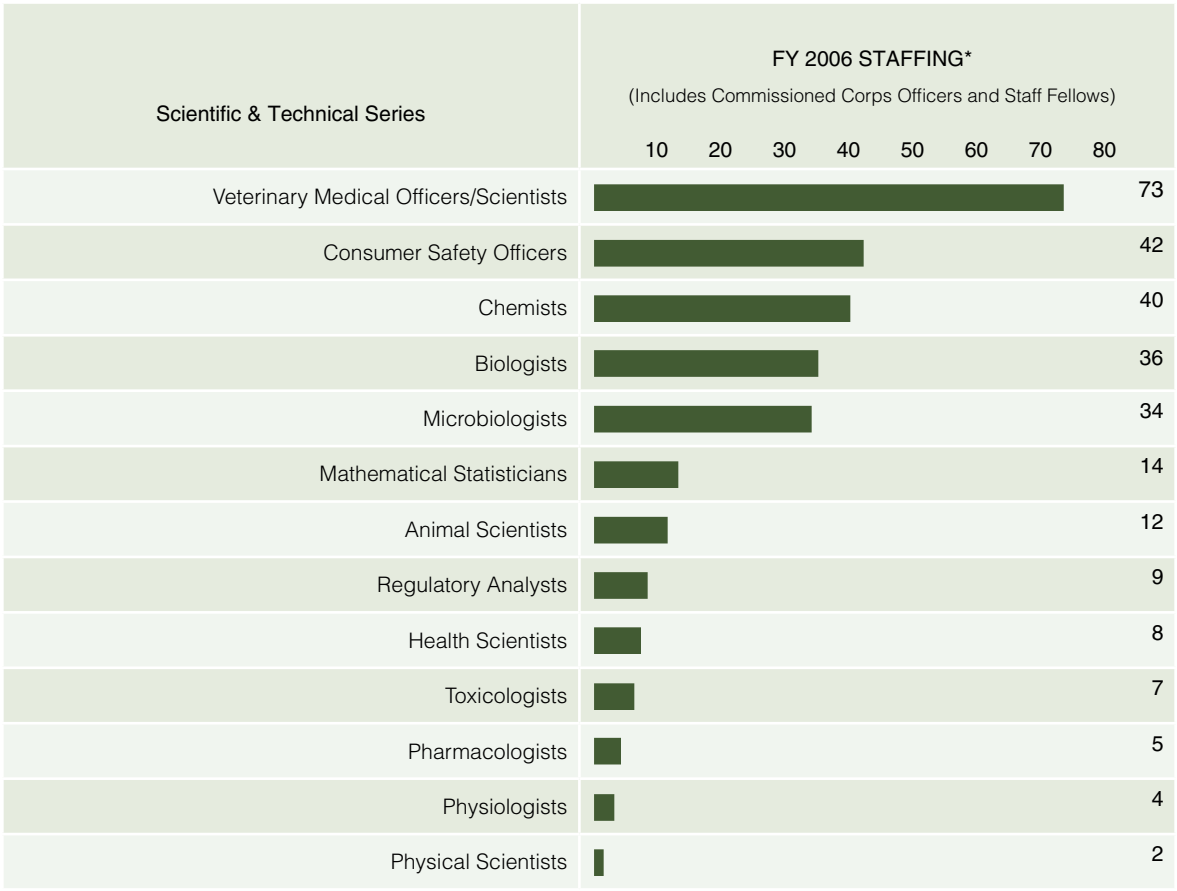
Budget and Staffing

FY 2006 Enacted Budget*	Pre-Market	Post-Market	FY 2006 Total(s)
Budget Authority (BA)	$27,455,000	$27,284,000	$54,739,000
User Fee (ADUFA)* *	$ 9,301,000		$ 9,301,000
Total Program Level	**$36,756,000**	**$27,284,000**	**$64,040,000**
Note: Estimates for the field are not included in the figures above.			
Field Activities:			
Animal Drugs & Feeds	$2,002,000	$32,840,000	$34,842,000

** Includes a 1 percent rescission.*
***ADUFA user fee amount does not include money for Other Activities.*

FY 2006 Enacted Budget Full-Time Equivalent	Pre-Market	Post-Market	FY 2006 Total(s)
Budget Authority (BA)	157	162	319
User Fee (ADUFA)	60		60
Total Program Level	**217**	**162**	**379**
Note: Estimates for the field are not included in the figures above.			
Field Activities:			
Animal Drugs & Feeds	13	218	231

Note: FDA has centralized the GSA rent and related activity costs into a central budget report, which no longer breaks out the costs by Center. Thus, the CVM Annual Report no longer contains data on such costs.



*Graph does not display 100 percent of CVM staffing (e.g., excludes consultants and advisory committee members).

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