# 2007 Annual Report

## Center for Veterinary Medicine

*Using Science and Law to Protect Public and Animal Health*

Fiscal Year 2007: October 1, 2006 - September 30, 2007

*Photo by Alfan Dangin,*
*Office of the Director.*

*Photo by Susan Storey,*
*Office of New Animal Drug Evaluation.*

*Photo by Bernadette Dunham,*
*Office of the Director.*

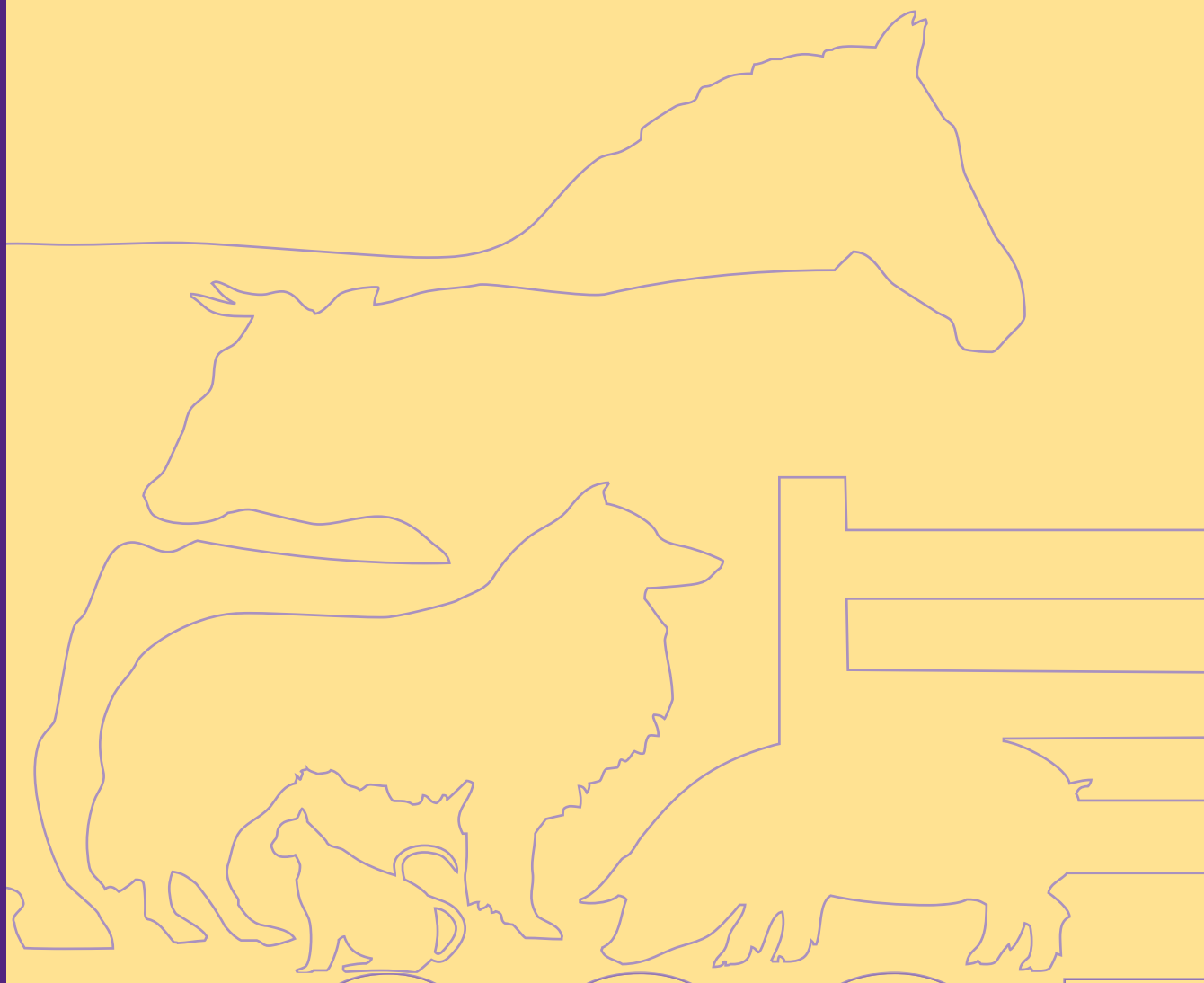

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*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

# Contents

*Photo by Bernadette Dunham,*
*Offfice of the Director.*

Photo by Susan Storey, Office of New Animal Drug Evaluation.

# SOME HIGHLIGHTS FROM FISCAL YEAR 2007

## *NEW ANIMAL DRUG APPROVALS—The Year of the Companion Animal*

From a drug approval standpoint, Fiscal Year (FY) 2007 was the year of the companion animal. The Center for Veterinary Medicine (CVM) approved 15 original or supplemental New Animal Drug Applications (NADAs) to improve companion animal health during the year. Several NADA approvals provided new therapeutic advances for companion animal health, including:

*SLENTROL*™ (*dirlotapide*), the first drug approved for the management of obesity in dogs in the United States. SLENTROL™ is a new chemical entity[1] that appears to reduce fat absorption and provide a "satisfied" signal from lipid-filled cells lining the dog's intestine so the dog will have a reduced appetite. Veterinarians generally agree that dogs weighing 20 percent more than ideal weight are obese. By this standard, many dogs in the United States are obese.

*VETMEDIN*® (*pimobendan*), a new drug for managing the signs of mild, moderate, or severe congestive heart failure in dogs due to certain conditions. Congestive heart failure is one of the more common heart problems seen in dogs, especially in certain breeds. A new chemical entity, VETMEDIN® is the first drug CVM has approved to treat congestive heart failure in dogs in more than 10 years. VETMEDIN® helps alleviate signs of heart failure by increasing the force of the heart muscle contraction and by dilating blood vessels to decrease resistance to blood flow.

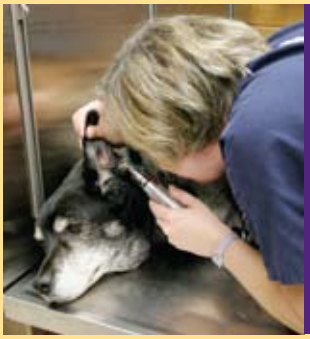


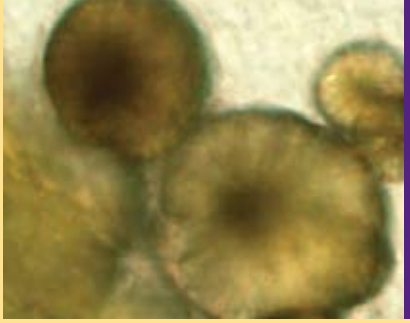
Photo by Christina Chambers, In the Moment Photography.

*CERENIA*™ (*maropitant citrate*), the first of a new class of drugs, approved in two formulations for prevention and treatment of vomiting in dogs: a tablet form for the prevention of acute vomiting, as well as vomiting due to motion sickness; and an injectable solution for the prevention and treatment of acute vomiting. An estimated 2.8 million dogs experience vomiting each year in the United States. Dogs undergoing cancer treatment or suffering from other ailments can suffer from acute vomiting, which can lead to weakness, dehydration, electrolyte imbalances, and even death. Motion sickness can be a major problem for dogs; some can become ill as quickly as 5 minutes after the start of a trip in a vehicle.

CVM approved six additional new chemical entities for use in companion animals in FY 2007. Details on these and other approvals are in the subsection on "Protecting the Health of Companion Animals" in the section on "FY 2007 Challenges and Accomplishments."

[1] A "new chemical entity" is a drug with an active ingredient that has not previously been approved.

## *SCIENTIFIC SOLUTIONS TO THE MELAMINE MYSTERIES*



Crystals created by melamine and cyanuric acid.
*Photo by Renate Reimschuessel, Office of Research.*

When reports of dog and cat deaths linked to pet food reached FDA in March 2007, CVM scientists had some questions to answer. First, what could have caused the apparent kidney failure that led to the deaths? Quick work by scientists from government, private industry, and academia led to a tentative identification – in just 2 weeks – of the culprit: melamine, an industrial chemical.

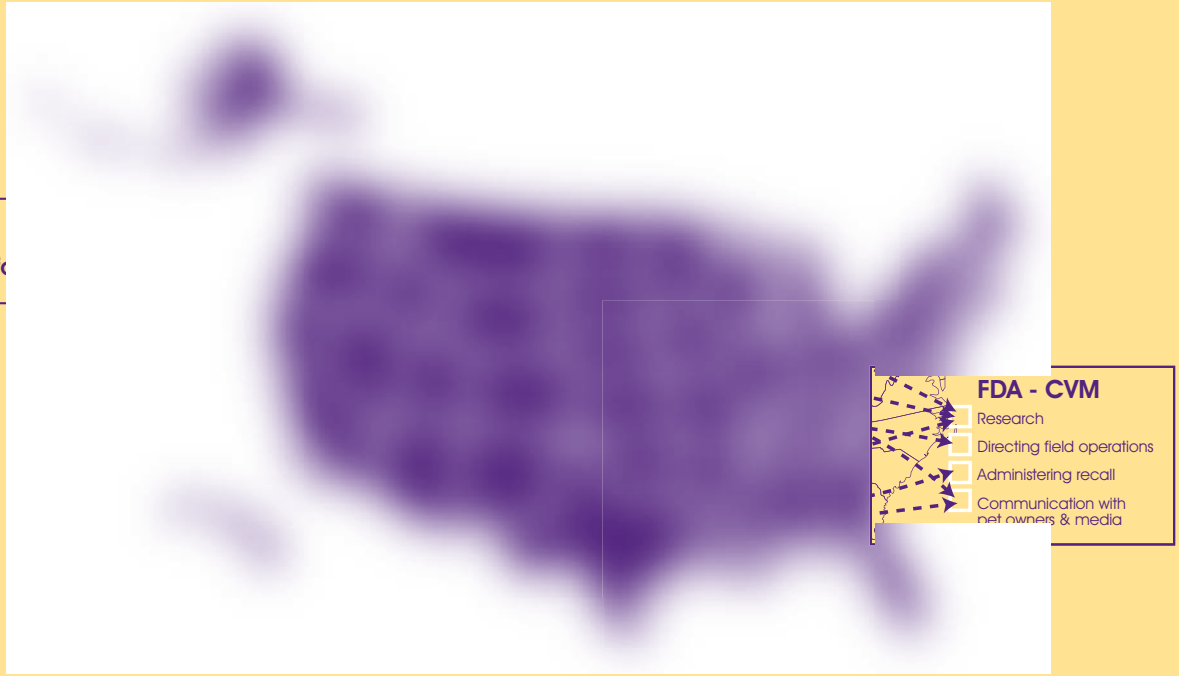
*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

*Photo by Christina Chambers, In the Moment Photography.*

But how could melamine, previously thought to be relatively innocuous, have had fatal results? Further study by pathologists at CVM's Office of Research and elsewhere revealed the formation of melamine-cyanurate crystals in animal kidneys, which led to tissue damage, followed by kidney failure. In other words, it seemed that the additional presence of cyanuric acid (or related chemicals) led to the animal deaths. Cyanuric acid, like melamine, is not authorized in pet food.

Confirming the melamine-cyanuric acid connection was not easy. CVM scientists initially proposed an association between the two chemicals, but the first tissue samples from dogs and cats that had died had few crystals. Office of Research scientist Dr. Renate Reimschuessel solved this mystery with the discovery that the crystals had been dissolved unintentionally when pathologists placed the samples in formalin prior to analysis. Further work by CVM scientists confirmed that neither melamine nor cyanuric acid alone produced crystals. However, a combination of the two compounds produced large numbers of crystals.

The scientists had more to do. There was a need for an efficient method to screen for the presence of melamine and cyanuric acid in pet food – and then in animal feed when investigators learned that melamine-containing feed was likely to have been fed to hogs, poultry, and fish. The compounds require two different extraction techniques. However, CVM's Office of Research scientists developed a unique provisional method – a liquid



chromatographic system – capable of simultaneous analysis of the two compounds.

Our Office of Research also shared information from its work with melamine and cyanuric acid in fish, swine, and chicken, with FDA's Office of Regulatory Affairs and U.S. Department of Agriculture (USDA) scientists for use in the development of methods for detecting the compounds in tissues. Fortunately, an interim risk assessment prepared quickly by FDA and USDA scientists, in consultation with scientists from three other federal agencies, concluded that the levels of the compounds in animal feed were not likely to pose a human health risk.

All this work was accomplished in a few weeks. CVM scientists were continuing to work at the end of the fiscal year to validate the provisional animal feed screening methods and to refine other work related to the melamine incident.

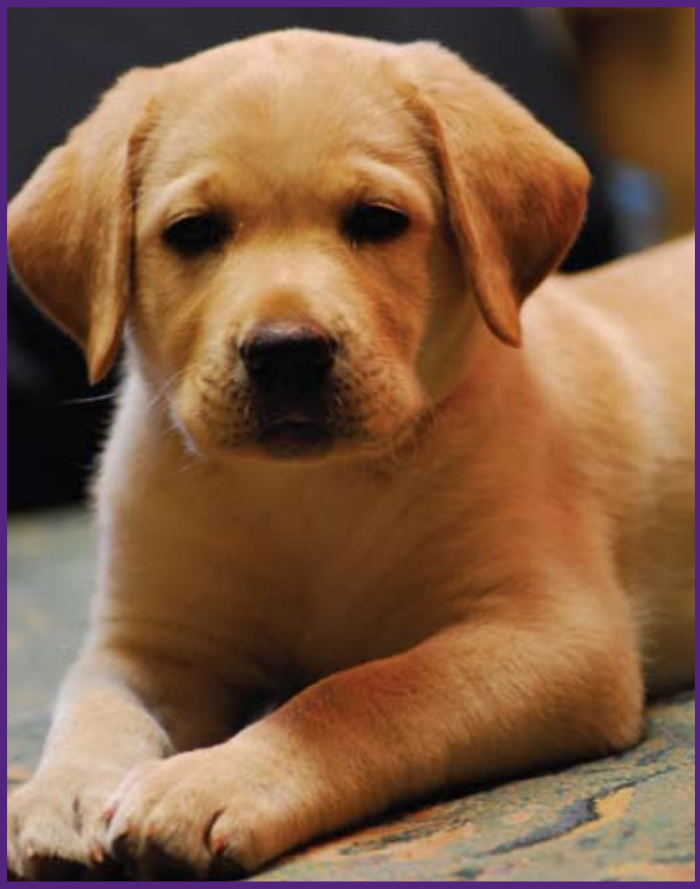


*Photo by Tracey Forfa, Office of the Director.*

The pioneering efforts of the CVM scientists, in collaboration with scientists in other agencies and organizations, were only part of CVM's mobilization to meet the melamine challenge. More details are in the subsection on "Protecting the Health of Companion Animals" in the section on "FY 2007 Challenges and Accomplishments."

## *FDA ISSUES ANIMAL CLONING RISK ASSESSMENT AFTER CAREFUL STUDY*

A decade ago, the birth of Dolly the sheep, the first mammal successfully cloned from an adult cell, sparked an ongoing ethical controversy. But it also intrigued livestock breeders, because of cloning's potential for spreading desirable characteristics rapidly through a breeding herd or flock.

When CVM learned in 2000 that commercial ventures were developing clones for use in breeding food-producing animals, the Center contracted with the National Academy of Sciences/National Research Council (NAS/NRC) for an independent, scientific peer review of available safety data on cloned animals and the food derived from them. (FDA's authority does not permit consideration of ethical concerns, but the Agency shares scientific information with groups that focus on ethical issues.)

The 2002 NAS/NRC report, titled "Animal Biotechnology: Science-Based Concerns," concluded that "there is no current evidence that food products derived from adult somatic cell clones or their progeny present a food safety concern" and that "the products of offspring of cloned animals were regarded as posing no food safety concern," but that "an evaluation of the composition of food products derived from cloned animals would be prudent to minimize any remaining food safety concerns."

In 2003, CVM presented a draft Executive Summary of a risk assessment for public discussion at a meeting of FDA's Veterinary Medicine Advisory Committee (VMAC). Following the VMAC deliberation, we undertook an exhaustive study to prepare a complete risk assessment to determine whether cloning poses risks to animals and whether food

*Cow clones. Photo courtesy of Cyagra, Inc.*

from clones or their offspring would pose any safety risk to humans, compared with animals bred using other assisted reproductive technologies.[2]

In the process of preparing the risk assessment, we performed a thorough search of the literature on clones, reviewing hundreds of peer-reviewed scientific journal articles. Clone producers provided data from independently analyzed blood samples of clones. We evaluated the data and the animals' health records, and compared the data with equivalent data from conventionally bred animals of the same age, breed, and raised on the same farms. In the end, we conducted the most comprehensive examination of the health of livestock clones to date. To evaluate food consumption risks, we used a Critical Biological Systems Approach (which incorporates a systematic review of the health of the animal clone and its progeny), and a Compositional Analysis Method (which involves an analysis of food products).

As required by the Office of Management and Budget, we asked for a peer review of the draft risk assessment by a group of independent scientific experts in cloning and animal health.

The multi-year effort culminated in FY 2007 when FDA issued a draft risk assessment and accompanying proposed risk management plan on the safety of animal cloning. The risk assessment encompasses cattle, swine, sheep, and goats, the livestock species that have been cloned to date. The document concludes that food products from healthy cattle, swine, and goat clones are as safe as food produced by conventionally bred animals. It presents the same conclusion for food from the progeny of clones. (The document does not draw conclusions with respect to food products from sheep clones, because of insufficient information on their health status.)

All of the data evaluated in the Draft Risk Assessment are available either in the Draft Risk Assessment itself or in peer-reviewed publications. The draft sets out the methodology used to evaluate the data, underlying assumptions, uncertainties, sources of potential bias, and the basis for our conclusions.

The public had an opportunity to comment on the draft risk assessment and proposed risk management plan following the documents' release in December 2006. We set out more details on the risk assessment and related documents in the section "Ensuring the Safety of Animal Clones and Animal Biotechnology" in "FY 2007 Challenges and Accomplishments."

[2] Cloning falls on a continuum of assisted reproductive technologies (ARTs) currently used in agriculture. Examples of other ARTs include artificial insemination, embryo transfer, and *in vitro* fertilization.

Stephen F. Sundlof, D.V.M., Ph.D., Director, Center for Veterinary Medicine.
*Photo by Catherine Brown, Program Support Center, HHS.*

# A MESSAGE FROM THE DIRECTOR

CVM's mission reaches to the protection of the health of all animals, in addition to human health. As in past years, our FY 2007 animal health-related achievements encompassed food-producing as well as companion animals. However, much of our activity during the year focused on the health of companion animals – ranging from therapeutic advancements, to protecting pets from food that is unsafe. Thus, we have chosen "protecting companion animal health" as a major theme in this Annual Report.

As our "Highlights" section reports, during the year we approved an unusually large number of drugs – 15 applications in total – to improve companion animal health. In addition to the three new chemical entities we highlighted in the previous section, we approved other drugs that represented therapeutic advances for use in cats, dogs, and horses.

Our most-publicized companion animal activity involved the melamine-related pet food recall, which may have been the most complex recall that FDA has ever had to deal with. (We previewed scientific achievements in the "Highlights" section and elaborate on the episode in "Protecting Companion Animal Health" and "Communicating with Stakeholders" in the section on "FY 2007 Challenges and Accomplishments.") The experience showed how much our food supply is interconnected with the global market, and it illustrated how a small number of companies can create an enormous problem. But it also allowed FDA to demonstrate how quickly and effectively it can mobilize in this kind of situation and establish a collaborative network with other agencies and organizations to deal with a major health problem.

The experience underscored the importance of communication with consumers and the significance of the human factor in pet food safety issues. During the several weeks following the first recall, FDA offices across the country – including CVM's – answered hundreds of phone calls a day from worried pet owners. FDA Complaint Coordinators received more than 18,700 calls during the first 6 weeks after announcement of the first recall; by contrast, in a normal year FDA receives no more than 6,000 complaints concerning all the products the Agency regulates.

It was an emotionally difficult, as well as physically draining, period for CVM and FDA staff members, who responded not only to consumer calls but also to many media inquiries; processed recall notices; guided inspections; and served in other ways. CVM and FDA scientists – working with colleagues in other agencies – did remarkable work in pinpointing the contaminants, validating detection methods, and screening hundreds of samples of pet food.

FDA, with CVM's direction and assistance, responded to the emergency quickly and effectively. FDA investigators

were at the first-affected company's manufacturing sites within 24 hours of the first notification. Investigators ultimately visited all of the pet food manufacturers involved in the recall (and animal feed manufacturers, when the investigation widened to include food animal species), and many retail establishments. FDA investigators even traveled to China when that nation was identified as the source of contaminated ingredients.

The melamine episode is having long-term effects far beyond CVM and FDA. To address food security, the Commissioner of Food and Drugs created a position of Assistant Commissioner for Food Protection. And the President created the Interagency Working Group on Import Safety to conduct a comprehensive review of the U.S. import system and to identify ways to further increase the safety of imports entering the United States. We can expect implications for CVM in FY 2008 and beyond, as the government implements the Working Group's recommendations.

The pet food recall highlighted the need for an improved, comprehensive pet food and animal feed safety system in the United States. At CVM, our Animal Feed Safety System (AFSS) Team has been working since 2003 to modernize the Nation's feed safety system to make it risk-based. The current system is limited and focused on a few known safety issues, such as bovine spongiform encephalopathy (BSE) and *Salmonella* infections. The AFSS will be more comprehensive; it will be designed to address gaps in our current system of feed safety oversight, and it will tie together regulation, policies, and guidance. The subsection on "Ensuring Feed Safety" in the section "FY 2007 Challenges and Accomplishments" reports progress made during the past year toward implementing the AFSS.

During the year, we assumed leadership of a coalition that includes representatives from the U.S. Department of Agriculture (USDA), the cattle industry, and the pharmaceutical industry, whose goal is to work collaboratively on a novel approach to reduce human exposure to *Escherichia coli* O157:H7. That organism, which can cause illness and death in humans, may be transferred from cattle to humans through ground beef. This undertaking is a "critical path" initiative to identify key problems and develop targeted solutions to this animal-originated human health problem. "Critical path" addresses the recent slowdown in innovative medical therapies reaching patients by focusing on the need to improve predictability and efficiency along the critical path from laboratory concept to commercial product.

Our past year's accomplishments are the direct result of the efforts of a skilled and dedicated staff. We have for a number of years worked diligently at enhancing the work culture at CVM as we move toward our goal of being a high performance organization. We place a high priority on improvement in individual performance through training and empowering our staff.

Surveys in previous years showed the success of the Center's efforts. One study showed that CVM ranked at the top among FDA Centers in the proportion of its staff that is actively engaged in carrying out the Center's mission. CVM's personnel turnover rate is about 8 percent – among the lowest, compared with other government agencies. In the Federal Human Capital Survey, the Center received higher ratings from our employees on average than did other agencies. For example, under "personal work experiences," CVM scored 5 percent to 15 percent higher than the average for all government organizations. Such results strongly reinforce the Center's reputation throughout FDA as a well-functioning, high performing organization. The Center has a prominent role in the FDA Commissioner's Workplace Culture Initiative.

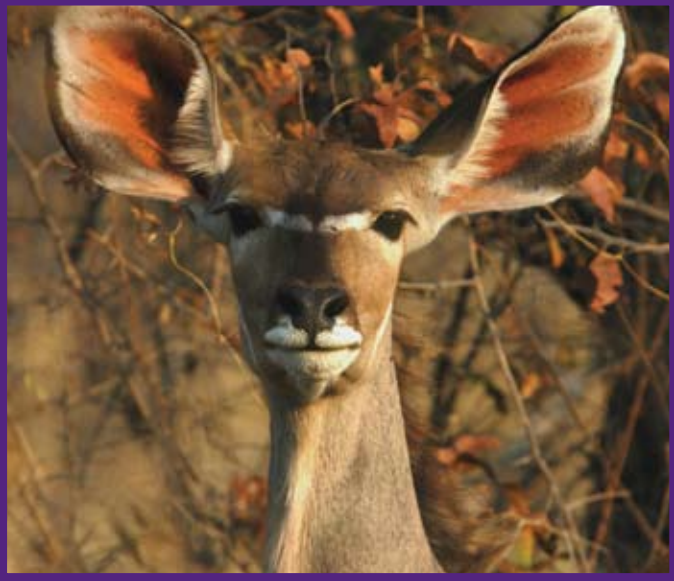


*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

The message from our Deputy Director, which follows this section, provides details on this past year's high performance initiatives. Dr. Bernadette Dunham joined CVM in 2002. Previously, she had a position in the American Veterinary Medicine Association's Governmental Relations Office. Upon coming to CVM, she served as Deputy Director of the Office of New Animal Drug Evaluation until her appointment during FY 2006 as Director of the Office of Minor Use and Minor Species Animal Drug Development, a position that she continues to hold. We were pleased to welcome her as the Center's Deputy Director.

We present in this Annual Report more details on the Center's many FY 2007 accomplishments. The pages following the Deputy Director's Message set out the challenges we face and our accomplishments during the past year. As highlighted throughout this report, our performance goals are aligned with Department of Health and Human Services and FDA objectives and goals. Where we reached our performance objectives and goals for FY 2007, 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.

This Annual Report 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 and participation of our stakeholders and partners as we work together for the public good.

*Photo by Bernadette Dunham, Office of the Director.*

*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

Bernadette Dunham, D.V.M., Ph.D., Deputy Director, Center for Veterinary Medicine.
*Photo by Catherine Brown, Program Support Center, HHS.*

# A MESSAGE FROM THE DEPUTY DIRECTOR

I have the privilege of following Dr. Sundlof's summary of our substantive FY 2007 achievements with additional information on developments in the organization that are behind the accomplishments.

We utilize a number of initiatives to facilitate improvement in individual performance, with some new emphases added during the past year. For example, we intend to extend the 360-degree assessment (evaluations by supervisors, peer, and others) to all staff members. Previously the assessment had been done only for supervisors.

During the year, we initiated a micro business evaluation pilot program to assess a team's interaction with internal and external partners. We continued to utilize other tools for improving the work culture, including: a list of managerial and Center-wide values and accompanying behaviors, used as a "reference standard"; personal coaching for managers and front line reviewers; High Performance Organization training; Myers-Briggs training; and our Staff College for continuing and accessible coursework.

An organization that strives to be high performance utilizes initiatives to improve its operating efficiency. The Center implemented project management several years ago, with a goal of helping the Center become more effective and efficient in carrying out its core and supporting functions. In simplest terms, project management is a systematic approach to planning and guiding a project from start to finish.

During the fiscal year, the CVM Project Management Team worked on tailoring project management to the needs of projects of various types, durations, and complexities. The team developed templates for several projects, created procedures to support the change management aspect of project management, and provided advice and consultation Center-wide concerning process and project management implementation and evaluation. The team also conducted a number of "lessons learned" sessions. Sponsors of several recent new animal drug application approvals have volunteered to participate in "lessons learned" sessions that included topics such as protocols, conduct of studies, summarization of statistical analyses, communication, and best practices for the future.

"Windows to Regulatory Research" is a scientific outreach program that we have sponsored for a decade. The program provides a 10-week educational work experience for outstanding college/university undergraduate, graduate, and professional students, and a 6-week internship for high school students. The goal of the intern program is to provide a foundation in biomedical and regulatory research that is integrated with scientific principles applicable to veterinary product development and regulation. The 2007 Summer Intern Program consisted of eight college students (from eight different colleges and universities) and two local high school students. CVM brings these students to the Center to encourage them to consider careers as leaders in regulatory science and research.

CVM's Center Leadership Team. *Photo by Jon Scheid, Office of the Director.*

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.[3] In making its decisions, the team considers scientific, economic, international, and environmental issues and their impact on the Center.

Appointments of individuals to serve in key positions are essential to the success of any organization. We made several such selections during the year. Dr. David White was selected as Director, Division of Animal and Food Microbiology in the Office of Research. Dr. Eric Dubbin was selected as Management Consultant. His role is to assist the Center Leadership Team in its focus on organizational development by training employees and maintaining objectivity in evaluating the Center's adherence to the vision we developed and the values that our behaviors reflect. Laura Alvey was selected as Director of the Communications Staff. Her job will be to coordinate CVM's outreach activities.

In addition, Gary Claywell was selected as Deputy Director, Office of Management; Connie Mahon was selected as Director, Staff College; and Dr. Neal Bataller was named Director, Division of Compliance.

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. Full details about all the awards are in Appendix C. But I want to make a special note of the FDA Commissioner's Special Citation awarded to Dr. Andrew Beaulieu, who retired in FY 2007 from CVM after 34 ½ years with the Center. The award is for his "outstanding career dedicated to public service, superior managerial performance, and excellence in regulatory science to support the Agency's critical public and animal health mission."

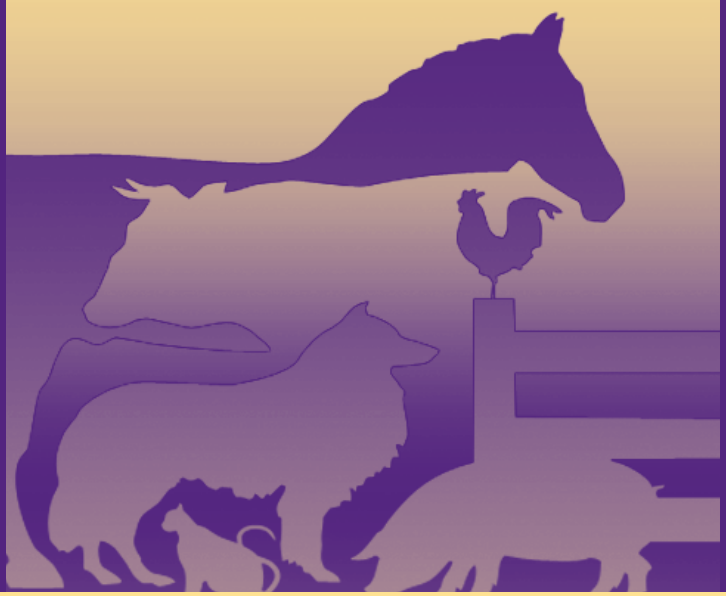
The number of articles published by CVM scientists during the year evidences their professional productivity. The article topics ranged from antimicrobial resistance to detecting drug residues in food products, feed safety, development of analytical methods, carcinogenicity of chemical compounds, and more. We have included a complete publications list in Appendix D.

It's been a busy, productive year – made possible by our staff of motivated, talented people. Each member of CVM makes a difference, and together we accomplished so much. Their contributions cause our Center Leadership Team to be very optimistic about our ability to meet the challenges of FY 2008 and beyond. We look forward to working with others in the FDA, and our stakeholders and partners, as we face the tasks ahead of us.

We believe that the reader can best appreciate the Center's FY 2007 accomplishments by understanding what CVM is all about – our mission, plans, organization, and sphere of influence. Thus, the next major section of our Annual Report is "About CVM."

[3] CVM's Center Leadership Team members are as follows:

Dr. Stephen F. Sundlof, Director, CVM
Ms. Catherine Beck,
Associate Director for Policy and Executive Programs
Dr. Eric Dubbin, Management Consultant
Dr. Bernadette Dunham, Deputy Director, CVM, and Director,
Office of Minor Use and Minor Species Animal Drug Development
Dr. Daniel G. McChesney, Director,
Office of Surveillance and Compliance
Mr. David Wardrop, Director, Office of Management
Dr. Marleen Wekell, Director, Office of Research
Dr. Steven D. Vaughn, Director,
Office of New Animal Drug Evaluation



# ABOUT CVM

## *OUR MISSION AND GUIDING PRINCIPLES*

### OUR MISSION…

The Center for Veterinary Medicine 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 decision-making.

*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 FDA'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; and
- 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 Management; the Office of Minor Use and Minor Species Animal Drug Development; 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

The Office of the Director directs overall Center activities, coordinates and establishes Center-wide 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.

### OFFICE OF MANAGEMENT

The Office of Management provides executive leadership and direction for management and administrative programs, policies, and issues at Center and Agency levels. The Office's management staff serves in strategic leadership positions on CVM and FDA councils and

Office of Management Director, David Wordrop; Deputy Director, Barbara Leach; Deputy Director, Gary Claywell. *Photo by Jon Scheid, Office of the Director.*

Office of Minor Use and Minor Species Animal Drug Development Director, Dr. Bernadette Dunham; Consultant to the Center for Minor Use and Minor Species issues and former Director of the Office, Dr. Andrew Beaulieu, and Dr. Meg Oeller. *Photo by Christopher Horstkamp, Office of New Animal Drug Evaluation.*

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.

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

The Office of Management 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, the Office represents management on issues regarding the FDA-National Treasury Employees' Union Collective Bargaining Agreement.

The CVM Staff College, also within the Office of Management, directs the development and implementation of the competency-based management, leadership, team-building curriculum, and an extensive scientific/technical curriculum.

The Office of Management supports the vital information resources management function to enhance employees' abilities to efficiently work with the integrated Information Technology systems to reach CVM goals.

## OFFICE OF MINOR USE AND MINOR SPECIES ANIMAL DRUG DEVELOPMENT

The Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act) provided for the establishment of the Office of Minor Use and Minor Species Animal Drug Development. 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 in cattle, horses, swine, chickens, turkeys, dogs, and cats) and minor species (including, for example, pet animals such as ornamental fish, parrots, ferrets, guinea pigs, iguanas, just to name a few; many animals of agricultural importance, such as sheep, goats, catfish, and honeybees; and zoo animals).

The Office of Minor Use and Minor Species Animal Drug Development 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 also 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, the Office will also be responsible for all aspects of animal drug indexing. The Office of Minor Use and Minor Species Animal Drug Development also performs a liaison role to the U.S. Department of Agriculture's minor use research program (NRSP-7) and provides outreach to stakeholders, including veterinarians, producers, consumers, government agencies, and the regulated industry.

Office of New Animal Drug Evaluation Director, Dr. Steven Vaughn; Deputy Director for Administration, Dr. David Newkirk.
*Photo by Jon Scheid, Office of the Director*

## OFFICE OF NEW ANIMAL DRUG EVALUATION

The Office'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. The Office of New Animal Drug Evaluation 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.

Drug sponsors must submit test results 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.

The Office of New Animal Drug Evaluation administers ADUFA, which authorizes FDA to collect fees in support of the review of new animal drugs. Under that Act, 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

Office of Surveillance and Compliance Director, Dr. Dan McChesney.
*Photo by Jon Scheid, Office of the Director.*

The Office has primary responsibility for three of CVM's four core functions: compliance-related actions, post-approval monitoring, and animal feed safety. The Office of Surveillance and Compliance monitors the safety and effectiveness of approved drugs after they enter the market. Working with the U.S. Department of Agriculture (USDA) and state agencies, the Office 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, the staff of the Office of Surveillance and Compliance utilizes epidemiological skills to protect public and animal health.

The Office of Surveillance and Compliance 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 (BSE) 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. The Office 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. The Office also coordinates the Center's administrative actions involving approved drugs, such as actions to withdraw drug approvals.

Office of Research Acting Deputy Director, Michael Thomas, and Office of Research Director, Dr. Marleen Wekell.
*Photo by Pat McDermott, Office of Research.*

## OFFICE OF RESEARCH

The Office 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, the Office of Research 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. The Office 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 the Office of Research, and the Office 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. The Office of Research 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.

The Office of Research 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 average, American consumers eat 110 lbs. of meat, 70 lbs. of poultry, 15 lbs. of fish, 590 lbs. of dairy products, and 30 lbs. 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 population of pets, 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 more than 70,000 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, livestock producers, 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 USDA's 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, 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. We work very closely with the Association of American Feed Control Officials (AAFCO). AAFCO membership consists of representatives from all 50 states, Puerto Rico, Costa Rica, Canada, FDA, USDA, and several universities.
- Veterinarians, who share with us numerous public and animal health goals, such as approval of new and better therapeutics, avoiding drug residues in food products, minimizing the development of antimicrobial resistance through prudent drug use practices, and educating producers 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.

*Photo by Bernadette Dunham, Office of the Director.*

# FY 2007 CHALLENGES AND ACCOMPLISHMENTS

## *INTRODUCTION*

Although we are organized into six separate offices, our Guiding Principles call for the staff members of CVM 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, we organize our presentation of FY 2007 accomplishments, not according to office structure, but according to crosscutting topics. These topics reflect issues of significant public interest. We introduce each of these areas of concern with a statement of the challenges that we face as we attempt to meet our "Back to Basics" goals and Agency and Department objectives.

Use of the topical areas we selected does not fully illustrate the interoffice and interdisciplinary nature of CVM's work. For example, ensuring the safety of animal feed and pet food by screening for contaminants is a common thread that runs through a number of the topical areas. In addition to the accomplishments related to assaying pet foods for chemical and biological contaminants,[4] CVM staff members were at work last year developing methods to detect prohibited material in ruminant feed;[5] developing screening methods for pesticides and antimicrobials in animal feed;[6] establishing baselines and sampling feeds for microbiological contamination and antibiotic resistance;[7] and sampling for the presence of aflatoxin in distillers dried grain (DDG), a by-product of ethanol production.[8] These efforts have significant implications for the development of the Animal Feed Safety System and for our work to limit the health effects of antibiotic resistance.

## *ACCOMPLISHING DEPARTMENT AND AGENCY OBJECTIVES*

The Department of Health and Human Services (HHS) established a number of broad-ranging objectives for FY 2007, and FDA adopted these objectives to guide the Agency in carrying out its mission to protect the public health. The objectives are divided into program results and executive leadership and management results. Following is a summary of our report card to show our success in achieving these objectives; details are in Appendix F.

[4] See "Scientific Solutions to the Melamine Mystery" under "Some Highlights from FY 2007" and "Protecting the Health of Companion Animals."
[5] See "Controlling Risk from BSE."
[6] See "Ensuring Feed Safety."
[7] See "Protecting Against Bioterrorism."
[8] See "Ensuring Feed Safety."

# 2007 Department of Health and Human Services Objectives

## Executive Leadership Results

## Management Results

## Program Results Objectives

### Improving Animal Health

### Approving Innovative New Animal Drug Products

### Timely Review of New Animal Drug Applications

### Improving Food Safety, Quantity, and Quality

### Improving Communications with Consumers

## PROGRAM RESULTS

Each program-results objective consists of one or more performance goals. (A complete list of objectives, along with related performance goals, and ratings, appear in Appendix F.) Our report card is based on an analysis of our achievements with respect to each of the performance goals within each objective. A ✓ for an objective means that we accomplished all of the performance goals within the objective. ✓X means that we accomplished some, but not all, of the performance goals within the objective. In that case, we explain the reason(s) for the X. Selected program results objectives for FY 2007, with brief explanations or examples, follow.

### Selected Program Results

✓ **Increase access to innovative animal drugs to improve animal health by the timely review of New Animal Drug Applications (NADAs).**

We have accomplished goals under the Animal Drug User Fee Act (ADUFA) for application review times, staff recruiting, and publication of policy and procedure documents to improve the animal drug application review process.

✓ **Increase access to innovative new animal drug products by bringing discipline into the review process.**

During the fiscal year, we met the goal of implementing a system of planning, execution, monitoring, and evaluation to improve and increase the efficiency of our business processes.

✓ **Increase access to innovative new animal drug products to improve animal health by providing rapid, transparent, and predictable science-based review of NADAs.**

One of the major accomplishments within this objective was the publication of the draft risk assessment on animal cloning.

✓ **Improve the safety of food products through better food-animal processing.**

We accomplished this objective in part by moving forward with a critical path approach to eliminating or reducing *Escherichia coli* O157:H7 in cattle prior to slaughter.

✓X **Improve quality, safety, and availability of food products through better manufacturing and product oversight.**

We accomplished most of the performance goals within this objective, except two, as indicated by the X. We did not accomplish a goal related to developing screening methods for bacterial pathogens in animal feed, because of the retirement of a key staff member. And we did not complete validation of a real time polymerase chain reaction method to detect material in animal feed prohibited by the bovine encephalopathy (BSE) rule, because of other priorities imposed on FDA laboratories.

✓X **Increase access to innovative animal drugs to improve animal health.**

We met this objective in part by completing work on the final rule for Indexing under the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act), and by preparing draft guidance on regulating transgenic drugs.

We did not complete the drafting of the proposed Conditional Approval regulations under the MUMS Act. These regulations are complex, because (unlike the other regulations implementing the MUMS Act) the regulations must fit within an existing structure of new animal drug approval regulations and procedures, but they also raise novel issues. The proposed regulations should be completed within the Agency early in 2008.

However, we have been able to review applications for Conditional Approval, and we were able to grant our first Conditional Approval during the year, even though the regulations are not yet in place. Our experience with these applications has provided insight for, but not delayed, promulgation of the proposed regulations.

**Enhance patient and consumer protection and empower these stakholders with better information about regulated products.**

As an example of how we accomplished this objective, we responded rapidly to communicate with the public and industry during the pet food recall incidents.

## EXECUTIVE LEADERSHIP AND MANAGEMENT RESULTS

In additional to the program objectives discussed above, we were challenged to achieve a number of Department- and Agency-wide objectives related to executive leadership and management results. We achieved all of the executive leadership and management objectives within CVM's scope of responsibilities.

Two examples relate to a leadership objective to *foster collaboration* with others outside the Center. First, during the melamine pet food contamination incident, CVM proactively established communications with the Centers for Disease Control and Prevention (CDC), veterinary professional organizations, and state diagnostic laboratories in identifying the nature and extent of the incident, and in communicating needed information to the veterinary community. CVM took the initiative in utilizing the resources of other organizations to pool information and direct the investigation to a successful outcome. This collaborative effort now serves as a model for responding to future animal illness outbreaks.

As a second example, CVM worked collaboratively with two pet food companies in the conduct of animal research studies that identified the causative factors involved with the incident. CVM fostered a cooperative and mutually respectful working relationship with the firms, whose work was critical to our understanding of the causes of the unprecedented contamination.

We provide further details on leadership and management objectives in "Achieving Productivity Through Achievement of Leadership and Management Objectives," in the section on "FY 2007 Challenges and Accomplishments" and elsewhere in this report.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

# *INCREASING THE AVAILABILITY OF SAFE AND EFFECTIVE ANIMAL DRUGS*

## THE CHALLENGE

Statutory standards and the needs of our stakeholders – and especially the needs of the billions of animals whose health we seek to protect – require that we make the right pre-approval decisions and do so efficiently and expeditiously. ADUFA 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 2007 ACCOMPLISHMENTS

We responded to the pre-approval challenges in a number of ways, as described below. In general, we directed these actions toward achieving several HHS objectives that involve increasing access to innovative new animal drug products.

## ADUFA

### Accomplishments

ADUFA authorizes the collection from sponsors and manufacturers 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. The law establishes performance goals to be implemented from FY 2004 through FY 2008. FDA's first 3 years under ADUFA (FY 2004 to FY 2006) were highly productive and successful. We met or exceeded all of the goals for review times and staff recruiting, as well as the development and dissemination of guidance, policy, and procedural documents.

ADUFA Financial Reports for FY 2004 to FY 2006 show that we met the legal conditions that must be satisfied before the Agency can collect and spend user fees. The ADUFA performance and financial reports for FY 2004 to FY 2006 are available on the CVM Web site. During FY 2007, we worked to achieve goals set for the year. Performance and financial reports for FY 2007 will be published separately.

### Renewing ADUFA

Congress authorized the ADUFA program through FY 2008. FDA has been working on a plan to reauthorize ADUFA for an additional 5 years. When Congress passed ADUFA, it directed the Secretary of Health and Human Services to consult with various groups in developing recommendations to Congress for the reauthorization of ADUFA, including recommendations for the goals and plans for meeting the goals associated with the process for reviewing animal drug applications. As directed by Congress, CVM convened a public meeting on ADUFA in April 2007 to seek public comments on the program's overall performance and reauthorization.

## FY 2007 APPROVALS

We have listed significant FY 2007 new animal drug approvals in Appendix B. During the year, we issued 17 original NADA approvals, 7 significant supplemental application approvals, and 20 significant generic animal drug application approvals.

We have highlighted approvals for companion animals and minor uses/minor species elsewhere in this report. An example of a significant approval for major species food animals was the approval of florfenicol as a Type A medicated feed article for control of swine respiratory disease.

## INITIATIVES TO PROTECT HUMAN AND ANIMAL HEALTH

### *Escherichia Coli* O157:H7

*Escherichia coli* serotype O157:H7 is a strain that causes severe damage to the lining of the human intestine, resulting in abdominal pain, bloody diarrhea, and

occasional vomiting, and it may lead to death. Each year, the organism is estimated to cause between 7,000 and 20,000 infections, resulting in 150 to 300 deaths, and a cost of $230 million to $600 million in medical and human productivity costs.

Although a number of foods have been linked to outbreaks of *Escherichia coli* O157:H7 infections, undercooked or raw hamburger is implicated in many cases, and cattle are therefore a source of the organism. An intervention for the reduction of the organism immediately prior to slaughter would, in conjunction with other risk management interventions during the slaughter and processing of beef, reduce the exposure of humans to *Escherichia coli* O157:H7.

During FY 2007, CVM began leadership of a coalition – which included representatives from the U.S. Department of Agriculture (USDA), the cattle industry and the pharmaceutical industry – that had the goal of working collaboratively to reduce human exposure to O157:H7. The coalition agreed to an approach to identify interventions from "farm to fork" framework and includes all stages of beef production and processing. Interventions could include pharmaceutical drugs, as well as vaccines and other approaches.

### Production and Therapeutic Drugs for Turkeys

The turkey industry has lost access to a number of significant therapeutic agents over the last 15 years. Many therapeutic and production animal drug needs of turkeys are not being met. Efforts to develop new animal drugs indicated for use in turkeys have been minimal. During FY 2007, CVM continued discussions, begun a year earlier with the National Turkey Federation, to explore the possibility of involving the Federation in establishing a national program to develop and seek approval for new animal drugs to fill the therapeutic needs of turkeys. This initiative is a proactive effort to pursue the approval of therapeutic drugs for turkeys by a mechanism other than traditional development by pharmaceutical sponsors.

*Photo by Susan Storey, Office of New Animal Drug Evaluation.*

## IMPROVING THE EFFICIENCY AND EFFECTIVENESS OF THE REVIEW PROCESS

### 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 work is a pharmacokinetics/pharmacodynamics (PK/PD)[9] 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 PK/PD study initiated in FY 2007, CVM scientists are studying the antibiotic tilmicosin in 16 beef steers, both in the healthy state and also following induction of pneumonia with *Mannheimia haemolytica*. The scientists are undertaking the investigation to determine whether target animal safety and PK/PD expectations may be

[9] Pharmacokinetics is the study of the bodily absorption, distribution, metabolism, and excretion of drugs, and pharmacodynamics is the study of the action of a drug in the body over a period of time.

biased when based on information obtained from healthy animals. This information will help CVM identify those classes of compounds for which we need to factor disease condition into our clinical efficacy and human food safety assessments.

In another research project started in FY 2007, our scientists are investigating the cause of acute deaths in cattle following subcutaneous injection. Several drug products designate the ear pinna (ear flap) as the site for such injection. Reports have attributed cattle deaths to the inadvertent injection of the drug into an artery. Scientists from CVM's Office of Research, in coordination with the Virginia-Maryland Regional College of Veterinary Medicine, are investigating possible pathways by which the improperly administered drug could reach the cerebral blood supply and cause death.

## Enhancing the Review Process Through the Development of Regulations and Guidance Documents

Regulations and guidance documents are important mechanisms for implementing improvements in the animal drug approval process. During FY 2007, FDA issued a final rule and a related guidance document describing requirements and procedures for making and reporting manufacturing changes to approved NADAs and generic applications. The final rule requires manufacturers to assess the effect on safety and effectiveness of a manufacturing change in the identity, strength, purity, and potency of a drug. It sets forth requirements for the timing of submission of a supplemental application related to manufacturing changes, e.g., when the supplemental application must be approved before the distribution of drugs manufactured using the change.

CVM during FY 2007 issued a series of guidance documents for electronic submission of various documents and information. We can now accept certain information from drug sponsors through an improved electronic submission system that includes an "Electronic Submission Gateway" developed by FDA. The key guidance is "Guidance for Industry #108: How to Submit Information in Electronic Format to CVM Using the FDA Electronic Submission Gateway," which describes the new electronic submission process.

We completed additional guidance documents and translated a number of guidance documents into Spanish. For additional information on publications, see Appendix A.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

## Actions to Increase the Efficiency of the Review Process

*Implementing a system to improve business processes.* One of our performance goals for FY 2007 was to increase access to innovative new animal drug products by implementing a system of planning, execution, monitoring, and evaluation to improve business process efficiencies. We accomplished this goal in a number of ways, including:

- Planning resource availability for various performance goals for FY 2008 so that resources can be balanced between animal drug review work and other essential non-review work.
- Working with increasing numbers of sponsors on projections for upcoming submissions, allowing the Office of New Animal Drug Evaluation to better manage its internal resources.

- Implementing the Office of New Animal Drug Evaluation's Quality System by making a gap analysis of our new animal drug review process, including assessing for gaps in our standard operating procedures.
- Assessments by Office of New Animal Drug Evaluation's Large Quality Assurance Initiative group of three major process areas that yield decisions communicated to industry sponsors. The three assessments resulted in improvements in the consistency of work output across the Office of New Animal Drug Evaluation.

*Collaborating With Stakeholders.* The Animal Health Institute and CVM in FY 2007 formed a working group to explore the use of PK/PD data in the development and evaluation of new animal drugs submitted for approval. (See PK/PD research, above, this section).

Working groups established with the Animal Health Institute in prior years continued to explore the reasons for multi-cycle reviews of safety and efficacy data for production and food animals. The goal of these working groups is to identify why submissions were found to be incomplete, so that the quality of future submissions can be improved. This information will reduce the number of multi-cycle submissions and accelerate the approval process.

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

# *PROTECTING THE HEALTH OF COMPANION ANIMALS*

## THE CHALLENGE

The increasing companion animal population in the United States, along with the growing affinity that pet owners have for their pets – evidenced by rising expenditures for pet care and aggressive marketing of pet products – illustrate the need for more safe and effective drugs for disease prevention and treatment in companion animals and for protecting the integrity of pet food.

## FY 2007 ACCOMPLISHMENTS

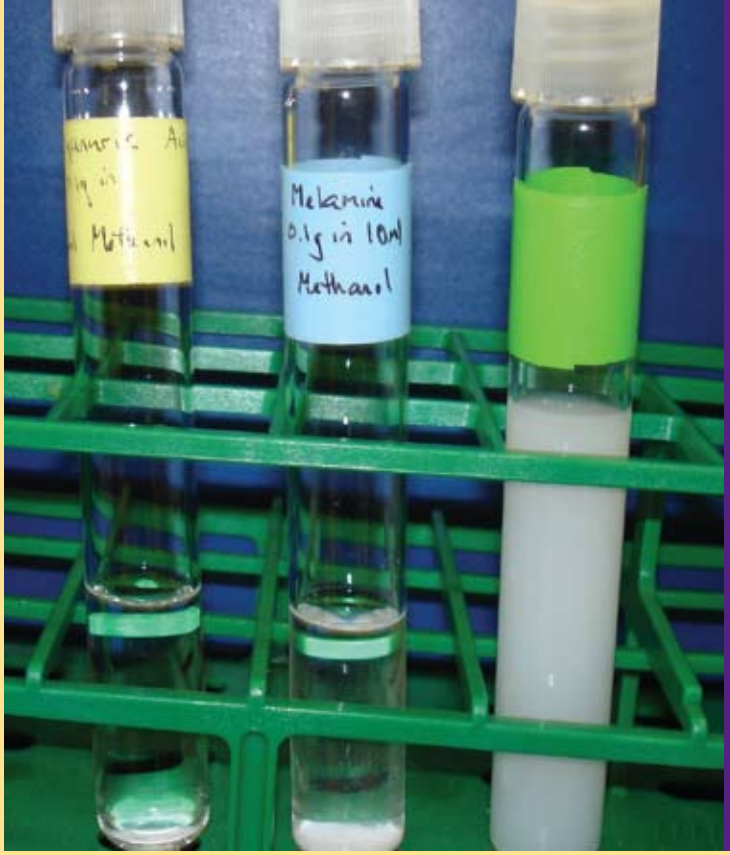
During the year, we met the challenge of pet food contamination – most prominently melamine-contaminated pet food, but also *Salmonella* contamination of pet food. In addition, we approved an unusually large number of significant new animal drugs and supplements for companion animal therapy.

## PET FOOD CHALLENGES AND ACCOMPLISHMENTS

### Melamine Contamination of Pet Food – What Happened, What CVM and FDA Did

In mid-March 2007, Menu Foods, based in Ontario, Canada, notified FDA that it was recalling certain of its pet food products due to complaints that included the deaths of a small number of dogs and cats. This notification – and a similar notification a month later from the Wilbur Ellis Co., San Francisco, CA, that it was recalling shipments of a pet food ingredient – set in motion a number of actions by CVM and FDA.

In the end, pet food manufacturers recalled hundreds of types of products and millions of servings, and the response by the Agency and the Center reached a virtually unprecedented level and intensity of effort. Recognizing the importance of pets to the American people and the magnitude of the problem, we dedicated significant staff time on a priority basis to determining the cause of the contamination and to resolving the problem. As one of many examples, CVM's Division of Compliance provided scientific support to FDA's field operations, using its scientific background to direct those operations. CVM was involved in many other initiatives:




When cyanuric acid combines with melamine, the result is crystals, as shown in the test tube on the right. *Photo by Renate Reimschuessel, Office of Research.*

*Finding the cause of the problem.* Veterinarians, toxicologists, pathologists, chemists, and other scientists from CVM and other parts of the Agency pitched in to pinpoint the problem. Fortunately, Menu Foods was able to target wheat gluten[10] quickly, and the scientists soon discovered melamine – suspected as a cause of the animal deaths – in the wheat gluten. The Wilbur Ellis Co. found melamine in the rice protein concentrate it had sold for use as a pet food ingredient. Soon, the scientists showed that melamine in combination with cyanuric acid caused the deaths. (For more details on the scientific effort to find the causes of the animal deaths and to assess the risk to humans from animals given feed thought to be contaminated by melamine, see "Scientific Solutions to the Melamine Mysteries" in the "Highlights" section at the front of this report.)

[10] Wheat gluten, made from wheat that has had the starch removed, is a high-protein ingredient often used to thicken sauces.

*Finding the source of the melamine, and the reason for its use in pet food.* Both Menu Foods and Wilbur Ellis Co. were able to establish swiftly their sources for the melamine-contaminated ingredients: suppliers in China. FDA eventually identified two Chinese distributors as the sources. We discovered later that the product labeled as wheat gluten feed was actually a mixture of wheat flour, wheat gluten, and melamine.

*Locating melamine-containing products.* Within 5 weeks after the first alert from Menu Foods, FDA personnel had collected and tested approximately 750 samples of wheat gluten; 330 were positive for melamine and/or melamine-related compounds. In the same timeframe, tests of 85 samples of rice products revealed 27 positives for melamine.

*Administering the recalls.* Menu Foods' recall involved 60 million individual packages of pet food from approximately 100 companies for which Menu Foods manufactured pet food. Wilbur Ellis Co. recalled 155 metric tons of pet food. Eventually, 31 firms recalled a total of 1,054 melamine-related products.

FDA's Office of Emergency Operations and Office of Regulatory Affairs handled the recalls, with scientific support and direction from CVM. We classified all the recalls according to health hazard (most were Class I).[11] We did this in less than 2 weeks through the coordinated efforts of CVM's Divisions of Animal Feeds and Compliance, and FDA's Office of Enforcement. CVM's Division of Compliance served as a clearinghouse and distributor of information about the recalls.

*Inspections to ensure compliance with the recalls and for other purposes.*

FDA's first priority was to identify and remove all contaminated product from the market. The complex distribution chain made our job much more difficult. FDA sent investigators to all manufacturing sites that used the contaminated ingredients and to storage locations. We also undertook the tedious process of tracking the effectiveness of the recall.

*Cutting off the source of contaminated ingredients.* In April 2007, FDA issued an import alert that required the detention without physical inspection of shipments of 11 different vegetable protein products from China entering the United States. The identified products included wheat gluten and rice protein products, among others. Agency personnel screened the detained products. A total of 1,108 entries of wheat gluten, rice, and diverse vegetable protein products were sampled for melamine and related compounds, and 357 tested positive. Those shipments were refused entry into the United States, and the shipments were referred to U.S. Custom and Border Protection for subsequent exportation or destruction.

During May 2007, FDA launched a month-long assignment to inspect ingredients imported from China. The assignment identified specific forms of wheat, corn, rice, and soy to test for melamine and related compounds.

*Other Actions.* CVM participated in an unprecedented communications initiative with consumers and industry stakeholders. Further details are in the subsection, "Communicating with Stakeholders," in the section on "FY 2007 Challenges and Accomplishments."

## *Salmonella* Contamination Assignment, Recalls, and Education

*Salmonella* in pet foods and treats can cause serious infections in dogs and cats and can potentially be transferred to people who handle contaminated pet food and treats.

Acting on several reports of human salmonellosis and *Escherichia coli* O157:H7 linked to contact with pets, CVM early in FY 2007 issued an assignment to FDA field

[11] FDA classifies recalls, according to degree of health hazard posed by the product, into class I, II, or III. Class I recall products present the highest health hazard.

offices to collect samples of direct-human-contact pet food and analyze them for the presence of *Salmonella* and *Escherichia coli* O157:H7. As a result of this effort, firms recalled 20 pet food products due to *Salmonella* contamination. The products included pet treats, dry dog food, raw cat foods, and pet food ingredients. Most of the recalls were Class I (highest health hazard).

The survey and resulting recalls have had a significant effect on the pet food industry's awareness of possible pet food microbial contamination and needed preventive measures. In addition, CVM provided instructions to pet owners for minimizing the incidence of foodborne illness associated with pet foods and treats. (See "FDA Tips for Preventing Foodborne Illness Associated with Pet Food and Pet Treats," CVM UPDATE July 27, 2007.)

### Recognition of Work Related to Aflatoxin in Pet Food

During the year, FDA recognized CVM's Aflatoxin in Pet Food Investigation and Recall Group with a Leveraging/Collaboration Award for exceptional effort in the investigation and removal of elevated aflatoxin[12] contaminated pet food.

## COMPANION ANIMAL DRUG CHALLENGES AND ACCOMPLISHMENTS

### Drug Approvals

CVM approved 14 significant original and one significant supplemental NADAs for companion animals in FY 2007. Of the 15 approvals, 12 were for dogs, 2 for cats and 1 for horses. In addition to the three approvals reported in the "Highlights" section under "Companion Animal Approvals," we approved the following six new chemical entities that provide therapeutic advances for companion animal health:

*Photo by Christopher Melluso, Office of Surveillance and Compliance.*

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

Dexmedetomidine hydrochloride – sedative, analgesic, and pre-anesthetic in dogs.

Moxidectin/imidacloprid – for treatment of roundworms, hookworms, whipworms, and fleas, and prevention of heartworm disease in dogs; and treatment of roundworms, hookworms, ear mites, fleas, and prevention of heartworm disease in cats.

*Photo by Alfan Dangin, Office of the Director.*

[12] Aflatoxin is a toxin produced by mold that can damage the liver and may lead to liver cancer. It causes cancer in some animals. The fungi that produce aflatoxin grow on crops such as peanuts, wheat, corn, beans, and rice.

Fluoxetine hydrochloride

– for treatment of separation anxiety in conjunction with behavior modification in dogs.

Diclazuril

– for treatment of equine protozoal myeloencephalitis.

Praziquantel/emodepside

– for treatment of roundworms, hookworms, and tapeworms in cats.

Spinosad

– to kill fleas and prevent and treat fleas on dogs for a month.

*Photo by Alfan Dangin, Office of the Director.*

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

*Photo by Dan Benz, Office of New Animal Drug Evaluation.*

## Meeting a Need for Treating Cushing's Disease in Horses

Cushing's Disease is an endocrine disorder that weakens a horse's immune system. For treatment of this disease, veterinarians have in the past prescribed pergolide – a human drug approved for treatment of Parkinson's Disease – as an authorized "extralabel" use. However, FDA's Center for Drug Evaluation and Research removed pergolide products from the market during FY 2007 due to concerns about cardiac side effects in humans. FDA has been working to ensure that pergolide remains available to treat Cushing's Disease in horses until an NADA is approved for that use. Options include making the approved product available through veterinary distribution channels, permitting pharmacy compounding of pergolide, and working with sponsors who are interested in seeking approval of an NADA.

# *INCREASING DRUG AVAILABILITY FOR AQUACULTURE AND OTHER MINOR USES/MINOR SPECIES*

## THE CHALLENGE

The MUMS Act 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 for farm-raised fish and other seafood is growing as well.

## FY 2007 ACCOMPLISHMENTS

As described in the following paragraphs, CVM made considerable progress during the year in adopting regulations to implement the MUMS Act and implementing the Act's provisions for drug approvals. The accomplishments included the first Conditional Approval and approval of the first two drugs for treatment of columnaris disease, a major disease of catfish.

## REGULATIONS IMPLEMENTING MUMS ACT

### Designation Regulations

During the fiscal year, FDA issued final regulations implementing the designation provisions of the MUMS Act and describing the procedure for designating a new animal drug as a minor use or minor species drug. MUMS Act designation of a new animal drug allows the drug sponsor 7 years of exclusive marketing rights to encourage the development of these limited demand drugs.

### Indexing Regulations

CVM made progress in developing the final rule to implement the MUMS Act's provision for an index of legally marketed unapproved new animal drugs and sent the rules to the Agency during FY 2007. The MUMS Act provides that under limited circumstances FDA may add a minor species to an index of unapproved new animal drugs that may legally be marketed even though the potential market for the drugs is too small to support the costs of the drug approval process, even under a Conditional Approval.

### Conditional Approval and Definitional Regulations

CVM is developing a proposed rule on Conditional Approval, as authorized by the MUMS Act. Conditional Approval allows the sponsor to market a drug before collecting all necessary effectiveness data, as long as the sponsor has demonstrated that there is a reasonable expectation that the drug is effective. The sponsor must also submit data to establish target animal and human food safety. The sponsor of a Conditional Approval drug may market the drug for up to 5 years, subject to annual renewals, while collecting substantial evidence of effectiveness.

The Center is also developing a regulatory definition of a "small number of animals" as that term relates to minor uses in major species.

## DRUG APPROVALS

### First Conditional Approval

During the year, CVM granted a Conditional Approval of Aquaflor®-CA1[13] (florfenicol) Type A medicated article for the control of mortality in catfish due to columnaris disease[14] due to *Flavobacterium comnare*, which is

[13] The "CA1" in the product name indicates that the drug is Conditionally Approved (CA) and that this is the first (1) Conditionally Approved application for this formulation.

[14] Columnaris disease occurs in external and systemic forms. Florfenicol was shown to be effective against both forms.

estimated to cause up to 25 percent of the disease losses in catfish annually. This is the first Conditional Approval under the MUMS Act. FDA also declared Aquaflor®-CA1 to be a "designated" new animal drug under provisions of the MUMS Act.

## First Approval for Coldwater Disease in Salmonids

CVM also approved Aquaflor® (florfenicol) Type A medicated feed article for the control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilum*. This is the first drug approved for use during coldwater disease outbreaks; up to 50 percent of affected fish may be lost during disease outbreaks, with greater mortality in younger fish.

The approval resulted from cooperation between the pharmaceutical sponsor and researchers from the U.S. Fish and Wildlife Service, U. S. Geologic Survey, and the Montana Department of Fish, Wildlife, and Parks.

Working with Atlantic salmon at CVM's Office of Research.
*Photo by Pat McDermott, Office of Research.*

## Approval for Hydrogen Peroxide – Environmental Risk Mitigation

CVM approved 35% PEROX-AID®, an external microbicide for the control of mortality in freshwater-reared finfish eggs due to saprolegniasis;[15] in freshwater-reared salmonids due to bacterial gill disease;[16] and in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare (Flexibacter columnaris)*. Approved with over-the-counter marketing status, 35% PEROX-AID® is the first new immersion drug[17] approved for finfish in 20 years. The drug is designated under provisions of the MUMS Act. The U.S. Geological Survey generated effectiveness and target animal safety data as well as the environmental assessment for the approval under a public master file.

The approved label contains risk mitigation language, which requests that users inform the appropriate authority of the National Pollutant Discharge Elimination System (NPDES) of their intent to use this drug, and of a water quality benchmark that has been derived for the hydrogen peroxide. The NPDES authority can use the benchmark in conjunction with site-specific information to determine if discharge limitation and/or effluent monitoring may be needed. The risk mitigation step is necessary because risk characterizations in the Environmental Assessment for 35% PEROX-AID® indicated that the effluent concentrations for some aquaculture facilities expected to use this drug could result in adverse effects on aquatic life in receiving waters. (Receiving waters are waters such as rivers or lakes into which the discharge from a facility flow.)

[15] Saprolegniasis is a fungal infection of fish that causes lesions on the skin.

[16] Bacterial gill disease is an infectious inflammatory disease of aquarium and salmonid species.

[17] An immersion drug is administered via the water as a bath treatment.

## Innovation for Environmental Assessment

**In most cases, new animal drugs for use in aquaculture will be used or discharged directly into surface waters. These drugs may have toxic effects on non-target organisms that serve important and valuable roles in the aquatic environment. There has been a critical need for consensus on a mechanism to evaluate and allow the safe use of new animal drugs in aquatic environments. A member of CVM's environmental staff, Dr. Eric Silberhorn, pioneered the use of the Environmental Protection Agency (EPA) numeric Water Quality Criterion in the application of numeric water quality benchmarks to the approval process for new aquatic animal drug products. The method allows for the discharge of effluents containing new animal drugs using safety data generated in a variety of non-target species together with site-specific data describing the composition of the receiving waters at the point of discharge. For his work, Dr. Silberhorn received the FDA Excellence in Review Science Award in 2007.**

Dr. Eric Silberhorn. *Photo by Jon Scheid, Office of the Director.*

## RESEARCH TO SUPPORT DRUG APPROVALS

### Food Safety Database

We expanded the online database (PhishPharm Database) to include more articles and placed the updated version on the CVM Web site July 2007 http://www.fda.gov/cvm/addaquainfo.htm. This resource, which contains detailed data on drug metabolism, residues, and pharmacokinetics in multiple fish species, is a valuable tool for veterinarians and for researchers developing therapeutics for minor species.

### Efficacy Studies

CVM researchers, using a disease model they developed for infecting channel catfish with a fungus (*Saprolegnia parasitica*) to test the efficacy of potential therapeutants, evaluated the efficacy of formalin to treat infected catfish. We completed the animal portion of this study in FY 2007 and began preparation of the final report.

### Antimicrobial Susceptibility Testing

During FY 2007, CVM researchers used Clinical and Laboratory Standards Institute standards that they had previously developed for antimicrobial susceptibility testing for aquatic organisms to begin to assemble a dataset that can be used by the Agency to develop interpretive criteria. Interpretive criteria assist veterinarians (or other users of antimicrobials, including lay persons for over-the-counter drugs) in selecting the most appropriate antimicrobial when more than one product is available for use, e.g., in determining whether a particular drug is likely to be effective in a specific situation.

## Methods Development

CVM researchers developed and "bridged"[18] a microbiologic method and a chemical high performance liquid chromatography method to test for active oxytetracycline in fish serum. We published these methods, which are used to evaluate pharmacokinetics of oxytetracycline in fish with and without a concurrent infection, thus providing important information for use in evaluating the effects of dose and clinical outcome in sick fish. The study was initiated in FY 2006, but most of the work was done in FY 2007.

*Photo by Dan Benz, Office of New Animal Drug Evaluation.*

Rainbow Trout. *Photo by Jennifer Matysczak, Office of New Animal Drug Evaluation.*

## Largemouth Bass Parasite Model

CVM researchers used their colony of Largemouth Bass infected with the renal parasite *Acolpenteron ureteroecetes* to study the effects of antiparasitic drugs on the monogenean parasite, thus helping identify potential therapeutic agents for diseases of minor species.

## Pharmacokinetic Comparison in Small Ruminants

CVM scientists are conducting a study, initiated in FY 2007, for PK characterization of small ruminant antiparasitic drugs. The information from the study will permit doses and dosing regimens to be based on the pharmacological understanding of the drugs, rather than – as in the past – assumptions and extrapolations from other drugs and species. The animal phases of the investigations of levamisole, albendazole, fenbendazole, and ivermectin have been completed. Sample collections after treatments with doramectin and moxidectin, as well as laboratory analyses of the samples from all six drugs, continued into FY 2008.

[18] "Bridged" means that the scientists analyzed for oxytetracycline using both methods and compared the results to determine the relationship of the two methods. Much of the older published research is based on microbiological methods. By bridging the methods, a comparison can be made between these older published results and the new studies conducted using high performance liquid chromatography methods.

# *REDUCING RISK FROM ANTIMICROBIAL RESISTANCE*

## THE CHALLENGE

Scientific evidence demonstrates that the use of antimicrobial drugs in food-producing animals can result in the survival of resistant bacteria, which can increase in number. 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's challenge is to develop policies and programs that reduce this risk to human health from the use of antimicrobial drugs in food-producing animals.

## FY 2007 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. We achieved significant progress in these efforts during the past year, responding to FDA strategic goals and Departmental objectives.

*Salmonella. Photo by Pat McDermott, Office of Research.*

## MONITORING FOR THE DEVELOPMENT OF RESISTANCE

CVM serves an active leadership role in the National Antimicrobial Resistance Monitoring System (NARMS), established more than a decade ago as a collaborative effort between CVM, USDA, and 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 useful life of approved drugs by promoting prudent and judicious use in animals of antimicrobial drugs and to identify areas for more detailed investigation.

During FY 2007, Dr. Beth Karp of the CVM Office of Research was selected as the NARMS Coordinator. Her responsibilities include coordination of the epidemiological activities of all three arms of the NARMS program – animal (administered by USDA), human (administered by CDC), and retail meat (administered by FDA) – as well as the development of the annual executive report. Much of the NARMS activity involves collaborative efforts, not only between federal agencies but also within FDA. For example, during the fiscal year NARMS personnel presented background on the NARMS program to senior leadership of CFSAN to foster collaborative efforts in food safety research and surveillance.

FY 2007 NARMS achievements included the following:

**Continued Implementation of the Recommendations of an Expert Panel**

During the fiscal year, we continued to implement several recommendations of a panel of outside experts, which was convened during FY 2005 for a review of the NARMS program. These changes included database improvement, greater international involvement, and additional hypothesis-driven research.

### Science Board Review

In fulfillment of program goals, CVM participated in strategic planning for, and provided leadership in support of, an FY 2007 review of the NARMS program by a Subcommittee of the Science Board to the FDA. In a public meeting, the Subcommittee addressed NARMS sampling strategies, research studies, data harmonization and reporting, and international activities. The meeting addressed the scope, strengths, weakness, and areas for improvement in the NARMS program. Following the Subcommittee meeting, FDA's NARMS personnel met with USDA and CDC representatives to develop responses to the Subcommittee's recommendations, which focused mainly on improving the sampling strategy and enhancing harmonization of databases and reporting. CVM expects to present a response to the Subcommittee's recommendations early in FY 2008.

### Web Site and Data Reporting

We have accelerated our NARMS data analysis to produce timelier reporting. During FY 2007, we published the first NARMS Executive Report (for 2003) and will publish the 2004 report early in calendar 2008. The 2005 NARMS Retail Meat Annual Report was expected to be on the Web site in November 2007, and the 2006 report was expected to publish early in calendar year 2008.

### Database Implementation

During the year, NARMS personnel developed and implemented the NARMS database application in the Center's Corporate Database Portal. This database provides information necessary to expedite the antimicrobial drug approval process, as well as provide post-approval monitoring information, which can facilitate FDA's response to important trends in antimicrobial resistance among foodborne pathogens.

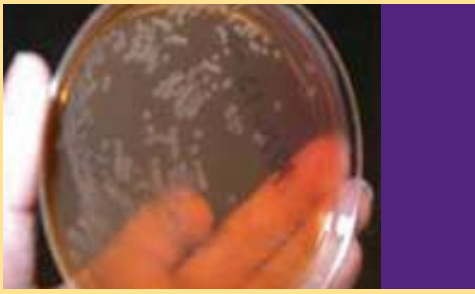
### International Activities

NARMS personnel participated in the World Health Organization Global *Salmonella* Surveillance (GSS) program by attending the annual GSS planning meeting and providing training to scientists from China, Russia, and the Caribbean. Such collaboration enhances the capacities of other countries in the surveillance of antimicrobial resistant *Salmonella* and significantly contributes to the global effort to contain enteric antimicrobial resistance in foodborne pathogens.

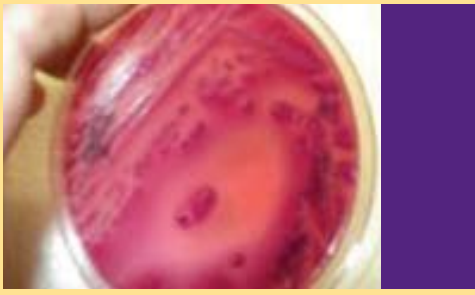
## PRE-APPROVAL AND POST-APPROVAL REVIEW FOR ANTIMICROBIAL RESISTANCE

During the year, CVM scientists reviewed microbial food safety information, including hazard characterizations and qualitative risk assessments, for 16 antimicrobial animal drugs. The drugs, from 14 different sponsors, are for uses in cattle, swine, poultry, and aquaculture species. A number of these drugs that were the subject of original and supplemental NADAs successfully met CVM's microbial food safety criteria. The scientists used CVM's Guidance for Industry #152 "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern." The guidance document provides a

*Salmonella.*



*Campylobacter.*



*Escherichia coli.*

*Enterococcus.*

pathway sponsors can use to show how an antimicrobial drug can be used in food-producing animals without endangering public health from promoting antimicrobial resistance.


Yolanda Jones, a biologist working in the laboratory at CVM's Office of Research.
*Photo by Michael Scott, Office of Research.*

## RESEARCH TO SUPPORT ANTIMICROBIAL RESISTANCE SURVEILLANCE AND REGULATION

### Developing Rapid Screening Methods

One of the Center's performance goals for FY 2007 was to develop rapid methods for screening antimicrobial resistant foodborne pathogens to identify specific animal origins for the pathogens. We accomplished this goal through several initiatives.

CVM scientists completed and published studies comparing different molecular fingerprinting techniques for characterizing multi-drug resistant *Salmonella* Newport and *Salmonella* Typhimurium isolates from food animals and retail meat and poultry. Results demonstrated that a combination of methods was necessary to determine the genetic relatedness of foodborne pathogens. This discovery will lead to improved tracking and characterization of outbreaks and will help guide anti-infective therapy in humans.

Using novel DNA fingerprinting techniques, CVM scientists are collaborating with investigators from the Max Planck Institute for Infection Biology to investigate the emergence of antimicrobial resistance phenotypes and evolutionary relatedness of veterinary diagnostic and retail meat *Salmonella* Newport isolates. Results obtained during FY 2007 indicate that multi-drug resistant *Salmonella* Newport emerged recently through both clonal expansion and acquisition of extrachromosomal plasmids containing multiple antimicrobial resistance genes.

### Food Animal Sources of *Enterococcus* Infections

CVM funded a cooperative research agreement with the University of Maryland to study *Enterococcus* from retail meats, healthy humans, and human infections. The goal of this project, which was essentially completed during FY 2007, is to determine whether food and food animals serve as an important source of human *Enterococcus* infections. Among the enterococci isolates examined, 62 percent were *Enterococcus* faecalis and 38 percent were *Enterococcus* faecium. *Enterococcus* infections, mainly *Enterococcus* faecalis, are among the most common hospital-acquired infections and include urinary tract infections, bacteremia, intra-abdominal infections, and endocarditis. Data obtained in the study suggest that *Enterococcus* faecalis strains are distributed across both human and food sources, while *Enterococcus* faecium sequence types likely occupy specific niches. Thus, *Enterococcus* faecalis may be more likely to move from food animals to humans and potentially cause human illness.

## Resistance Links From Food to Humans

NARMS personnel are currently collaborating with academic investigators at the University of Minnesota and Iowa State University in characterizing potential links between antimicrobial resistant *Escherichia coli* recovered from retail foods and human extra-intestinal pathogenic *Escherichia coli* infections (e.g., urinary tract infections and septicemia). Preliminary findings indicate some similarity between isolates of humans and poultry; however, most appear to have distinct differences, indicating that it is unlikely that these isolates are involved in human extra-intestinal pathogenic *Escherichia coli* infections.

## Resistant Pathogens

NARMS personnel continue to partner with USDA scientists in characterizing antimicrobial resistance patterns among *Salmonella* and *Escherichia coli* obtained from their Microbiological Data Program, which collects data regarding the incidence and identification of targeted foodborne pathogens on fresh fruit and vegetables.

## Other Research

CVM scientists partnered with researchers at the University of Maryland to study contribution of target gene mutations and efflux (outflow) to decreased susceptibility of fluoroquinolones and other antimicrobials in *Salmonella* Typhimurium.

*Photo by Devaraya R. Jagannath, Office of New Animal Drug Evaluation.*

# CONTROLLING RISK FROM BSE

## THE CHALLENGE

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 include several ruminant and nonruminant animal diseases. Laboratory and epidemiological evidence strongly suggests that people can contract a human TSE, variant Cruetzfeldt-Jakob Disease, 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.

## FY 2007 CHALLENGES

We continued to provide the expert scientific knowledge and review on BSE for the Agency. Much of our effort during the year focused on enforcing and strengthening our BSE feed regulation, which prohibits the use of certain mammalian-origin proteins in ruminant feed. The purpose is to prevent the establishment and amplification of BSE in the United States through feed. Following are highlights of some of our achievements that accomplished FDA's strategic goal of consumer protection and the Department-wide objective of improving the safety of food products.

## U.S. BSE RISK STATUS

Unlike the several previous fiscal years, FY 2007 did not see the discovery of any BSE-infected cattle in the United States. Due in part to the work of CVM staff, the United States in 2007 achieved controlled-risk status through the OIE (World Organization for Animal Health). Although this category requires presentation of an international veterinary certificate attesting that certain conditions have been complied with, the status is an improvement from a trade standpoint over the previous status of "undetermined."

A scene from the CVM video, "Preventing the Spread of BSE."

## TRAINING, EDUCATION, AND ENFORCEMENT

### Education for the Regulated Industry

During the fiscal year, CVM released a video," Preventing the Spread of BSE," on FDA's Web site at http://www.fda.gov/cvm/bseOtherInfo.htm. The approximately 11-minute video is intended to help truckers prevent the spread of BSE. The video explains the requirements under FDA's BSE feed regulation that truckers clean out their trucks to prevent cross-contamination when carrying materials prohibited for use in the feed of ruminants. We developed the video in cooperation with FDA's Office of Regulatory Affairs, the American Feed Industry Association, the National Grain and Feed Association, and the National Renderers Association.

### Inspections

To implement the goal of improving the safety of food products through better manufacturing and product oversight, through the FY 2007 work-planning process we allocated field resources to allow for targeted inspections of all known renderers and feed mills processing products containing prohibited materials (approximately 500 high-risk firms). We estimate that the total number of FY 2007 BSE-related inspections of all firms that process or handle animal feed – including inspections both by state and FDA investigators – will approximate the confirmed number for FY 2006, which was 8,934.

We added a new inspectional emphasis in FY 2007 – targeted BSE inspections of the animal feed transportation industry. The transportation industry is a critical element in the promotion of animal feed safety through the

prevention of cross-contamination. We issued an assignment to the FDA Districts to identify transportation firms and to conduct transporter inspections, and we made significant revisions to the inspection checklist by adding transportation questions.

During FY 2007, the Agency conducted BSE inspections at far more than 1,000 firms marked "transporter/hauler" on the BSE checklist. Although most of these inspections were done at firms/sites that also fit other categories on the checklist (such as feed mills, renderers, and distributor/retailers), the increased focus on transportation by these firms will provide public health benefit as well.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

### Enforcement Actions

Although inspections show that the rate of violations of the BSE feed rule remain low, violations may lead to enforcement actions. For example, during the year an Ohio renderer of bovine and poultry materials and two of its officers entered into a consent decree of permanent injunction due to continuing, significant violations of FDA's ruminant feed ban. The defendants agreed to come into compliance with the regulations including labeling products with the statement "Do not feed to cattle or other ruminants," maintaining separate lines of equipment for producing various products, and/or sufficiently cleaning existing equipment between uses. Further, the consent decree provides for FDA to require a recall or shutdown in the event of future violations.

### Field Training

CVM staff conducted 9 BSE feed regulation training sessions, ranging from 2-hour updates to 2-day comprehensive training, for FDA field staff and state regulators.

## STRENGTHENING THE BSE FEED REGULATION

During the year, CVM completed work on a final rule that would amend the BSE feed rule regulation to remove the highest risk tissue from all animal feed to prevent the spread of BSE. In addition, the revisions would augment the current animal feed regulation by further reducing the risks of BSE associated with cross-contamination and on-farm mis-feeding. Responding to comments on the proposed rule issued in October 2005, we have conducted a new economic analysis and revised our environmental assessment, focusing in both instances on carcass disposal.

## DEVELOPING ANALYTICAL METHODS FOR DETECTING PROHIBITED PROTEINS

Because of changing demands on the FDA field laboratories, the validation of the real time polymerase chain reaction method for detecting prohibited animal proteins in animal feed was not completed this year. However, the information needed for validation was collected from the participating laboratories, and the data are currently being analyzed. When it is validated, the method will detect prohibited proteins produced according to U.S. processing conditions. CVM's Office of Research during the year validated the real time polymerase chain reaction method for use in detecting prohibited proteins (bovine, ovine, and porcine materials) processed according to European Union conditions. Thus, the method can be used to detect prohibited materials in imported products.

## *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 that repeatedly present animals for slaughter that are adulterated with illegal drug residues – identified through the USDA's National Drug Residue Monitoring Program – may cause a significant public health concern. In fact, investigation of repeat violators is a top priority. Investigating first-time violations of residues from drugs prohibited from extralabel use in food animals, residues of drugs not approved for food animal use, and very high-level drug residues are also high priorities.

### FY 2007 ACCOMPLISHMENTS

The following summarizes our FY 2007 efforts to avoid unsafe drug 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 295 firms under the Tissue Residue Program. FDA issued 47 tissue residue-related Warning Letters. CVM's Division of Compliance also reviewed and approved one proposed tissue residue-related injunction action in FY 2007.

Enforcement actions resulted in consent decrees of injunction entered during FY 2007 against several firms whose actions resulted in illegal drug residues in edible tissues. Following is an example.

In August 2007, a U.S. District Court issued an order of permanent injunction against two Puerto Rican dairies and the owner of the dairies, after the USDA found five illegal drug residues in cows marketed by the dairies, and after follow-up inspections confirmed that the dairies continued to use animal drugs in an improper manner. The drug residues included antibiotics, such as sulfamethazine, sulfathiazole, sulfadimethoxine, and penicillin at levels not permitted by FDA. Under the terms of the order, the defendants were required to implement record-keeping systems to ensure that their use of drugs will not result in illegal residues, and the defendants were not permitted to resume marketing milk or animals for slaughter until they were in compliance with the order.

### IMPORT TOLERANCES

We continued during the year to coordinate the drafting of several regulations to implement the import tolerances provisions of the Animal Drug Availability Act of 1996.

That Act authorizes FDA to establish tolerances (import tolerances) for residues, found in imported food products of animal origin, of drugs that are used in other countries but are unapproved new animal drugs in the United States. If no tolerance has been established for a drug, 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.

### INTERNATIONAL COORDINATION RELATED TO ANIMAL DRUG RESIDUES

Delegates at the 17th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) reviewed and took action on Maximum Residue Limits for a number of drugs, including colistin, ractopamine, erythromycin, and triclabendazole. The delegates, from 46 member countries and 1 member organization, also discussed "Draft Guidelines for the Design and Implementation of National Regulatory Food Safety Assurance Programmes Associated with the Use of Veterinary Drugs in Food Producing Animals," and CCRVDF created or re-established working groups on several topics, including risk management. CVM's Director chairs CCRVDF, the Director

of our Office of New Animal Drug Evaluation leads the U.S. delegation, and other CVM staff members serve as subject matter experts.

*Photo by Bernadette Dunham, Office of the Director.*

## RESEARCH TO SUPPORT SAFETY OF IMPORTED AND DOMESTIC FOOD PRODUCTS

### Drug Residues in Imported and Domestic Honey

We continued to find samples of imported and domestic honey contaminated with residues of a significant number of drugs that are not approved for use in apiculture (beekeeping) in the United States. (Only tylosin, oxytetracycline, and fumagillin are so approved.) As a result, there is a need to monitor honey for a broad range of antimicrobial agents. During FY 2007, CVM scientists completed the development and validation of a multi-class monitoring method for this purpose. The analytical method is capable of determining and confirming the presence of 17 antibiotics in honey, including tetracyclines, fluoroquinolones, macrolides, sulfonamides, phenicols, and fumagillin in the low parts per billion level using liquid chromatography tandem mass spectrometry.

The method is suitable for surveillance and regulatory programs, and it can be used to monitor for unsafe levels of approved drugs, in addition to residues of unapproved drugs. Its development is especially significant for FDA's Center for Food Safety and Applied Nutrition (CFSAN) in its regulation of honey for use in human food and to the states that produce honey for use in human food.

### Antiparasitic Drug Residues in Farmed Fish

Aquatic parasitic infestations, a major problem in fish farming, are often treated successfully with albendazole or ivermectin. However, these antiparastic agents must be metabolized and eliminated to below tolerance levels before the treated fish may be used for human food. Sensitive and specific analytical methods are required to monitor the parent drug and metabolite residue levels of these antiparasitic agents. The last depleting and most persistent metabolite of the drug is usually used as a marker residue to monitor the complete removal of the drug residue to below an accepted tolerance level. Extensive species-by-species metabolism studies are often needed to determine if the parent drug or one of the metabolites is the most important drug residue to monitor.

During FY 2007, CVM scientists completed a multi-year study of the metabolism and residue depletion of albendazole in farmed fish. For catfish, the species studied in 2007, the albendazole sulfone metabolite is the last depleting compound in muscle tissue and should serve as the marker residue. The CVM scientists also found that parent drug, ivermectin, is the marker residue for Atlantic salmon, tilapia, and catfish.

Atlantic Salmon at the Woods Hole Science Aquarium.
*Photo by Jennifer Matysczak, Office of New Animal Drug Evaluation.*

# *ENSURING FEED SAFETY*

## THE CHALLENGE

Threats to the safety of the Nation's animal feed supply could come from several sources. 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 2007 ACCOMPLISHMENTS

Following are highlights of our FY 2007 accomplishments with regard to feed safety. In addition to the actions described below, we 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. We also participated in the development of new regulations intended to provide greater assurance that the manufacture, distribution, and use of all animal feed ingredients and mixed feeds results in safe feed products.

## RISK-BASED SYSTEM – ANIMAL FEED SAFETY SYSTEM

Led by a team consisting of members within and outside CVM, we are developing a nationwide, comprehensive risk-based system designed to prevent contamination. We are designing the Animal Feed Safety System (AFSS) to detect hazards before feed products are distributed, and thus minimize detrimental animal and human health effects. Additional background on AFSS is available on the AFSS page, http://www.fda.gov/CVM/AFSS.htm. We describe some of the AFSS accomplishments during the year in the following paragraphs.

### Public Meeting on Risk Exposure

The AFSS Team used its fourth public meeting, held in May 2007, to present information about methods for determining likely exposure to risks, specifically the concept of exposure scoring for feed contaminants. The exposure scoring system addresses the presence of contaminants in source materials for feed ingredients and those factors in manufacturing or processing that may affect the levels of contaminants in final feed formulations. The AFSS Team used the production of swine feed as an example to illustrate how the risk-ranking method will estimate exposure to contaminants due to the presence of the contaminants in the feed that animals consume.

The Team also discussed the ways that processing steps could increase or mitigate exposure to some of the feed contaminants. The Team used available data, but encouraged the submission of additional data on contaminant levels in both feed ingredients and finished feed, including data on the effects of processing.

### Revision to Draft Framework

The AFSS team revised the Draft Framework document during the year. The document now lists 11 operating principles, an increase from the 7 listed in the first draft framework. It also lists five components, with the addition of a component that emphasizes the importance of complete training for inspectors and outreach to the industry to help firms comply with the feed safety rules. The Draft Framework is available at http://www.fda.gov/cvm/AFSS2ndDraftFramework.html.

### Definitions for Animal Feed Ingredients

As part of the AFSS initiative, CVM in August 2007 signed a Memorandum of Understanding with the Association of American Feed Control Officials (AAFCO) that provides for cooperating to establish definitions for animal feed ingredients. The Memorandum clarifies the responsibilities of FDA and AAFCO during the AAFCO feed ingredient definition process, and provides mechanisms for modifying the process as well as resolving disputes. AAFCO, which is not a regulatory body, provides a mechanism for state

Unloading gluten feed. *Photo by Shannon Jordre, Office of Surveillance and Compliance.*

regulatory agencies to develop and uniformly implement rules, regulations, standards, definitions, and enforcement policies for the manufacturing, labeling, and sale of animal feeds and ingredients in all of the states.

## COMPLIANCE CHALLENGES IN ANIMAL FEED SAFETY

### Sampling for Aflatoxin in Ethanol Byproduct

CVM's Office of Research began method development in FY 2007 to address a potentially significant feed safety issue involving DDG. DDG is the residue from fermented grain, and with the expansion of corn fermentation for ethanol production, increasing amounts of DDG are available for incorporation into animal feeds. The process raises two residue concerns: antibiotics, which are used to kill bacteria prior to seeding corn with yeast; and aflatoxins in the corn, which may be concentrated to high levels in DDG. Both could lead to unhealthful residues in animal feed.

At the end of the fiscal year, the Office of Research had two method development tracks underway for DDG screening by liquid chromatography/mass spectrometry, one for antimicrobials and one for mycotoxins, such as aflatoxin. A comprehensive mycotoxin screen could be used, not only for surveillance of commercial DDG, but also as a general test for counterterrorism and feed security. Our plan is to ask the FDA field offices to collect samples for analysis during FY 2008.

### Self-Inspection of Medicated Feed Manufacturing Facilities

During the year, we issued a draft Compliance Policy Guide[19] that provides guidance to FDA field offices for prioritizing medicated feed manufacturing facilities inspections, based on factors that include whether the facility conducts self-inspections. The draft Compliance Policy Guide describes a proposed approach that medicated feed manufacturing facilities might follow in conducting self-inspections to determine compliance with the Federal Food, Drug, and Cosmetic Act and the appropriate regulations. Self-inspection is a cost-effective method for ensuring the use of prudent feed manufacturing practices and helps the regulatory agencies prioritize their inspections, among other benefits.

### Changes in Veterinary Feed Directive Guidance

During the year, CVM revised its guidance document for Veterinary Feed Directive (VFD)[20] drugs to define the term "appropriately licensed veterinarian" as it pertains to the VFD regulation. Specifically, the term refers to a veterinarian who has a valid license to practice veterinary medicine in the state in which the animals are located and who is treating the animals within the parameters of a valid veterinarian-client-patient relationship. The guidance also now states that the Center considers the Internet an acceptable electronic means of transmitting VFD orders, provided that certain requirements are met. We made these changes in response to requests for clarification made to the Center.

[19] See Draft Compliance Policy Guides Manual, Voluntary Self-Inspection of Medicated Feed Manufaturing Facilities, http://www.fda.gov/ora, under "Compliance References."

[20] Guidance for Industry #120, Veterinary Feed Directive Regulation.

## FOOD AND COLOR ADDITIVES

During the year, we changed our regulations to permit the use of selenium yeast in feed supplements for beef cattle and in salt mineral mixes for free-choice feeding of beef cattle. This approval is the first to allow selenium yeast supplementation other than through its addition to complete feed. We also issued a "Generally Recognized As Safe" affirmation of a source of vitamin D for poultry.

We coordinated the development of a proposed rule to amend the regulations regarding the declaration of certified color additives on the labels of animal food including animal feeds and pet foods. This amendment is in response to the need to make the animal feed regulations consistent with the regulations regarding the declaration of certified color additives on the labels of human food.

## RESEARCH RELATED TO FEED CONTAMINANTS

During FY 2005 and FY 2006, CVM developed and validated two screening methods for detecting 27 drug compounds from 9 chemical classes in feed. Because of the significant time commitment made to melamine method development, our progress during FY 2007 in feed contaminant method development related to other chemical contaminants was limited. Nevertheless, we completed development of a provisional liquid chromatography/mass spectrometry screening method for detecting select organophosphate pesticides and ionophore antimicrobials.

Karen Blickenstaff, a microbiologist with the Division of Animal and Food Microbiology, Office of Research. *Photo by Pat McDermott, Office of Research.*

# *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. FDA is responsible for implementing certain provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 relating to protection of the Nation's food and drug supplies. CVM is working with other federal agencies to help the Nation prepare for a biological emergency, natural disaster, or terrorist attack by making sure there is a safe animal feed supply system.

## FY 2007 ACCOMPLISHMENTS

As we continue to clarify our role and goals with respect to bioterrorism, we have been actively working on initiatives that are in line with Agency, Department, and government-wide priorities.

## BIOTERRORISM VULNERABILITY ASSESSMENTS

In July 2007, CVM and CFSAN participated in the conduct of a CARVER+Shock vulnerability analysis of an animal feed manufacturer in a feed producing region in the central part of the United States. This exercise was part of the Strategic Partnership Program Agroterrorism (SPPA) initiative. SPPA is an ongoing program involving the Department of Homeland Security, Federal Bureau of Investigation (FBI), USDA, FDA, the states, and industry to protect important sub-sectors from a terrorist attack. The information from this year's exercise will be used by industry to harden potential soft targets for terrorists.

The CARVER+Shock vulnerability analysis is a tool that analysts use to determine the desirability of a target to terrorists. "CARVER" is an acronym for criticality, accessibility, recuperability, vulnerability, effect, and recognizability. The "Shock" part of the evaluation is a combination of health, economic, and psychological effects of an attack.

CVM, CFSAN, and FDA's Office of Crisis Management participated in a table-top exercise with a scenario, designed with CVM's assistance that included deliberately contaminated feed. The "virtual" contaminated feed affected the dairy and poultry industries with human illness that also induced a public health response. The exercise focused on communications between the stakeholders in an ongoing outbreak with simultaneous investigations. (A "table top" exercise is intended to focus on the overall response, decision-making process, and coordination and communications with community members; it is not a test of detailed response procedures.) Other participants included representatives from the USDA, FBI, industry, and five states.

CVM assisted the University of Tennessee College of Veterinary Medicine in conducting pilot training for an "Agriculture and Food Vulnerability Assessment Training Program" in Tulare, CA, in January 2007. Other participants were from the wine, dairy, and nut industries, as well as academia.

Ron Miller in Division of Animal Research. Office of Research, working with a high-performance liquid chromography unit. *Photo by Pat McDermott, Office of Research.*

## RESEARCH RELATED TO BIOTERRORISM

The recent attention to biosecurity in animal agriculture has renewed interest in development and evaluation of rapid microbiological screening methods for use in animal feeds and feed commodities. CVM was challenged in a FY 2007 performance goal to develop and adopt methods to culture feeds and feed commodities for the

presence of bacterial pathogens of veterinary and public health significance. Accomplishing this goal meets the Department objective of improving quality, safety, and availability of food products through better manufacturing and product oversight. In addition to contributing to the Center's work on antimicrobial resistance, this work also supports development of the Animal Feed Safety System.

CVM's approach to this challenge has two aspects:

### Establishing a Baseline for *Bacillus* and *Clostridium* Contamination of Animal Feed

Office of Research scientists have conducted survey programs to determine 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. During the past year, the Office of Research completed development and instillation of isolation methods to be used in screening feeds and feed commodities for the presence of the *Bacillus cereus* group (including *B. anthracis*). We will address the development of methods for *Clostridium* in FY 2008. Our objective is to use survey samples collected by the FDA field offices to begin feed analysis to determine baseline rates for *Bacillus* and *Clostridium* spp.

### Sampling of Several Microbial Species for Prevalence and Antibiotic Susceptibility Profiles

This new project will evaluate rapid screening methods for their applicability to feed and feed commodities in the United States. We will establish culture methods to determine the presence and antibiotic susceptibility of various organisms of interest. This program will result in a better assessment of the role animal feed plays in the introduction of pathogens into the animal production environment and will assess the potential for feed to disseminate resistance determinants in the animal population.

The immediate objective is to develop and implement a national swine feed survey. During FY 2007, Office of Research scientists worked with the CVM Division of Animal Feeds and the FDA Office of Regulatory Affairs to sample complete swine feeds for *Salmonella*, *Escherichia coli*, and *Enterococcus* prevalence and to determine antimicrobial susceptibility profiles of recovered isolates.

*Photo by Dan Benz, Office of New Animal Drug Evaluation.*

# *ENSURING THE SAFETY OF ANIMAL CLONES AND ANIMAL BIOTECHNOLOGY*

## THE CHALLENGE

The application of cloning and biotechnology to the production of animals and products derived from animals continues to grow. Animal cloning, an assisted reproductive technology, is seen as a means of expanding populations of cattle, swine, and goats with desired characteristics. Animal biotechnology includes genetic engineering, which involves adding or taking away genes (unlike cloning, which does not change the gene sequence). Genetic engineers are investigating broader ranges of applications in animals. Producing animals through cloning and biotechnology raises potential food and animal safety issues, and CVM needs to act based on a thorough understanding of the scientific and risk issues that are involved.

## FY 2007 ACCOMPLISHMENTS

We focused much of our effort during the year on our draft risk assessment related to animal cloning. However, we also participated in the development of draft guidance on genetically engineered animals. The guidance is intended to acknowledge FDA's regulation of genetically engineered animals and to clarify and formalize FDA's recommendations to producers and developers of genetically engineered animals regarding the commercialization of these animals.

## ANIMAL CLONING

FDA in December 2006 issued for public comment three documents that address the safety of animal cloning: a draft risk assessment,[21] a proposed risk management plan,[22] and a draft guidance for industry.[23] Publication of these documents, accompanied by a communications initiative, met two of CVM's FY 2007 program goals. (Information about the cloning risk assessment and related documents is available on CVM's Web site, www.fda.gov/cvm.)

Calf clones. *Photo courtesy of Cyagra, Inc.*

### Draft Risk Assessment

The risk assessment encompasses livestock species that have been cloned (cattle, swine, sheep, and goats). The document's purposes are to determine whether (1) cloning poses any unique health risks to animals involved in cloning, compared with other assisted reproductive technologies, and (2) foods (human food and animal feed) derived from animal clones or their progeny pose consumption risks greater than those posed by foods derived from animals produced by conventional breeding.

The assessment concluded that:

- Food products from healthy cattle, swine, and goat clones that meet existing requirements for meat and milk in commerce pose no increased food and feed consumption risk(s) relative to comparable

[21] A Risk-Based Approach to Evaluate the Food Safety of Animal Clones and Their Progeny: Data Analysis, Preliminary Conclusions, and Data Needs. DRAFT

[22] Animal Cloning: Proposed Risk Management Plan for Clones and their Progeny – December 29, 2006.

[23] Guidance No. 179 – Guidance for Industry Use of Edible Products from Animal Cloning or their Progeny for Human Food or Animal Feed. DRAFT

products from sexually reproduced animals. The risk assessment did not make a finding with respect to food from sheep clones, because of limited data. In addition, food and feed from any progeny of a clone poses no more risk than food from any other sexually reproduced animal.

- Some animals involved in the cloning process (i.e., cattle and sheep surrogate dams, and some clones) are at increased risk of adverse health outcomes relative to conventional animals. The same adverse outcomes have been observed with other assisted reproductive technologies currently used in agriculture, but cloning increases the frequency of the outcomes. The frequency is expected to decrease as cloning technology improves. Progeny of clones are expected to be normal.

## Proposed Risk Management Plan

The goal of the proposed risk management plan is to identify the relevant issues to be considered in managing risks associated with animal cloning and to present proposed actions to manage those risks. We proposed the risk management plan, even though the risk assessment found little risk, because uncertainties persist in all science judgments. Specifically for the risk assessment, uncertainties arise from three sources: our reliance on empirical[24] data, which was limited; our use of biological assumptions; and, perhaps most importantly, ongoing changes in the technology used to produce clones. The plan discusses these uncertainties in detail. The major features of the plan include surveillance for changes in cloning technology, the state of knowledge that could affect food safety, and measures related to risk to the health of animals involved in cloning.

## Guidance for Industry

The draft Guidance for Industry provides no recommendations for additional safeguards, except that it recommends that edible products from sheep clones not be introduced into the human food supply at this time.

## Voluntary Moratorium

For a number of years, CVM has asked industry to voluntarily refrain from introducing food products from animal clones and their progeny into the human or animal food supply, pending completion of the risk assessment process. FDA reaffirmed its request when it released the draft documents in 2006, which allowed time for the Agency to complete the final documents.

*Photo by Steve Brynes, Office of New Animal Drug Evaluation.*

[24] Empirical refers to that which can be seen or observed alone, often without reliance on theory.

# *ADDITIONAL SURVEILLANCE AND COMPLIANCE ACTIONS TO PROTECT PUBLIC AND ANIMAL HEALTH*

## THE CHALLENGE

Surveillance and compliance activities are key parts of our efforts with regard to addressing the issues of antimicrobial resistance, BSE, drug residues, feed safety, and other crosscutting issues described above. We have had challenges in additional areas that are related to our 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, regulating animal drug compounding, and controlling the marketing of unapproved drugs.

## FY 2007 ACCOMPLISHMENTS

Following are highlights of our accomplishments during the past fiscal year.

## COMPLIANCE ACTIONS

### Risk-Based Inspection Planning

During the year, the Center initiated the use of risk-based assessment methods for identifying firms of highest risk, as part of the inspection planning process. The methods will be applied to drug and medicated feed good manufacturing practices and tissue residue inspections. The risk-based methods use a variety of factors – such as process, product, facility, and time from last inspection – that affect product safety. The use of this process means that the Agency will be utilizing its resources in the inspection of firms associated with the greatest risk of adversely affecting public and animal health. The lists of assignments CVM developed during FY 2007 will be used by our District offices in scheduling inspections during FY 2008.

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

### Inspection of Registered Establishments

We collaborated with ORA to complete the inspection of registered animal drug establishments (domestic and foreign) and 700 feed manufacturing facilities. These are statutorily required biennial inspections to ensure the safety of marketed animal drugs and animal feeds.

### Compliance Action Processing

We received 77 requests for regulatory actions (Warning Letters, injunctions, and seizures) and processed the requests in an average time of 16 working days per request.

### Regulation of Extralabel Use

*Flunixin*. Responding to reports that veterinarians were administering flunixin meglumine by means of an intramuscular route in cattle, FDA published an Update[25] reminding veterinarians that the only approved route is intravenous administration. The intramuscular route may be more convenient for veterinarians, but has the potential to cause violative drug residues; in fact, the Agency has investigated a number of violative drug residues in cattle that resulted from extralabel use of flunixin. Under the Animal Medicinal Drug Use Clarification Act, extralabel use is limited to treatment when the health of an animal is threatened or suffering or death may result from failure to treat. Extralabel use is not permitted where the purpose is to make the administration more convenient.

*Medicated Feed in Minor Species*. Following up on inquiries that indicated possible confusion about extralabel use of medicated feed in minor species, CVM restated the conditions under which such use can be made:

[25] "FDA Reminds Veterinarians on the Correct Use of Flunixin Meglumine," CVM Update May 10, 2007.

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

veterinarian involvement, treatment use only (no extralabel use for production purposes), and no feed reformulation or relabeling.

### Use of Unapproved Clenbuterol in Horses

As a result of the deaths of several horses in Louisiana associated with the use of an unapproved product labeled as "Clenbuterol HCL," CVM issued a warning to horse owners and veterinarians against such use. The warning listed the only approved clenbuterol products.

## SURVEILLANCE ACTIONS

### Adverse Drug Events

During FY 2007, the Division of Surveillance received approximately 36,000 adverse experience reports and was able to review 23,000 of these reports.

The Division has continued to work on the Pilot Vet-Works project, which will facilitate the electronic submission of adverse drug experience reports. This program will enhance the Center's ability to process and evaluate adverse drug experience reports.

We also facilitated Drug Experience Report reviews by implementing a process that converts paper submissions of Drug Experience Report components (such as promotion and advertising documents and labels) to electronic form. This improvement enables electronic review of an entire Drug Experience Report submission, increasing the efficiency of the review process.

### Drug Promotion and Advertising

The Division of Surveillance received more than 5,168 Drug Experience Reports containing promotional labeling and advertising pieces as of August 2007. During the year, the Division reviewed more than 8,700 promotional labeling and advertising pieces submitted by drug sponsors. As a result, the Center in FY 2007 issued five Warning Letters and four Untitled Letters requesting discontinuation of violative labeling and advertising materials, an increase from previous years due to reprioritization of violations as they relate to public health. The issues prompting the letters included unsubstantiated claims for prevention of zoonotic disease (disease that can be transmitted from animals to humans), omission of pertinent information, and inappropriate minimization of risk.

### Labeling Changes

As part of a risk communication initiative, CVM staff reviewed the labeling of all nonsteroidal anti-inflammatory drugs with a focus on improving the level of risk communication and improving the consistency in labeling across the drug class. All the sponsors contacted for changes provided positive responses and the labeling for all the products has been revised.

## Medically Necessary Veterinary Products

We conducted veterinary medical reviews of several animal drug products to determine their Medically Necessary Veterinary Product status and made appropriate recommendations for mitigating drug shortages.

## Drug Listing

To improve the Center's ability to make regulatory decisions about products for which it is responsible, CVM has designed a proactive annual program for updating the list of animal drugs that are in commercial distribution. The program involves mailing to each animal drug manufacturer or distributor a printout of the drug products that are included in the firm's drug product listing, accompanied by instructions to update the list. CVM completed its 2007 Drug Listing Verification Program mailing at the end of June. Information from the verification reports will allow us to evaluate actions that might have to be taken to avoid shortages of medically necessary animal drugs, enhance our ability to conduct our regulatory duties, and help us accurately assess user fees under ADUFA.

*Photo by Alfan Dangin, Office of the Director.*

# *ENHANCING PRODUCTIVITY THROUGH ACHIEVEMENT OF LEADERSHIP AND MANAGEMENT OBJECTIVES*

## THE CHALLENGE

The challenge for the Office of Management was to provide the essential executive leadership and knowledgeable support necessary for CVM to meet the 2007 Departmental objectives for executive leadership and management and certain CVM-specific program objectives. The organization's challenge also includes continued implementation and guidance of the improved management systems and business practices, as outlined by HHS and FDA.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

## FY 2007 ACCOMPLISHMENTS

Through the leadership and active guidance of the Office of Management, the Center successfully met specific objectives for FY 2007, as described in the following significant outcomes and achievements.

## EXECUTIVE LEADERSHIP AND MANAGEMENT RESULTS OBJECTIVES

As summarized above in the section "Accomplishing Department and Agency Objectives," CVM successfully met the FY 2007 Departmental executive leadership and management objectives as applied to CVM's sphere of activity. Here are just a few examples to illustrate:

### Executive Leadership Results Objective: Foster Collaboration

*New Process for Procurement Submissions*. In FY 2007, in collaboration with the FDA Office of Acquisitions and Grants Services, the Office of Management initiated a new process to ensure that all procurement packages are reviewed by a subject matter expert to ensure that the paperwork is complete and correct. The process has decreased the number of questions and amount of paperwork requests between the Center and Office of Acquisitions and Grants Services, resulting in more accurate, timely awards.

### Executive Leadership Results Objective: Develop Staff

*Performance Management Program*. Effective January 1, 2007, CVM implemented the new four-level Performance Management Appraisal Program aimed at aligning individual and organization performance for all non-Senior Executive Service employees. The implementation of the new appraisal system is in compliance with the President's Management Agenda and in accordance with Departmental guidelines. This new process will help employees understand the broader context of how their performance contributes to the success of CVM as a high performing organization.

### Management Results Objective: Recruit, Develop, Retain, and Strategically Manage a World Class HHS Workforce

*Talent Resource Center (TRC)*. During FY 2007, FDA established the TRC, a pilot organization that focuses on FDA's recruitment efforts. The goal of this initiative is to develop a process to bring new hires on board within 45 days of the closing date of an announcement. In support of this effort, CVM's Office of Management has designated a Human Capital Strategy Advisor, who will compile a comprehensive recruitment package for the TRC. This strategic recruitment process will help eliminate delays that were encountered in the past.

## PROGRAM RESULTS OBJECTIVES

In the introductory section, "Accomplishing Department and Agency Objectives," we summarized the outcome of CVM's achievement of the Center-specific program-results objectives. In the following paragraphs, we elaborate on the Center's accomplishments with respect to four of the program results objectives. These objectives, all of which were achieved, have a common focus on leadership and management, and therefore are closely related to the Departmental Executive Leadership and Management objectives.

**Program Results Objective: Provide for the efficient and effective administration of the ADUFA financial program to enhance the review of NADAs and the investigational submissions.**

In addition to meeting the program objective, achievements in this area helped reach the Departmental management-results objective to improve financial performance. For example, we created a baseline invoicing database to facilitate efficient administration of the ADUFA Financial Program. Specific program goals included:

- Develop and publish fee schedules by August 2007.

The Office of Management developed and announced rates and payment procedures for FY 2008 animal drug user fees in a notice published in the August 2, 2007, *Federal Register*. Thus, fees were established within 60 days before the start of the new fiscal year, as required by ADUFA.

- Provide a proactive and timely response to industry and citizen requests for information on billings, fees, and payments.

We developed a process so that ADUFA electronic mailbox and voice messages are checked daily, so that questions are answered in a timely manner. In addition, we posted "CVM Updates" on the CVM Internet site when critical information related to ADUFA was released from the Agency.

**Program Results Objective: Provide staff and management with the mechanism to run reports and utilize the hourly cost and data to better manage resources and programs.**

In addition to meeting the program objective, achievements in this area helped achieve the Departmental Executive Leadership Objective to Ensure Accountability for Business Results. Specific program goals included:

- The release of the Consolidated Reporting Environment (CRE), which houses hourly and cost data.

The CRE, released in production (which means that the data for this reporting application were made available to an appropriate group of employees for everyday use) in August 2007, is a real-time environment that allows users to obtain hourly and cost data down to the reference identification level (lower level/subset of an activity). Users can access canned reports, query data, and run *ad hoc* reports. This effort assists the Center in understanding the true costs of doing business, which in turn assists in leveraging assets. As a result, CVM can better manage its resources and programs to ensure that they are aligned with the Agency and Department goals.

**Program Results Objective: Create opportunities for greater collaboration of scientific data through the NARMS within CVM.**

We met a program goal by successfully developing and implementing the NARMS application in the Center's Web-based Corporate Database Portal. As a result, CVM/FDA can better determine the prevalence of antimicrobial resistance among *Salmonella*, *Campylobacter*, *Escherichia coli* and *Enterococcus* isolated from meat and poultry purchased from selected grocery stores. This NARMS application provides CVM, FDA, and HHS personnel with necessary information to help expedite the antimicrobial drug approval process, as well as providing necessary post-approval monitoring information that will facilitate FDA's response to public health threats.

**Program Results Objective: Broaden the scope and curriculum of the CVM Staff College/University of Maryland collaboration that offers a Master of Public Health (MPH) degree with concentration in veterinary public health to include eligible employees from elsewhere in the Agency and Department (through HHS University).**

In addition to meeting the program objective, accomplishments in this area helped achieve the Departmental Executive Leadership Results Objectives to develop staff and foster collaboration. Specific program goals included:

- Initially explore a working partnership with other Agency centers to join with CVM in offering the MPH degree program to eligible employees.

The CVM Staff College initiated meetings with other Staff College Directors in other centers throughout the Agency to determine the level of interest. The staff then explored creative and productive ways to collaborate, develop, implement, and evaluate an MPH program working in partnership with the University of Maryland, Baltimore School of Public Health.

- Engage in the development of the MPH degree program to include those centers that express interest in the program.

The collaborative MPH degree program, with concentration in veterinary public health, started with the offering of Principles of Epidemiology and Exposure, Risks, and Public Health in 2006. Two courses were offered in the fall of 2007: Principles of Epidemiology and Pharmacoepidemiology in Veterinary Medicine. These courses are offered Agency-wide to all eligible employees.

## VIRTUAL TRAINING OFFERED BY CVM STAFF COLLEGE

During the year, Office of Management created within the CVM Staff College a virtual environment using Internet technology to connect CVM scientists with colleagues and educators around the world. The first course, Pharmacoepidemiology in Veterinary Medicine (part of the new MPH program), was offered in Fall 2007. The instructor, from the University of Maryland (UMD) School of Pharmacy, facilitated lectures designed for collaborative interactions via the Internet with CVM staff in the CVM Staff College Computer Laboratory, their own office, or on their home desktop computers. Other professionals from UMD also participate in this program.


CVM Staff College; students can attend in person, or remotely through virtual training. *Photo by Jon Scheid, Office of the Director.*

# *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 available resources. Our success in promoting and protecting the public health depends in large part not only on active involvement by our stakeholders, but also partnerships with those whose goals align with ours.

*Photo by Bernadette Dunham, Office of the Director.*

## FY 2007 ACCOMPLISHMENTS

We continued work under a number of partnering arrangements during the year. These mutual-benefit arrangements have influenced CVM policies and practices and have enhanced our research and epidemiological efforts.

Twenty 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 the FY 2007 FDA awards ceremonies. This large number of award winners is a powerful demonstration of CVM's extensive involvement in leveraging and collaboration arrangements.

To illustrate the importance of collaboration with others outside CVM, we set out below an example related to each of the major areas of accomplishment that are included in this year's Annual Report.

Drug approvals. Proactive initiatives to facilitate animal drug approvals to meet critical health needs – including human health – are part of our mission. For example, CVM has engaged representatives from the cattle industry, pharmaceutical industry, and USDA to form a coalition to collaboratively work within our respective areas to reduce/eliminate *Escherichia coli* O157:H7 from human food.

Companion Animal Health. There were many examples of effective collaboration and resource leveraging during the pet food recall, including:

- FDA shared information and worked with its regulatory partners in all 50 state agricultural and health agencies, and we collaborated on investigative and analytical efforts.
- We coordinated with Banfield, the Pet Hospital®, a nationwide network of veterinary hospitals, whose extensive database of the animals it treats was especially helpful in determining the prevalence of acute renal failure in cats and dogs.
- We worked with the Veterinary Information Network, the American Society for the Prevention of Cruelty to Animals, university faculty, and others to help us assess the extent of the outbreak.
- The American Veterinary Medical Association and other professional organizations partnered with us, providing advice and communicating important information to the public.
- FDA and the Food Safety Inspection Service of the U.S. Department of Agriculture, in consultation with the Centers for Disease Control and Prevention, the EPA, and the Department of Homeland Security, prepared an interim safety/risk assessment on melamine and related compounds during the pet food recall. The Agency prepared the interim report in response to an ongoing investigation of contaminated vegetable protein products imported from China that were mislabeled as "wheat gluten" and "rice protein concentrate."

The experience solidified CVM's relationships with many of these groups, so that the Agency can in the future utilize their databases, expertise, and networks to facilitate investigations of emerging crises and improve the reporting of illnesses by veterinary professionals.

Minor Uses/Minor Species. CVM's FY 2007 approval of 35% PEROX-AID® (hydrogen peroxide) for three indications was a direct result of collaboration between the public and private sectors. In addition to work by the sponsor, the U.S. Geological Survey's Upper Midwest Environmental Sciences Center, La Crosse, WI, generated effectiveness and target animal safety data in addition to the environmental assessment needed for the approval and made these data available in a public master file. This kind of collaboration is fostered by the Annual Aquaculture Drug Approval Coordination Workshop that brings together participants from aquaculture companies, the pharmaceutical industry, and chemical companies, as well as state and federal agencies.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

Antimicrobial Resistance. Research is an essential component of the Center's efforts to control the development and transfer of animal-originated antimicrobial resistance. The importance of collaborative efforts with scientists from the academic world is underscored by the fact that during the fiscal year CVM researchers worked with scientists from the Max Planck Institute, North Carolina State University, The Ohio State University, University of Maryland, University of Minnesota, and Iowa State University on various projects related to antimicrobial resistance.

BSE. The value of collaboration with industry is seen in the development and dissemination of the video for truckers, "Preventing the Spread of BSE," which was the result of a collaborative effort involving CVM and FDA's Office of Regulatory Affairs, working with the American Feed Industry Association, the National Grain and Feed Association, and the National Renderers Association.

Animal Drug Residues. During the year, CVM and FDA continued to work closely with partners in state and federal agencies in a combined effort to limit the occurrence of illegal drug residues in edible animal products. For example, one mechanism for interaction between federal agencies is the Interagency Residue Control Group (IRCG), consisting of representatives of FDA, several USDA agencies, and the EPA. The IRCG's objective is to attempt to solve the complex problem of tissue residue violations through communication and cooperative efforts in investigation and enforcement.

Animal Feed Safety. The August 2007 signing of a Memorandum of Understanding with AAFCO to cooperate on the definitions for animal feed ingredients provides a timely opportunity to acknowledge an important

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

collaborative relationship. The Association is a voluntary organization comprised largely of regulatory officials who have responsibility for enforcing their state's laws and regulations concerning the safety of animal feeds. Its membership is comprised of representatives from each state in the United States, as well as representatives from Puerto Rico, Costa Rica, Canada, FDA and USDA.

Protecting Against Bioterrorism. A partnership example is the SPPA initiative, under which CVM, FDA, and other federal agencies collaborate 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.

Animal Cloning and Biotechnology. The publication of our draft risk assessment on animal cloning provides an occasion to highlight international partnerships. We are working with international groups with expertise in cloning, assisted reproductive technologies, and animal health to develop animal care standards to help manage animal health risks associated with cloning. We are also developing an international clone database in association with the International Embryo Transfer Society.

Achieving Leadership and Management Objectives. Creation of a virtual environment within the CVM Staff College makes it possible to connect CVM scientists with colleagues and educators around the world using Internet technology. Such virtual technology will provide participating staff the opportunity to develop cross-cultural communication and global scientific collaboration to maintain cutting edge-science in the 21st century. In addition, collaboration with the University of Maryland, Baltimore, to create opportunities for CVM reviewers to earn an MPH degree, with concentration in veterinary public health, will provide expertise that will facilitate a more effective response to veterinary public health issues.

## *COMMUNICATING WITH STAKEHOLDERS*

### THE CHALLENGE

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 need to have their questions answered and know what steps CVM has taken to protect the food supply and keep their pets safe. CVM must present clear information to diverse audiences about programs and initiatives that are sometimes technical and usually quite complex. 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.

### FY 2007 ACCOMPLISHMENTS

We undertook a broad range of initiatives to provide important information on public health issues and CVM programs and accomplishments during the year. Our Communications Staff provides leadership in many of the Center's outreach initiatives, but all of our offices also provide leadership and play active roles in the Center's effort to communicate with our constituents. The following highlights illustrate the range of Center-wide participation in communications efforts.

### PET FOOD RECALL

CVM provided timely written and oral information for consumers about the pet food recall and disseminated it through FDA's Web site, press interviews, and interactions with individuals via our consumer line and home page e-mail inquiries. We developed, posted, and frequently updated press releases, "Frequently Asked Questions," a searchable pet food recall list, and other sources of information. At the height of the recall, CVM's Communications Staff received and responded promptly to between 50 and 75 phone calls daily. In addition, the Staff responded to more than 5,000 home page e-mail inquiries and comments.

Some of the highlights included the following.

Web site information. We used FDA's and CVM's Web sites to give consumers the sometimes complex information about the recall in the most user-friendly, straightforward way possible. We also posted all recall press releases. During the first 2 months following the recall, CVM's Web site received more than 1.3 million hits on its recall-related pages (the FDA Web site had 6.1 million hits related to the recall).

Posting analytical information. To get manufacturers involved in preventing the further spread of the problem, we posted analytical methods on our Web site that companies could use to test for melamine and related compounds in ingredients.

Reminder to feed and pet companies. We posted an open letter on CVM's Web site reminding feed and pet food manufacturers that they are legally responsible for making sure the ingredients they use are safe and that they should have procedures in place to ensure ingredient safety.

Partnering with the press. FDA scheduled telephone briefings twice weekly to recap events, explain new developments, and answer reporters' questions. FDA held 13 scheduled press briefings during the 2 months following the first recall.

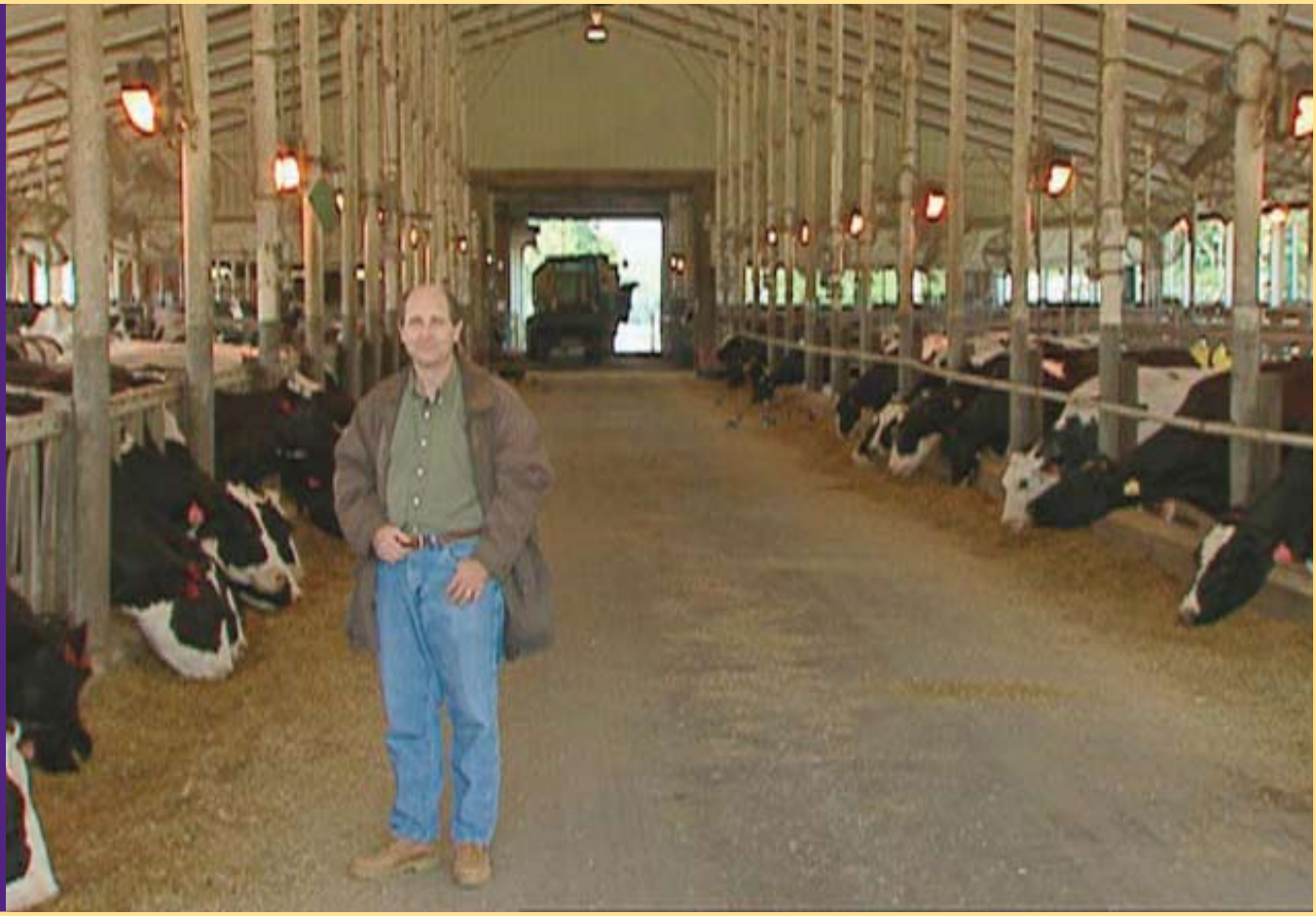
These actions and others helped CVM meet the performance objective of enhancing consumer protection and empowering consumers with better information about regulated products.

## ANIMAL CLONING RISK ASSESSMENT

A Center performance goal was to plan and lead a communication effort for the release of the draft risk assessment and related documents on animal clones and their progeny. We arranged for numerous press calls and media interviews at the time of the release of these documents. In addition, CVM posted the draft documents on its Web site along with a CVM Update and additional background materials related to animal cloning. This included three consumer information documents the Center prepared – "Cloning Primer," "FAQs (Fequently Ask Questions) for Consumers," and "Cloning Myths."

## BSE TRUCKER VIDEO

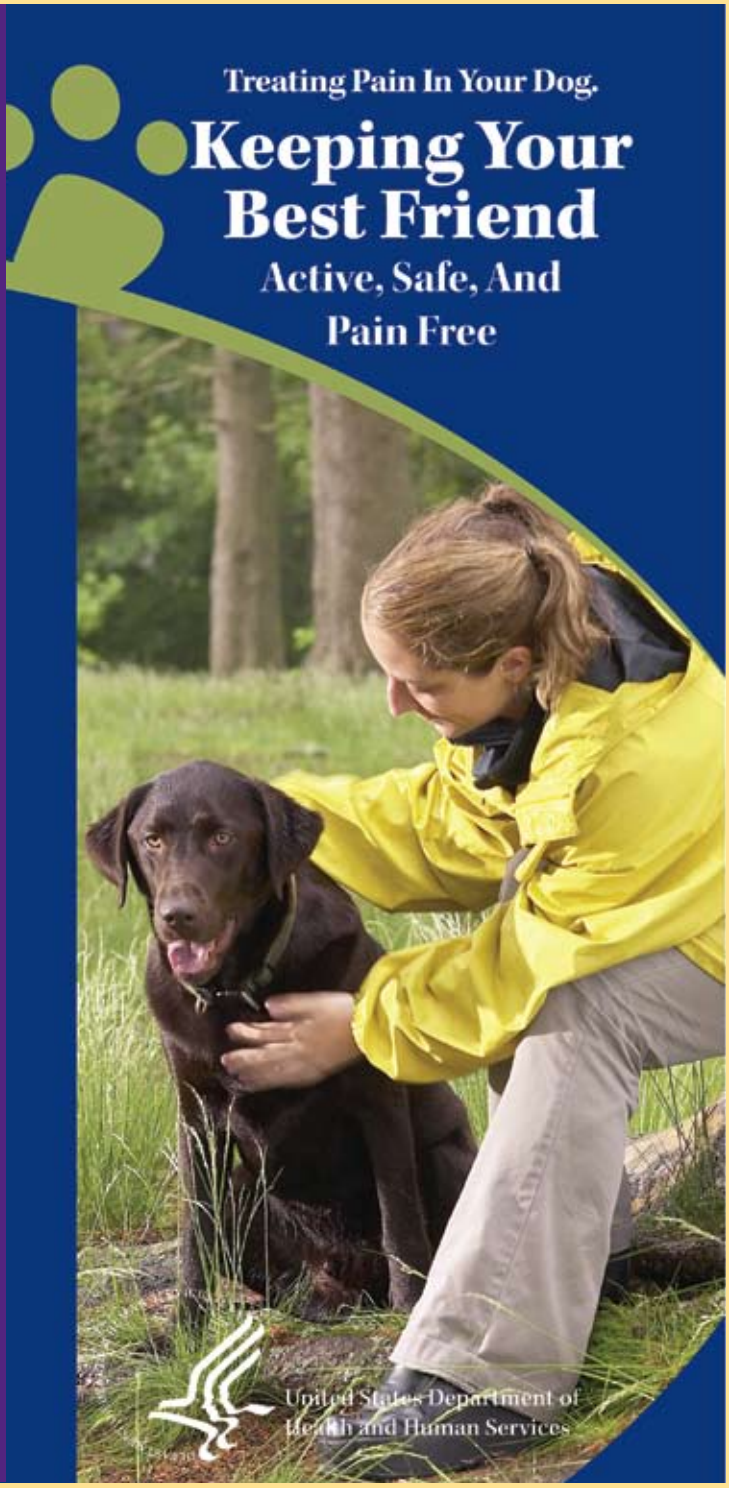
One of our performance goals is to communicate with livestock producers, veterinarians, industry, and the public to ensure a clear understanding and acceptance of FDA veterinary programs and policies. A significant achievement was the video/DVD for ingredient truck drivers, which explains the truck cleanout procedures to prevent cross-contamination of feed ingredients with prohibited material. Trade associations representing the feed industry distributed more than 1,500 copies to member trade organizations and state/regional grain and feed association members. In addition, many feed manufacturers are copying and sending the video to their feed mills. The video has won several awards, including a "Communicator Award" Award of Distinction, bronze "Mercury Award," Gold Screen award from the National Association of Government Communicators, and a Bronze statue from the Telly Awards.



*From the CVM video, "Preventing the Spread of BSE."*

## NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) FOR DOGS

As part of a broad strategy to facilitate proper use of NSAIDs and specifically to educate dog owners about the side effects of NSAIDs, we published a 2-page brochure, "Treating Pain in Your Dog." By the end of the fiscal year, we had mailed more than 9,500 copies. We worked with the Veterinary Information Network, American Animal Hospital Association *NEWStat*, and the American Veterinary Medical Association to announce availability of the brochure and post links to it. We also arranged with the U.S. General Services Administration's Federal Citizen Information Center for promotion and free distribution of our brochure. In recognition of its efforts, CVM's NSAID Education Outreach Team received a CVM Team Excellence Award during 2007 award ceremonies.



NSAID brochure cover.

## ADDITIONAL COMMUNICATIONS ACCOMPLISHMENTS

Other accomplishments included:

- Providing responses to FDA's Office of Public Affairs on more than 190 inquiries from media organizations concerning the cloning risk assessment, SLENTROL™, cefquinome, the New Animal Drug Application approval process, POSILAC®, CERENIA™, roxarsone, genetically engineered animals, the pet food recall, and many other subjects.
- Responding to more than 300 CVM home page inquiries on topics that included animal cloning, illegal sale of turtles, exporting/importing pet food, regulations on pet treats and pet food, veterinary medical devices, Internet drug sales, and how to access the Adverse Drug Experience database.

## WEB SITE INNOVATIONS

During the year, we:

- Drafted and launched a new Web page on CVM – Information for Dog Owners http://www.fda.gov/cvm/infodogowners.htm, which compiles and consolidates information related to dogs.
- Drafted and launched a newly revised page on CVM's regulation of turtles http://www.fda.gov/cvm/turtles.htm.
- Redesigned and updated the CVM Aquaculture Page with a "front" page and table of contents, http://www.fda.gov/cvm/aqualibtoc.htm.
- Made revisions in the NARMS page and the MUMS Act drug designation page.

*Photo by Devaraya R. Jagannath, Office of New Animal Drug Evaluation.*

# APPENDIX A

## 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 regulations. This responsibility includes ensuring that rules comply 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 – Supplements and Other Changes to Approved New Animal Drug Applications. December 13, 2006.

Final Rule – Designation of New Animal Drugs for Minor Uses or Minor Species. July 26, 2007.

### Guidances

Draft Guidance for Industry #181 – Blue Bird Medicated Feed Labels. October 27, 2006.

Guidance for Industry #35 – Bioequivalence. (Revised.) November 8, 2006.

Draft Guidance for Industry #179 – Use of Edible Products from Animal Clones or Their Progeny for Human Food or Animal Feed. December 28, 2006.

Guidance for Industry #183 – Animal Drug User Fees: Fees Exceed Costs Waiver/Reduction. March 9, 2007.

Guidance for Industry #150 – Concerns Related to the Use of Clove Oil as an Anesthetic for Fish. (Revised.) April 24, 2007.

Guidance for Industry #136 – Protocols for the Conduct of Method Transfer Studies for Type C Medicated Feed Assay Methods. April 26, 2007.

Guidance for Industry #137 – Analytical Methods Description for Type C Medicated Feeds. May 8, 2007.

Guidance for Industry #83 – Chemistry, Manufacturing and Controls Changes to an Approved NADA or ANADA. May 30, 2007.

Draft Guidance for Industry #143 – Pharmacovigilance of Veterinary Medicinal Products: Controlled List of Terms - VICH GL30. (Revised.) June 20, 2007.

Guidance for Industry #59 – How to Submit a Notice of Claimed Investigational Exemption in Electronic Format to CVM. June 29, 2007.

## Other Documents

Animal Drug User Fee Rates and Payment Procedures for FY 2008. August 2, 2007.

*Photo by Michelle Stull, Office of New Animal Drug Evaluation.*

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

# Appendix B

## Significant Drug Approvals

### Original Approvals

**IVERHART MAX™ (ivermectin/praziquantel/ pyrantel pamoate)**

An original combination approval for treatment of roundworms, hookworms, and tapeworms and for the prevention of heartworm disease in dogs.

**ANTISEDAN® (Atipamezole hydrochloride)**

A supplemental approval to reverse the sedative and analgesic effects of dexmedetomidine hydrochloride in dogs.

**DEXDOMITOR® (dexmedetomidine hydrochloride)**

An original approval as a sedative and analgesic and as a pre-anesthetic in dogs.

**ADVANTAGE MULTI™ (moxidectin/imidacloprid)**

An original combination approval for treatment of roundworms, hookworms, whipworms, and fleas and for the prevention of heartworm disease in dogs.

**ADVANTAGE MULTI™ (moxidectin/imidacloprid)**

An original combination approval for treatment of roundworms, hookworms, ear mites, fleas and for the prevention of heartworm disease in cats.

**SLENTROL™ (dirlotapide)**

An original approval for the management of obesity in dogs.

**RECONCILE® (fluoxetine hydrochloride)**

Original approval for the treatment of separation anxiety in dogs in conjunction with behavior modification.

**CERENIA™ (maropitant citrate tablets)**

An original approval for the prevention of acute vomiting and prevention of vomiting due to motion sickness in dogs.

**CERENIA™ (maropitant citrate injectable)**

An original approval for the prevention and treatment of acute vomiting in dogs.

**WORMXPlus™ (praziquantel/pyrantel pamoate)**

Original combination approval for the treatment of roundworms, hookworms, and tapeworms in dogs.

**PROTAZIL™ (diclazuril)**

An original approval for the treatment of Equine Protozoal Myeloencephalitis.

**VETMEDIN® (pimobendan)**

An original approval for the management of congestive heart failure due to atrioventricular valvular insufficiency or dilated cardiomyopathy in dogs.

**PROFENDER® (praziquantel/emodepside)**

Original combination approval for the treatment of roundworms, hookworms, and tapeworms in cats.

**ETOGESIC® Injectable (etodolac)**

An original approval for the control of pain and inflammation associated with osteoarthritis in dogs.

**COMFORTIS® (spinosad)**

An original approval to kill fleas and for the prevention and treatment of fleas on dogs for one month.

## Original Generic

**SMZ-Med™ 454 (sodium sufamethazine) Soluble Powder**

An original ANADA for use in chickens, turkeys, swine, and cattle. For treatment and control of disease caused by organisms sensitive to sulfamethazine. It is a generic copy of SULMET™ (sodium sulfamethazine) Soluble Powder.

**RESPIRAM™ (doxapram hydrochloride)**

An original ANADA for use in dogs, cats, and horses to stimulate respiration during and after anesthesia; to speed awakening and return of reflexes after anesthesia in dogs, cats, and horses; and to stimulate or initiate respirations following cesarean or dystocia in neonate dogs and cats. It is a generic copy of Dopram®-V Injectable.

**NOROMECTIN® (ivermectin) Injection**

An original ANADA for the treatment and control of gastrointestinal roundworms, lungworms, grubs, sucking lice, and mange mites in cattle; and for gastrointestinal roundworms, lungworms, lice, and mange mites in swine. It is a copy of IVOMEC® (ivermectin).

**PRIMEX® (pyrantel pamoate) Equine Liquid Wormer**

An original ANADA is an over-the-counter generic product for the removal and control of mature infections of large strongyles, pinworms, large roundworms, and small strongyles in horses and ponies. It is a generic copy of PAMOBAN (pyrantel pamoate) Horse Wormer.

**NOROMECTIN® (ivermectin and clorsulon) PLUS Injection**

An original ANADA approved for the treatment and control of internal parasites, including adult liver flukes, and external parasites in cattle. It is a copy of IVOMEC® (ivermectin and clorsulon) PLUS.

**Melengestrol acetate, monensin sodium, ractopamine hydrochloride**

An original ANADA for the use of a Type A medicated article, HEIFERMAX™ 500 (melengestrol acetate), in combination with OPTAFLEXX™ (ractopamine hydrochloride) and RUMENSIN® (monensin) sodium for the manufacture of three-way Type B or Type C medicated feeds. This combination product is a generic copy of MGA® 500 (melengestrol acetate) plus OPTAFLEXX™ and RUMENSIN®.

**Oxytet™ 10 (oxytetracycline HCL)**

An original ANADA to treat various infections in cattle. It is a generic copy of MEDAMYCIN®-100 Injectable.

**TETROXY® (oxytetracycline hydrochloride) Aquatic**

An original ANADA to mark skeletal tissues, most often the otoliths, of all finfish fry and fingerlings for subsequent identification. It is a generic copy of OXYMARINE™ (oxytetracycline hydrochloride) soluble powder.

**Lasalocid sodium, melengestrol acetate**

An original ANADA approval for the use of HEIFERMAX™ 500 (melengestrol acetate) in combination with BOVATEC® (lasalocid sodium). Type A medicated articles are approved for use in combination of two-way Type B or Type C medicated feeds. It is a copy of MGA® 500 (melengestrol acetate) in combination with BOVATEC® (lasalocid sodium).

**SUPERIORBUT® (phenylbutazone) Powder**

An original ANADA for the relief of inflammatory conditions associated with the musculoskeletal system of horses. It is a generic copy of Phenylbutazone (phenylbutazone) Tablets.

**Ampicillin sodium**

An original ANADA approval for the use of Ampicillin sodium, sterile powder, in horses for the treatment of respiratory tract, skin, and soft tissue infections caused by susceptible organisms. It is a generic copy of AMP-EQUINE (ampicillin sodium).

**Glycopyrrolate Injectable (0.2 mg/mL)**

This is an original approval for use as a pre-anesthetic anticholinergic agent for use in dogs and cats. It is a generic copy of ROBINUL®-V Injectable.

**Neomycin Liquid (neomycin sulfate)**

An original approval for the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin sulfate in cattle, swine, sheep, and goats. It is a generic copy of BIOSOL® Liquid (neomycin sulfate).

**Gentamicin (gentamicin sulfate) Piglet Injection**

An original approval for the treatment of porcine colibacillosis caused by strains of *Escherichia coli* sensitive to gentamicin. It is a generic copy of GARACIN® Piglet Injection.

**Clindamycin Oral Drops (clindamycin hydrochloride)**

An original ANADA for use in dogs and cats for treatment of infections caused susceptible organisms. It is a copy of ANTIRODE AQUADROPS.

**Lincomycin-Spectinomycin Water Soluble Powder**

An ANADA for use as an aid in the control of air sacculitis casused by either *Mycoplasma synoviae* or *Mycoplasma gallisepticum* susceptible to lincomycin-spectinomycin and complicated chronic respiratory disease (air sac infection) caused by *Escherichia coli* and *Mycoplasma gallisepticum* susceptible to lincomycin-spectinomycin in chickens up to 7 days of age. It is a generic copy of L-S 50 Water Soluble Powder.

**Butorphanol Tartrate Injection**

An original ANADA for the relief of pain in cats caused by major or minor trauma or pain associated with surgical procedures. This product is a generic copy of TORBUGESIC-SA® (butorphanol tartrate).

**Formacide-B (formalin)**

This is an original generic approval for use in the environmental water as a parasiticide for all cultured finfish, penaeid shrimp, and as a fungicide for all finfish eggs. It is a generic copy of PARASITE-S® (formalin).

**Gentamicin Sulfate (gentamicin sulfate, betamethasone valerate) Topical Spray**

An original ANADA for use in dogs for treatment of infected superficial lesions caused by bacteria sensitive to gentamicin. This product is a generic copy of GENTOCIN® Topical Spray.

**MURICIN™ (mupirocin) Ointment 2%**

An original approval for dermatological use in dogs for topical treatment of bacterial infections of the skin. It is a generic copy of BACTODERM® Ointment.

## New Minor Species Approvals

**HYDROGEN PEROXIDE**

Administrative NADA approval for 35% PEROX-AID® for the control of mortality in freshwater-reared finfish eggs due to saprolegniasis, for the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium branchiophilum*, and for the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare* (*Flexibacter columnaris*).

**FLORFENICOL**

Supplemental approval for the control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilum*.

## Conditional Approval

**FLORFENICOL**

Conditional Approval granted for the control of mortality in catfish due to columnaris disease.

## Supplemental Approvals

**Dexmedetomidine ghydrochloride**

This supplemental NADA provides for addition of feline species for the sedation/analgesia indication.

**Tulathromycin**

This supplemental NADA provides for the addition of *Mycoplasma bovis* to the list of target pathogens for the bovine respiratory disease control at high risk indication.

**Florfenicol**

This supplemental approval for the control of mortality in freshwater-reared salmonids due to coldwater disease.

## New Dosage Form

**Estradiol, trenbolone acetate**

This original approval is for the use of an implant containing 200 mg trenbolone acetate and 40 mg estradiol (REVALOR-XS) as a slow-release delivery system that increases rate of weight gain and improves feed efficiency for up to 200 days in steers fed in confinement for slaughter.

## New Species/Class

**NUFLOR® (florfenicol)**

This original approval is for an antibiotic Type A medicated article for swine.

## Revised Labeling

**Tylosin phosphate**

This supplement provides for the addition of an alternative feeding regimen for the control of porcine proliferative enteropathies (PPE, ileitis) to include "feed 100 g tylosin per ton of complete feed for at least 3 weeks. Follow with 40 g tylosin per ton of complete feed until pigs reach market weight." Additional corrections to regulation.

**Ivermectin**

The effect of the supplement is to add claims to the generic labeling that are no longer protected by 3 years of marketing exclusivity and to incorporate CVM-requested labeling changes to the Environmental Safety section, Disposal statement, and Residue Information. This product is a generic copy of IVOMEC® (ivermectin) Pour-on for Cattle.

## Publication of Data Availability

**Hydrogen peroxide**

Announcement of data available in Public Master File 5639 for the effectiveness and safety of hydrogen peroxide.

## Rx/OTC Status Change

**Oxfendazole**

Approved change of marketing status from prescription to over-the-counter for the 22.5% bovine oxfendazole formulation only. The grounds for this change are based on relinquishing the intra-ruminal route of administration.

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

# APPENDIX C

## CVM* 2007 HONOR AWARD RECIPIENTS

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

### FDA COMMISSIONER'S SPECIAL CITATION

***Andrew J. Beaulieu, D.V.M.***

For an outstanding career dedicated to public service, superior managerial performance, and excellence in regulatory science to support the Agency's critical public and animal health mission.

***CVM Avian Influenza Rapid Response Team***

For demonstrated international leadership in pandemic influenza preparedness as it directly relates to the avian influenza virus.

***CDR Alfred W. Montgomery***
***Mary C. Carson, Ph.D.***
***William T. Flynn, D.V.M.***
***Jeffery S. Jones, D.V.M., Ph.D.***
***Beth E. Karp, D.V.M., M.P.H.***
***Dragan Momcilovic, D.V.M., Ph.D.***
***Terry A. Proescholdt, D.V.M., Ph.D.***
***Jeffrey L. Punderson, D.V.M.***
***Jon F. Scheid***
***Nadine R. Steinberg, J.D.***
***Kim R. Young***

### AWARD OF MERIT

***Glenn A. Peterson, Ph.D.***

For collaboration and leadership in developing Agency-wide standards and in promoting excellence in post-marketing safety reviews and product quality processes for FDA and internationally.

***Roxanne K. Schweitzer***

For exceptional leadership managing CVM's financial management program contributing significantly to the Center and Agency's public health mission.

### OUTSTANDING SERVICE AWARD

***Karen S. Alder***

For outstanding leadership in application development, effective management of technology resources, and superior efforts to leverage existing technology solutions for business process improvements.

***Rachel A. Breeden***

For outstanding performance and personal initiative transitioning and implementing CVM from Travel Manager to GovTrip, the new Agency travel management system.

***Orton J. Cartwright***

For extraordinary leadership and accomplishment in review of an FDA study.

Color Guard for CVM's Award Ceremony in May 2007.
*Photo by Catherine Brown, Program Support Center, HHS.*

***Angela K. Clarke, D.V.M.***

For sustained superior performance reviewing new animal drug applications and for significant contributions to Center scientific policy development.

***Lesley J. Groves***

For her teamwork, mentoring, timeliness, and high quality work that supports the Office in the receipt of electronic submission and the archiving of electronic files.

***Connie R. Mahon***

For superior performance and exceptional contributions to the CVM Staff College, as well as demonstrating a strong commitment as a productive, effective team player.

***Anna B. Nevius, Ph.D.***

For sustained superior performance in recruiting biostatisticians to CVM and in leading a high-performing statistics review team.

***David G. White, Ph.D.***

For extraordinary leadership and accomplishment in addressing scientific and regulatory issues related to antimicrobial resistance in foodborne pathogens.

***Linda M. Wilmot, D.V.M.***

For sustained exemplary performance in fostering collaboration and scientific excellence within the Team, Division, and Office.

## GROUP RECOGNITION AWARD

***ADUFA Collection Management Module Team***

For superior performance despite stringent budget and time constraints in building a fully automated process for managing Animal Drug User Fee Act user fee collection.

***Charles E. Eastin, D.V.M., Ph.D., M.P.H., DACVPM***
***Lowell P. Fried (deceased)***
***Charise S. Kasser, Pharm.D.***
***A. Robert Miller***
***David R. Newkirk, Ph.D.***
***Glenn A. Peterson, Ph.D.***
***Herman M. (Marty) Schoenemann III, Ph.D.***
***Margaret A. Zabriski, Ph.D.***
***Contractor Team Members (Booz Allen Hamilton)***
***Jill Kay***
***Irina Degileva***
***Anna Filina***
***Heather Goodman***
***Angela Loui***
***Esperanza Greene***

***Animal Cloning Risk Assessment Roll Out Group***

For outstanding teamwork in developing, coordinating, and conducting the national and international public roll-out of the FDA's Animal Cloning Risk Assessment.

***Amey L. Adams, Ph.D.***
***M. Cecilia Aguila, D.V.M.***
***Michaela G. Alewynse, Ph.D.***
***Mary J. Bartholomew, Ph.D.***
***Catherine P. Beck***
***Rial A. Christensen, Ph.D.***
***Siobhan M. DeLancey***
***Eric S. Dubbin, D.V.M.***
***William T. Flynn, D.V.M.***
***Tracey H. Forfa, J.D.***
***Linda A. Grassie***
***Kevin J. Greenlees, Ph.D.***
***Barry H. Hooberman, Ph.D.***
***Christopher T. Horstkamp***
***Jeffrey S. Jones, D.V.M., Ph.D.***
***Vashti D. Klein***
***John C. Matheson, III***

***Thomas J. Moskal, D.V.M.***
***Julia A. Oriani, Ph.D.***
***Larisa Rudenko, Ph.D.***
***Timothy C. Schell, Ph.D.***
***Cuc N. Schroeder***
***Stephen F. Sundlof, D.V.M., Ph.D.***
***Steven D. Vaughn, D.V.M.***

***Microbial Food Safety Team***

For sustained and exceptional team expert contribution to Center, Agency, and Inter-Agency on issues of antimicrobial resistance due to non-human drug uses and many other emerging but challenging issues.

***Bernadette Abela-Ridder, D.V.M., Ph.D.***
***Jeffrey M. Gilbert, Ph.D.***
***Joshua R. Hayes, Ph.D.***
***Roger A. Jones, Ph.D.***
***Karen E. R. Lampe, Ph.D.***
***Ruby Singh, Ph.D.***
***S. Steve Yan, Ph.D.***

***ONADE SOP Working Group***

For ongoing and dedicated service in developing and revising Standard Operating Procedures that ensure the efficient and effective review and approval of new animal drugs.

***Mary E. Allen, Ph.D.***
***Kristen L. Anderson, Ph.D.***
***Steven M. Fleisher, D.V.M.***
***Lynn G. Friedlander, Ph.D.***
***Harlan J. Howard, Ph.D.***
***Rosilend A. Lawson, V.M.D.***
***Virginia F. Recta***
***Michelle "Chellie" L. Stull, D.V.M.***
***Katherine P. Weld, Ph.D.***

## LEVERAGING/COLLABORATION AWARD

***Aflatoxin in Pet Food Investigation and Recall Group***

For exceptional effort in the investigation and removal of elevated aflatoxin contaminated pet food.

***William J. Burkholder, D.V.M.***
***Karen B. Ekelman, Ph.D.***
***Linda A. Grassie***
***Michael H. Henry, Ph.D.***
***Shannon T. Jordre***
***Randall A. Lovell, D.V.M., Ph.D.***
***Barbara A. Rodgers***
***Jon F. Scheid***
***Merton V. Smith, II., Ph.D., J.D.***
***Michael R. Talley, D.V.M.***
***Kim R. Young***

***Ana Haydée Fernández, D.V.M.***

For outstanding efforts in working with regulatory agencies and others in Latin America to promote understanding and acceptance of CVM's human food safety standards.

***CVM Learning Management System Evaluation Team***

For exceptional collaboration effort in support of FDA and HHS University's major initiative to evaluate and select a single, Department-wide Learning Management System.

***Connie R. Mahon***
***Karen L. Tracey***
***Sherri Stephenson-Washington***

***Shannon T. Jordre***

For significant and exceptional performance in managing the Center for Veterinary Medicine's BSE Compliance Program.

***Quality Assurance Training Session Team***

For providing exceptional scientific and regulatory expertise in the collaborative development and presentation of training session material for the Society of Quality Assurance Animal Health pre-conference training session.

***Zollie A. Perry, Ph.D.***
***George A. Prager***
***Fredda C. Shere-Valenti***
***Vernon D. Toelle, Ph.D.***

## QUALITY OF WORK LIFE AWARD

***Bernadette Abela-Ridder, D.V.M., Ph.D.***

For creating a quality work environment and motivating her Team and Division to perform the best job possible.

***Carmela G. Stamper, D.V.M.***

For her outstanding level of commitment and service to improving the morale and quality of life for the Division of Therapeutic Drugs for Non-Food Animals and for the Office of New Animal Drug Evaluation.

***Michelle "Chellie" L. Stull, D.V.M.***

For outstanding leadership and mentorship of new reviewers.

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

## FDA SCIENTIFIC ACHIEVEMENT AWARDS

***Eric M. Silberhorn, Ph.D.***

**FDA EXCELLENCE IN REVIEW SCIENCE**

For recognizing the need and championing the development and adoption of numeric water quality benchmarks to provide a path forward across the Federal Food, Drug, and Cosmetic Act, National Environmental Policy Act, and Clean Water Act to approve and regulate new animal aquaculture drugs.

***Melanie J. McLean, D.V.M.***

**FDA OUTSTANDING NEW REVIEWER**

For significant contributions toward the public health objectives of the Agency and an exceptional grasp of the review process for new animal drugs.

## CVM DIRECTOR'S HONOR AWARD

***Joseph C. Kawalek, Ph.D.***

**First place recipient**

For sustained leadership and dedication in conducting research activities critical to the Center for Veterinary Medicine's mission.

***Margaret A. Zabriski, Ph.D.***

**Second place recipient**

For exemplary performance and leadership to the Center for Veterinary Medicine's IT activities.

## CVM PROJECT MANAGEMENT EXCELLENCE AWARD

***John H. Bartkowiak***

For excellence in leadership in projects intended to facilitate the Center's movement toward electronic submission of labeling and adverse event reports.

***Zoe Ann Gill***

For providing highly efficient and effective support as the project manager for the Center's Animal Feed Safety System Team.

***Kimberly A. Sanders***

For outstanding leadership among OITCVM project managers and implementation of the Project Management Office within OITCVM.

## CVM EXCELLENCE IN MENTORING AWARD

***Karyn D. Howard***

For your outstanding gift in mentoring with an unselfish dedication that enables others to grow professionally and support the goals and mission of CVM.

***Barbara E. Leach***

For her admirable teaching skills and unselfish dedication in mentoring CVM employees, both within and outside the Office of Management.

***Douglass S. Oeller, D.V.M.***

For exceptional efforts mentoring others to enhance their strengths, overcome their weaknesses, and broaden their skills to achieve professional growth, career advancement, and job satisfaction.

## CVM ADMINISTRATIVE EXCELLENCE AWARD

***Denise B. Durham***

For providing administrative management support to the supervisors, Management Officer, and employees of the Center for Veterinary Medicine, Office of Research.

***Sonia C. Gallagher***

For providing extraordinary administrative management support to UFMS users, Management Officers, and employees of the Center for Veterinary Medicine.

***Arleen G. Wang***

For providing extraordinary administrative management support to the supervisors, Management Officers, and employees of the Center for Veterinary Medicine.

## CVM COMMUNICATIONS EXCELLENCE AWARD

***Michelle D. Talley***

For outstanding leadership of CVM's Internet/Intranet technical effort and serving as IT project manager for ONADE's Smart Templates Project.

## CVM SUPPORT STAFF EXCELLENCE AWARD

***Jessica Rae Lawrence***

For exceptional performance and support to the Division of Manufacturing Technologies.

***Robin E. Nguyen***

For outstanding technical support and initiative to enhance the companion animal new animal drug approval process.

## CVM TEAM EXCELLENCE AWARD

***STARS Approved Facilities Working Group***

For exceptional teamwork in the design and implementation of the STARS Approved Facilities Database at CVM.

***Karen S. Alder***
***Kristen L. Anderson, Ph.D.***
***Matthew D. Anderson, Ph.D.***
***Dennis M. Bensley, Ph.D.***
***Renee S. Blosser***
***Mary Beth Borsetti***
***Stephanie C. Bowman, Ph.D.***
***Daniel C. Burnette***
***Jean-Michel 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.***
***Sharri R. Graham (Booz Allen Hamilton)***
***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***
***Mary G. Leadbetter***
***June Liang, Ph.D.***
***Charli M. Long, Ph.D.***
***William G. Marnane***
***Marina Mizina (Booz Allen Hamilton)***
***James K. Nitao, Ph.D.***
***Charles P. O'Brien, Ph.D.***
***Michael E. Oehlsen, Ph.D.***
***Rebecca L. Owen, Ph.D.***
***Michael J. Popek***
***J. Kevin Rice, Ph.D.***
***Anthony M. Stone***


CVM Director Dr. Sundlof talking with attendees at CVM's 2007 Awards Ceremony.
*Photo by Catherine Brown, Program Support Center, HHS.*

***Robin M. Stone***

***Faye Y. Wei, Ph.D.***

***Geoffrey K. Wong***

**PHS Unit Commendation**

***CDR M. Thomas Hendricks, Jr.***

***LCDR Wei Guo***

***Dairy Drug Labeling, Storage, and Residue Avoidance Guidance Team***

For superior performance in streamlining the FDA Milk Safety Program Guidance Memoranda.

***Randal E. Arbaugh***

***Michael R. Talley, D.V.M.***

## CVM TEAM EXCELLENCE AWARD

***Mediator Development Team***

For development of an innovative and collaborative solution which can be used across the Agency to quickly and efficiently integrate document management functionality into existing IT applications.

***Elaine A. Johanson***

***Kimberly A. Sanders***

**Contractor Team Members (Booz Allen Hamilton)**

***Ali Abbas***

***Howard Conrad***

***Irina Dergileva***

***Jan Dreisbach***

***Gregory Dyer***

***Heather Goodman***

***Venkatesan Gopalaswamy***

***Sharri R. Graham***

***Brett Larrabee***

***Kent McNickle***

***Marina Mizina***

***Sam Rossoshek***

***Rajan Subramanium***

***NSAID Education Outreach Team***

For outstanding and creative teamwork in identifying a critical information need and designing a highly successful outreach strategy to address that need: the NSAID Education Outreach Program.

***Laura C. Alvey***

***John D. Baker, D.V.M.***

***Melanie R. Berson, D.V.M.***

***Deborah H. Brooks***

***Margarita A. Brown, D.V.M.***

***Stephanie W. Dove***

***Bernadette M. Dunham, D.V.M., Ph.D.***

***Roderick J. Hudson***

***Joanne M. Kla***

***Vashti D. Klein***

***Barbara M. Leotta, D.V.M.***

***Mary Cacia Masser, D.V.M.***

***Thomas J. Moskal, D.V.M.***

***Douglass S. Oeller, D.V.M.***

***Amy L. Omer, D.V.M.***

***Lee Anne Palmer, D.V.M.***

***Jon F. Scheid***

***Mohammad I. Sharar, D.V.M.***

***Michele J. Sharkey, D.V.M.***

***Ann Stohlman, V.M.D.***

***Michelle D. Talley***

***Linda M. Wilmot, D.V.M.***

**PHS Unit Commendation**

***CAPT Lynn O. Post***

## FDA SCIENTIFIC ACHIEVEMENT AWARDS

## EXCELLENCE IN ANALYTICAL SCIENCE

**CVM ANALYTICAL SCIENCE EXCELLENCE AWARD**

***Philip J. Kijak, Ph.D.***

For his efforts and leadership in developing, evaluating, and standardizing test methods for drug residues in animal-derived foods.

## OUTSTANDING SUPPORT SCIENTIST

**CVM OUTSTANDING SUPPORT SCIENTIST AWARD**

***Patti Cullen***

For dedicated support and outstanding research contributions to CVM's NARMS and PulseNet programs.

## OTHER AGENCY AWARDS

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

## COMMISSIONER'S SPECIAL CITATION

***Centennial Planning Committee***

(Nominated by the Office of the Commissioner)

For dedication to planning commemorations to highlight 100 years of the Food and Drug Administration's contribution to promoting and protecting public health.

***Deborah H. Brooks***
***Jean-Michel Campagne, Ph.D.***
***Elizabeth P. Cormier, Ph.D.***
***Joseph W. Cormier, Ph.D.***
***Bharati R. Dhruva, Ph.D.***
***Bernadette M. Dunham, D.V.M., Ph.D.***
***Norman R. Gregory***
***Vashti D. Klein***
***James K. Nitao, Ph.D.***
***Walter D. Osborne, J.D.***
***Rebecca L. Owen, Ph.D.***
***Michael J. Popek***
***Carmela G. Stamper, D.V.M.***

***FDA Pandemic Influenza Preparedness Task Force***

(Nominated by the Office of the Commissioner)

For outstanding leadership in developing the FDA Pandemic Influenza Preparedness Strategic Plan and in advancing the Nation's preparedness for an influenza pandemic.

***Beth E. Karp, D.V.M., M.P.H.***
***Dragan Momcilovic, D.V.M., Ph.D.***
***Terry A. Proescholt, D.V.M., Ph.D.***
***Stephen F. Sundlof, D.V.M., Ph.D.***
***Kim R. Young***

**PHS Unit Commendation**

***CDR Alfred W. Montgomery***

## COMMISSIONER'S SPECIAL CITATION

***The 21 CFR Part 207 Proposal Group***

(Nominated by the Office of the Commissioner)

For extraordinary and exemplary contributions to the CDER, CBER, CVM, and FDA missions by developing and publishing proposed regulations governing drug establishment registration and listing.

***Lowell P. Fried (deceased)***
***Martine L. Hartogensis, D.V.M.***
***Charise S. Kasser, Pharm.D.***
***Isabel W. Pocurull***

## GROUP RECOGNITION AWARD

***FDA Performance Management Appraisal Program Implementation Team***

(Nominated by the Office of the Commissioner)

For exemplary team effort and outstanding performance in implementing the new Performance Management Appraisal Program throughout FDA.

***Holly A. Ballance***
***Susan M. Banks***
***Jacqueline M. Salter***
***Arleen G. Wang***

***Mobile Laboratory Fort Sam Houston Chemistry Team***

(Nominated by the Office of Regulatory Affairs)

For recognition of outstanding teamwork and special accomplishments during the inaugural development of the Mobile Lab Chemistry Team to Ft. Sam Houston (FSH).

***Diane T. Bargo***

***Performance Budget Writing Project Workgroup***

(Nominated by the Office of the Commissioner)

For outstanding contribution to developing and implementing writing principles that ensure an effective and clear presentation of FDA's Performance Budget.

***Roxanne K. Schweitzer***

***David E. Wardrop, Jr.***

## LEVERAGING/COLLABORATION AWARD

***Collaborative Efforts Assessing Widespread Impact of a Sterility Failure***

(Nominated by the Office of Regulatory Affairs)

For outstanding team effort assessing the wide spread impact of a veterinary drug manufacturer's sterility failure investigation.

***William L. Bargo***

***H. Gregg Claycamp, Ph.D.***

***Julie V. Conwell***

***Gloria J. Dunnavan***

***Elizabeth A. Grove***

***Mai X. Huynh***

***Kim R. Young***

***Interagency Honey Import Alert Collaboration Group***

(Nominated by the Office of Regulatory Affairs)

For an exceptional collaboration effort using state laboratory analyses to support an FDA regulatory action resulting in protection from adulterated imported honey.

***Neal Bataller, D.V.M.***

***Deborah A. Cera***

***David N. Heller***

***Philip J. Kijak, Ph.D.***

***Mayda I. Lopez, Ph.D.***

***Daniel G. McChesney, Ph.D.***

***Frances M. Pell***

***Nadine R. Steinberg, J.D.***

***Michael H. Thomas***

***Kim R. Young***

## OUTSTANDING INTERCENTER SCIENTIFIC COLLABORATION AWARD

***The FDA Microarray Quality Control (MAQC) Project Committee***

(Nominated by National Center for Toxicological Research)

For exceptional intercenter scientific collaboration in working toward consensus on the generation, analysis, and application of microarray data in the discovery, development, and review of FDA-regulated products.

***Heather C. Harbottle, Ph.D.***

*Photo by Angela Clarke, Office of New Animal Drug Evaluation.*

*Photo by Devaraya R. Jagannath, Office of New Animal Drug Evaluation.*

# APPENDIX D

## Publications

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


Aarestrup, F. M., R. S. Hendriksen, J. Lockett, K. Gay, K. Teates, **P. F. McDermott, D. G. White**, H. Hasman, G. Sørensen, A. Bangtrakulnonth, S. Pornreongwong, C. Pulsrikarn, F. J. Angulo, and P. Gerner-Smidt. 2007. International Spread of Multidrug-resistant *Salmonella* Schwarzengrund in Food Products. *Emerging Infectious Diseases*. 13(5):726-31.

Billal, D. S., D. P. Fedorko, **S. S. Yan**, M. Hotomi, K. Fujihara, N. Nelson, and N. Yamanaka. 2007. *In vitro* induction and selection of fluoroquinolone-resistant mutants of *Streptococcus pyogenes* strains with multiple emm types. *Journal of Antimicrobial Chemotherapy*. 59(1):28-34.

Chen, S., S. Cui, **P. F. McDermott, S. Zhao, D. G. White**, I. Paulsen, and J. Meng. 2007. Contribution of target gene mutations and efflux to decreased susceptibility of *Salmonella* Typhimurium to fluoroquinolones and other antimicrobials. *Antimicrobial Agents and Chemotherapy*. 51:535-542.

**Chu, P.-S.** and **M. I. Lopez**. 2007. Determination of nitrofuran residues in milk of dairy cows using liquid chromatography-tandem mass spectrometry. *Journal of Agricultural and Food Chemistry*. 55:2129-2135.

Culp, S. J., P. W. Mellick, R. W. Trotter, **K. J. Greenlees,** and F. A. Beland. 2006. Carcinogenicity of malachite green chloride and leucomalachite green in B6C3F1 mice and F344 rats. *Toxicology*. 44(8):1204-2.

**De Alwis, G. K. H.**, L. L. Needham, and D. B. Barr. 2007. Automated solid phase extraction and quantitative measurement of 2,3-dibromo-1-propanol using gas chromatography-mass spectrometry. *Archives of Environmental Contamination and Toxicology*. 53:134-139.

Fanatico, A. C., **P. B. Pillai**, J. L. Emmert, and C. M. Owens. 2007. Meat Quality of Slow- and Fast-Growing Chicken Genotypes Fed Low-Nutrient or Standard Diets and Raised Indoors or with Outdoor Access. *Poult. Sci.* 86:2245-2255.

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 3569-3577.

Foley, S. L., **S. Zhao**, and **R. D. Walker**. 2007. Molecular typing methods for determining the source of *Salmonella* foodborne pathogens. *Food borne Pathogens and Disease*. 3:253-276.

Fritsche, T. R., **P. F. McDermott**, T. R. Shryock, **R. D. Walker**, and T. Y. Morishita. 2007. Agar dilution and disk diffusion susceptibility testing of *Campylobacter* spp. *Journal of Clinical Microbiology*. 45(8):2758-9; author reply 2759.

**Gilbert, J. M., D. G. White**, and **P. F. McDermott**. 2007. The National Antimicrobial Resistance Monitoring System. *Future Microbiology*. 2(5):493-500.

Gladwin, R., **K. J. Greenlees**, and K. Mitsumori. 2006. Colistin. Toxicological evaluation of certain veterinary drug residues in food. WHO Food Additive Series: 57. World Health Organization, Geneva. IPCS. pp. 3-30.

**Heller, D. N.** 2007. Ruggedness testing of quantitative atmospheric pressure ionization mass spectrometry methods: the effect of co-injected matrix on matrix effects. *Rapid Communications in Mass Spectrometry*. 21:644-652.

**Lopez, M. I.**, M. F. Feldlaufer, A. D. Williams, and **P.-S. Chu**. 2007. Determination and confirmation of nitrofuran residues in honey using LC-MS/MS. *Journal of Agricultural and Food Chemistry*. 55:1103-1108.

Lynne, A. M., B. S. Rhodes-Clark, K. Bliven, **S. Zhao**, and S. L. Foley. (In press.) Antimicrobial resistance genes associated with *Salmonella enterica* serovar Newport isolates from Food Animals. *Antimicrobial Agents and Chemotherapy*.

**McDermott, P. F.**, J. Simala-Grant, **R. D. Walker**, D. E. Taylor. (In press.) Antimicrobial Resistance in *Campylobacter* and *Helicobacter*. *Antimicrobial Drug Resistance: Principles for the Clinic and Bench*. (D. Mayers, J. Sobel, M. Ouellette, S. Lerner, eds.) Humana Press, Totowa, NJ.

**Okelo, P. O., D. D. Wagner**, L. W. Carr, F. W. Wheaton, L. W, Douglass, and S. W. Joseph. 2006. Optimization of extrusion conditions for elimination of mesophilic bacteria during thermal processing of animal feed mash. *Animal Feed Science and Technology*. 129: 116-137.

**Shaikh, B., N. Rummel, C. Gieseker, P.-S. Chu**, and **R. Reimschuessel**. (In press.) Residue depletion of tritium labeled ivermectin in rainbow trout following oral administration. *Aquaculture*.

**Shere-Valenti, F. C., G. A. Prager**, and **V. D. Toelle**. 2007. Quality Systems for the 21st century: A look at FDA's Center for Veterinary Medicine's (CVM) Bioresearch monitoring quality system. *Proceedings for 22nd Annual Society of Quality Assurance meeting April 29th to May 3rd*.

Simjee, S., **P. F. McDermott, D. G. White,** C. Hofacre, R. D. Berghaus, **P. J. Carter**, L. Stewart, T. Liu, M. Maier, and J. J. Maurer. (In press.) Antimicrobial susceptibility and distribution of antimicrobial resistance genes among *Enterococcus* and coagulase-negative *Staphylococcus* isolates recovered from poultry litter. *Avian Diseases*, vol. 51.

Tabasi, S. H., **R. Fahmy, D. Bensley, C. O'Brien**, and S. W. Hoag. (In press.) Quality by Design, Part I: Application of NIR Spectroscopy to Monitor Manufacturing Process for Orbifloxacin Tablets. *Journal of Pharmaceutical Science*.

Tabasi, S. H., **R. Fahmy, D. Bensley, C. O'Brien**, and S. W. Hoag. (In press.) Quality by Design, Part II: Application of NIR Spectroscopy to Monitor Coating Process for Pharmaceutical Sustained Release Product. *Journal of Pharmaceutical Science*.

Tabasi, S. H., **R. Fahmy, D. Bensley, C. O'Brien**, and S. W. Hoag. (In press.) Quality by Design, Part III: Study of Curing Process of Sustained Release Polymer Products Using NIR Spectroscopy. *Journal of Pharmaceutical Science*.

Welch, T. J., W. Florian Fricke, **P. F. McDermott, D. G. White**, M-L. Rosso, D. A. Rasko, M. K. Mammel, M. Eppinger, M. J. Rosovitz, **D. Wagner**, L. Rahalison, J. E. LeClerc, J. M. Hinshaw, L. E. Lindler, T. A. Cebula, E. Carniel, and J. Ravel. 2007. Multiple antimicrobial resistance in plague: An emerging public health risk. *PLoS ONE* 2(3):e309.

Zaidi, M. B., J. J. Calva, M. T. Estrada-Garcia, V. Leon, G. Vazquez, G. Figueroa, E. Lopez, J. Contreras, **J. Abbott, S. Zhao**, **P. F. McDermott**, and L. Tollefson. (In press.) An integrated food chain surveillance system for *Salmonella* in Mexico: A model for developing countries. *Emerging Infectious Diseases*.

Zaidi, M. B., V. Leon, C. Canche, C., Perez, **S. Zhao, S. K. Hubert, J. Abbott, K. Blickenstaff**, and **P. F. McDermott**. 2007. Rapid and widespread dissemination of multidrug-resistant *bla*CMY-2 *Salmonella* Typhimurium in Mexico. *Journal of Antimicrobial Chemotherapy*. 60(2):398-401.

**Zhao, S., P. F. McDermott, D. G. White, S. Qaiyumi, S. L. Friedman, J. W. Abbott, A. Glenn, S. L. Ayers**, K. W. Post, W. H. Fales, R. B. Wilson, C. Reggiardo, and **R. D. Walker**. 2007. Characterization of multidrug resistant Salmonella recovered from diseased animals. *Veterinary Microbiology*. 123(1-3):122-32.

Zheng, J., S. L. Keys, **S. Zhao**, J. Meng, and E. W. Brown. (In press.) An enhanced discriminatory scheme for PFGE-based subtyping of *Salmonella enteritidis*. *Emerging Infectious Diseases*.

*Photo by Bernadette Dunham, Office of the Director.*

*Photo by Steve Brynes,*
*Office of New Animal Drug Evaluation.*

*Photo by Steve Brynes,*
*Office of New Animal Drug Evaluation.*

*Photo by Cathy Beck, Office of the Director.*

# APPENDIX E

## CVM BUDGET AND STAFFING

| FY 2007 Enacted Budget | Pre-Market | Post-Market | FY 2007 Total |
|---|---|---|---|
| Budget Authority | $29,999,000 | $28,356,000 | $58,355,000 |
| User Fee (ADUFA)* | $ 9,434,000 | | $ 9,434,000 |
| ***Total Program Level*** | **$39,433,000** | **$28,356,000** | **$67,789,000** |
| Note: Estimates for the field are not included in the figures above. | | | |
| Field Activities: Animal Drugs and Feeds | $2,116,000 | $34,278,000 | $36,394,000 |

* ADUFA user fee amount does not include money for Other Activities.

| FY 2007 Enacted Budget Full-Time Equivalents | Pre-Market | Post-Market | FY 2007 Total |
|---|---|---|---|
| Budget Authority | 170 | 154 | 324 |
| User Fee (ADUFA) | 54 | | 54 |
| **Total Program Level** | **224** | **154** | **378** |
| Note: Estimates for the field are not included in the figures above. | | | |
| Field Activities: Animal Drugs and Feeds | 12 | 197 | 209 |

| Scientific and Technical Series | FY 2007 STAFFING* (Includes Commissioned Corps Officers and Staff Fellows.)<br>10 20 30 40 50 60 70 80 |
|---|---|
| CVM employs a total of 99 veterinarians in a variety of positions, including 79 that are classified as Veterinary Medical Officers/Scientists. | |
| Veterinary Medical Officers/Scientists | ----------/ 79 |
| Chemists | ----------/ 42 |
| Consumer Safety Officers | ----------/ 40 |
| Biologists | ----------/ 36 |
| Microbiologists | ----------/ 34 |
| Mathematical Statisticians | -----/ 13 |
| Animal Scientists | ---/ 11 |
| Pharmacologists | --/ 6 |
| Toxicologists | --/ 5 |
| Health Scientists | -/ 4 |
| Physiologists | / 2 |
| Physical Scientists | / 1 |

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

*Photo by Jennifer Matysczak, Office of New Animal Drug Evaluation.*

# Appendix F

## CVM Performance Goals – Program Results

**1. Increase access to innovative animal drugs to improve animal health by the timely review of New Animal Drug Applications.**

- Complete review and action on 90 percent of Original New Animal Drug Applications and reactivations for those applications received during FY 2007 and acted on by September 30, 2007.

**2. Increase access to innovative new animal drug products by bringing discipline into the review process.**

- Implement a system of planning, execution, monitoring and evaluation to improve business process to increase efficiencies.

**3. Increase access to innovative new animal drug products to improve animal health by providing rapid, transparent, and predictable science-based review of New Animal Drug Applications.**

- Prepare draft guidance on regulating transgenic animals as new animal drugs and respond in a timely manner to all questions raised during the Agency and Department review process, thereby facilitating the Agency and Department decision on publishing the guidance.
- Release for public comment the draft risk assessment analysis on animal clones and their progeny. (Also included under Performance Goal #6.)
- Review and respond to comments received on draft risk assessment and related documents for animal clones and their progeny. (Also included under Performance Goal #6.)

**4. Improve the safety of food products through better food-animal processing.**

- Foster the development of a critical path framework with outside stakeholders to identify, evaluate, and approve for marketing therapeutic animal drugs intended to reduce/eliminate *Escherichia coli* O157:H7 in cattle prior to slaughter.
- Lead and participate in strategic planning to develop a coalition to foster the development of therapeutic interventions intended to reduce/eliminate *Escherichia coli* O157:H7 in cattle prior to slaughter.
- Provide leadership for the development of the final BSE animal feed rule and submit by April 2007 for Agency clearance; respond in a timely manner to all questions raised during the Agency, Department, and Office of Management and Budget review process, thereby facilitating the decision on publishing the guidance.
- Respond in a timely manner to all questions raised during the Agency, Department, and OMB clearance process of the BSE animal feed rule, thereby facilitating the Agency and Department decision on publishing the BSE animal feed rule.

✓ • Develop rapid methods (e.g., microarray, biomarkers) for screening antimicrobial resistant foodborne pathogens to identify specific food-producing animal origins.

✓X **5. Improve quality, safety, and availability of food products through better manufacturing and product oversight.**

✓ • In the FY 2007 work plan, allocate resources to be able to conduct annual, targeted BSE inspections of all known renderers and feed mills processing products containing prohibited materials. (This performance goal is to be acted upon in conjunction with ORA.)

✓ • Perform a vulnerability assessment of a major feed manufacturing facility in the United States as part of the Strategic Partnership Program Agroterrorism initiative.

✓ • In the FY 2007 work plan, allocate resources to perform Prior Notice Import Reviews on 46,700 food and animal feed line entries considered to be high risk. (This performance goal is to be acted upon in conjunction with the CFSAN and ORA.)

X • Develop and adopt isolation methods to be used in screening feeds and feed commodities for the presence of bacterial pathogens of veterinary and public health significance. (This performance goal is to be acted upon in conjunction with ORA.)

*This goal was not met, due to the departure of a key staff member who has not yet been replaced.*

X • Complete validation of the real time polymerase chain reaction method to detect prohibited materials in animal feeds to support BSE rule. (This performance goal is to be acted upon in conjunction with ORA.)

*CVM was unable to complete this item because several FDA laboratories could not commit the resources to the validation study due to other priorities.*

✓ • Complete the development of procedures to include select pesticides in the multi-class, multi-residue method for drugs and other contaminants in animal feeds and initiate the development of procedures to include mycotoxins.

✓X **6. Increase access to innovative animal drugs to improve animal health.**

✓ • Prepare draft guidance on regulating transgenic drugs as new animal drugs and respond in a timely manner to all questions raised during the Agency, Department, and OMB review process, thereby facilitating the decision on publishing the guidance.

✓X • Increase the availability of more medications legally available to veterinarians and animal owners to treat minor animal species and uncommon diseases in the major animal species by completing the proposed rule for "Conditional Approval" and complete final rule for "Indexing."

*CVM completed the final rule for Indexing, but did not complete the proposed rule for Conditional Approval. CVM approved the first application for Conditional Approval in April, 2007, and continues to review applications for Conditional Approval as they are received. The Center's experience with these applications has informed, but not delayed, promulgation of the proposed regulations. Drafting of the proposed Conditional Approval regulations is complex because (unlike the other regulations implementing the MUMS Act) these regulations must fit within an existing structure of new animal drug approval regulations and procedures, but they also raises novel issues. The proposed regulations were expected to be completed by the Agency by the end of the year.*

✓ • Complete review and action on 90 percent of Original New Animal Drug Applications and reactivations for those applications received during FY 2007 and acted on by September 30, 2007.

✓ • Release for public comment the draft risk assessment analysis on animal clones and their progeny. (Also included under Performance Goal #3.)

✓ • Review and respond to comments received on draft risk assessment and related documents for animal clones and their progeny. (Also included under Performance Goal #3.)

**7. Enhance patient and consumer protection and empower consumers by providing better information about regulated products.**

- Plan and lead the Center's communication efforts for the release of the draft risk assessment and related documents on animal clones and their progeny for public comment.
- Participate in strategic planning and provide leadership in support of the FY 2007 FDA Science Board review of the NARMS program.
- Communicate with livestock producers, veterinarians, industry, and the public to ensure a clear understanding and acceptance of FDA veterinary programs and policies.
- In FY 2007, publish the first NARMS Executive Report and also publish the FY 2005 NARMS retail Annual Report.
- Implement recommendations from the 2005 NARMS external review (e.g., data reporting and harmonization, improving timeliness of reporting).

**8. Provide for the efficient and effective administration of the Animal Drug User Fee financial program to enhance the review of New Animal Drug Applications and the investigational submissions.**

- Develop and publish fee schedules by August 2007.
- Provide a proactive and timely response to industry and citizen requests for information on billings, fees, and payments.

**9. Provide staff and management with the mechanism to run reports and utilize the hourly and cost data to better manage resources and programs.**

- The release of the Consolidate Reporting Environment, which houses hourly and cost data.

**10. Create opportunities for greater collaboration of scientific data (NARMS) within CVM.**

- Migrating NARMS data into the Web-based Corporate Database Portal.

**11. Broaden the scope and curriculum of the CVM Staff College/University of Maryland Collaboration that offers a Master of Public Health (MPH) with concentration in veterinary public health to include eligible employees from elsewhere in the Agency and Department (through HHS University).**

- Initially explore a working partnership with other Agency centers to join with CVM in offering the MPH degree program to eligible employees.
- Engage in the development of the MPH degree program to include those centers that express interest in the program.

*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

*Photo by Angela Clarke,*
*Office of New Animal Drug Evaluation.*

2007 Annual Report

CENTER FOR VETERINARY MEDICINE

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