

EXHIBIT E

**TO THE THIRD DECLARATION
OF JENNIFER A. SORENSON**

FDA CENTER FOR VETERINARY MEDICINE
USING SCIENCE AND LAW TO PROTECT PUBLIC AND ANIMAL HEALTH
ANNUAL REPORT
FISCAL YEAR 2004 OCTOBER 1, 2003–SEPTEMBER 30, 2004

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**CVM Director
Dr. Stephen F. Sundlof**

A MESSAGE FROM THE DIRECTOR ...

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Fiscal year (FY) 2003 – the year covered by our first annual report – was a year of anticipation. We looked forward throughout the year to the passage of animal drug user fee legislation. We were also hopeful that legislation benefiting minor species and minor drug uses would soon be passed. At the end of the year, we completed much needed guidance for assessing antimicrobial resistance risks from drugs that were candidates for approval; we were ready to put the guidance into operation.

Fiscal year 2004 has been a time of implementation, as we put into place significant changes in law and policy. These innovations will, in the long run, profoundly improve the availability of safe and effective drugs for major and minor species and drug uses. We have worked diligently to put into place the mechanisms, procedures, and personnel required by the Animal Drug User Fee Act of 2003 (ADUFA), signed by the President in November 2003. This legislation will help us expedite and improve our review of applications for new animal drugs so that safe and effective new products will be available more quickly.

Toward the end of the year, we began to organize to implement the Minor Use and Minor Species Animal Health Act of 2004 (MUMS), which became law in August 2004. The new law contains measures that will significantly expand the availability of drugs for minor uses and minor species of animals. Further, we have fully implemented Guidance for Industry (GFI) #152, which provides a scientific risk-based process for assessing the likelihood that a drug will cause antimicrobial resistance problems in humans. For example, as provided in the guidance document, we asked our Veterinary Medicine Advisory Committee (VMAC) to assess the food safety of an antimicrobial drug that is under CVM review for use in food-producing animals.

We expanded our monitoring related to antimicrobial resistance during FY 2004. Data and information collected in the surveillance efforts support risk assessments for antimicrobial resistance and we will use this information to guide us in applying risk management measures.

Antimicrobial resistance is receiving increased attention worldwide, because expansion of international food marketing increases the chances of country-to-country movement of resistant organisms. For example, the Codex Committee on Residues of Veterinary Drugs in Food expedited its draft Code of Practice to Minimize and Contain Antimicrobial Resistance at its 2004 meeting. CVM's Deputy Director, Dr. Linda Tollefson, chaired the drafting group.

Developments concerning another international issue, the occurrence of bovine spongiform encephalopathy (BSE), occupied our attention during the past year. The diagnosis of the first BSE-infected cow in the United States brought immediate

compliance action by the Food and Drug Administration to prevent the spread of BSE through animal feed. Working with the U.S. Department of Agriculture, we took steps toward implementing several measures that would strengthen our BSE feed regulation, which is intended to prevent the establishment and amplification of BSE through feed. FDA and State investigators met a Department of Health and Human Services program objective in their inspections of feed manufacturers and renderers during FY 2004.

We moved ahead during fiscal year 2004 to evaluate and plan regulatory activities in areas of new and emerging emphasis. This included completion of a draft risk assessment on animal cloning, and participation in a number of initiatives involving our nation's counterterrorism efforts related to bioterrorism.

We also provided new guidance for activities that we have regulated for years. This included educational and regulatory actions related to compounding of drugs for use in animals, an area of considerable activity and some controversy.

And of course we continued with the essential ongoing activities of the Center, including the approval of a number of new animal drug applications. An example was Vetsulin™, the first veterinary insulin approval, approved to treat hyperglycemia and hyperglycemia-associated clinical signs in dogs with diabetes mellitus. Another example was the approval of Simplicef® (cefepodoxime proxetil), which gives veterinarians a new once-daily treatment option to treat skin infections (wounds and abscesses) that are common among dogs.

We present more details on these and many other activities in this annual report. The following pages set out the challenges we face and our accomplishments during the past year. Where we reached our performance goals for FY 2004, we so indicate. Where we fell short of the goals, we indicate this also. We believe we best serve the public by reporting our shortcomings along with our accomplishments.

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

With the passage of ADUFA and MUMS, Congress has passed five major laws for animal drugs during the past 16 years. We will work diligently during FY 2005 to implement these new laws, just as we have worked hard to respond to Congress' directives relating to generic drugs, extralabel use, and drug availability. Above all, we value the trust the public bestows on us, and we will continue to earn that trust by upholding these and other laws for which we have responsibility.



**CVM Deputy Director
Dr. Linda Tollefson**

A MESSAGE FROM THE DEPUTY DIRECTOR ...

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Following on Dr. Sundlof's summary of our substantive FY 2004 achievements, I will report on developments in the organization that are behind the accomplishments.

CVM is managed collaboratively by its Senior Management Team, which participates in the day-to-day management and policy decisions facing the Center, as well as long range planning, budgeting, and policy development. In making its decisions, the team considers scientific, economic, international, and social issues and their impact on the Center. A project manager documents action items and decisions to assure that these actions and decisions are implemented.¹

The new laws discussed by the Director require that organizational changes and personnel additions be established, starting in FY 2004. We met our goals for hiring new professional staff to review new animal drug applications under ADUFA, and we were pleased with the high caliber of those we were able to employ. We also developed procedures, and established fee rates and payment procedures, under ADUFA.

Following passage of the MUMS legislation, we began the process of establishing a new Office of MUMS Animal Drug Development. We are establishing the functional statements, reporting relationships, delegations of authority, and position descriptions required to implement the new law.

We made some additional organizational changes that will facilitate implementation of management initiatives. For instance, as part of the growth and enhancement of the retail meat arm of the National Antimicrobial Resistance Monitoring System (NARMS), several epidemiologists from the Office of Surveillance and Compliance were reassigned to the Division of Food and Animal Microbiology in the Office of Research.

Efforts continued during the year to incorporate science-based risk management, to maximize public protection with limited resources. We fully implemented activity time reporting (ATR) to – among other purposes – allow us to determine the percentage of time each office spends on animal drug review process-related activities. With ATR, we can perform activity-based costing (ABC). This allows us to identify the full cost of all our pre- and post-market and overhead activities.

We implemented new strategic human capital management activities, as part of our results-oriented management emphasis. For example, we implemented educational programs directed toward the goal of resolving new and emerging scientific issues that affect our ability to make drug approval decisions. Responding to continuing

budget restraints, we were able to achieve our goal of reducing the number of administrative positions in the Center.

Appointments of individuals to serve in leadership positions are essential to the success of any organization. We made one such selection during the year, the appointment of David Wardrop as Director of the Office of Management.

The accomplishments of an organization are often reflected in the public recognition of its people. The Food and Drug Administration 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 for all the awards are in Appendix A.

The professional productivity of our scientists is demonstrated clearly by the large number of articles they published during the year. The article topics ranged from antimicrobial resistance to drug metabolism and residues, biotechnology, drug manufacturing and more. Of special note, Dr. Nabil Anis won the outstanding FDA 2004 Science Forum poster award for the use of a new biotechnology for the detection of drug residues in milk. We have included a complete publications list in Appendix B.



Members of CVM's Senior Management/Leadership Team: Dr. Tollefson, Dr. McChesney, Dr. Beaulieu, Dr. Sundlof, Ms. Beck

The "Windows to Science and Regulatory Research Program," a summer internship for outstanding college and high school students, illustrates the diversity of the Center's activities. The program's goal is to provide the interns with a foundation in regulatory-based research that is integrated with scientific principles applicable to veterinary product development and regulation. The 2004 program consisted of 11 participants, including one student from Croatia. Each student was assigned to a CVM scientist who served as his or her mentor. CVM invests in the program to provide the students with an experience that will encourage them to consider regulatory science and research as a career.

It has been a busy, productive year – made possible by our staff of motivated, talented people. Their contributions cause our Senior Management Team to be optimistic about meeting the challenges of FY 2005 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 2004 accomplishments by understanding what CVM is all about – our mission, plans, organization, sphere of influence, and so on. Thus, the first major section of our annual report is "About CVM."

¹ CVM's Senior Management Team members are as follows:

Dr. Stephen E. Sundlof, Director, Center for Veterinary Medicine

Dr. Linda Tollefson, Deputy Director, Center for Veterinary Medicine

Dr. Andrew J. Beaulieu, Director, Office of Minor Use and Minor Species Animal Drug Development

Ms. Catherine Beck, Associate Director for Executive Programs and Acting Associate Director for Policy and Regulations

Dr. David Grau, Senior Management Consultant

Dr. William Flynn, Deputy Associate Director for Policy and Regulations

Dr. Daniel G. McChesney, Director, Office of Surveillance and Compliance

Mr. David E. Wardrop, Jr., Executive Officer; Director of Office of Management

Dr. Steven D. Vaughn, Director, Office of New Animal Drug Evaluation

Dr. Linda D. Youngman, Director, Office of Research

Ms. Vashri Klein, Project Manager

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 external 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 "one HHS" initiative of the Secretary of Health and Human Services, and the Food and Drug Administration's Strategic Action Plan.

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

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

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

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

OUR ORGANIZATION AND RESPONSIBILITIES

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

OFFICE OF THE DIRECTOR (OD)

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

The Director approves new animal drug applications, and exercises other statutory authority that has been delegated to him. Other functions are performed through a Deputy Director and Associate Directors for executive programs, and policy and regulations.



CVM Deputy Director Dr. Linda Tollefson and CVM Director Dr. Stephen F. Sundlof

The Office conducts communication and education programs, provides project management support for the Center, offers the services of the CVM Ombudsman, manages the Veterinary Medicine Advisory Committee, and coordinates international activities in the Center.

OFFICE OF MUMS ANIMAL DRUG DEVELOPMENT (OMUMS)

The Minor Use and Minor Species Animal Health Act of 2004 (MUMS) provided for the establishment of the Office of Minor Use and Minor Species Animal Drug Development. The Office reports directly to the Director of the Center for Veterinary Medicine, and is responsible for overseeing the development and legal marketing of new animal drugs for minor uses (disease conditions that are rare) and minor species (including small or unusual animal species, fish, and zoo animals).



**ONADE Director Dr. Steve Vaughn (left)
and Supervisory Program Analyst
Dr. David Newkirk**

OFFICE OF NEW ANIMAL DRUG EVALUATION (ONADE)

ONADE's mission is to protect the public health by ensuring the availability of an adequate number of safe and effective animal drugs to meet the therapeutic and production needs of animals. ONADE administers the core function of drug review – it directs 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 clinical tests to establish drug safety and effectiveness. Sponsors of drugs intended for food animals must also prove that food products derived from treated animals do not contain unsafe drug residues, and that the food products are safe with respect to microbial safety. The sponsors must develop analytical methods to detect and measure drug residues in edible animal products. The Federal Food, Drug, and Cosmetic Act provides for approval of both pioneer and generic animal drugs, and for FDA-granted authority to use investigational animal drugs. CVM classifies the animal drugs it approves, for distribution and use purposes, as over-the-counter, prescription, or veterinary feed directive.

ONADE administers the Animal Drug User Fee Act of 2003, which authorizes FDA to collect fees in support of the review of new animal drugs.

OFFICE OF SURVEILLANCE AND COMPLIANCE (OS&C)

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

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

OFFICE OF RESEARCH (OR)

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

In support of the drug review function, OR conducts studies in animal drug safety and efficacy, antimicrobial resistance mechanisms, metabolism, standardization of test methods and pharmacokinetics/pharmacodynamics. The goal of these efforts is to provide a science base for guideline development. OR supports the compliance program of the Center through the development of analytical methods and evaluation of screening tests for detection of drug residues in imported and domestic food products. The Office is responsible for the post-approval monitoring of retail meats for drug resistant foodborne pathogens under the NARMS, and molecular typing of those



OS&C Director Dr. Dan McChesney (right) and Deputy Director Dr. George Graber



OR Director Dr. Linda Youngman (right) and Deputy Director Dr. Marleen M. Wekell

pathogens as part of the national PulseNet program. OR conducts research to understand the microbiology of animal feeds, and the dissemination of resistant organisms via livestock feeds. The Office is also developing methods to detect material, prohibited in ruminant feeds by the BSE feed regulation, that could compromise animal feed safety.

OR prepares a detailed annual report; for a copy, write to Center for Veterinary Medicine, Office of Research, 8401 Muirkirk Road, Laurel, MD 20708, attention Denise Strekal.

OFFICE OF MANAGEMENT (OM)

The Office of Management has primary responsibility in four administrative management program areas: budget and finance; management services; planning, procurement and facilities; and information resources management. OM plans, develops, and implements Center management policies as follows:

- Provides leadership and direction for the planning, development, and execution of the CVM budget. This includes analysis, formulation, and presentation of budget issues.
- Directs the development and implementation of the competency-based Staff College and accompanying curriculum.
- Sets the Center's expectations with regard to required competencies through the Staff College Knowledge Center.
- Serves as the focal point for management and administrative interaction with other FDA offices to assist in the efficient delivery of administrative services to the Center's employees.
- Provides liaison services for activities that include space and workplace planning, facilities management and operations, and workplace safety.
- Represents management on Center issues that involve the National Treasury Employees' Union and the implementation of the FDA/NTEU Collective Bargaining Agreement.
- Serves as Center's liaison with the Agency's Office of Shared Services, the Rockville Human Resources Center, and the Office of the Chief Information Officer to ensure efficient and effective administrative management and Information Technology services.
- Manages and provides leadership for the implementation and delivery of financial activities associated with the Center's user-fee program.
- Provides leadership and coordination and serves as the Center liaison with the Agency concerning GAO and IG studies/inquiries.
- Supports and enhances employees' abilities to efficiently work with integrated systems to reach CVM goals.
- Provides coordination and leadership for the Center's activity-based costing/activity time reporting system, and integrates it into the business culture of the Center's operations.



OM Director David Wardrop and Deputy Director Barbara Leach

OUR SPHERE OF INFLUENCE

CVM's efforts to help assure that domestic and imported animal food products are safe affect millions of consumers. American consumers eat – on the average – 180 pounds of red meat and seafood, 65 pounds of poultry, 580 pounds of dairy products, and 30 pounds of eggs each year. Besides protecting the health of consumers, CVM works to safeguard the health of food-producing animals in the United States: 103 million cattle, 61 million pigs, 8.8 billion chickens, 270 million turkeys, and 6 million sheep and goats. The United States produces more than \$100 billion worth of livestock and livestock products each year.

CVM approvals are now in effect for 692 drug products on the market for use in food-producing animals. We have approved many of these drugs for administration through animal feed. CVM has licensed 1,141 firms that manufacture medicated feeds under a law passed by Congress several years ago. And we have published regulations that authorize use of more than 50 food (feed) additives.

A total of 779 currently approved drug products are available to maintain the health of our nation's growing population of pets, which now numbers 62 million dogs and 71 million cats, in addition to 5.5 million horses.

Altogether, we regulate activities of some 6,600 feed manufacturers and related firms, nearly 300 animal drug manufacturers and other sponsors of animal drug applications and Type A Medicated articles, many thousands of livestock and poultry producers, and firms in a variety of specialized industry groups. The drugs we approve help the nation's 69,000 veterinarians accomplish their task of maintaining the health of the nation's animals.



CVM staff members at the Center's picnic, showing off their pets

OUR STAKEHOLDERS AND PARTNERS

OUR STAKEHOLDERS

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

We use a variety of methods to keep stakeholders informed, and to seek their advice and opinions about our policies and programs. These methods include public meetings; requests for comment on proposed regulations and guidance documents; the CVM website (www.fda.gov/cvm); and a variety of informal means, such as letters, phone calls, and emails.

OUR PARTNERS

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

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

Our partners include:

- Other Federal agencies with whom we share related regulatory responsibilities, such as the 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 (e.g., pesticides). For example, the Interagency Residue Control Group, with members from FDA, USDA and the Environmental Protection Agency, coordinates information on residues of animal drugs, pesticides, and environmental contaminants in animal food products.
- Centers for Disease Control and Prevention (CDC), 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, who 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).
- Veterinarians, who share with us numerous public and animal health goals such as testing and surveillance of animal drugs for safety and effectiveness, avoiding drug residues in food products, minimizing the development of antimicrobial resistance through prudent drug use practices, and educating producers and related industries as to their public health responsibilities.
- Foreign regulatory agencies who 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 Registration of Veterinary Medicinal Products (VICH), the Codex Committee on Residues of Veterinary Drugs in Food (CCRVDF), and other multilateral organizations.

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

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



FISCAL YEAR 2004 CHALLENGES AND ACCOMPLISHMENTS

INTRODUCTION

Although we are organized into six separate offices, our Guiding Principles call for the staff 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 2004 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.

To help us achieve our strategic goals in FY 2004, we established targets for the year – a number of specific performance goals. Individual Offices have primary responsibility for achieving some of the performance goals, but two or more Offices share many of the performance goals because the goals relate to activities that require collaborative efforts.

We highlight our performance goals below, in the appropriate sections, and indicate (with ✓ for yes and ✗ for no) whether we accomplished the goals.

We have worked during the past year to focus on the priorities in the DHHS-wide program and management objectives. We also focused on the priorities stated in FDA’s Strategic Action Plan: efficient risk management, better informed consumers, improved patient and consumer safety, protection from terrorism, and more effective regulation through a stronger workforce. We have indicated below some examples of how our FY 2004 accomplishments responded to the Agency’s priorities.

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 preapproval decisions, and do so efficiently and expeditiously. CVM's challenge is to protect the public health by assuring that there is an adequate supply of animal drugs to meet therapeutic and production needs. The newly passed Animal Drug User Fee Act 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.

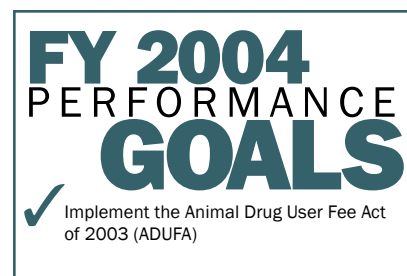
FY 2004 ACCOMPLISHMENTS

We responded to the challenges in a number of ways, as described below. In general, we directed these actions toward achieving the FDA Strategic Plan priorities of increased productivity in new drug development, and improving the quality of health care services. We also focused efforts on the Strategic Plan's objective of providing a timely, high quality, and cost-effective process for review of pre-market submissions.

ANIMAL DRUG USER FEE ACT

The law. Implementing ADUFA was a major CVM emphasis during FY 2004. Similar to a very successful user fee law for human drugs, ADUFA authorizes FDA to collect fees in support of the review of new animal drugs. The fees are for certain new animal drug applications, and for the establishments, products, and sponsors associated with these and previously approved applications. The legislation authorizes the collection of fees totaling approximately \$43 million over five years, to enable FDA to hire and train additional scientific reviewers and implement enhanced processes to accelerate and improve the review process and build necessary support infrastructure.

The benefits. This legislation will help FDA expedite and improve its review of applications for new animal drugs so



that safe and effective new products will be available more quickly. Specifically, our goals are to:

- eliminate existing backlogs of new animal drug applications within 2 years;
- over a 5-year period, move toward the goal of completing the review of 90 percent of new animal drug applications within 180 days;
- resolve new and emerging scientific issues that affect CVM's ability to make approval decisions; and
- achieve an enhanced and predictable review performance.

The new law will promote animal health by increasing the availability and diversity of safe and effective drug products that relieve animal pain and suffering. And it will reduce potential threats to the public health by spurring development of drugs for food-producing animals, decreasing the likelihood of drug residue and antimicrobial resistance problems. In addition, we anticipate substantial savings to the animal drug industry in regulatory review and developmental expenses. A faster, more predictable review process is expected to spur more research and development by the animal drug industry.

Finally, the law requires the Agency to adopt administrative processes to ensure that review times for generic animal drugs do not increase from their current level due to activities under ADUFA.

Implementation. The President signed the law in November 2003, and Congress authorized receipt of user fees in appropriations language enacted in January 2004. The Center was engaged in implementing the new law – by hiring reviewers, developing procedures for applying the new law, and establishing fee rates and payment procedures. The Agency published Guidance for Industry (#170) on ADUFA's fee waiver provision. GFI #170 describes the types of fee waivers and reductions CVM may grant, including those related to significant barriers to innovation, situations in which fees exceed costs, and minor uses or minor species.

Reports. The law requires the Agency to submit two reports to Congress – a performance report and a financial report. These reports for FY 2004 will be published separately.

ACTIONS TO INCREASE THE EFFICIENCY OF THE REVIEW PROCESS AND ENSURE THE SAFETY AND EFFECTIVENESS OF ANIMAL DRUGS

As we prepared to implement ADUFA during FY 2004, we continued to undertake strategic initiatives – started during the previous fiscal year – designed to improve the effectiveness of the pre-market review process and assure the safety of approved products. These efforts included guidance to expedite the approval process, clarify standards and processes for drug approvals, and harmonize preapproval guidance to assure the submission of adequate studies.

For example, the Center issued:

- A regulation describing the procedures for requesting, conducting, and documenting presubmission conferences. The conferences provide an opportunity for a drug sponsor to reach an agreement with FDA establishing a submission or investigational requirement.
- Draft Guidance for Industry (#169) on the chemistry, manufacturing, and controls information to be submitted for certain drug substances to ensure continued drug substance and drug product quality.¹
- Draft Guidance for Industry (#162) for preparing and using comparability protocols for changes in chemistry, manufacturing, and controls of protein drug products.² A comparability protocol is a comprehensive plan that describes certain tests, studies, and limits to be achieved to demonstrate the effect of manufacturing changes on safety and effectiveness of drug products.
- Draft Guidance for Industry (#135) for validation of analytical procedures for Type C medicated feeds. The draft guidance provides recommendations on how to consider the various validation characteristics for each analytical procedure used in medicated feed assays.
- Draft Guidance for Industry (#171) for waiver of *in vivo* demonstration of bioequivalence of animal drugs in soluble powder oral dosage form products and Type A medicated articles. The draft guidance expands on CVM's bioequivalence guidance, explaining how CVM intends to evaluate requests for waiver.
- Draft and final guidance documents resulting from collaborative efforts with industry and international regulatory partners within VICH³ to harmonize preapproval guidance. This will further assure the submission of adequate studies to protect public health and to support the efficient use of industry resources. It includes six documents related to human food safety.

¹ Prepared by the Chemistry Manufacturing and Controls Coordinating Committee, including representatives from CVM and FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

² Prepared by the Comparability Protocol Working Group, including representatives from CVM and FDA's CDER and CBER.

³ VICH is the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.

SIGNIFICANT NEW APPROVALS

FY 2004 was a productive year for approval of original, supplemental, and generic animal drug applications. The following tables document approvals that we consider to be significant.

TABLE 1 – ORIGINAL APPROVALS

SIMPLICEF (cefpodoxime proxetil)	New chemical entity for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of <i>Staphylococcus intermedius</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus canis</i> (group G, β hemolytic), <i>Escherichia coli</i> , <i>Pasteurella multocida</i> , and <i>Proteus mirabilis</i> .
EXCEDE for Swine (ceftiofur crystalline free acid) sterile suspension	EXCEDE for Swine is an antimicrobial indicated for the treatment of swine respiratory disease (SRD) associated with <i>Actinobacillus pleuropneumoniae</i> , <i>Pasteurella multocida</i> , <i>Haemophilus parasuis</i> , and <i>Streptococcus suis</i> .
METACAM Injectable Solution (meloxicam)	Original approval for the control of pain and inflammation associated with osteoarthritis in dogs.
NAVIGATOR Oral Paste (nitazoxanide)	New chemical entity for the treatment of equine protozoal myeloencephalitis (EPM).
ULCERGARD (omeprazole)	Oral Paste original OTC approval for the prevention of gastric ulcers in horses.
VETSULIN (insulin)	New chemical entity and the first veterinary insulin approval. The product is approved to treat hyperglycemia and hyperglycemia-associated clinical signs in dogs with diabetes mellitus.
BUSCOPAN Injectable Solution (N-butylscopolammonium bromide)	New chemical entity for the control of pain associated with spasmodic colic, flatulent colic, and simple impactions in horses.
SURPASS Topical Anti-Inflammatory Cream (diclofenac)	New chemical entity for the control of pain and inflammation associated with osteoarthritis in horses.
SEDIVET Injectable Solution (romifidine hydrochloride)	New chemical entity for the control of pain and inflammation associated with osteoarthritis in horses.
PREVICOX TABLETS (firocoxib)	New chemical entity for the control of pain and inflammation associated with osteoarthritis in dogs.

TABLE 2 – SUPPLEMENTAL APPROVALS

BANAMINE (flunixin meglumine) Injectable Solution	Adds lactating dairy cattle to the existing indications for the control of pyrexia associated with bovine respiratory disease and endotoxemia, and for the control of inflammation in endotoxemia. Additionally, this supplement adds a new indication for the control of pyrexia associated with acute bovine mastitis, and it establishes a tolerance for residues of flunixin in milk.
OXYMARINE (oxytetracycline hydrochloride soluble powder)	Provides for the immersion marking of the skeletal tissues of finfish fry and fingerlings. This supplemental NADA relied on publicly available data contained in Public Master File (PMF) 5667, which were compiled under National Research Support Project 7 (NRSP-7), a national agricultural research program for obtaining clearances for use of new drugs in minor animal species and for special uses.
EQUIMAX (ivermectin, praziquantel)	Supplemental approval for use of the deworming product in breeding, pregnant, or lactating mares without adverse effects on fertility.
IVOMEK (ivermectin) Pour-On for Cattle	Adds new persistent activity indications for <i>Dictyocaulus viviparus</i> for 28 days after treatment, <i>Cooperia surnabada</i> for 14 days after treatment, and <i>Damalinia bovis</i> for 56 days after treatment. Extends the persistent activity periods for <i>Oesophagostomum radiatum</i> from 14 to 28 days after treatment and <i>Cooperia punctata</i> and <i>Trichostrongylus axei</i> from 14 days to 21 days after treatment.
IVOMEK PLUS (ivermectin & clorsulon) Injection for Cattle	Extends the persistent effect periods for <i>Oesophagostomum radiatum</i> from 14 to 28 days after treatment and <i>Cooperia punctata</i> and <i>Trichostrongylus axei</i> from 14 to 21 days after treatment.
IVOMEK (ivermectin) Injection for Cattle and Swine	Extends the persistent effect periods for <i>Oesophagostomum radiatum</i> from 14 to 28 days after treatment and <i>Cooperia punctata</i> and <i>Trichostrongylus axei</i> from 14 to 21 days after treatment.
DECTOMAX (doramectin) Pour-On for Cattle	Extends the persistent effect periods for <i>Cooperia punctata</i> from 28 to 35 days after treatment and <i>Dictyocaulus viviparus</i> and <i>Cooperia oncophora</i> from 21 to 28 days after treatment.
LEVASOLE (levamisole hydrochloride) Soluble Drench Powder for Cattle and Sheep	Provides for combining NADAs 112-050 and 112-051 for sheep and cattle, respectively, with labeling for the 1.8 oz. and 21.34 oz. containers bearing the indications for both these species and the 0.46 oz. container bearing the indications for sheep only.
WAZINE Pork Pack Soluble Powder (dipiperazine sulfate; piperazine hydrochloride)	Adds a swine-only label for a 35 lb. container of soluble powder (piperazine dihydrochloride) with directions for administering in water or by feed. Also, adds directions for individual administration in feed using a provided beaker as a measuring device.
TM-50, TM-100, TM-50D, and TM-100D Type A Medicated Articles (oxytetracycline)	Establishes a zero-day pre-slaughter withdrawal period in cattle after administration of TM-50, TM-100, TM-50D, and TM-100D Type A Medicated Articles (oxytetracycline) at a dosage of 10 mg oxytetracycline per pound of body weight daily for 14 days.
TERRAMYCIN 50, TERRAMYCIN 100, and TERRAMYCIN 200 Type A Medicated Articles (oxytetracycline)	Establishes a zero-day pre-slaughter withdrawal period in cattle after administration of TERRAMYCIN 50, TERRAMYCIN 100, and TERRAMYCIN 200 Type A Medicated Articles (oxytetracycline) at a dosage of 10 mg oxytetracycline per pound of body weight daily for 14 days.
NAXCEL Sterile Powder (ceftiofur sodium)	Establishes a 4-day pre-slaughter withdrawal time in swine after administration of NAXCEL Sterile Powder.

TABLE 2 – CONTINUED

EXCENEL RTU Sterile Suspension (ceftiofur hydrochloride)	Establishes a 4-day pre-slaughter withdrawal time in swine after administration of EXCENEL RTU Sterile Suspension (ceftiofur hydrochloride).
BOVATEC 68 (lasalocid)	To be used in the manufacture of CRYSTALYX IONO-LYX Free-Choice Type C Medicated Protein Feed Block for pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) for increased rate of weight gain.
COMPONENT TE-IS with TYLAN (trenbolone acetate and estradiol, and tylosin tartrate) ear implant containing trenbolone acetate (80 mg), estradiol (16 mg), and tylosin tartrate (29 mg)	For increased rate of weight gain and improved feed efficiency for steers fed in confinement for slaughter.
COMPONENT TE-200 with TYLAN Implant containing trenbolone acetate (200 mg), estradiol (20 mg) and tylosin tartrate (29 mg)	For use in steers fed in confinement for slaughter. Trenbolone acetate and estradiol increase rate of weight gain and improve feed efficiency, while tylosin tartrate acts as a local antibacterial.
COMPONENT TE-200 with TYLAN (trenbolone acetate and estradiol, and tylosin tartrate) ear implant containing trenbolone acetate (80 mg), estradiol (8 mg), and tylosin tartrate (29 mg)	For increased rate of weight gain for heifers fed in confinement for slaughter.



Scientists confer at CVM's Office of Research

TABLE 3 – COMBINATION APPROVALS

<p>MECADOX 10 (carbadox) & TERRAMYCIN 50, TERRAMYCIN 100, & TERRAMYCIN 200 (oxytetracycline) – Provides for the combined use of carbadox (MECADOX 10, NADA 041-061) and oxytetracycline (TERRAMYCIN 50, TERRAMYCIN 100, and TERRAMYCIN 200, NADA 095-143) Type A medicated articles to make a Type C medicated feed for swine</p>	<p>For treatment of bacterial enteritis caused by <i>Escherichia coli</i> and <i>Salmonella choleraesuis</i> susceptible to oxytetracycline, and treatment of bacterial pneumonia caused by <i>Pasteurella multocida</i> susceptible to oxytetracycline; and increased rate of weight gain and improved feed efficiency. This application was eligible for approval in accordance with the Animal Drug Availability Act (ADAA) provisions for combinations of approved drug products in animal feeds.</p>
<p>DECCOX (decoquinatate) plus RUMENSIN (monensin sodium) Type A Medicated Article</p>	<p>ADAA combination – Increases the feeding range of decoquinatate to 12.9 to 90.8 g/ton.</p>
<p>DICLAZURIL and ROXARSONE</p>	<p>An ADAA feed combination for the prevention of coccidiosis caused by <i>Eimeria tenella</i>, <i>E. necatrix</i>, <i>E. acervulina</i>, <i>E. brunetti</i>, <i>E. mitis</i> (<i>mivati</i>), and <i>E. maxima</i>, and for increased rate of weight gain, improved feed efficiency, and improved pigmentation in broiler chickens.</p>
<p>MONENSIN, RACTOPAMINE and TYLOSIN</p>	<p>An ADAA feed combination for use in beef cattle.</p>
<p>MONENSIN and RACTOPAMINE</p>	<p>An ADAA feed combination for use in beef cattle.</p>
<p>MELENGESTROL ACETATE, MONENSIN, RACTOPAMINE and TYLOSIN</p>	<p>An ADAA feed combination for use in beef heifers.</p>
<p>MELENGESTROL ACETATE, MONENSIN and RACTOPAMINE</p>	<p>An ADAA feed combination for use in beef heifers.</p>

RESEARCH TO SUPPORT ANIMAL DRUG REVIEW

Drug sponsors are responsible for submitting studies to prove that their drugs are safe and effective. Complementary work – accomplished by CVM, its contractors and collaborators – may alter the type and number of studies required for approvals, thus improving the efficiency of the drug approval process. An example of this is an ongoing pharmacokinetics/pharmacodynamics study that will help assess the effects of drugs in diseased animals, an important contribution because most data submitted to CVM are generated in healthy animals. The animal phase of the study utilizing enrofloxacin in both healthy and diseased animals is completed, and we are in the final stages of the laboratory analyses. In addition, we have begun preparations for a second study using tilmicosin.

Another example is an ongoing investigation of the rate and extent of sulfamethazine absorption from fast and slow release boluses. Information from this study in calves will be compared to *in vitro* dissolution data. Results of these comparisons will be used to evaluate the possible use of Process Analytical Technology (PAT) as a new quality control tool for the manufacture of drug products. PAT is a scientific, risk-based framework that will help manufacturers develop and implement new, efficient tools for use during pharmaceutical development, manufacturing, and quality assurance while maintaining or improving the current level of product quality assurance.

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

FY 2004 PERFORMANCE GOALS

- ✓ Provide technical assistance to the staff of the Senate Health, Education, Labor, and Pensions (HELP) Committee chair in preparing the Committee report that accompanied the Minor Use and Minor Species Animal Health Act of 2004 when it passed.
- ✓ After it passed in FY 2004, began implementation of provisions of the Minor Use and Minor Species Animal Health Act of 2004.

THE CHALLENGE

“The Minor Use and Minor Species Animal Health Act of 2004” (MUMS) challenges CVM to implement measures that will significantly expand the availability of drugs for minor uses and minor species. Because the potential sales volume is low, animal drug manufacturers lack economic incentive to seek animal drug approvals for minor uses (diseases that are rare) or minor species (animal species other than cattle, horses, pigs, chickens, turkeys, dogs, or cats). The need in aquaculture is a good example. Aquaculture is becoming an increasingly important source of fish for human consumption. The U.S. aquaculture industry is expanding – approaching \$1 billion in annual sales – and the need for therapeutic and production drugs is growing as well.

FY 2004 ACCOMPLISHMENTS

We focused much of our effort during FY 2004 on MUMS. Prior to the law’s passage, CVM provided technical assistance to the Senate with respect to the language of the law itself and in preparing the committee report that accompanied the bill when it was passed. After passage, we started the process of implementing the new law. We also made significant progress in research that will support MUMS approvals and protect consumers of aquacultured products.

IMPLEMENTATION OF MUMS LEGISLATION

The law and its benefits. Signed by the President in August 2004, this legislation provides innovative, flexible ways to provide drugs to treat minor animal species as well as uncommon diseases in the major animal species. It is designed to help pharmaceutical companies overcome the financial roadblocks they face in providing limited-demand animal drugs. The new law is expected to benefit agricultural groups such as those in aquaculture; also it will help sheep and goat producers and beekeepers. It will also help people who own small or unusual pets such as guinea pigs or

ornamental fish, and it will likely be a great help to zoo veterinarians. The new law modifies provisions of the Federal Food, Drug, and Cosmetic Act in three key ways, providing for:

- **Conditional Approval:** Under MUMS, the sponsor of a veterinary drug can ask CVM for “conditional approval,” which allows the sponsor to make the drug available after proving the drug is safe and establishing a reasonable expectation of effectiveness, but before collecting all of the effectiveness data needed to support a full approval. The drug sponsor can keep the product on the market for up to five years, through annual renewals, while gathering the required effectiveness data.
- **Indexing:** In some cases, the potential market for a minor species drug is just too small to support the costs of the drug approval process, even under a conditional approval. In such instances, FDA now may add the drug to an index of unapproved new animal drugs that may be legally marketed. This provision will be especially helpful to veterinarians treating zoo or endangered animals, or owners of minor pet species such as ornamental fish or caged reptiles, birds, or mammals.
- **Designation:** This aspect of the legislation provides incentives for approvals. It is similar to the “Orphan Drug Act” for humans, which helps pharmaceutical firms develop drugs for limited human uses. Grants to support safety and effectiveness testing will be available. Companies that gain approval for designated new animal drugs will be granted seven years of marketing exclusivity.

Implementation. After the President signed MUMS into law, the Center began the process of establishing the mandated new Office of MUMS Animal Drug Development. This involves establishing functional statements, reporting relationships, delegations of authority, and position descriptions. We also began to establish interim processes to deal with designations and conditional approvals that became effective immediately upon enactment of MUMS. In addition to dealing with the day-to-day business of implementing these provisions of MUMS, we will begin the process of proposing and finalizing the needed implementing regulations – starting with those relating to designation.

RESEARCH TO SUPPORT DRUG APPROVALS

CVM’s extensive research program related to minor species illustrates the Center’s commitment to facilitating the approval process for drugs for minor uses and minor species. The research will be a valuable adjunct as CVM implements the MUMS legislation. Below we describe research and related activities concerning drug effectiveness and human food safety.

Formalin effectiveness. During FY 2004, we completed a study of the efficacy of formalin for treating fungal infections in



Aquaculture research at CVM's Office of Research

rainbow trout. To conduct the trials, we optimized fungal culture conditions and developed a consistent disease model in trout. The results of our study indicate that at several dosage levels formaldehyde significantly reduced mortality in fish with a *Saprolegnia* fungal infection. The final report will provide pivotal data for the Public Master File for use by drug sponsors in obtaining approvals.

Food safety database. As part of CVM's commitment to streamlining the drug approval process for minor species, we have begun to develop a database of literature detailing drug metabolism, residues, and pharmacokinetics in multiple fish species. At the close of FY 2004, this database consisted of more than 250 articles that included data from 50 species (40 genera) of fish. The database will be a valuable resource to investigators of drug metabolism in aquatic species, as well as to government and private organizations involved in the drug approval process for aquatic species.

Drug Residues in Seafood. During FY 2004, we made significant progress in improving the efficiency of drug residue testing, including the development of multi-residue methods for screening/confirmation and quantification of drug residues. This included:

- **Multi-residue procedures for screening/confirmation in shrimp.** During FY 2004, we completed the development and validation of a multi-residue procedure for shrimp that screens and confirms the presence of residues of 17 different drugs in a single assay. The previously existing procedures in ORA laboratories could test shrimp for only two of the drugs included in the new multi-residue procedure.
- **Multi-residue procedures for screening/confirmation in salmon and other finfish.** We started to extend the multi-residue procedure developed for shrimp to salmon and other finfish, an important step because more drugs (approximately 40) potentially can be used for finfish than for shrimp.
- **Multi-residue procedures for quantitative analysis in shrimp.** Screening and confirmation testing for the presence of drugs is an essential regulatory tool, but it is also important to be able to determine the amount of residue. For example, information on drug concentration will be needed if the Agency establishes import tolerances for seafood. Additionally, quantitative procedures will provide tools for approval of needed aquaculture drugs under the new MUMS legislation. However, quantitative procedures do not exist for many of the drugs detected in the screening/confirmation procedure described above. Accordingly, we began the development of a multi-residue quantitative procedure for shrimp during FY 2004.
- **Procedures for nitrofurans residues in shrimp and channel catfish.** Through visitation and on-site method demonstration, CVM Office of Research

scientists during FY 2004 transferred to the FDA's Northeast Regional Laboratory a previously developed method for screening/confirmation of nitrofurans residues in shrimp. Because nitrofurans residues are chemically attached to the tissue matrix, it was not possible to incorporate these compounds into the multi-residue shrimp procedure. Applying the same approach used in shrimp, OR scientists validated methods for both quantitative and screening/confirmation of nitrofurans-bound residues in channel catfish. In addition, in collaboration with the Gulf Coast Seafood Laboratory in FDA's Center for Food Safety and Applied Nutrition, we initiated a study to further investigate the metabolism and depletion of nitrofurans in channel catfish.

Drug residues in honey. Only one antibiotic, oxytetracycline, is currently approved for use in honeybees. However, the drug is believed to be ineffective in some circumstances, leading to the use of unapproved drugs to treat sick colonies. Few methods currently exist for detecting drug residues in honey, but during FY 2004 we started to develop procedures to screen for such residue.

Distinguishing transgenic fish from nontransgenic fish. CVM scientists conducted a study during FY 2004 to determine if transgenic fish could be distinguished from non-transgenic fish using the isoelectrical focusing (IEF) developed by FDA to identify recognized finfish. The IEF patterns showed no differences in the banding patterns between transgenic and non-transgenic salmon. Thus, we have established that the IEF procedures cannot be used to distinguish transgenic salmon from nontransgenic salmon for regulatory purposes.

REDUCING RISK FROM ANTIMICROBIAL RESISTANCE

THE CHALLENGE

Scientific evidence demonstrates that the use of antimicrobial drugs in food-producing animals can result in the selection for resistant bacteria. Resistant foodborne bacteria can then be transferred to humans, resulting in illness. If the consumer needs antimicrobial drug treatment, that therapy may be compromised because the drugs of choice may be ineffective. The first Food and Agriculture Organization (FAO)-World Organization for Animal Health (OIE)-World Health Organization (WHO) expert consultation on “Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific Assessment” in December 2003 (which had CVM participation) concluded that there is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials.



CVM Advisory Committee discussed the pending application for an antimicrobial drug as part of the Center's approach to addressing an issue of antimicrobial resistance

FY 2004 ACCOMPLISHMENTS

In cooperation with other agencies, CVM has undertaken proactive risk assessment and risk management, surveillance, research, and education 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 the FDA Strategic Plan priority of reducing the major public health threat caused by foodborne illness.

ASSESSING RISK AND TAKING APPROPRIATE RISK MANAGEMENT ACTION

Guidance for assessing risk. The Center has fully implemented the Guidance for Industry (GFI #152)⁴, which provides a scientific risk-based process for assessing the likelihood that an antimicrobial drug used to treat an animal may cause an antimicrobial resistance problem in humans. As an example of the implementation of the guidance, CVM's Veterinary Medicine Advisory Committee (VMAC) in October 2004 considered the microbiological food safety of an antimicrobial drug application under review for use in food-producing animals.

FY 2004 PERFORMANCE GOALS

- ✓ Enhance the transparency of National Antimicrobial Resistance Monitoring System (NARMS) to stakeholders, the public, and other interested parties by increased reporting and communications of NARMS results and program information by publishing annual reports of NARMS data from animals (provided by the USDA), humans (provided by the CDC) and retail meat (provided by FDA); posting NARMS publication references on the website; and presenting NARMS susceptibility testing results at scientific meetings via posters or oral presentations.
- ✓ Support an advanced World Health Organization (WHO) training course on the surveillance of Salmonella and antimicrobial resistance in foodborne pathogens.
- ✓ Participate in the cooperative agreement with four sites in Mexico to determine prevalence of Salmonella species and quinolone-resistant *E. coli* in symptomatic and asymptomatic humans.
- ✓ Enhance the robustness of the NARMS retail meat arm by training participating State public health labs in isolation and testing methodologies and expanding the number of labs participating in the retail meat arm.
- ✗ Although we did meet the goal of training State laboratory personnel, the retail meat arm of NARMS did not expand to new sites this year because all 10 FoodNet sites are currently participating. As FoodNet expands, we will consider expanding to additional sites.
- ✓ Continue to review penicillin and tetracycline approvals for microbiological food safety concerns.
- ✓ Develop a database that will be searchable from the web containing a listing of all antimicrobials approved for use in food animals.

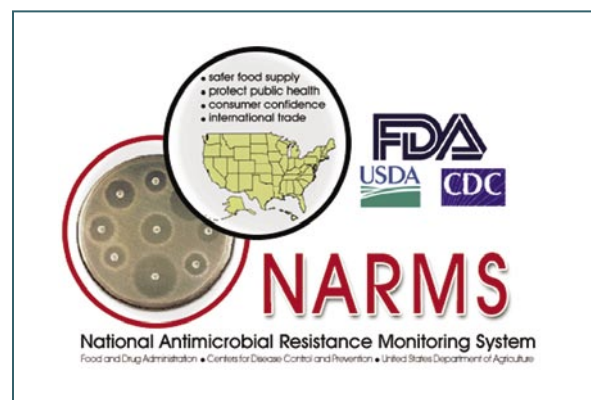
⁴ "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern."

Continuation of penicillin and tetracycline review. As a follow up to long-standing proposals to withdraw approvals of subtherapeutic feed uses of penicillin and tetracycline, CVM during FY 2004 completed microbiological food safety reviews of the last of seven approved penicillin and penicillin combination products. Review of several approved tetracycline products is underway. These reviews are using GFI #152 as a guide to develop an overall estimate of the risk to humans from the continued use of these drugs.

Progress in risk assessments. In accordance with a plan to evaluate risks associated with use of approved antimicrobials, we completed a risk assessment for Virginiamycin use in food animals. We will use information from the risk assessment to determine what risk management measures we should take, if any.

MONITORING FOR THE DEVELOPMENT OF RESISTANCE

Federal/State monitoring program. We collaborate with the USDA and the CDC in the operation of NARMS, which tracks changes in susceptibilities to a number of antimicrobial drugs of animal pathogens that can cause disease in humans.



Data from the program provides timely information to veterinarians and physicians, prolonging the useful lives of approved drugs by promoting prudent use. NARMS data have stimulated research in molecular characteristics of resistance emergence and transfer, improved our knowledge of risk factors associated with the development of antimicrobial resistant infections, and triggered research projects related broadly to prudent antimicrobial use in animals.

NARMS consists of three kinds of testing sites, or arms: human (led by CDC), animal (administered by USDA), and retail meats (directed by FDA/CVM). The sites use identical isolation, identification, and susceptibility testing procedures. Surveillance includes non-typhoidal *Salmonella*; *Escherichia coli*, including *E. coli* O157:H7; *Campylobacter* and *Enterococcus* isolated from human stool samples, animals at slaughter, and retail meat; and human isolates of *Shigella*, non-cholerae *Vibrio*, *Listeria* and *Salmonella Typhi*.

CVM's Office of Research scientists coordinate the NARMS retail meat arm. Sites in 10 States that are part of FoodNet participate by collecting samples from local grocery stores and submitting isolates to the CVM/OR laboratory for antimicrobial susceptibility testing. The work of the FoodNet sites has allowed FDA to monitor the antimicrobial susceptibility profiles of foodborne pathogens at the point of consumer purchase, providing a more representative picture of the contribution of the food supply to antimicrobial resistance. This information serves

as an early warning system should foodborne pathogens begin to show increased resistance to various antimicrobial agents being used in animal husbandry and clinical human medicine. The data also helps sponsors with their submissions to CVM under Guidance for Industry #152.

NARMS retail meat arm accomplishments in FY 2004 included:

- CVM/OR matched the PFGE (pulsed-field gel electrophoresis) patterns of bacteria isolated from retail meat collected in the State of Iowa to bacteria collected from humans in Iowa who were ill from foodborne disease. By matching PFGE patterns (DNA fingerprints) for bacteria from different sources, it is possible to show a link between isolates from animals, retail meats, and bacteria isolated from infected humans. In fact, this work showed that bacteria in retail meat caused the people in Iowa to become ill.
- The first annual report of the retail meat arm, representing data for year 2002 isolates, went on line at the CVM website in September 2004. In January 2005, all 10 FoodNet sites that are part of the retail meat sampling program will adopt more statistically robust sampling procedures.
- Because a number of laboratories are involved in purchasing retail meats and conducting the microbiological analysis, we developed a training program to ensure that all sites use identical methods to collect, isolate, and identify the bacteria. Representatives of nine State laboratories participated in our second training session, in November 2003. CVM microbiologists and epidemiologists provided lectures and laboratory demonstrations for this successful training session.



Participants in ResistVet program in Mexico learn to test for resistant strains of bacteria

International expansion of NARMS: Mexican resistance surveillance.

Responding to increases in U.S. importation of meat and poultry from Mexico after passage of the North American Free Trade Agreement, CVM collaborated with the Mexican government to establish a novel surveillance initiative, ResistVet, in January 2002. The cooperative agreement involves development of a surveillance system for *Salmonella*, *Campylobacter* and quinolone-resistant *E.coli* at sites in four Mexican states with high agricultural activity. The surveillance system is designed to identify outbreaks of foodborne illness, in particular those that are multi-drug resistant, in time to respond with interventions to stop the spread of resistant pathogens.

In FY 2004, the principal investigator initiated training in slaughter plant sampling in the state of Yucatan, with the participants learning how to sample the carcasses and submit the samples to the health department laboratory. As a result of the successful training, the state agriculture authorities plan to initiate sampling in all slaughter plants in Yucatan.

ResistVet has strengthened Mexico's capacity to monitor foodborne disease and resistant pathogens. During FY 2004, work continued on determination of the prevalence of *Salmonella*, *Campylobacter*, and quinolone-resistant generic *E. coli* both in asymptomatic and ill humans, as well as from poultry, beef, and pork. The project also made progress in identification and comparison of the susceptibility profiles of the *Salmonella*, *Campylobacter*, and *E. coli* isolates.

Animal feed surveillance. Several studies have shown that human foodborne illness can be traced back to animal feed. During FY 2004 we instituted surveillance of resistant pathogens in animal feed, including *Salmonella*, *E. coli* and *Enterococcus*. Although limited, the data obtained suggest that animal feed components may be an important vehicle for the dissemination of zoonotic (animal to human) pathogens and antibiotic resistance. We plan to continue the sampling project in the future.

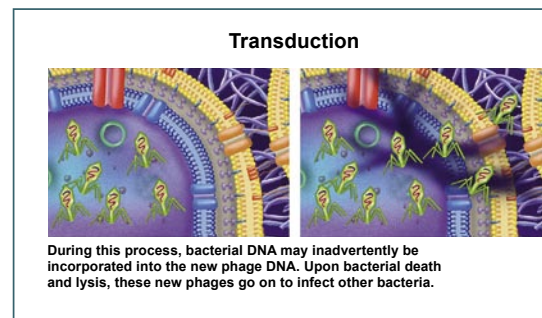
INTERNATIONAL TRAINING IN FOODBORNE ILLNESS CONTROL

Global Salm-Surv (GSS) is a worldwide network of laboratories and individuals involved in surveillance, isolation, identification, and antimicrobial susceptibility testing of foodborne pathogens. It is part of an effort by the WHO to strengthen the capacities of its Member States in the surveillance and control of major foodborne diseases, and to contribute to the global effort of containment of antimicrobial resistance in foodborne pathogens.

To help meet these goals, CVM provides financial support and personnel with expertise in the epidemiology and microbiology of foodborne disease. In FY 2004, CVM microbiologists participated as trainers in two training courses, one in Trinidad for participants from the English-speaking Caribbean nations (the CVM participant was Dr. Patrick McDermott), the other in Nanjing, China, for participants representing 20 cities/provinces (the CVM participant was Dr. Shaohua Zhao, who speaks Mandarin). At the end of each training course, participants are asked to present specific action plans for improving surveillance of foodborne diseases in their home regions.

OUTREACH AND EDUCATIONAL EFFORTS

Animated Video on Antimicrobial Resistance. During the year, our scientists and communications specialists collaborated to produce an animated video that shows the ways in which bacteria can develop resistance to antimicrobials. The



During FY 2004, CVM produced an animated video to show the processes bacteria can use to become resistant to antimicrobials. This is a scene from that video.

purpose of the video is to advance understanding by key audiences, particularly veterinary students and livestock producers, of the issue of antimicrobial resistance by showing how the process works.

CVM scientists presented results, strategies and design issues related to NARMS to a number of audiences during FY 2004. For example, OR scientists presented susceptibility testing results via posters or oral presentations at seven scientific meetings, including the American Society for Microbiology annual meeting and the Annual Conference on Antimicrobial Resistance.

NEW DATABASE OF APPROVED NEW ANIMAL DRUGS

The Center made substantial progress during FY 2004 in developing a web-based database with enhanced search capability that will allow members of the public to search for approved drugs by type as well as species. The project, originally conceived to help members of the public learn more about approved antimicrobial veterinary products, has been expanded to boost the ability of FDA and the public to search by type and species for all approved new animal drugs. The final version of the database is scheduled to be available in FY 2005.

FY 2004 PERFORMANCE GOALS

✓ Conduct research that will provide information that has the potential to reduce the transfer of resistant animal pathogens to humans.

RESEARCH TO SUPPORT ANTIMICROBIAL RESISTANCE SURVEILLANCE AND REGULATION

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

taken to control antimicrobial resistance will be based on sound science. Our FY 2004 research included several broad objectives, as follows.

Multi-drug resistant *Salmonella* serotype Newport has recently been spreading on an epidemic scale in both animals and humans throughout the United States. During FY 2004, OR scientists used PFGE to characterize a collection of *S.* Newport isolates (recovered from animals, retail meats, and ill humans) with regard to antimicrobial resistance phenotypes as well as genetic relatedness. Results demonstrated that resistant isolates spread between animals and humans. The research supports the conclusion that bacterial pathogens isolated from animals and humans that have identical DNA fingerprints can be considered to have come from a single source. If the pathogen is a zoonotic foodborne pathogen, then the animal from which it was isolated would be considered the source. This research removes any doubts that humans can become infected and ill from the use of antimicrobials in food-producing animals.

This accomplishment was possible because of CVM's association with the PulseNet program, a national molecular subtyping (genotypic) network for foodborne disease surveillance. The program uses PFGE as the DNA fingerprinting method to identify the source of foodborne illness outbreaks. CVM's efforts as part of PulseNet focus on characterizing bacterial strains obtained from food-producing animals and retail meats. Data from these samples provide a critical link with NARMS, a surveillance program that is based on phenotypic characterization of bacteria, e.g., isolation, identification, and antimicrobial susceptibility testing. The PulseNet database represents a powerful epidemiological tool to conduct trace-back studies during outbreaks of foodborne illness leading to faster intervention and establishment of control measures.

Our FY 2004 PulseNet-related accomplishments included subtyping of more than 1,200 *Salmonella*, *E. coli*, *Campylobacter* and *Vibrio* isolates by PFGE. We also analyzed approximately 400 *Salmonella* isolates (obtained from four State veterinary diagnostic laboratories) using PFGE and antimicrobial susceptibility testing. We found varying but generally high rates of drug resistance, including multiple resistance among some isolates. We also identified several resistance genes.

To better interpret the public health threat represented by current antimicrobial resistance levels, CVM contracted with the American Type Culture Collection (ATCC) to measure resistance among banked historical collections of *Salmonella*, *Campylobacter* and *E. coli*. ATCC had received 1,513 *E. coli*, 1,876 *Salmonella*, and 1,138 *Campylobacter* strains as of September 2004. Once we complete antimicrobial susceptibility testing of these isolates, we will use resistant isolates to examine the genetic bases of resistance. Data from this study will help us better assess the impact over the past six decades of antimicrobial use in veterinary and human medicine.

CVM's Bacterial Source Tracking project investigates the animal origin of human *Salmonella* and *Campylobacter* infections. OR scientists are using a variety of techniques to determine with some level of certainty if a human *Salmonella* infection can be traced to food-producing animals of a particular species (e.g., cattle, pigs, poultry, etc.). Results obtained during FY 2004 show that, while serotyping, antibiograms, and PFGE can show some host-specific clustering, it will require a combination of phenotypic and genotypic methods to identify the animal source of a human infection. Thus, we plan to conduct further research in this area.

FY 2004 PERFORMANCE GOALS

- ✓ Use existing microbiological collections to examine historical susceptibility of foodborne bacterial pathogens to antimicrobial agents. Search, assess, and acquire collections of *Escherichia coli*, *Salmonella*, and *Campylobacter*.

FY 2004 PERFORMANCE GOALS

- ✓ Conduct research to identify the food-producing animal species that contribute to antimicrobial resistance in foodborne pathogens.

CONTROLLING RISK FROM BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

THE CHALLENGE

The discovery of a BSE-infected cow in the United States during 2003 added to CVM's challenge to strengthen controls that will prevent the spread of BSE through feed. BSE, commonly known as "mad cow disease," 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 (vCJD), by consuming food from BSE-infected cattle. In the absence of adequate controls, BSE could spread among the cattle population through feed ingredients derived from infected cattle.

FY 2004 ACCOMPLISHMENTS

Much of our effort during the year focused on follow-up action related to the BSE case; this included compliance activities and steps toward strengthening our BSE feed regulation. We made significant progress in developing analytical methods that will enhance efficient, effective compliance with the regulation. Following are highlights of some of our achievements during the year just ended, as we focus on the FDA strategic priorities of protecting consumer and animal health, and efficient risk management.

FY 2004 PERFORMANCE GOALS

- ✓ Finalize an interim final rule that revises the existing feed ban rule.
- ✓ Conduct targeted BSE inspections of 100 percent of all known renderers and feed mills processing products containing prohibited material (in conjunction with FDA's Office of Regulatory Affairs).
- ✓ Provide technical assistance and research methods to State and FDA analytical laboratories for detecting bovine-derived proteins in animal feeds.
- ✓ Work on validating a simpler, faster version of the Polymerase Chain Reaction (PCR) method.
- ✓ Work on developing an immuno-chemical-based test that can be used as an adjunct to the PCR test, to identify exempt proteins in animal feeds that will support the FDA's feed ban.
- ✓ Begin to evaluate commercially available diagnostic test kits marketed for the detection of mammalian protein in animal feed or feed ingredients.



FDA feed controls designed to prevent BSE

RESPONDING TO THE BSE CASE IN THE UNITED STATES

In December 2003, the USDA's Animal and Plant Health Inspection Service (APHIS) notified FDA that a dairy cow slaughtered at a Washington State slaughterhouse was positive for BSE. The FDA took immediate actions, aided by State regulatory authorities, to identify, control, and dispose of all rendered animal feed that could have contained remnants of the BSE-positive cow. CVM's activities in this investigation included providing staffing to the FDA and

USDA/APHIS emergency operation centers, tracking the distribution and disposition of suspect material, communicating with State authorities, and overseeing the final disposition or destruction of the suspect material. CVM has also issued a Guidance for Industry (#174) for the disposition of material from BSE-positive cattle in animal feed.

STRENGTHENING THE BSE FEED REGULATION

FDA acted in 1997 to prevent the establishment and amplification of BSE in the United States through feed, and thereby minimize any risk to animals and humans. We did so by adopting our BSE feed regulation, which prohibits the feeding of certain mammalian protein – known as “prohibited material” – to cattle and other ruminants.

After discovery of the BSE-infected cow, FDA announced plans to publish interim final rules modifying the BSE feed regulation. Soon after, however, an International Review Team convened by USDA issued a report that included proposals for public health actions that differed significantly from those planned by FDA.

In lieu of an interim final rule, in July 2004 FDA and the USDA published an advance notice of proposed rulemaking (ANPRM) requesting comments and scientific information on several additional regulatory measures that would strengthen the feed regulation. Some of the measures under consideration would prevent cross contamination of prohibited material to feed intended for cattle and other ruminants. These measures include: removing specified risk materials (SRMs) from all animal feed, including pet food; requiring dedicated equipment or facilities for handling and storing feed and ingredients during manufacturing and transportation; and prohibiting the use of all mammalian and poultry protein in ruminant feed. (“SRMs” are the materials such as brain and spinal cord considered most likely to be infected with BSE.) Another measure would exclude the use of materials from non-ambulatory disabled cattle and dead stock in any animal feed. The agencies were reviewing the comments as the fiscal year closed.

STRENGTHENING THE RUMINANT FEED BAN INSPECTIONAL EFFORTS

In November 2003, FDA published a compliance program guidance manual, “Bovine Spongiform Encephalopathy/Ruminant Feed Ban Inspections,” for use by State and FDA regulatory officials. The document is intended to assist investigators in determining compliance with the BSE feed regulation that prohibits the use of specified animal proteins in ruminant feeds. The new guidance provides a more comprehensive description of inspectional efforts than had previously been available. Throughout the year, CVM continued its educational efforts by conducting a number of State-by-State workshops on the specifics of conducting these inspections.

During FY 2004, FDA and State investigators inspected 647 firms as part of our BSE feed inspection program. This included 100 percent of all known renderers and feed mills processing products containing prohibited material. Some of the firms were no longer handling prohibited material, reducing to 570 the number of firms that are known to be handling prohibited material.

SURVEILLANCE ASSIGNMENT FOR DETECTING PROHIBITED MATERIAL IN DOMESTIC ANIMAL FEEDS

In further support of the BSE prevention efforts, CVM during FY 2004 issued an assignment to sample and analyze a wide variety of animal feeds to determine whether feed intended for ruminants might contain material prohibited by FDA's BSE feed regulation. Due to limitations of analytical methods (which could detect mammalian protein but could not definitively detect the presence of prohibited mammalian protein), it was necessary to follow positive analytical findings with investigations to determine whether the positive results were due to the presence of prohibited material. The follow-up investigations (at feed mills and elsewhere in the feed chain) revealed a high level of compliance with the BSE feed regulation.

DEVELOPING ANALYTICAL METHODS FOR DETECTING PROHIBITED MATERIALS

The availability of practical, validated methods to detect protein from different animal species could improve effectiveness and efficiency in the enforcement of the BSE feed regulation. Methods to detect mammalian protein have been available for some time. But, because not all mammalian proteins are prohibited from ruminant feed, methods are needed to identify protein from prohibited species, such as cattle. The development and use of such methods would be consistent with the FDA Strategic Plan priority of targeting limited resources for maximum protection.

In FY 2003, the CVM Office of Research validated a DNA-based method for detection of bovine-derived material, and has made the method available for routine use by FDA field laboratories and several State laboratories. In FY 2004, a second DNA-based method trial successfully validated the use of a commercially available forensic kit for detecting bovine and ovine (sheep) meat and bone meals. OR scientists are working with FDA field scientists to integrate this PCR method into current work assignments in the field laboratories. In addition, the two groups have begun efforts to configure the method to be a confirmatory test for feed microscopy, which is the official FDA methodology for detecting the presence of animal components in feed.

Recent efforts have resulted in the development of a real-time PCR method capable of detecting bovine (cattle), porcine (swine), ovine (sheep), caprine (goat), equine (horse), or cervid (deer) material, along with fowl. ("Real-time" means that we can detect the presence of prohibited material as the reaction is taking place, so we do not have to further process the sample.) This method is capable of detecting meat and bone meals prepared under conditions of time, temperature,

and pressure used in the European Union as well as the United States. (Most other available tests detect only material rendered in the United States.) Additional work is focused on developing a multiplex, real-time method that would permit the simultaneous detection of up to four different species within a single PCR reaction tube. Successful development and validation of such a method would allow field laboratories to use the same PCR method for imports and U.S. produced feeds. During FY 2004, our Office of Research also began evaluating commercially available diagnostic tests marketed for the detection of mammalian proteins in animal feed and feed ingredients. We completed our evaluation of two tests intended for field use, concluding that with labeling changes the tests can be important tools for surveillance and quality assurance, although they appear to be less sensitive than the laboratory methods in current use.

AVOIDING UNSAFE DRUG RESIDUES IN HUMAN FOOD

FY 2004 PERFORMANCE GOALS

- ✓ Modify Compliance Program Guidance Manual 7371.006 Illegal Residues in Meat and Poultry to include residues of domestic seafood. The program's name will be changed to Illegal Residues in Meat, Poultry and Seafood.
- ✓ Conduct surveys of drug residues in imported foods to support a risk assessment of the hazards from these residues.
- ✓ Perform laboratory validation of chemical analytical methods submitted to support pre-market product applications.
- ✓ Use new technologies in the development of multi-residue methods for the detection of drug residues in imported aquaculture products.

THE CHALLENGE

Improper use of approved drugs or use of unapproved drugs in domestic food-producing animals can result in unsafe residues in meat, poultry, seafood, and milk. Firms or individuals who repeatedly present animals for slaughter that are adulterated with illegal drug residues may represent a significant public health risk. In fact, investigation of repeat violators is our top priority. In addition, investigating first-time violations of drugs prohibited from extralabel use in food animals, drugs not approved for food-producing animal use, and very high-level drug residues are high priorities for investigation. Also, we are challenged by the FDA Strategic Plan's emphasis on the need for safety oversight to catch up with the rapid growth in the volume of imports of products, especially seafood, that are under FDA's jurisdiction.

FY 2004 ACCOMPLISHMENTS

The following summarizes our FY 2004 efforts to avoid unsafe residues in meat, poultry, milk, and seafood.

ENFORCEMENT TO CONTROL DRUG RESIDUES IN MEAT

Controlling unsafe hormone implants in veal calves. CVM played a major role in developing a viable interagency approach to controlling the use of hormone implants in veal calves. Working with the USDA, our Division of Compliance prepared temporary guidance providing conditions under which veal calves that had been implanted could be marketed safely for human food. The Division worked closely with regulated industry and other Federal agencies to develop adequate education and oversight programs to ensure continued industry compliance. In addition, as a result of efforts by our Division of Surveillance, manufacturers of several hormonal implant products added warning statements on their products' labels, cautioning against improper use of the products in veal calves.

Neomycin residue in bob veal calves. In response to increased numbers of violative neomycin residues in bob veal calves, the Center published a CVM UPDATE in July 2004 to

inform producers that using a milk replacer product containing neomycin in calves that might go to slaughter as veal may cause antibiotic residues. (Bob veal calves are calves that are a few days to three weeks of age, weighing up to 150 pounds and being fed milk or milk-based diets.)

Actions against tissue residue violators. Under CVM's direction, FDA and States working on the Agency's behalf under contracts or cooperative agreements investigated 743 tissue residue violations during the year. FDA issued 105 tissue residue-related Warning Letters. Enforcement actions resulted in consent decrees of injunction against several dairy farms that had marketed cows and calves whose edible tissues contained illegal drug residues. We initiated six residue-related injunction actions, one contempt-of-injunction action, and two criminal prosecutions during the year.

Drug inventory survey. During FY 2004, we initiated use of a drug inventory survey form by investigators who make on-farm visits. Information on drug use that will be reported on this form will help establish priorities for drugs to be included in the USDA's national residue testing program.

RESEARCH TO SUPPORT REGULATORY EFFORTS TO PREVENT UNSAFE DRUG RESIDUE IN MEAT AND MILK

Research conducted or funded by CVM supports the development and use of analytical methods for detecting drug residue in meat and milk. For example, during FY 2004 we performed laboratory validation of chemical analytical methods (used to detect residue in edible products) submitted to support pre-market product applications for three new animal drugs.

Another example is our work during FY 2004 related to tissue-fluid correlation in beef steers. CVM scientists have studied the distribution of the drugs gentamicin and penicillin in the blood, urine, and kidney tissue of beef steers. By knowing the relationship of drug levels in these parts of the animal, producers, processors, and regulatory officials will be able to quickly test the blood or urine of a live animal to determine if the kidney tissue contains violative levels of these frequently used veterinary drugs. Screening test kits that provide a positive response to drug levels in the urine, saliva, or plasma and that correlate to a violative drug concentration in the kidney can then be developed for field use. This will allow a rapid decision regarding the slaughter status of a drug-treated steer.

In the course of this research, CVM scientists developed laparoscopic techniques to periodically biopsy the kidneys of drug-treated steers. These techniques will be useful in drug residue research supporting new animal drug approvals. They permit simultaneous monitoring of drug depletion in biological fluids and kidney tissue for the establishment of the most precise correlation with a minimum number of animals. Typically, kidney tissue samples can be obtained only from slaughtered

animals; this restricts the sampling of kidney tissue of each animal to a single time point. The laparoscopic procedure allows researchers to obtain tissue samples at various time points from the same animal. This reduces the total number of animals required, and limits the impact of between-animal biological variation.

CONTROLLING UNSAFE DRUG RESIDUES IN DOMESTIC AND IMPORTED SEAFOOD

CVM's Office of Research has conducted surveys of drug residues in imported aquaculture foods to support a risk assessment of the hazards from these residues. Specifically, OR has developed a fish database that provides, among other things, pharmacokinetic and pharmacodynamic data that could be used for a risk assessment. Also, as mentioned in the section on MUMS, OR has used new technologies to develop multi-residue methods that can be used to detect drug residues in both imported and domestic seafood.

During FY 2004, CVM updated its compliance program aimed at reducing illegal drug residues in meat and poultry, by adding coverage of drug residues in domestic seafood and other animal-derived foods, such as honey, to the program. Program implementation will be modified by the issuance of directed assignments for investigations of repeat violators.

ENSURING FEED SAFETY

THE CHALLENGE

Threats to the safety of the nation's animal feed supply could come from several sources, including bioterrorism. Contaminants and unsafe additives in animal feed can harm the animals, as well as humans who consume animal products – and 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 2004 ACCOMPLISHMENTS

Following are highlights of our FY 2004 accomplishments with regard to feed safety.

RISK-BASED SYSTEM – ANIMAL FEED SAFETY SYSTEM

CVM is developing a comprehensive risk-based feed safety system that would be preventive. 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. A Work Group that included representatives from State regulatory agencies and several FDA components sponsored a two-day public meeting in September 2003 to gather input from representatives of the feed industry and other sectors.

During FY 2004 we reviewed and summarized the comments from the public meeting, and made the summaries available on the CVM website (www.fda.gov/cvm). To assist us in the development of the AFSS, we also performed a study of the strengths and weaknesses of the current measures used by the FDA in animal feed safety. And we sought comment on key definitions and the essential elements of the AFSS.

SAFETY REVIEW OF FEED INGREDIENTS

Food additives. CVM is responsible for the review and approval of new substances added to animal feed. We approved one food additive petition, for natamycin, during the fiscal year. Natamycin is added to broiler chicken feed to retard the growth of *Aspergillus parasiticus*, a fungus known to produce mycotoxins that can adversely affect human and animal health.

FY 2004 PERFORMANCE GOALS

- ✓ Continue the process of generating an Animal Feed Safety System (AFSS), establish a project plan and monitor progress. Develop process control guidance and model regulations for State adoption.
- ✓ Maintain biennial coverage by inspecting 50 percent of 1,440 registered animal drug and feed establishments (in conjunction with ORA).
- ✓ Prepare final guidance for industry on raw meat diets.



CVM feed mill

Safety of enzymes. The development of novel technologies to engineer protein products with improved functionality in animal feed has spurred interest in the feed use of enzymes. When added to animal feed, enzymes improve nutrient digestibility. Use of enzymes, therefore, can reduce the amount of nitrogen and phosphorus entering the environment, and thus help mitigate environmental concerns related to animal waste. Our Division of Animal Feeds conducted safety reviews of several new sources of the enzyme phytase in FY 2004. Phytase increases the digestibility of phosphorus bound to phytate, so its use can reduce the amount of phosphorus in animal waste.

Plant biotechnology. Utilizing a voluntary notification system, FDA reviews the safety of biotechnology-derived plant varieties that have been developed for traits such as herbicide resistance, insect pest resistance, enhanced nutrient availability or modification of nutrient composition (e.g., high laurate canola and high oleic acid soybeans). Although not all of the new varieties are used in animal feed, CVM has participated in the review of many of the varieties. During the past year, we participated in the review of all 13 of the new submissions received by the Agency. This included completion of consultations with the sponsors of new varieties of creeping bent grass, alfalfa, and wheat that express a protein that makes these plants tolerant to the herbicide glyphosate, and a cotton variety whose seed expresses a protein that imparts resistance to certain types of insect pests.

UPGRADING REGULATIONS FOR LIQUID AND FREE-CHOICE MEDICATED FEED

FDA changed its regulations for the manufacture of medicated liquid and free-choice feeds in June 2004. Liquid medicated feed is an animal feed that contains an approved new animal drug, while free-choice medicated feed is used in a feeding system in which animals have access to medicated animal feed (dry or liquid) at any time. We changed the liquid medicated feed regulations to clarify the data needs for the approval of animal drugs intended for this type of feed. The change in the free-choice medicated feed regulations ensures consistency with the requirements for liquid medicated feed.

COMPLIANCE CHALLENGES IN ANIMAL FEED SAFETY

Feed recalls. The Center handled 50 feed recall events during FY 2004. FDA issued seven recalls based on nutrient sub-potency or super-potency in finished feeds. Fifteen feed recalls were due to issues related to our BSE feed regulation.

Review of labeling for States. When State feed regulatory officials review feed labeling, the officials will request CVM's guidance when they encounter labeling that lists questionable ingredients and/or contains questionable label statements. CVM assists the States in reviewing the labeling and will pursue regulatory action if necessary. Our Division of Animal Feeds completed 131 label reviews in FY 2004.

Medicated feed mill inspections. During FY 2004, FDA and State inspectors completed inspections of more than half of the approximately 1,100 FDA-licensed medicated feed mills in the United States. State inspectors accomplished more than half of the inspections.

SAFETY OF PET FOOD

In May 2004, CVM issued the final Guidance for Industry (#122) for “Manufacture and Labeling of Raw Meat Foods for Companion and Captive Noncompanion Carnivores and Omnivores.” We developed this guidance in response to the growing use of raw meat as animal food, and the human and animal safety problems that can occur if these products are not manufactured, stored, and handled appropriately. The final guidance contains recommendations to manufacturers as to the source of meat; measures that can be taken to prevent bacterial contamination of the meat; information on how to ship the meat; and labeling guidelines for the benefit of those who handle and feed the meat to animals.

PROTECTING AGAINST BIOTERRORISM

FY 2004 PERFORMANCE GOALS

- ✓ Develop a list of priority products for countermeasures and a plan to periodically review and update list.
- ✓ The Submission Tracking and Reporting System (STARS) module containing facility information from approved New Animal Drug Applications (NADA) will be 75 percent populated and quality controlled.
- ✓ Evaluate rapid laboratory analytical methods to permit analysis of products for microbiological hazards and compare them to existing cultural methods.
- ✓ Develop analytical methods to detect the presence of toxic substances that could be introduced into U.S. animal feed supplies, and by developing the methods we would thus be supporting the FDA's counterterrorism initiatives.
- ✓ Assist the USDA and industry in the development of an acceptable cross-jurisdictional animal identification system.
- ✓ Work with Department of Homeland Security and CDC on a bioterrorism surveillance system.
- ✓ Develop a database containing a comprehensive inventory of registered animal drug establishments.

THE CHALLENGE

There is widespread concern that microbial and/or other toxic agents could be used in the food chain as weapons to harm human and animal health. Bioterrorism against the human food and animal feed supplies would also harm the U.S. economy. FDA-regulated products such as animal drugs would play a central role in countering the effects of such terrorism. Stockpiling veterinary drugs and compiling information on animal drug manufacturing facilities could provide valuable assistance in countering bioterrorism efforts.

FY 2004 ACCOMPLISHMENTS

Several CVM bioterrorism initiatives during the past year support FDA's Strategic Action Plan priorities of preparing for and effectively responding to bioterrorism and other public health emergencies. For instance, we worked with other parts of FDA and with other Federal agencies to help the United States prepare for a biological emergency, natural disaster, or terrorist attack by making sure there are safe and adequate supplies of animal drug products and animal feeds. We participated in drafting the food and animal feed portion of the National Infrastructure Protection Plan, established under a Presidential Directive related to homeland security. In addition to these examples and actions mentioned elsewhere in this report (e.g., in sections related to BSE and animal feed safety), we participated in the following initiatives during FY 2004.

INITIATIVES RELATED TO ANIMAL DRUGS

Priority products for countermeasures. We collaborated during FY 2004 with other government agencies on the development of a list of priority products for countermeasures. The list will be used in assembling a National Strategic Veterinary Stockpile. Our work in this area helped meet the FY 2004 FDA program commitment of developing a list of high-priority projects for countermeasures. CVM is represented on a steering committee established to continue development of strategies related to this objective.

Facility database. We achieved our FY 2004 goal of populating a database that includes information about facilities for the manufacture of approved new animal drugs. The database gives CVM quick access to facility information for each approved new animal drug application. If we find a problem with a particular drug, we can readily define the scope of the problem because the database has information on other products that use the same ingredients, formulations, manufacturing processes, and the like. Thus, we would be able to respond quickly to a bioterrorism incident involving a new animal drug.

ANIMAL FEED INITIATIVES

Microbiological hazards. Office of Research scientists are evaluating rapid laboratory methods to permit analysis of feedstuffs for microbiological hazards, and comparing these methods to existing cultural methods such as the isolation and identification of *Salmonella* from animal feces. Animal feed commodities are often retained for a very short period of time at feed manufacturing facilities, and thus rapid detection methods are essential for timely decision making with regard to the ultimate disposition of these materials.

Testing for Contaminants. CVM scientists have begun a program to develop rapid tests to detect contaminants and threat agents (toxic substances) in animal feed. We are looking at both the applicability of commercially available field tests originally intended for individual commodities, and the development of advanced laboratory techniques using mass spectrometry to measure 30 or more agents in one analysis. We plan to use techniques from the multi-class methods for eggs, meat, and seafood that we have developed successfully.

Biosecurity awareness guidelines for the feed industry. Building on a Guide to Biosecurity Awareness developed by the American Feed Industry Association, our Office of Surveillance and Compliance is educating the industry on performing tailored assessments of vulnerability. This process began with a consultation with the Department of Defense on the CARVER/Shock process (a method used to evaluate potential threats to regulated products), and was followed with meetings with trade groups to explain the process.

DEVELOPING AND TESTING EMERGENCY RESPONSE PLANS

As part of the Agency's preparation for potential bioterrorist acts, CVM participated during FY 2004 in the development and testing of emergency response plans for chemical, biological, and radiological incidents. OS&C continues to update its counterterrorism plan on emergency preparedness and response, including scenarios in which animal feeds may be a vector.

DEVELOPING AND IMPLEMENTING BIOTERRORISM REGULATIONS

CVM participated in the development of two FDA regulations (and guidance for industry) for implementing the Bioterrorism Act. The regulations, published in

October 2003, are intended to enhance the security of the food and feed supplies by establishing rules related to facility registration and prior notice of imports. In addition, the Division of Compliance participated in a number of public meetings on the regulations, providing information on the requirements for the animal feed/food industry and answering questions from the industry.

ASSISTING IN LIVE ANIMAL INITIATIVES

Animal identification system. We are assisting the USDA and industry in the development of an acceptable cross-jurisdictional animal identification system. We provided needed information during a meeting sponsored by the White House Office of Science and Technology Policy to identify research and development needs relative to counterterrorism. We assisted in the identification of gaps and the preparation of recommendations in this area.

Bioterrorism surveillance system. OS&C participated in a workshop for surveillance of animal disease outbreaks with the Department of Homeland Security, USDA, CDC, and academia also participating. We followed up by awarding contracts pertaining to the accomplishment of these goals.

ASSURING THE SAFETY OF ANIMALS PRODUCED BY BIOTECHNOLOGY

THE CHALLENGE

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

FY 2004 ACCOMPLISHMENTS

CVM provided scientific support and participated in White House-level deliberations on the appropriate regulatory framework for genetically engineered animals, while continuing to work with sponsors of animal biotechnology products to ensure that their progress is responsible but not unduly burdened as the Federal government prepares a policy on transgenic animals.

Cloning received considerable attention in CVM during the year, as we focused on a topic that is an FDA Strategic Plan priority. Our major efforts began with the issuance of a draft Executive Summary of the Animal Cloning Risk Assessment in October 2003, and presentations to a public meeting of the Veterinary Medicine Advisory Committee in November 2003. By the end of the fiscal year, CVM had completed the draft Risk Assessment and the Proposed Risk Management Plan for Animal Clones and their Progeny. The documents were ready for release following development of risk communication strategies.

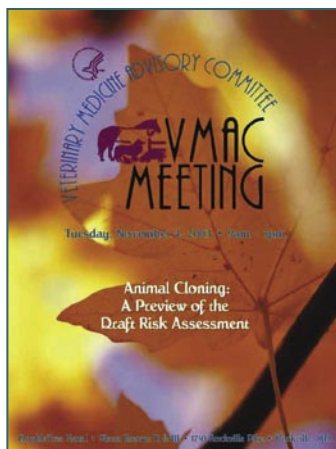
FY 2004 PERFORMANCE GOALS

- ✓ Work with the Office of the Commissioner, Office of Chief Counsel, and the USDA to develop an appropriate approach to regulating animal biotechnology.
- ✓ Animal Cloning:
 - Complete and release a draft executive summary for Risk Assessment on Animal Cloning.
 - Publish draft risk assessment for public comment (out of Center along with a Proposed Risk Management Plan).
- ✓ Provide scientific leadership and develop staff expertise for addressing the regulatory needs of CVM's animal biotechnology efforts.

GENETICALLY ENGINEERED ANIMALS

CVM continued developmental work during the year on a transgenic animal policy. This included preparation of a survey of potential hazards of a range of known animal biotechnology products under development, and consideration of alternative approaches to regulating plant biotechnology products.

As the primary agency in the Federal government that has been actively working with developers of animal biotechnology products, CVM served as the leader in the science-based discussions with the USDA, the Environmental Protection Agency, the National Institutes of Health, the Fish and Wildlife Service, and others in deliberations moderated by the Office of Science and Technology Policy (OSTP) on the appropriate approach to regulating animal biotechnology. CVM participated in “listening sessions” organized by OSTP to bring stakeholders from industry, consumers, and academia to several meetings to voice their concerns. These interagency deliberations continue.



CVM advisory committee, VMAC, discussed the cloning risk assessment at its fall meeting during FY 2004

ANIMAL CLONES

CVM completed and released the draft Executive Summary for the draft Risk Assessment on Animal Cloning and spent a day presenting the Animal Cloning Risk Assessment before the Veterinary Medicine Advisory Committee and the public in November 2003. The risk assessment addresses both animal health and the safety of food derived from animal clones and their progeny. VMAC discussed whether the risk assessment adequately identified the hazards and characterized the risks related to animal health and to food for human consumption. CVM asked for the committee’s views and scientific opinions concerning questions posed to it. The transcript, which provides important information on the committee’s responses, is available on the CVM website.

After considering the comments received from the public and the advisory committee, CVM completed the draft risk assessment for public release. Risk communication planning began in August 2004 and is continuing for FY 2005.

CVM staff gave several presentations to scientific and trade associations during the year on the methodology being developed to conduct the risk assessment for animal cloning.

ANIMAL BIOTECHNOLOGY EXPERTISE DEVELOPMENT

We continued during the year to use staff additions, and internal training through the CVM Animal Biotechnology Working Group (ABWG), to develop the appropriate expertise to address the scientific issues presented by animal

biotechnology. The ABWG concentrated its effort on ensuring that CVM personnel are aware of the critical issues in biotechnology; possess the scientific skills necessary to address the rapidly evolving and highly technical issues associated with animal biotechnology; and are familiar with the regulatory environment surrounding those issues.

We pursued several avenues to accomplish this objective during FY 2004. This included instituting an Expertise Development Program. We chose three topics for development by work groups: genomics and proteomics, allergenicity and novel proteins, and viral vectors (mobilizable transposable elements). These work groups focused on defining the critical issues that may face CVM staff in reviewing a biotechnology product, identifying key resources (e.g., scientific literature; websites; and subject matter experts in CVM, FDA, or elsewhere), and determining the best manner in which those resources can be applied to address the critical issues.

ADDITIONAL SURVEILLANCE AND COMPLIANCE ACTIONS TO PROTECT PUBLIC AND ANIMAL HEALTH

FY 2004 PERFORMANCE GOALS

- ✓ Finalize curricula for cGMP's (current Good Manufacturing Practices) for the pharmaceutical inspectorate and begin training inspectors.
- ✓ Animal Drug Compounding: Develop a "Field Guide to AMDUCA" (the Animal Medicinal Drug Use Clarification Act) that will include compounding as part of our educational efforts; work with ORAU (FDA's Office of Regulatory Affairs University) in developing two AMDUCA/Compounding modules; issue an assignment to inspect 20 compounding firms; and issue a letter to all State Boards of Pharmacy.
- X The AMDUCA Field Guide has been drafted and placed into clearance, but was under review at the close of the fiscal year. As explained elsewhere in this Annual Report, the inspection assignment and letter to Boards of Pharmacy have been issued. The modules were not developed due to lack of funding.

THE CHALLENGE

Surveillance and compliance activities are key parts of our efforts with regard to antimicrobial resistance, BSE, drug residues, feed safety, and other crosscutting issues described above. We have had challenges in other areas, related to our core functions of compliance-related actions and post-approval monitoring. These challenges include surveillance to assess post-approval drug safety, taking steps to assure proper manufacture of approved drugs, compounding, regulation of the marketing of unapproved drugs, and acting against other threats to public and animal health.

FY 2004 ACCOMPLISHMENTS

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

RECALL OF HEARTWORM DRUG

At FDA's request, the manufacturer of the heartworm medication ProHeart6® agreed in September 2004 to cease production immediately and recall the drug from the market until the FDA's concerns about adverse reaction reports associated with the product could be resolved. ProHeart6 is an approved injectable sustained-release heartworm prevention product for dogs, containing the active ingredient moxidectin. Heartworm disease is a serious and potentially fatal condition of dogs, cats, and other species of mammals.

FDA based its request on unexplained adverse drug event reports, some of them severe. The Agency has requested that the firm continue to conduct research to determine the cause of related adverse reactions, and develop a strategy to help prevent such problems in the future before the product is marketed again. The FDA will convene an independent scientific advisory committee to thoroughly evaluate all available data.

ADVERSE DRUG EVENTS

One of FDA's Strategic Plan priorities is to increase attention on adverse events connected with drug use. During FY 2004, the Division of Surveillance received 28,424 adverse

experience reports, an increase of more than 5,000 from FY 2003. We were able to review 18,625 of these complaints. Because of the severity of this year's complaints, we spent considerably more review time than in previous annual periods reviewing certain individual adverse drug event (ADE) submissions involving heartworm drug safety and lack of effectiveness.

LABELING AND ADVERTISING CHANGES

On our recommendation, the sponsor of a cattle antibiotic undertook a major relabeling and education program after a human death that occurred following accidental injection of this product. Under our continuous post-approval pharmacovigilance program, the Division of Surveillance implemented label changes that included the addition of environmental safety, disposal, and veal calf warning information for ivermectin drug products in cattle; and modification and updating of the indications for ivermectin drug products in horses.

We also implemented revisions in the labeling of a number of other drug products, incorporating post-approval adverse drug experience information, and combining this action with notification to veterinarians of the important changes. Altogether, we reviewed more than 7,700 promotional labeling and advertising pieces submitted by drug sponsors, and issued a number of action letters requesting discontinuation of violative labeling and advertising materials.

COMPLIANCE WITH GOOD MANUFACTURING PRACTICES

FDA inspectors during FY 2004 conducted 170 inspections of manufacturers of dosage form drugs and Type A medicated articles for compliance with the cGMP regulations. This was well over half of the 299 registered establishments in the United States. Thus, we met the statutory goal of inspecting half of the establishments during the year.

We participated with others in the FDA in finalizing a curriculum for cGMP training, and in the initiation of the Pharmaceutical Inspectorate Training Course in August 2004. This supports the FDA's priority of modernizing the health care system through improved cGMPs.

An FY 2004 cGMP inspection at a sterile products manufacturing facility resulted in the issuance of a Warning Letter for serious deviations from cGMP regulations that caused the sterile products manufactured at the facility to be adulterated. The firm is a leading manufacturer and distributor of prescription and over-the-counter animal health care products for the livestock and companion animal industries. In response to the Warning Letter, the firm recalled all of its sterile products made during the time frame covered by the inspection, and has continued to work with FDA to resolve its manufacturing control problems.

DRUG LISTING

Animal drugs in commercial distribution must be listed by the Agency. To improve the Center's ability to make regulatory decisions about products for which it is responsible, CVM has designed a proactive program for updating the drug list. The program involves mailing each animal drug manufacturer or distributor a printout of the drug products that are listed in the firm's Drug Product Listing, accompanied by instructions to update the list. CVM initiated its Drug Listing Verification Program information at the end of July 2004. We had received responses from approximately 50 percent of the firms by the end of the fiscal year. 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 to accurately assess user fees under ADUFA.

REGULATING DRUG COMPOUNDING

Inspection program. In response to the increased availability of compounded veterinary drug products, CVM implemented a plan to reduce the risk from use of these products in food-producing and non-food-producing animals. CVM accomplished this task by issuing a position paper on compounding to each State Board of Pharmacy, meeting with various trade associations, and issuing an assignment to FDA District Offices to inspect 20 compounding pharmacies. The Agency issued five Warning Letters, and one seizure of compounded drugs was accomplished in FY 2004. Altogether, half of the inspections that had been completed by the end of the year resulted in regulatory action or were being considered for regulatory action. The communication efforts, inspections, and enforcement activities have led to a decrease in the use of compounded veterinary drugs for food-producing animals.

Revised CPG on veterinary drug compounding. The current Compliance Policy Guide (CPG), published in July 2003, describes our thinking as to the types of veterinary compounding that might be subject to enforcement action. FDA has received numerous letters from veterinarians, pet owners, compounding pharmacists, and associations expressing concern that the CPG lacks sufficient clarity on the circumstances in which veterinary compounding, particularly compounding from bulk drugs, would be permitted. Many of the letters also disagreed with the current policy, stating that it was not within FDA's legal authority, and complained about the lack of prior public comment. After meeting with several groups and considering the comments it has received, CVM is revising the CPG and will release it for public comment during FY 2005.

ENHANCING PRODUCTIVITY THROUGH ACHIEVEMENT OF MANAGEMENT GOALS

The Center fully supported the reshaping of the Agency's management systems and business practices in response to the President's Management Agenda, the Department of Health and Human Services Department-wide Management Objectives, and the Agency's Strategic Plan, creating an even stronger organization through the implementation of new, more customer-responsive processes. The Center successfully met the specific management goals for 2004, as described in the following significant outcomes and achievements.

IMPLEMENTED RESULTS-ORIENTED MANAGEMENT

Integration of performance with budget. In FY 2004, CVM worked on the Agency's FY 2006 integrated performance plan and budget that contains narratives on increases, changes in program resources, justification of base resources, output data, and performance goals. Increasingly, over the past few years, the Department of Health and Human Services and the Office of Management and Budget (OMB) have stressed the integration of performance measures and accomplishments into the budget request. DHHS-level budget decisions will be the basis for the next budget submitted to OMB. The final OMB decisions are the basis for the Congressional Justification. The performance plan and budget will be integrated in FY 2006 to ensure that budget decisions are linked with performance, as intended by the Government Performance and Results Act.

Activity-based costing. The Center implemented an activity-based costing system to provide data to measure our performance. This system includes an activity time reporting system that documents time spent by CVM staff on the major activities performed each day. CVM implemented 100 percent time reporting for all staff during FY 2004. The activity-based costing, derived from the time reporting, allows for the identification of the full costs (direct and indirect) of all of CVM pre- and post-market, research activities and overhead. During FY 2004, we used the system to determine the percentage of time each office spends on activities related to the animal drug review process. The system, when fully

FY 2004 PERFORMANCE GOALS

- ✓ Implement results-oriented management, such as integrating the budget and performance plans for FY 2006 to begin the development of a performance budget.
- ✓ Implement strategic human capital management by targeting recruitment outreach efforts.
- ✓ Complete the FY 2004 Competitive Sourcing Program: Focus on the clerical staff.
- ✓ Improve Information Technology (IT) Management by supporting the transformation of how the Agency/Center conducts IT operations and consolidates reporting lines of the IT organization in CVM.
- ✓ Create administrative efficiencies and consolidate management functions by reducing administrative positions.
- ✓ Participate with the Agency in creating new training, employee development programs, including those that allow academic and esteemed individuals to spend time in the Center to inject innovative thinking into the current regulatory science and review process.

operational, will give CVM managers a key tool for planning and using their resources. They will better understand, manage, and assign true costs to CVM business processes, activities, services, and products. It will also communicate Center priorities to front line staff.

Project Management Implementation. CVM continues its support of four project management pilot projects. During FY 2004, one pilot project team, the CVM



Project Management team at work

Communications Clearance Team, successfully planned and implemented a policy and process for clearing Center communications. The Document Control Unit Facilities Team is developing plans to relieve document unit space problems. The Animal Feed Safety System Team, described in more detail in the Animal Feed section of this report, has successfully completed two milestones in its plan – to conduct a public meeting for gathering stakeholder input and to develop an animal feed safety system framework document. The Office of New Animal Drug Evaluation (ONADE) continues to improve its Office-wide project management process for planning and monitoring progress on all non-review projects.

To support these project management pilot projects, the Project Management Staff (PMS) has undertaken several initiatives to assist the pilot project teams and to enhance project management skills throughout the Center. The PMS organized a project management “Community of Practice” that provides a forum for sharing lessons learned and best practices, and engages in group problem-solving for project planning and implementation issues. An Enterprise Project Management Team, consisting of Office Project Managers from each CVM Office, tracks high priority projects with critical timelines and potential cross-Office implications. In collaboration with ONADE and the Staff College a new project management training format was developed that integrates project management principles, tools and techniques with Microsoft Project 2003 software skills. The PMS has also drafted a set of performance metrics for project management implementation and begun work on a searchable database for collecting and tracking performance data.

IMPLEMENTED STRATEGIC HUMAN CAPITAL MANAGEMENT

Hiring innovations. The Center is hiring new animal drug reviewers to meet the workload increase with the initiation of the Animal Drug User Fee Act of 2003. In doing so, CVM is using the Staff College Competency Model in the recruiting and interviewing process to ensure identification and selection of the best-qualified candidates possessing the necessary technical, team, leadership, and management skills and learning agility. The Center is also taking part in Agency Job Fairs to reach out to areas not previously tapped when searching for qualified candidates.

Diversity initiatives. CVM worked with the Agency's Office of Equal Employment Opportunity and Diversity Management (OEEODM) to implement the mandatory EEO and Diversity Management Training Program for all managers and supervisors. The Center also has been an active participant in the Agency's new OEEODM Council that has been established to serve as an advisory body to the FDA Commissioner, the Management Council, and the Director, OEEODM. The representatives are the communications link between FDA employees and top management.

COMPLETED THE COMPETITIVE SOURCING PROGRAM FOR CLERICAL POSITIONS

OMB circular A-76 directs all Federal agencies to conduct cost comparison studies of commercial activities performed by Federal employees. The FDA's 2001 Federal Activities Inventory Reform Act (FAIR Act) inventory lists the number of commercial, full time equivalent position within the Agency. The most recent phase of A-76, the analytical assessment of selected functions within the clerical support services, was publicly announced in February 2004. The solicitation of competitive sourcing was released in September 2004, with bids due in November 2004.

IMPROVED INFORMATION TECHNOLOGY MANAGEMENT

Expanded E-government. The Center continues to enhance IT management consistent with the President's expanded E-government initiative. As an example, CVM acquired a pilot system to permit electronic reporting to enhance the efficiency of the Safety Review Team in the Center's Division of Surveillance. In addition, CVM awarded a contract for the development of the electronic submission of adverse drug events to greatly enhance the process.

IT migration. CVM supported the implementation of the FDA IT Directors' Migration Plan that moved the Agency IT managers and staff into the Agency's Office of the Chief Information Officer. The Director and staff will continue to provide a high quality of service for the Center's IT projects. They remain closely integrated in meeting the business needs of CVM through intervention of IT solutions and technologies.

Corporate document management. The Center's Corporate Document Management System (CDMS) promotes an integrated decision support environment, as well as optimizes and streamlines critical business activities. This has included preparing final requirements and system design documents for CDMS Dynamic Indexing; and completing CDMS user training for appropriate users within the Office of New Animal Drug Evaluation and the Office of Surveillance and Compliance.

Integrated systems. CVM continued to support and enhance the ability of employees to efficiently work with integrated systems to reach CVM goals. For the pre-market arena, systems were enhanced and released to CVM users and stakeholders to facilitate increased data collection and detailed analysis including

the ADUFA Evaluation initiative, Electronic Submissions Systems (ESS) Portable Document Format (PDF) Smart Forms, which provide increased data collection and accuracy of sponsor submitted data. For the post-market arena, enhancements to systems were developed and released including the Drug Experience Reporting Systems (DERS), Bioresearch Monitoring System Establishment Inventory Module (BIMO) and design and development of the Adverse Drug Event (ADE) Extensible Markup Language (XML) document repository and the ADE XML schema. Also, we began upgrades for the Outlook Notification Form Integration (ONFI) to enable reviewers to perform online review and information processing.

CREATED ADMINISTRATIVE EFFICIENCIES AND CONSOLIDATED MANAGEMENT FUNCTIONS

The Center created administrative efficiencies and consolidated management functions by reducing administrative positions in the following ways.

Reduction in administrative positions. The Center not only met its 2004 targeted administrative position reductions as directed by the Agency, but also exceeded the requirement. To meet the goal, CVM reduced and redistributed the administrative workload and consolidated functions and tasks that are required in this organizational area.

Consolidation of administrative positions. In response to the Department's mandate for a consolidation of administrative services, the Center fully supported the Agency's implementation of the Office of Shared Services. The Center's participation includes the reengineering of work processes, participation on functional committees, transfer of payroll and operational funds to support Shared Services, and the assignment of liaisons to specific Shared Services functions. Shared Services is a service model for internal administrative support functions that combines the best of centralized and decentralized organization structures. Shared Services provides services in a competitive market environment model, ensuring the effective and efficient delivery of services. As a result, the business unit has considerable input into the make-up of services it receives.

PARTICIPATED IN NEW TRAINING AND EMPLOYEE DEVELOPMENT PROGRAMS

We participated with the Agency in the formulation of new training and employee development programs, including initiatives to allow academics and others to bring their ideas and programs to CVM, as follows.

Visiting academics. The Center encouraged interaction with local universities and colleges to increase the time scientists spend at CVM. This was achieved through the Center's Staff College curriculum with the inclusion of visiting professors, as well as experts from industry who provided cutting-edge information regarding current scientific issues and research.

Staff College expansion. The Center continued to develop and expand the CVM Staff College that we established in FY 2002. Through the state-of-the-art Knowledge Management Center, the College provides the framework to support the development and delivery of a robust scientific, management, leadership, and team building curriculum based upon researched and established core competencies necessary for high performance in specific positions and functional areas. During 2004, the Staff College enhanced the learning activities and educational opportunities offered to Center employees by providing seminar series and courses intended to meet the management goal of presenting new and emerging scientific issues that strengthen the employees' ability to make required scientific decisions. Some of these series/courses include the following:

Emerging Technology Series. Focuses on innovative advances in technology and science. It was leveraged with the University of Maryland, Baltimore County, to provide training in the use of Bioreactors, including scale-up, validation, and monitoring.

Scientific Seminar Series. Highlights the use of scientific methods in problem solving and analysis. The series covers risk assessment, analysis, and management. Another Scientific Seminar Series addresses current issues related to antimicrobial use in human and animal medicine, both companion and food-producing animals.

Rounds Series. Developed in partnership with the ONADE Quality Assurance Team, the series features targeted instruction in the creation and review of drug approval packages. A Reference Manual and learning objectives assist new animal drug reviewers and Consumer Safety Officers to better implement the policies and procedures that will decrease review cycle time for approval packages and improve the overall quality of package submissions.

New Reviewer Training. Designed to achieve the management goal of a more enhanced and predictable drug review performance. The 2004 series included statistical instruction to aid reviewers in data analysis and study design.

LEVERAGING PRODUCTIVITY THROUGH PARTNERSHIPS

FY 2004 PERFORMANCE GOALS

✓ Continue leveraging activities through contractual agreements and informal collaboration.

THE CHALLENGE

FDA and CVM continuously seek out partnering opportunities to maximize the use of our 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.

FY 2004 ACCOMPLISHMENTS

We initiated several partnering arrangements during the year and continued a number of others. These mutual-benefit arrangements have influenced CVM policies and practices, and have enhanced our research and epidemiological efforts. They are in line with the FDA Strategic Plan priority to ensure effective communication and working relationships with key external stakeholders.

We have highlighted a number of partnership agreements in this report. Examples include the collaborative effort with the USDA and CDC in NARMS; collaboration with the Mexican government to detect resistance in pathogens that may contaminate food imported to the United States and also pose a hazard to U.S. travelers; and arrangements with State regulatory agencies to conduct BSE feed rule and medicated feed inspections.

There are many other arrangements that we have not highlighted elsewhere in this report. For example, we continued to work very closely with the Association of American Feed Control Officials. The purpose of this organization is to provide a mechanism for State and Federal government regulatory officials to explore the problems encountered in administering feed laws. The goals are to develop just and equitable standards, definitions, and policies to be followed in enforcing feed laws; promote uniformity in feed laws, regulations, and enforcement policies; and cooperate with members of the industry producing feed products in order to promote the effectiveness and usefulness of such products. CVM continues to work with FDA's Center for Food Safety and Applied Nutrition and Office of Regulatory Affairs, and

the National Conference on Interstate Milk Shippers (State regulators and industry) on milk safety issues. This includes regulatory compliance work and education on issues such as dairy farm biosecurity, antimicrobial resistance development, BSE prevention, rapid milk antibiotic screening test kit development, and residue avoidance.

During FY 2004, CVM approved a supplemental new animal drug application for Oxymarine (oxytetracycline hydrochloride soluble powder), which provides for the immersion marking of skeletal tissues of finfish fry and fingerlings. This approval will be useful to State and Federal hatcheries to determine the success of stocking programs or to track fish populations. The method is an improvement over external tags, which can damage the fish and often are lost. The approval relied on publicly available data compiled under National Research Support Project 7 (NRSP-7), a national agricultural research program for obtaining clearances for use of new animal drugs in minor animal species and for special uses. Created by the USDA, NRSP-7 includes participants from a number of universities as well as the USDA and CVM.

Another example of collaboration: In developing the procedure to screen for residues of unapproved drugs in honey, CVM researchers are collaborating with the USDA Bee Laboratory. The bee laboratory is providing control and incurred (drug-containing) honey samples, and knowledge about drugs that may be used in apiculture.

During the year, FDA recognized the collegial efforts of CVM staff members through leveraging/collaboration awards such as the award to the AFSS that included members from State regulatory agencies and several offices within FDA. Other CVM staff members received leveraging/collaboration awards for process analytical technology and cGMP leadership; several collaborative efforts involving counterterrorism activities; regulatory actions involving monkeypox; and additional achievements that are listed in the Awards Appendix.

These and other partnerships allow us to devote our scarce resources to those activities that we are uniquely qualified to perform. They provide a means to expand our capabilities by allowing us to use our intellects, time, money, and other resources in a manner that maximizes their value.

STAFFING, SPACE AND BUDGET

Staff and Budget. Budgeted staffing levels for CVM and CVM-related field activities are in Appendix C.

Space. With the passage of ADUFA, CVM required new space to house approximately 80 additional personnel over the next three years. To meet this requirement CVM has since ADUFA's passage secured 18,156 sq. ft. of office space on the second floor of Metro Park North IV. Consolidation of Office of Surveillance and Compliance offices in this new space will facilitate the ADUFA-related growth and consolidation of ONADE offices in Metro Park North II. Full implementation of the ADUFA-driven space plan will be completed during 2005.

APPENDICES

APPENDIX A – AWARDS

CENTER FOR VETERINARY MEDICINE* 2004 HONOR AWARD RECIPIENTS

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

FDA COMMISSIONER'S SPECIAL CITATION

For innovative and exceptional service involving emerging public health issues of the Center for Veterinary Medicine, including BSE, monkeypox, and animal drug compounding efforts.

Neal Bataller, D.V.M.

CVM Activity Time Reporting/ABC Project Team

For outstanding leadership and achievement in designing, developing and delivery of CVM's Activity Time Reporting System in the context of the Center's Activity-Based Costing (ABC) initiative.

Karen S. Alder
 Russell A. Frobish, Ph.D.
 George Graber, Ph.D.
 Gwendolyn Jones
 David L. Lynch
 Daniel G. McChesney, Ph.D.
 Jerome J. McDonald, Ph.D.
 Robert Miller
 David R. Newkirk, Ph.D.
 Jacquelyn L. Pace
 Glenn A. Peterson, Ph.D.
 Vernon D. Toelle, Ph.D.
 Stephen T. Trostle
 Michael H. Thomas
 Madeline C. Van Hoose
 Steven D. Vaughn, D.V.M.
 Juandy S. Walston

CVM Antibiotics in Milk Test Kit Team

For outstanding contributions to the development of a third-party quality assurance system, which will ensure the nation a safe milk supply through improved test kits.

Gloria J. Dunnavan
 Philip J. Kijak, Ph.D.
 Daniel G. McChesney, Ph.D.
 Michael R. Talley, D.V.M.
 Jurgen D. von Bredow, Ph.D.

A-76 Study Teams

For untiring effort in the development of comprehensive Performance Work Statements and cost effective Most Efficient Organizations, which resulted in six successful competitions.

Deborah H. Brooks

Linda L. English

David L. Lynch

ERIC Development and Implementation Team

For outstanding service in establishing the FDA Employee Resource and Information Center.

Stephanie W. Dove

FDA/Booz Allen Hamilton Shared Services Team

For outstanding commitment to and collaborative support of the many activities related to the design and implementation of a new service delivery model in FDA.

Stephanie W. Dove

Robert Miller

Don R. Peterson

FDA EU Seafood and Dairy Audit Teams

For hard work, dedication, teamwork, and continued collaboration during the European Union audits of the FDA Seafood and Dairy Regulatory Systems.

Michael R. Talley, D.V.M.

FDA TOPOFF2 Exercise Team

For participation in conducting a successful exercise of the Federal Response Plan government wide, in a response to simulated terrorist events in multiple cities of the United States.

Neal Bataller, D.V.M.

Gloria J. Dunnavan

CDR Alfred W. Montgomery, D.V.M.

Kim R. Young

Intercenter Consultative/Collaborative Review Process Working Group

For outstanding contributions in the development of the Agency's Standard Operating Policy and Procedure for the intercenter consultative/collaborative review process.

Tracey H. Forfa, J.D.

Registration Interim Final Rule Team

For extraordinary contributions in reviewing numerous public comments and drafting interim final rules to implement the registration and provisions of the Bioterrorism Act in an expedited timeframe.

Mark H. Hackman
CDR Alfred W. Montgomery, D.V.M.
Isabel W. Pocurull
Kim R. Young

AWARD OF MERIT**Antimicrobial Resistance Guidance Group**

For extraordinary leadership developing guidance for industry urgently required by CVM to protect human and animal health in evaluating antimicrobial drugs for food-producing animals.

Carole R. Andres
Mary J. Bartholomew, Ph.D.
Monica Brown-Reid, D.V.M.
H. Gregg Claycamp, Ph.D.
Susan J. Dewitt
William T. Flynn, D.V.M.
Jeffrey M. Gilbert, Ph.D.
Kevin J. Greenlees, Ph.D.
Barry Hooberman, Ph.D.
Wendelyn R. Jones, Ph.D.
Karen R. Lampe, Ph.D.
Judith M. O'Haro
Julia W. Punderson, V.M.D., Dip.ACT
Aleta M. Sindelar
Charlotte A. Spires, D.V.M.
Stephen F. Sundlof, D.V.M., Ph.D.
Linda Tollefson, D.V.M.
Madeline C. Van Hoose
Robert D. Walker, Ph.D.
David G. White, Ph.D.
S. Steve Yan, Ph.D.

For extraordinary leadership and performance that contributed to the incorporation of Risk Analysis and Risk Management into the Center for Veterinary Medicine's operating environment.

H. Gregg Claycamp, Ph.D.

For exemplary service and admirable dedication to the Center for Veterinary Medicine, the Center employees, and the public who benefit from this organization's endeavors.

Barbara E. Leach

Bioterrorism Proposed and Interim Final Rule Outreach Strategy Group
For outstanding contributions in devising and implementing a successful outreach strategy related to the Bioterrorism Proposed and Interim Final Rules.

Aleta M. Sindelar

For sustained outstanding leadership of FDA's Laboratory Animal Care and Use programs.

Mack A. Holt, D.V.M.

OUTSTANDING SERVICE AWARD

For sustained and significant contributions to the development and implementation of major administrative management programs in the Center for Veterinary Medicine.

Linda J. Callahan

For outstanding performance and service in managing critical administrative, personnel and budget activities for the Office of the Center Director and the Office of Management.

Heidi M. Jackson

For sustained superior performance managing three technically complex public health communications projects while also supporting the CVM leadership team as project manager.

Vashti D. Klein

For superior performance in the development of analytical methods to detect banned veterinary drugs in imported shrimp and the transfer of the methodology to ORA.

Mayda I. Lopez, Ph.D.

For outstanding leadership in development and implementation of the Center for Veterinary Medicine's Continuation of Operations Plan (COOP).

David L. Lynch

For outstanding service in the development and implementation of Project Management within the Office of New Animal Drug Evaluation.

Nancy L. Mach

For outstanding service to the Agency through significant contributions to the regulatory, administrative, and managerial needs of the Office of New Animal Drug Evaluation and the Center for Veterinary Medicine.

Gail L. Schmerfeld, J.D.

For sustained excellence in regulatory review work.

Michelle L. Stull, D.V.M.

GROUP RECOGNITION AWARD

The Animal Cloning Risk Assessment Group

For outstanding achievement in developing the Animal Cloning Risk Assessment and presenting the Risk Assessment document to the VMAC members at the fall public meeting.

Amey L. Adams, Ph.D.

Michaela G. Alewynse, Ph.D.

H. Gregg Claycamp, Ph.D.

Eric S. Dubbin, D.V.M.

Jodie M. Fleming

Kevin Greenlees, Ph.D.

Barry Hooberman, Ph.D.

Wendelyn R. Jones, Ph.D.

Ibrahim Kamara

Nancy L. Mach

John C. Matheson, III

Tomislav Modric, D.V.M., Ph.D.

Thomas J. Moskal, D.V.M.

Larisa Rudenko, Ph.D.

Gary B. Sherman, D.V.M., Ph.D.

Codex Outreach Working Group

For outstanding achievement in effective outreach to Central and South America to facilitate harmonization, participation and capacity building in Codex Alimentarius.

Richard L. Ellis, Ph.D.

Ana Haydee Fernandez, D.V.M.

Lynn G. Friedlander, Ph.D.

L. Thomas Mulligan, Ph.D.

FDA/CVM/OR QA/GLP Team

For exceptional performance resulting in a successful GLP evaluation for the Food and Drug Administration's Center for Veterinary Medicine's Office of Research.

Sonya M. Bodeis

Orton J. Cartwright

Pak S. Chu, Ph.D.

Carol V. Cope

R. Bruce Craig

Denise B. Durham

Linda L. English

Russell A. Frobish, Ph.D.

Charles M. Giesecker

David N. Heller

Joseph C. Kawalek, Ph.D.

Philip J. Kijak, Ph.D.

D. Shawn Matheny

Patrick F. McDermott, Ph.D.

Renate Reimschuessel, V.M.D., Ph.D.

Stanley G. Serfling

Michael H. Thomas

Linda D. Youngman, Ph.D.

NARMS Retail Meat Group

For exceptional performance in implementing the Retail Meat Arm of the National Antimicrobial Resistance Monitoring System (NARMS) including a pilot study conducted in Iowa.

Jason W. Abbott

Sherry L. Ayers

Mary J. Bartholomew, Ph.D.

Sonya M. Bodeis

Peggy J. Carter

Patricia Cullen

Linda L. English

Sharon L. Friedman

Stuart A. Gaines

Confidence M. Gbarayor

Althea Glenn

Elvira L. Hall-Robinson, D.V.M.

Marcia L. Headrick, D.V.M.

Susannah Hubert

Gwendolyn Jones

Scott S. Komo, Ph.D.

Kyung Y. Lee, Ph.D.

Patrick F. McDermott, Ph.D.

Shawn D. McDermott

Anna B. Nevius, Ph.D.

Terry A. Proescholdt, D.V.M., Ph.D.

Sadaf Qaiyumi

Lisa E. Rojas

Ruby Singh, Ph.D.

Charlotte A. Spires, D.V.M.

Teresa R. Thomas

Linda Tollefson, D.V.M.

Stephen T. Trostle

Vivian G. Vontress

David D. Wagner, Ph.D.

Loretta A. Walker, D.V.M.

Robert D. Walker, Ph.D.

David G. White, Ph.D.

Shaohua Zhao, Ph.D.

cGMP Steering Committee

For outstanding performance in organizing and delivering the six seminar series on "Quality Systems and Risk-Based Approaches."

Geoffrey K. Wong

Dioxin Strategy Development and Implementation Group 2000 – 2003

For outstanding efforts and dedication in the development and implementation of the dioxin strategy for monitoring, method development, and reducing human exposure.

Randall A. Lovell, D.V.M., Ph.D.

Daniel G. McChesney, Ph.D.

FDA Animal Drug User Fee Legislative Team

For leadership and sustained commitment to Public and Animal Health in collaborating with Congress, industry, and consumers to develop and enact legislation for a results-oriented program to review animal drugs.

Andrew J. Beaulieu, D.V.M.

William C. Keller

William G. Marnane

Robert Miller

David R. Newkirk, Ph.D.

Elizabeth L. Parbuoni

Don R. Peterson

Robert W. Sauer

Gail L. Schmerfeld, J.D.

Herman M. Schoenemann, III

Stephen F. Sundlof, D.V.M., Ph.D.

Steven D. Vaughn, D.V.M.

David E. Wardrop, Jr.

FDA Competitive Sourcing Team

For extraordinary effort in designing FDA's approach to competitive sourcing as well as the successful competition and award of six cost comparisons for FDA employees.

Don R. Peterson

LEVERAGING/COLLABORATION AWARD

Animal Feed Safety System Team

For outstanding stewardship in the planning and conduct of the Animal Feed Safety System public meeting designed to initiate the process for improving animal feed safety.

Kim E. Bell
David S. Conklin
Gloria J. Dunnavan
Karen B. Ekelman, Ph.D.
Henry E. Ekperigin, D.V.M., Ph.D.
Zoe A. Gill
George Graber, Ph.D.
Linda A. Grassie
David W. Grau, D.M.D.
Jo W. Gulley
Mark H. Hackman
Ibrahim Kamara
Shannon T. Jordre
Daniel G. McChesney, Ph.D.
John Dennis McCurdy, Ph.D.
Dragan Momcilovic, D.V.M., Ph.D.
Jacquelyn L. Pace
Frances M. Pell
Isabel W. Pocurull
Barbara A. Rodgers
Jon F. Scheid
Ronald R. Scherzberg
Madeline C. Van Hoose
David D. Wagner, Ph.D.
Toni V. Wooten
Kim R. Young

For providing expert scientific knowledge and efforts to assure completion of a comparison table of U.S. and Canadian veterinary drug maximum residue limits/tolerances in foods.

Richard L. Ellis, Ph.D.

The FDA Training Consortium Team

For establishing the CVM sponsored FDA Training Consortium that leverages Center resources and achieves economies of scale that substantially increase electronic training program efficiencies.

Melissa A. Starinsky
Sherri Stephenson-Washington

The Process Analytical Technology and Current Good Manufacturing Practices
Leadership Group

For outstanding achievement in establishing successful collaborations between FDA and industry that embrace innovative technological advances and implement risk-based approaches focused on critical manufacturing areas.

Dennis M. Bensley, Jr., Ph.D.
Raafat M. Fahmy, Ph.D.
William G. Marnane

Bioterrorism Act – Administrative Detention Proposed Rule Team

For extraordinary contributions in drafting a clear and understandable proposed rule implementing the Administrative Detention provisions of the Bioterrorism Act, to ensure the protection of the U.S. food supply.

William L. Bargo

Bioterrorism Act – Recordkeeping Proposed Rule Team

For extraordinary contributions in drafting a clear and understandable proposed rule to implement the Establishment and Maintenance of Records provision in the Bioterrorism Act.

William L. Bargo

FDA BIO 2003 Exhibit Group

For collaborative achievement in organization and staffing of the FDA exhibit booth at the BIO 2003 Conference to provide FDA education and outreach efforts.

Deborah H. Brooks
Melanie A. Fleming
Jon E. Scheid

Minnesota Partnership Laboratory Group

For successful partnership between the Food and Drug Administration and Minnesota Department of Agriculture in furtherance of the President's Food Safety Initiative and protecting the public health.

Marleen M. Wekel, Ph.D.

Monkeypox Interagency Work Group

For superior performance and innovation in implementing a collaborative multi-Federal, State, and local Agency approach that minimized the spread of Monkeypox, a zoonotic disease.

Neal Bataller, D.V.M.
Deborah A. Cera
Gloria J. Dunnavan
Shannon T. Jordre
Joseph C. Paige, D.V.M.
Frances M. Pell
Sue Ann Williams
Toni V. Wooten

New York District Tissue Residue Outreach Group
For exceptional collaboration/leveraging with Federal, State and Academic partners in addressing tissue residue problems in New York State.
Neal Bataller, D.V.M.
Gillian A. Comyn, D.V.M.

QUALITY OF WORK LIFE AWARD

For leadership and innovation in providing an improved quality of work life for employees in the Division of Human Food Safety.
Mark M. Robinson, Ph.D., D.V.M.

For enhancing the quality of work life in the Division of Therapeutic Drugs for Non-food Animals by coordinating the assignment of computer equipment and software.
Michele J. Sharkey, D.V.M.

COMMISSIONER'S ADMINISTRATIVE MANAGEMENT AWARD

OC Travel Manager Team
For successful implementation of Travel Manager through FDA.
Dawn E. Calhoun
Anita L. Heinrich
Heidi M. Jackson

FDA SCIENTIFIC ACHIEVEMENT AWARD (CVM NOMINATIONS)

CVM ANALYTICAL SCIENCE EXCELLENCE AWARD

For the development of sensitive methods for the detection and confirmation of animal drug residues in meat, milk and eggs.
Pak-Sin Chu, Ph.D.

CVM OUTSTANDING JUNIOR INVESTIGATOR AWARD

For outstanding performance which resulted in developing new techniques, troubleshooting procedures and working independently to provide incurred residue tissues of multiple drugs in multiple fish species.
Charles M. Giesecker

CVM OUTSTANDING SUPPORT SCIENTIST AWARD

For outstanding performance, as evidenced by working independently, improving existing procedures, innovating new techniques, and demonstrating enthusiasm and teamwork.

Cristina B. Nochetto

CVM OUTSTANDING NEW REVIEWER AWARD

For efficient and effective recommendations to approve eleven generic animal drug products, and for exceptional scientific insight and response to citizen petitions.

John K. Harshman, D.V.M.

PHS COMMISSIONED CORPS HONOR AWARDS**PHS OUTSTANDING UNIT CITATION AWARD (OUC)**

For establishing a program in Mexico to detect antimicrobial resistance in foodborne pathogens to better assure the safety of domestic and exported food to the United States.

RADM Linda Tollefson, D.V.M.

CAPT Marcia L. Headrick, D.V.M.

PHS COMMENDATION MEDAL (CM)

For essential leadership and coordination in development of a new scientific database to assess the safety of cloned animals and feed derived from their progeny.

LT Ibrahim Kamara

CVM AWARDS AND RECOGNITION**THE CVM DIRECTOR'S HONOR AWARD**

First place recipient

For exemplary scientific expertise and leadership concerning BSE and animal feed controls following the 2003 discovery of two cows in North America with BSE.

Burt A. Pritchett, Ph.D.

Second place recipient

For exemplary performance in coordinating the Center's efforts in establishing regulations for import tolerances.

Fran M. Pell

CVM ADMINISTRATIVE/COMMUNICATIONS EXCELLENCE AWARD

For exceptional accomplishments in providing outstanding support for the personnel management function in the Center for Veterinary Medicine.

Lisa M. Durphy

For superior performance in producing the CVM NEWS and for efforts as Project Manager for the CCCP.

Joanne M. Kla

CVM SUPPORT STAFF EXCELLENCE AWARD

For unparalleled, consistent support in performance of tasks critical to the performance of the Division and as a back-up throughout ONADE.

Marjorie A. Lidard

CVM/OR Support Staff

For providing consistent outstanding support and dedication in managing the enormous volume of purchase order requests for the Office of Research.

Denise B. Durham

Ettie Karpman

Denise M. Strekal

CVM TEAM EXCELLENCE AWARD

360-Degree Working Group

For excellence in designing, developing and implementing a 360-degree feedback program based on the CVM managerial behaviors for all the team leaders and above.

Laura A. Adam

Norris E. Alderson, Ph.D.

Richard L. Arkin, J.D.

Andrew J. Beaulieu, D.V.M.

Frances A. Benedict

Bessie M. Cook

Gloria J. Dunnavan

Charles E. Eirkson, III

Russell A. Frobish, Ph.D.

Jeffrey M. Gilbert, Ph.D.

David W. Grau, D.M.D.

Elizabeth A. Grove

Carol J. Haley, Ph.D.

Philip J. Kijak, Ph.D.

Vashti D. Klein

Barbara E. Leach

William G. Marnane

Daniel G. McChesney, Ph.D.

Anna B. Nevius, Ph.D.

Glenn A. Peterson, Ph.D.

Kim R. Young

CVM Animal Drug/Biologic Working Group

For sustained superior performance in resolving difficult inter-agency jurisdictional issues involving novel animal biological products and for updating the FDA/USDA MOU accordingly.

Neal Bataller, D.V.M.

Michael J. Myers, Ph.D.

Lisa M. Troutman, D.V.M.

Vitolis E. Vengris, D.V.M., Ph.D.

Schibblehut and Schrider Team

For exceptional craftsmanship, creativity, and commitment in supporting mission oriented research within CVM.

Neil T. Schibblehut

John V. Schrider

Veterinary Drug Compounding Compliance Policy Guide Team

For providing exceptional policy clarification and coordination during the development of a guidance document furthering the protection of public health.

Neal Bataller, D.V.M.

Alfred W. Montgomery, D.V.M.

Lynn O. Post, D.V.M.

Gail L. Schmerfeld, J.D.

APPENDIX B – PUBLICATIONS

Note: Names of CVM Staff Members are in bold type

Bloom, R. A. 2004.

Use of veterinary pharmaceuticals in the United States. *Pharmaceuticals in the Environment: Sources, Fate, Effects and Risks*. Kümmerer, Klaus (Ed.) 2d Ed. Springer-Verlag, Berlin.

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P. F. McDermott, T. Donkar, C. Bolin, S. Bolin, S. Munro, E. J. Baron,
and **R. D. Walker.** 2003.

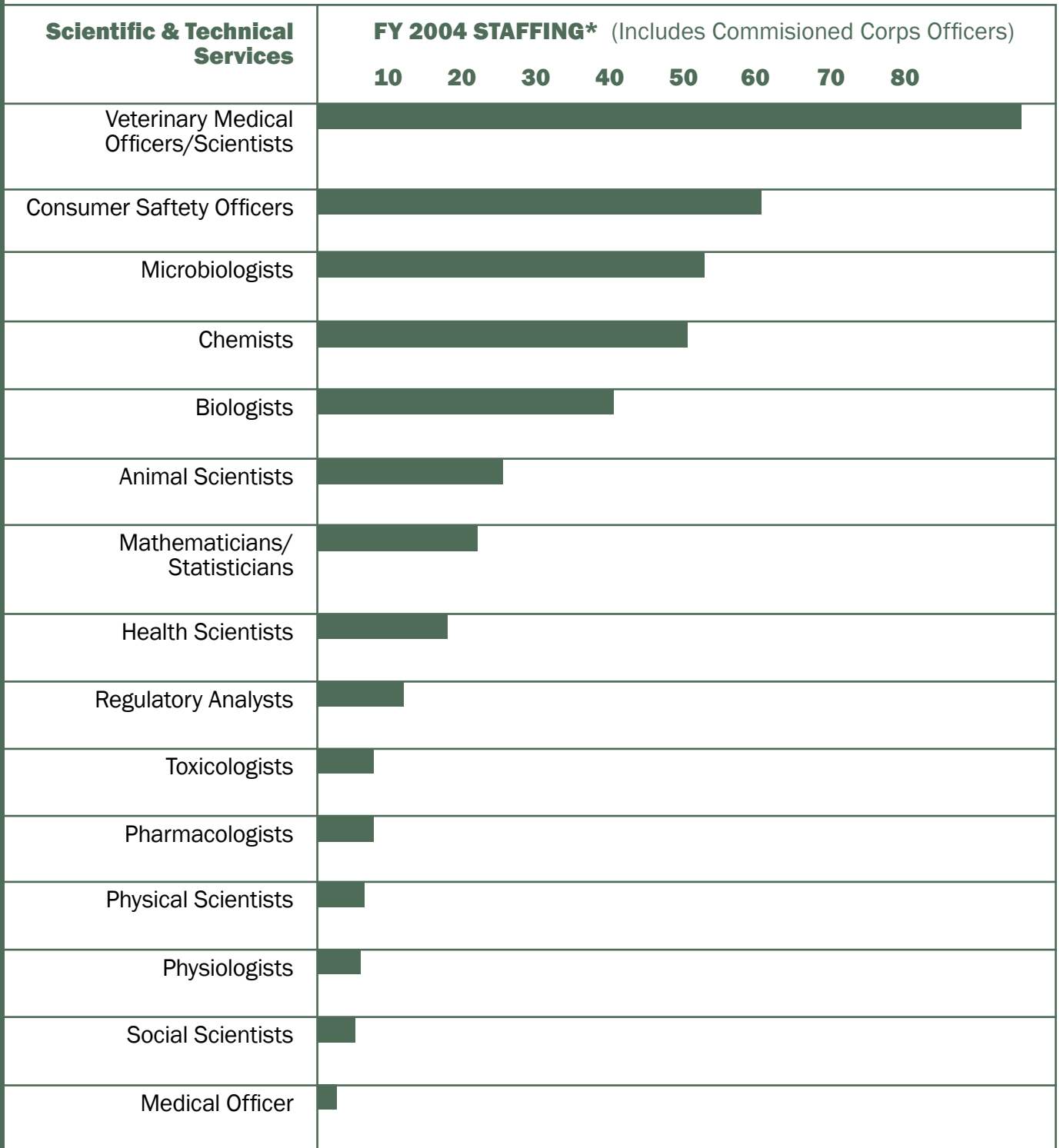
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APPENDIX C – BUDGET DETAILS**BUDGET**

Full Time Equivalent Employees	Pre-Market	Post-Market	FY 2004 Total(s)
Budget Authority (BA)	183	132	315
User Fee (ADUFA)	40		40
Total Program Level	223	132	355
Note: Estimates for the field are not included in the figures above. Field Activities-Animal Drugs & Feeds info:	20	243	263

*FY 2004 Enacted Budget	Pre-Market	Post-Market	Rent	FY 2004 Total(s)
Program	\$26,160,000	\$28,442,000		\$54,602,000
GSA Rent & Rent Related Activities			\$12,358,000	\$12,358,000
ADUFA	\$4,750,000			\$4,750,000
ADUFA GSA Rent & Rent Related Activities			\$250,000	\$250,000
Total Program Level	\$30,910,000	\$28,442,000	\$12,608,000	\$71,960,000
Note: Estimates for the field are not included in the figures above. Field Activities-Animal Drugs & Feeds info:	\$2,148,000	\$26,708,000		\$28,856,000

*FY 2004 enacted budget as of August 2004 (reflects GSA rent reprogramming).



*Graph does not display 100 percent of FTEs.