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FDA VETERINARIAN

TRYING TO KEEP "MAD COW DISEASE" OUT OF U.S. HERDS

by Linda Bren

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Millions of British television viewers watched the harrowing final days of 14-year-old Zoe Jeffries in October 2000. The ordeal of the young girl from Manchester, England, began more than two years earlier. First she cried for two weeks, then came the hallucinations and continuous screaming. As the disease progressed, the pain in her legs worsened until she couldn't walk. Bedridden, her brain wasting away, she was reduced to communicating through moans and grunts.

Zoe's mother, Helen Jeffries, let the television cameras into her home to demonstrate the plight of people like her daughter—victims of new variant Creutzfeldt-Jakob disease, or nvCJD. The neurological illness is thought to be the human form of bovine spongiform encephalopathy, or BSE—commonly called "Mad Cow Disease." The disease is thus far untreatable, incurable, and ultimately fatal.

"It's a bad disease," says Lawrence Schonberger, MD, MPH, an epidemiologist at the Centers for Disease Control and Prevention (CDC). "We believe that it is transmitted by food that has been contaminated with the agent that causes BSE. Every case of nvCJD is a major tragedy." Although the incubation period after initial exposure can be quite long, once clinical signs and symptoms begin, death usually occurs within about a year.

The recent increase in reported cases of BSE in European cows and the increasing number of human nvCJD cases in the United Kingdom have raised fears throughout the European Union (EU) of the risk of eating beef possibly contaminated with the BSE agent. Although these concerns may have spread to the United States, the diseases have not. No cases of nvCJD in humans or BSE in cows have ever been identified in this country.

BSE and nvCJD have thus far been kept out of the United States largely through the combined efforts of the Food and Drug Administration, the U.S. Department of Agriculture (USDA), the CDC, other federal organizations, and state regulatory and health agencies. These organizations have taken aggressive actions to reduce the risk that BSE could be introduced and spread in this country.

BSE has infected more than 180,000 cattle in the UK and about 1,800 cattle elsewhere in the EU, according to the European Commission's Health and Consumer Protection Directorate, an agency of the EU. Because of UK actions to eradicate BSE since it was first identified in 1986, the number of BSE cases is falling sharply in that country, but it is rising in a number of other European countries.

The sudden rise in reported BSE cases may, in part, reflect increased testing to detect infected cattle by some EU member countries, particularly France, according to Burt Pritchett, a veterinarian in FDA's Center for Veterinary Medicine. "And because of the long incubation period of BSE (two to eight years), cows being identified with BSE now would have become infected several years ago," says Pritchett. "In December

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PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION CENTER FOR VETERINARY MEDICINE

2000, the EU imposed BSE testing EU-wide, which will likely further increase the number of cases being reported."

How BSE Spreads Within Cattle Herds

Evidence suggests that certain contaminated cattle feed ingredients are the source of BSE infection in cattle. The process that leads to the contaminated feed starts when livestock already harboring the BSE agent are slaughtered. After cows and sheep are killed, the edible parts are removed. The inedible remnants are taken to a special plant, where they undergo a process called "rendering." This process creates two major products:

- fat, which is used in an amazing array of products (such as soap, lipstick, linoleum, and glue), and
- meat-and-bone meal (MBM), a powdery, high-protein supplement that is often processed into animal feed.

Although the animal remnants are "cooked" at high temperatures during the rendering process, the BSE agent, if present, is able to survive.

When this contaminated MBM is fed to cattle as a protein supplement, the BSE agent can be passed on to many new cattle. It is believed that this is how BSE was spread through the UK cattle herds.

In 1997, scientists at the Institute for Animal Health in Edinburgh, Scotland, and the Imperial College School of Medicine in London presented studies that strongly pointed to the agent that causes BSE as the most likely cause of human nvCJD. The UK government concluded that victims of nvCJD most likely acquired the disease by consuming food that had been made from cattle infected with BSE.

Although BSE and nvCJD occur in different species, they both belong to a family of fatal neurological diseases known as transmissible spongiform encephalopathies (TSEs), so named because of the sponge-like holes they leave in the brain. Currently, no test can reliably detect BSE in live cattle or nvCJD in live humans. A diagnosis is confirmed by examining brain tissue after death. The agent that causes TSEs is not well understood. The prevailing theory of the scientific community is that the agent is a "prion," an abnormal, slowly replicating protein.

"So little is known about prion diseases," says James Voss, DVM, of the College of Veterinary Medicine and Biomedical Sciences at Colorado State University. "It's a very difficult area to study because of the long incubation period of these diseases," says Voss, who is also the co-chairman of the TSE Task Force of the Council for Agricultural Science and Technology, a nonprofit research consortium. "We believe the risk is very, very low that BSE could gain entry to this country, but no one can say with 100 percent certainty that it won't happen."

"We know that our cattle are not immune to this disease just because they live on this side of the Atlantic Ocean," says Murray Lumpkin, senior medical advisor in FDA's Office of the Commissioner. "Renderers, cattle ranchers, feed manufacturers, feed lot operators, and state and federal government agencies will all have to continue to work together vigilantly to assure safe cattle-feeding practices are scrupulously followed. This is our first line of defense against the disease getting into American cattle herds."

Other TSEs are known to occur in sheep, mink, deer, elk, and cats. The recent European outbreak of BSE may have originally resulted from feeding cattle with MBM-supplemented feed made from sheep carcasses infected with scrapie—a TSE found in sheep and goats.

Unlike BSE, other animal TSEs do not appear to be naturally transmitted to humans, according to an October 2000 report of the TSE Task Force. However, five TSEs do occur in humans—all of them rare. In 1957, scientists first recorded a human TSE, called kuru, in the Fore natives

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LIGHTS, CAMERA, ACTION!

With all the press attention on BSE, CVM Director, Dr. Stephen Sundlof, has spent countless hours in interviews with reporters from the major networks, and a multitude of newspapers, radio, and television stations. His office has been transformed into a television studio, and camera men and network producers abound. Recently, Dr. Sundlof was interviewed by Scott Pelley, correspondent for CBS' 60 MINUTES II, for an upcoming show about the threat of BSE.

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of the New Guinea highlands. The Fores were cannibals—they ate parts of their fellow humans, especially brain tissue. It is believed this practice contributed to further spread of kuru in the population.

Two Forms of CJD

Another human TSE, Creutzfeldt-Jakob disease, in its classic form, occurs worldwide at a rate of approximately one case per 1 million people per year. Classic CJD, unlike its new variant, nvCJD, is not known to be caused by consuming food made from cows infected with BSE.

"CJD and nvCJD are best thought of as two different diseases," says CDC's Schonberger. "CJD was around long before the emergence of BSE in cattle."

Victims of classic CJD and nvCJD may share some symptoms, but the patterns of the brain lesions are distinct. To date, nvCJD has caused disease in younger patients, and the mean duration of illness is more prolonged. (The average age for death of nvCJD has been 27.5 versus 68 for CJD, and the average time to death after the onset of clinical symptoms is 13 months for nvCJD versus less than six months for CJD.)

As of Feb. 2, 2001, a total of 94 cases of nvCJD have been confirmed or suspected in the UK, according to the UK Department of Health. Three cases in France and one in Ireland were reported by the European Commission's Health and Consumer Protection Directorate.

The U.S. Response

The focus for American animal and human health officials has been prevention. "Using the best science known at this time, the United States has an aggressive, multi-faceted program in place to try to prevent the establishment and spread of BSE," says Stephen Sundlof, DVM, PhD, Director of FDA's Center for Veterinary Medicine. FDA's restrictions on certain cattle feed ingredients and its import alerts on cattle products are critical parts of this program. In addition, USDA has prohibited certain animals and animal products from entering the country.

Since 1989, USDA's Animal and Plant Health Inspection Service (APHIS) has banned the import of live ruminants (cattle, sheep, and goats) and most ruminant products from countries where BSE has been reported. In addition, in 1990, APHIS began a program of active surveillance of certain American cows for evidence of BSE. While FDA inspects feed production facilities, the USDA surveillance program condemns and tests any cows displaying signs of neurological problems at slaughter. As of October 2000, approximately 12,000 cattle brains from nearly every state and Puerto Rico had been examined, with no evidence of BSE found. More than 60 diagnostic laboratories continue to examine hundreds of cattle brains each year.

In August 1997, FDA established a regulation that prohibits the use of most mammalian protein in the manufacture of animal feeds for ruminants. With the strong support of renderers, cattle owners, feed manufacturers, and feed lot owners, FDA launched a compliance and education program, including a rigorous inspection program. The goal of these efforts is to achieve as close to 100 percent compliance with this new regulation as possible. FDA and state regulators have conducted nearly 10,000 inspections of renderers, feed mills, ruminant feeders, dairy farms, protein blenders, feed haulers, and distributors since January 1998. More than three-quarters of these establishments were found to be in compliance. And most of the establishments that initially had problems were found in compliance upon re-inspection.

Education is also an extremely important part of the compliance program. "We've put a lot of effort into getting the word out about the regulation," says Sundlof. FDA has sponsored workshops for state veterinarians and feed control officials from all 50 states, Puerto Rico, the U.S. Virgin Islands, and Canada. In addition, FDA has held briefing sessions with trade associations and consumer groups, and has developed additional guidances for complying with the regulation.

FDA is continuing its compliance efforts by conducting additional inspections and re-inspecting noncompliant facilities. Based on an evaluation of the inspections conducted from 1998 through 2000, FDA will revise its compliance strategy to try to assure its goal of 100 percent adherence to the feeding regulations.

FDA and USDA recently took emergency action to prevent potentially cross-contaminated products from entering the United States. On December 7, 2000, APHIS banned all imports of rendered animal proteins, regardless of species, from the more than 30 countries that either are known to have BSE in their cattle or otherwise present undue risk for introducing BSE into the United States. FDA has also announced an import alert, allowing its inspectors to detain shipments from these countries of animal feed (including pet food), animal feed ingredients, and certain other products of animal origin intended for animal use.

FDA and USDA will continue to aggressively enforce their regulations and to work closely with those in the cattle and feed industries to minimize the risk of BSE introduction or spread in U.S. cattle herds. FDA will develop new guidances and regulations as the scientific knowledge about BSE expands. Working together with many counterpart agencies in the United States and around the world and with various industry and consumer groups, FDA will continue to do its best to protect the health of Americans and of our American cattle herds.

Linda Bren is a Writer-Editor with the ***FDA Consumer****.*

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4 NEW COMMITTEE MEMBERS FOR VMAC

Six new members have been selected to join FDA's Veterinary Medicine Advisory Committee (VMAC). The new members are Deborah Kochevar, D.V.M., Ph.D., Alexander MacDonald, Ph.D., Anne Parkhurst, Ph.D., Marguerite Pappaioanou, D.V.M., Ph.D., John Waddell, D.V.M., and Dennis Wages, D.V.M. They replace former members Janis Cleland, D.V.M., Steven Barker, Ph.D., Ling-Jung Koong, Ph.D., Frederick Angulo, D.V.M., Ph.D., Keith Sterner, D.V.M., and Oscar Fletcher, D.V.M., Ph.D., respectively.

Deborah Kochevar, D.V.M., Ph.D.

Alexander MacDonald, Ph.D.

John Waddell, D.V.M.

Dr. Kochevar is an Associate Professor in the Department of Veterinary Physiology and Pharmacology at Texas A & M University. Her expertise is **companion animal medicine** and she is Board-Certified as a Diplomate, American College of Clinical Pharmacology.

Dr. MacDonald is the Scientific Director at Pharma Science, Inc., in North Caldwell, New Jersey. He is an expert in analytical methodology development and evaluation for veterinary drug tissue residues, **chemistry.**

Anne Parkhurst, Ph.D.

Dr. Parkhurst's expertise is **Biostatistics**. She is currently Professor of Biometry, University of Nebraska-Lincoln and has extensive research experience and publications on farm animal topics.

Dr. Pappaioanou is a Captain in the U.S. Public Health Service stationed at the Centers for Disease Control, Atlanta, Georgia. With expertise in **Public Health Epidemiology**, Dr. Pappaioanou is an Honorary Diplomate in the American Veterinary Epidemiology Society.

Marguerite Pappaioanou, D.V.M., Ph.D.

Dennis Wages, D.V.M.

Dr. Waddell is an expert in **food animal medicine**. He is currently Corporate Vice President of Nutrition Services, Inc., a swine nutrition company. Dr. Waddell is also Corporate President of Dreisohn, Inc., a contract finishing swine operation.

Dr. Wages is Professor of Poultry Health Management, Department of Farm Animal Health and Resource Management, College of Veterinary Medicine, North Carolina State University. **Avian medicine** is his expertise, and he is Board-Certified as a Diplomate, American College of Poultry Veterinarians.

Dr. Vernon C. Langston whose expertise is **pharmacology,** is the new chairman of VMAC, replacing Dr. Sterner. Other members include Dr. Thomas Carson, Dr. Michael Doyle, Dr. Barbara Glenn, Dr. Wanda Haschek-Hock, Dr. Robert E. Holland, and Mr. Richard Wood. VMAC members normally serve four-year terms. □

NEW PET FOOD SPECIALIST AT CVM

Dr. William J. Burkholder, D.V.M., Ph.D. ACVN joined FDA's Center for Veterinary Medicine (CVM) on December 18, 2000, as the canine and feline nutrition and pet food specialist in CVM's Division of Animal Feeds. Prior to coming to CVM, Dr. Burkholder was an Assistant Professor of Veterinary Clinical Nutrition in the Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, Texas A & M University, College Station, Texas. While at Texas A & M he completed research regarding obesity in dogs and cats and assessed methods to measure body composition of dogs.

Dr. Burkholder received his B.A. from the University of Virginia, D.V.M. from Virginia Tech in 1985, and Ph.D. in veterinary nutrition from Virginia Tech in 1994. He is board certified in veterinary nutrition holding Diplomate status in the American College of Veterinary Nutrition. His address is: FDA/Center for Veterinary Medicine, Division of Animal Feeds, 7500 Standish Place, HFV-228, Rockville, MD 20855, telephone: 301-827-0179, e-mail: bburkhol@cvm.fda.gov.

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TOLLEFSON APPOINTED CVM DEPUTY DIRECTOR

Linda Tollefson, D.V.M., M.P.H. has been appointed as Deputy Director of FDA's Center for Veterinary Medicine (CVM) effective February 1, 2001. Dr. Tollefson succeeds Dr. Andrew Beaulieu who will assume the new position of Associate Director for Animal Health Policy and Operations in CVM.

Dr. Tollefson joined CVM in 1993 and has been the Director of the Center's Office of Surveillance and Compliance since January 1997. She came to FDA in 1984 at the Center for Food Safety and Applied Nutrition (CFSAN.) Dr. Tollefson's last position before coming to CVM was Chief of the Epidemiology Branch.

During her CVM tenure, Dr. Tollefson has provided outstanding leadership in the direction and oversight of many of the Center's activities in the area of food safety. She is the senior manager who has been primarily responsible for managing major elements of CVM's efforts under the Food Safety Initiative (FSI.) This Presidential initiative, which for CVM is almost entirely associated with the issue of antimicrobial resistance, has been growing in recent years to the point that it now represents about 40% of the Center's budget. Food safety issues, in general, now account, directly or indirectly, for about 80% of the Center's budget.

Dr. Linda Tollefson

Dr. Tollefson is one of the founders of the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS). NARMS monitors development of resistance of zoonotic enteric pathogens from human and animal clinical specimens, from healthy farm animals, and from carcasses of food-producing animals at slaughter. NARMS was established in 1996 as a collaboration among several Federal agencies in response to concerns associated with the approval of antibiotics important to human medical therapy for use in food animals.

CVM Director Stephen Sundlof says "Dr. Tollefson is the CVM senior manager best suited by training and experience to deal with the complexities of food safety issues, in general, and antimicrobial resistance issues, in particular. I look forward to working with her in her new role as Deputy Center Director."

Dr. Tollefson received both her B.S. and D.V.M. degrees from the University of Illinois, and a M.P.H. from the Johns Hopkins University with special training in Epidemiology and Biostatistics. Dr. Tollefson has been awarded numerous Public Health Service medals and commendations, including the Meritorious Service Medal in 1997, and has published over 50 articles in scientific journals.

Dr. Beaulieu has been with CVM for 28 years and has a thorough working knowledge of the animal product-related provisions, limitations, and practical applications of the Food, Drug, and Cosmetic Act. He has served as Deputy Center Director since July 1999. As Associate Director for Animal Health Policy and Operations, Dr. Beaulieu now will deal primarily with issues relating to animal health including products intended for minor uses or minor species and with internal operations such as the Center's ongoing initiative to become a higher performing organization. □

DEADLINE EXTENDED FOR SUBMITTING DATA FOR POULTRY FLUOROQUINOLONE NOOH

The Center for Veterinary Medicine (CVM) has extended the deadline for Bayer Corporation, Agriculture Division, to submit data and information in response to CVM's proposal to withdraw approval of the company's fluoroquinolone product for use in poultry.

The extension was granted because some of the data cited in the October 31, 2000, Notice of Opportunity for Hearing (NOOH) were found to be incorrect. The data used in the NOOH were taken from reference number 2 of the NOOH, the risk assessment entitled "The Human Health Impact of Fluoroquinolone Resistant Campylobacter Attributed to the Consumption of Chicken." CVM discovered that corrections were needed to two cell references in the risk assessment model. Since CVM needs to make these corrections to the risk assessment, it also intends to incorporate the final FoodNet data for 1999. The NOOH stated that in 1999, a mean estimate of 11,477 persons were infected with fluoroquinolone-resistant Campylobacter from chicken and subsequently prescribed a fluoroquinolone. As a result of the correction of the two cell references in the risk assessment model and the incorporation of the final FoodNet data for 1999, that number will be revised to 9,261 persons. The numbers given for the 5th and 95th percentiles in the NOOH—6,412 and 18,978 persons—will also be revised to 5,227 and 15,326 persons.

CVM does not believe that the revisions alter the premise of the NOOH. In the NOOH, CVM has proposed to withdraw the approval of the new animal drug application for use of enrofloxacin in poultry on the

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DEADLINE EXTENDED FOR SUBMITTING DATA FOR POULTRY FLUOROQUINOLONE NOOH (Continued)

grounds that new evidence shows that the product has not been shown to be safe as provided for in the Federal Food, Drug, and Cosmetic Act, the statute that covers the use of new animal drugs in the U.S.

A notice to revise the data in the NOOH and the Campylobacter risk assessment was published in the *Federal Register* on January 22, 2001. Bayer must submit data and information supporting the company's request for a hearing by February 21, 2001. Other interested persons may also submit comments on the NOOH during the additional 30-day time period.

Bayer's original deadline for submitting data and information was January 2, 2001. However, the company was informed that the deadline would be extended and, therefore, did not submit any data or information by the original deadline. Except for data and information prohibited from public disclosure, e.g., trade secret information, any information that is submitted may be seen in FDA's Dockets Management Branch.

CVM continues to encourage public review of the NOOH and information connected to it. The Center has made the risk assessment and the program to run the calculations publicly available through its Web site. □

ONADE DEPUTY APPOINTED

CVM recently announced the selection of Allen Rudman, Ph.D. as Administrative Deputy of the Office of New Animal Drug Evaluation (ONADE). Dr. Rudman was previously with FDA's Office of Generic Drugs, Center for Drug Evaluation and Research (CDER), where he was the Deputy Director in the Division of Chemistry I.

Since joining the FDA, Dr. Rudman has been recognized as an FDA Peer Review Expert and CDER Master Reviewer. He has direct experience in scientific assessment of applications and related submissions and in the evaluation of industry proposals and comments on draft policies and guidances developed by CDER. In addition, he has received over a dozen FDA awards including the FDA Commissioner's Award of Merit as Chairman of the SUPAC Working Group, FDA Commissioner's Special Citation as a member of the Vice-President's Reinventing Government Working Group, and the Vice Presidential National Partnership for Reinventing Government (Hammer) Award. Dr. Rudman has been involved in a number of projects and committees including: FDA Topic Leader to the International Conference on Harmonization (ICH) Working Group on Impurities in Drug Products, Chair of the CDER Scale-up and Post Approval Changes (SUPAC) Task Force, Chair of the CDER Drug Product Technical Committee, member of the Research Project Advisory Group, Chair of the OGD Parenterals Advisory Group, representative to the World Health Organization, member of the Reviews Evaluation Steering Committee, and member of the MDI/DPI Working Group.

Before joining the FDA, Dr. Rudman received his Ph.D. in bio-inorganic chemistry and was employed at several large international pharmaceutical companies in research, manufacturing and quality control including SmithKline Beecham and Novartis Pharmaceutical Corporation. He was recently elected as Vice Chair of the U.S. Pharmacopoeia (USP) Pharmaceutical Dosage Forms Expert Committee by the USP Council of Experts and is a member of the AAPS/FDA Product Quality Initiative Science Management Committee. □

EXTRAMURAL RESEARCH MEETING

On December 5 - 6, 2000, FDA/Food Safety Initiative (FSI) held its second annual Extramural Research Meeting in College Park, Maryland. Dr. Stephen Sundlof, CVM's Director, Lou Carson, FSI, and Dr. Bernard Schwetz, Acting Deputy Commissioner, opened the meeting. FDA staff from CFSAN and CVM chaired the sessions on exposure, controls, dose response, and resistance.

Researchers funded by FSI through CVM or through CFSAN presented their in-progress results. Newly funded (September 2000) researchers presented their research plans and preliminary findings. Dr. Norris Alderson, Director of CVM's Office of Research, made closing remarks. □

CVM OFFICIALS ATTEND AAEP

Veterinary Medical Officers from CVM's Division of Surveillance attended the American Association of Equine Practitioners (AAEP) 46th Annual Convention from November 26 - 29, 2000, in San Antonio, Texas. AAEP reaches approximately 5.1 million horse owners worldwide through its 6,500 members. More than 2,000 veterinary health professionals were in attendance. The president of the AAEP requested the participation of CVM's Division of Surveillance because of a concern that questionable veterinary products were being promoted at the Convention trade show. There were 190 exhibitors representing five countries at the trade show. CVM officials collected promotional materials and product samples from several exhibitors, primarily pharmaceutical compounding companies and manufacturers of nutraceuticals. The materials will be reviewed for violations and necessary action will be taken. □

CVM's MINI-SABBATICAL PROGRAM

by Douglass Oeller, D.V.M., Tania Woerner, V.M.D., and Lisa Troutman, D.V.M.

This year, CVM's Office of New Animal Drug Evaluation offered the opportunity for scientific reviewers to apply for funding of individually developed short-term training projects. The program is called CVM's mini-sabbatical program. It is part of former FDA Commissioner Jane Henney's commitment to keep the agency's scientific knowledge current.

The mini-sabbatical is described as "any developmental opportunity that involves more than 40 work hours/year." It can be a training opportunity out of the Center, or a temporary reassignment of work. Each applicant prepared a proposal describing the project, how it would benefit the employee, and how it would benefit CVM. The proposals were reviewed based on cost, workload considerations, and applicability to the Center's priorities. CVM's Division of Therapeutic Drugs for Non-Food Animals (HFV-110) approved funding for three Veterinary Medical Officers to spend time at Colleges of Veterinary Medicine.

Dr. Douglass Oeller spent three weeks at the Virginia-Maryland Regional College of Veterinary Medicine (VMRCVM), in Blacksburg, Virginia. *http://www.vetmed.vt.edu/* Founded by the Virginia General Assembly in 1978, the VMRCVM is a regional professional school built upon the strong foundations of two of the nation's leading land-grant universities: Virginia Tech in Blacksburg and the University of Maryland at College Park. The Veterinary Teaching Hospital at Virginia Tech is a comprehensive, advanced care facility that provides primary and referral care for animals throughout the States of Virginia and Maryland.

Veterinary Medical Officers in HFV-110 are expected to have current knowledge about the diagnosis and treatment of the diseases of companion animals. Dr. Oeller spent the time working with students and faculty in the Small Animal Internal Medicine section of the teaching hospital. Most clinical faculty members are board certified specialists in areas like medicine, surgery, ophthalmology, radiology, anesthesiology, neurology, dermatology and other areas who apply advanced diagnostic and therapeutic techniques in caring for hospital patients. Dr. Oeller's visit provided immersion in clinical medicine as practiced by experts. He examined patients, participated in clinical rounds, and observed echocardiography, ultrasound, and endoscopic procedures. The visit offered an opportunity to meet with faculty members who may conduct studies that will be submitted for FDA review. The visit also provided opportunities to establish better communication between FDA/CVM and the clinical faculty of VMRCVM.

Dr. Tania Woerner participated in a mini-sabbatical June 5 -17, 2000, at Colorado State University. Dr. Woerner reviews many of the drugs designed to enhance the reproductive functions of horses. The Animal Reproduction and Biotechnology Laboratory (ARBL) *http://www.cvmbs.colostate.edu/physio/arbl.html*, is an integral part of the Department of Physiology in the *College of Veterinary Medicine and Biomedical Sciences*. Twelve departmental faculty members are associated with the ARBL and devote full-time to the area of reproductive biology. In addition, two members of the Department of Clinical Sciences are considered integral members of the ARBL due to their interactive commitments and expertise. Faculty members in other departments, colleges, and universities contribute in joint research projects.

In addition to the faculty members, 6 - 10 postdoctoral trainees or postdoctoral research associates, and 20 - 30 graduate students, contribute to the activities of the laboratory. Because of the large number of trainees involved, unique interactions are possible and openings for highly qualified postdoctoral trainees and graduate students usually exist.

ARBL is located at the Foothills Campus which also includes pasture and housing for the hundreds of cattle, horses, sheep and laboratory animals used for research. Construction of a 22,000 square foot laboratory/office building was completed in 1995, and an adjacent 15,000 square foot building, which houses the gamete preservation and embryo transfer laboratories, also underwent extensive renovation in 1995. This new facility allows most personnel of the program to be housed at a single location, and enhances interactions among faculty and students. The new laboratory includes specific facilities for cloning, sequencing and characterization of genes; measurement of hormones, receptors, and other compounds of biologic interest; transmission electron microscopy; isolation and culture of cells; immunology and immunochemistry; production of transgenic animals; seminal analyses; and cryopreservation of sperm and embryos. The facilities have been designed to allow maximum flexibility in teaching, research and service programs.

Researchers associated with the ARBL have international reputations, having received over 20 major awards for excellence in research and service and have been elected as officers of major professional societies. One is a member of the National Academy of Sciences. Many serve on the editorial boards of major journals devoted to reproductive biology and reproductive endocrinology and sit on national review boards for research funding.

For more information on ARBL contributions to research on reproduction please visit the following web site: *http://www.cvmbs.colostate.edu/physio/arbl_reprotech.html*.

Dr. Woerner interacted predominantly with Dr. Edward L. Squires, *http://www.cvmbs.colostate.edu/physio/squires.html*, and a world-renowned equine reproductive specialist. During her two-week visit she

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CVM's MINI-SABBATICAL PROGRAM (Contin.)

participated in an ongoing stallion reproductive safety study. Dr. Woerner had reviewed the protocol for this study and was able to view the conduct of the study and participate in the collection and evaluation of the semen.

Dr. Woerner was also educated on the XY Project, which is currently being evaluated as a means of sorting equine sperm using the technology of flow cytometry. This technology has worked well in cattle sperm; however, equine sperm is more susceptible to damage caused by the procedure with resultant lower recovery rates. To date, several foals have been born with sorted equine sperm with 100% accuracy.

During her two-week visit she also began work on a Reproductive Safety Guidance for Equines. Based on the suggestions of Dr. Squires and collaboration with Dr. Dickson Varner of Texas A&M and other experts in this field, she was able to create specific recommendations for detecting drug induced effects on the reproductive function of the stallion and the mare. Currently CVM's Target Animal Safety Guidance Document #33, only briefly mentions how a reproductive safety study should be conducted. The revised guidance will make more specific recommendations, and save considerable time in protocol formation and review.

Dr. Woerner continues to interact with Dr. Squires and recently participated in the Equine Stallion Reproductive Seminar held January 11 - 12.

Dr. Lisa Troutman spent two weeks in the oncology service at Colorado State University College of Veterinary Medicine, in Fort Collins, Colorado. *http://www.cvmbs.colostate.edu/cancercure/animalcancerctr.htm*

The comparative oncology program at the Veterinary Teaching Hospital is the largest and most comprehensive of its kind in the United States. In operation since 1974, the program has more than 40 professionals who evaluate and treat more than 1,000 animal cancer patients each year.

Animals brought to the oncology program often are in advanced stages of the disease. They are treated with the most current and innovative forms of cancer therapies and care. Staff personnel include experts in radiation therapy, medical oncology, surgery, pathology, physics, nutrition, and specialty nursing. Single and multifaceted treatment regimes include photon and electron radiation, and chemotherapy.

The oncology program also is a center of research activity, ensuring the patients get the latest treatments available. In addition, much of the research conducted and applied here has direct application to diagnosis and treatment of similar cancers in people. Through the oncology treatment and research program, they help not only our animal friends, but their human companions as well.

Dr. Troutman spent time under the direction of Dr. Greg Ogilvie *http://www.vin.com/promo/Consultants/consultant23.htm* on the clinical service with students, residents, and clinicians. This enabled her to examine cancer patients, learn the latest cancer treatment therapies as well as monitor patients involved in a clinical field trial for an investigational anticancer drug. She also spent time in the laboratory learning about ongoing research projects. For example, many projects were examining the role that matrix metalloproteinases (MMP's) play in cancer metastases. This is a new area of research that many pharmaceutical companies are hoping to design potential new anticancer drugs for both humans and companion animals. This minisabbatical provided the opportunity to create a new collaboration with a renowned oncology researcher as well as enhance Dr. Troutman's knowledge in cancer diagnosis and treatment.

Drs. Oeller, Woerner, and Troutman are Veterinary Medical Officers in CVM's Office of New Animal Drug Evaluation, Division of Therapeutic Drugs for Non-Food Animals.

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CONSENT DECREE SIGNED IN TISSUE RESIDUE CASE

On December 4, 2000, the judge for the United States District Court for the Eastern District of California signed a Consent Decree of Permanent Injunction against Heduino V. Brasil, an individual doing business as H & I Dairy, Tipton, California. This dairy was producing and selling cattle that contained excessive and illegal residues of antibiotic drugs in edible tissues. Some cattle that Mr. Brasil sold were adulterated because they contained unsafe new animal drugs and were held under insanitary conditions whereby they may have been rendered injurious to health.

The court order permanently enjoined Mr. Brasil and H & I Dairy from directly or indirectly introducing or causing to be introduced into interstate commerce, or delivering or causing to be delivered for introduction into interstate commerce, any food animals or their edible tissues, until the firm has come into compliance with the Federal Food, Drug, and Cosmetic Act, and fulfilled various regulatory requirements.

On December 14, 2000, an inspection of H & I Dairy was conducted by an investigator from FDA's San Francisco District Office to determine the state of compliance with the provisions of the Consent Decree. The inspection revealed minor areas of concern which require corrective action. Based upon the findings of the inspection and the promise of immediate correction, the District Office authorized Mr. Brasil and H & I Dairy to begin selling cattle. FDA will periodically monitor the dairy. Any future violations of the Consent Decree could result in the initiation of civil or criminal contempt proceedings.

FDA's San Francisco District Office conducted all investigative work for this case. CVM's Division of Compliance, FDA's Office of the Chief Counsel and the U.S. Department of Justice's Office of Consumer Litigation handled the case processing, litigation and negotiation.

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CVM VETERINARIANS TEACH IN CHILE

by Thomas Letonja, D.V.M.

On December 18 to 21, 2000, Drs. Ana Fernández and Thomas Letonja from CVM's Office of New Animal Drug Evaluation participated as speakers in a seminar entitled "Prudent Use of Veterinary Drugs". The seminar was organized by the School of Veterinary Medicine, University of Chile, and sponsored by the Chilean Ministry of Agriculture and the Ministry of Health. The seminar was held at the Veterinary School Campus in Santiago, Chile. Over 40 veterinarians and other health professionals affiliated with the veterinary pharmaceutical industry and regulatory agencies were in attendance.

Dr. Ana Fernández (left) instructs Chilean officials.

The objectives of the seminar were (a) To examine veterinary drug approval process in Chile and developed countries including Europe, USA, Canada, Australia, and Japan, with emphasis on the legal framework and determination of effectiveness and safety (animal, environmental, consumer, and handler safety) of veterinary drugs, (b) To examine control and surveillance of approved drugs in Chile and developed countries, (c) To discuss the responsibilities of veterinarians in the management of animal drugs.

The program on the first day examined the legal framework and government organizations involved in the veterinary drugs approval process including the following topics: (a) Chile: Overview of product registration; (b) Livestock and veterinary drugs products for export from Chile, (c) USA: Veterinary drug approval process; (d) Drug approval process in Europe, Canada, Australia, and Japan.

During the second day of the seminar, the registration process and studies necessary for an approval for the use of veterinary drugs were examined. The following topics were discussed in detail: (a) Chile: Registration process and review of scientific and technical data; (b) USA: Registration process and review of scientific and technical data; (c) USA: Studies needed for the evaluation of animal safety and effectiveness; (d) USA: Studies needed to evaluate environmental safety; (e) USA: Studies needed for the evaluation of veterinary drug residues; (f) USA: Studies needed to determine safe handling of veterinary drugs.

On the third day, the prudent management of veterinary drugs to protect the public health was discussed, emphasizing the following topics: (a) Approval and use of antibiotics in veterinary medicine and impact on human and animal health, (b) Chile: Bacterial resistance to antibiotics and public health impact, (c) Veterinary drug residues: The importance of the withdrawal periods. The presentations were delivered in Spanish.

The attendees had a lively discussion on the impact of the recommendations and requirements of the regulatory authorities on the drug approval process of developed countries on other areas of the world. The European Union and the United States are the major suppliers of veterinary pharmaceuticals for developing countries.

Dr. Letonja is a Veterinary Medical Officer in CVM's Office of New Animal Evaluation. □

PREPARE FOR NATIONAL PET WEEK

During the week of May 6 - 12, veterinarians, veterinary technicians, and others will celebrate "People and Pets, The Perfect Combination."

National Pet Week 2001 is sponsored by the American Veterinary Medical Association (AVMA), the Auxiliary to the AVMA, the American Animal Hospital Association (AAHA), and the North American Veterinary Technician Association. The theme recognizes the warmth, joy, love, and companionship that pets bring into our lives and the vital role of the veterinarian in that relationship.

For more information about this celebration, please visit the AVMA's web site at *http://www.avma.org*. CVM is proud to endorse this worthwhile campaign. □

CORRECTION

On page 14 of the January/February 2001 *FDA Veterinarian*, the following correction should be made. Enrofloxacin, Silver Sulfadiazine Emulsion, under Routes/Remarks, should read "The NADA provides for ototopical (in the ear) use in dogs depending on weight." This product is not an eye drop as indicated incorrectly. We apologize for this mistake. □

10 MICHIGAN STATE STUDIES ANTIMICROBIAL RESISTANCE ON ORGANIC VERSUS CONVENTIONAL DAIRY FARMS

by Vash Klein

Researchers are looking into the question of what difference organic farming may have on the levels of resistant bacteria in a dairy operation, and on the farm's revenue situation.

Organic dairy farms, which among other things use no or very little antibiotics, will be compared with conventional dairy farms with regard to management, disease incidence, economic inputs, and measures of animal welfare.

A three-year study is funded by the Center for Disease Control and the Food and Drug Administration. The study will determine if 30 dairy farms with at least a five-year history of zero or minimal use of antibiotics have lower rates of antibiotic resistance than do 30 region-matched conventional dairy farms that routinely use antibiotics.

Results will be compared internationally, most notably with a parallel study of antibiotic resistance in Denmark, to determine if dairy farms in countries with minimal use of antibiotics have lower rates of antibiotic resistance than what is found in the U.S. The Danes are currently involved in comparing antibiotic susceptibility between their organic farms and their conventional farms and have found some evidence of differences. A unique opportunity is being realized to compare antibiotic susceptibility of bacteria between organic and conventional dairy herds in an agricultural system that makes minimal use of antibiotics (Denmark), and organic and traditional dairy herds in a country which makes maximal use of antibiotics (U.S.).

Questions Raised

A preliminary study conducted last year indicated that the responding organic dairy farms had somatic cell counts (subclinical mastitis), clinical mastitis incidence rates, and cull rates well within normal ranges for Midwestern dairy farms.

The fact that some organic dairy herds can successfully compete without using any antibiotics suggests that this area is ripe for more study.

Vash Klein is a Public Affairs Specialist in CVM's Communications Staff. □

REGULATORY ACTIVITIES

The following firms/individuals received warning letters for offering animals for slaughter that contained illegal drug residues:

- Dale E. Senestraro, Coolidge Dairy Farm L.L.C., Coolidge, KS
- Peter H. Schouten, P. & L Schouten Dairy, Hico, TX
- Gregory L. Ziegler, Ziegler Dairy Farm, Middleton, WI
- Terrence J. Seubert, Seubert Calf Ranch, Dorchester, WI
- Andrew J. Slenders, Jr., AJ Slenders Dairy, Laton, CA
- Dale Shulfer, Shulfer Dairy, Amherst Junction, WI

These violations involved illegal residues of sulfadimethoxine in a cow; oxytetracycline in a holstein dairy cow; gentamicin in a cow; neomycin in a bob veal calf; sulfadimethoxine in a cow; and gentamicin in a bob veal calf.

All of these individuals were instructed to notify the FDA District Office within 15 working days of steps they have taken to correct the violations and prevent their recurrence. Failure to take prompt action to correct the stated violations may result in regulatory action without further notice such as seizure and/or injunction.

A warning letter was issued to Mark Boyd, Acting President/CEO, Control Solutions, Inc., Pasadena, TX, for significant deviations from the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals (21 CFR Parts 210 - 211). In addition, this veterinary drug manufacturing facility, doing business as C.J. Martin, was found to be misbranding the following drugs: Martin's Brand Pet Wormer, D-Worm, Scarlet Oil Smear for Horses, Violet Wound Dressing, Horse Antiseptic Ointment, Amine-Iodide, and Pine Tar Oil, since the labeling bears the incorrect address of the manufacturing facility. Also, the Martin's Brand Pet Wormer for Dogs and Cats was found to be adulterated since analysis showed the product differed from the labeled amount.

Dr. Charles R. Bray, Taylorsville Veterinary Clinic, Mt. Airy, MD, received a warning letter as a result of a follow-up investigation to findings of illegal drug residues of gentamicin in cows located on three farms in Maryland that were treated for mastitis using D.G.S. (Lincomix, Dexamethazone, Gentocin and Spectam) manufactured and prescribed by Dr. Bray's veterinary clinic. The D.G.S. is manufactured, in part, using Gentamicin Sulfate, labeled for use in the treatment of horses only, and not approved for oral or injectable use in cattle.

Mr. M. Yamamota, President, Uni-Heartous Pet Products, USA, Inc., Tokyo, Japan, received a warning letter for introducing animal food into the United States interstate commerce that was misbranded. The products were labeled only in the Japanese language. 21 CFR Part

(Continued, next page)

501.15(c)(1) states that "all words, statements, and other information required on a pet food label . . . shall appear thereon in the English language."

Mr. Allen Petro, Owner, Ana-Tech, Monroe, WI, received a warning letter for manufacturing the product, "BLU-HOOF Topical" without a new animal drug application on file with the FDA. Therefore, the product is considered unsafe, and adulterated, in that it was not manufactured in accordance with Current Good Manufacturing Practice regulations. In addition, other products, such as "ANA-KETO," "CAL-B4," "X-IT(W)," are labeled with therapeutic claims, but are not approved new animal drugs.

Warning letters were sent as a result of violative conditions found during investigations of the following medicated feed manufacturing facilities:

- Xtra Factors, Greeley, CO
- Fourth & Pomeroy Associates, Inc., Clay Center, KS
- Farmers Coop Association, Manhattan, KS
- Koch Poultry Company, Inc., Chicago, IL

These violations included failure to properly identify, store and control medicated articles to maintain their identity and integrity; failure to perform assays on medicated feeds as required; failure to assure that all medicated articles used in production of medicated feeds are within their expiration date; failure to assure that medicated feed labels are accurate and complete; failure to establish adequate procedures for the receipt, storage, and inventory control of drugs; failure to conduct daily drug inventories; failure to document all flushes of the pellet mill between runs of medicated and withdrawal feeds; failure to have master record files include all necessary manufacturing and control directions; and failure to review batch production records to ensure all production steps were completed and documented. □

UPDATE ON FY 2000 APPROVALS

CVM's Office of New Animal Drug Evaluation (ONADE) processed 5,497 submissions for new animal drug applications (NADAs), abbreviated new animal drug applications (ANADAs), investigational new animal drug files (INADs) and generic investigational new animal drug (JINADs) files during FY 2000, compared to 5,968 in FY 99.

Approximately 74 percent of NADAs, ANADAs, and supplements were processed within the applicable statutory timeframe of 180 days. Of the 5,497 submissions, 72 were for original NADAs and ANADAs and 977 were for supplements to previously approved NADAs and ANADAs. In addition, CVM reviewed 367 phased data submissions under INADs and JINADs to support approvals.

FDA published 53 documents relating to significant NADA and ANADA approvals in the *Federal Register*. Significant approvals included: 3 new chemical entities, 8 products for use in new animal species, 1 new dosage form of a previously approved product, and 4 products available in new dosages.

TABLE
New Chemical Entities Approved in FY 2000

Drug	*Species*	*Sponsor*	*NADA Number*
Sevoflurane	Dogs	Abbott Labs	141 - 103
Ractopamine Hydrochloride	Swine	Elanco	140 - 863
S-Methoprene	Dogs	Wellmark International	141 - 162

The new chemical entities approved in FY 2000 are listed in the table above.

A complete list of all FY 2000 animal drug approvals is available from the *FDA Veterinarian.* Additional information about FDA-approved veterinary drugs is included on the Center's Home Page at *http://www.fda.gov/cvm/fda/greenbook/greenbook.html*. □

VETERINARY ACCREDITATION REVOKED

by Jeff Spykerman

On October 4, 2000, the United States Department of Agriculture ordered the revocation of veterinary accreditation of Dr. Bradley J. Rabe in the State of Nebraska. This revocation will be effective for a period of not less than 2 years.

On November 22, 1999, Bradley J. Rabe D.V.M. was sentenced in U.S. District Court, District of Nebraska. District Court Judge Urban sentenced Dr. Rabe to one-year probation, two hundred hours of community service, a one thousand dollar fine, and one hundred-dollar special assessment. The terms of Rabe's probation included that he must provide court access to his financial records; that he must provide FDA access to his place of business and veterinary practice records upon request; that he must comply with all Nebraska Department of Health Veterinary license requirements; and that he must comply with all rules, regulations and policies of the Food and Drug Administration.

(Continued, next page)

VETERINARY ACCREDITATION REVOKED (Continued)

Between the time of Rabe's plea agreement and sentencing the Nebraska Department of Agriculture reported to FDA's Office of Criminal Investigations (OCI) that they had evidence that Rabe was continuing to misbrand prescription veterinary drugs which resulted in the adulteration of two loads of Grade A milk. The state's report was provided to the court and taken into consideration during the sentencing phase.

Rabe's sentencing stemmed from a Federal Grand Jury indictment on March 16, 1999 after OCI determined that he was relabeling Baytril (enrofloxacin) as "Vitamin B-1 No Withdrawal" and selling to local food animal producers both with and without the producers knowledge of what the product contained. The indictment charged Rabe with 5 counts of Title 21, intent to defraud by adulterating and misbranding Baytril after receipt in interstate commerce. The indictment also charged Title 18, Aiding and abetting. At the time of Rabe's Baytril distribution, the drug was not approved for use in food-producing animals.

At the end of two years after the effective date of the revocation of Dr. Rabe's veterinary accreditation, he may reapply for accreditation in accordance with 9 CFR 161.2(b).

The Food and Drug Administration's Office of Criminal Investigations, FDA's Forensic Chemistry Center and the Nebraska Department of Agriculture, Bureau of Dairies & Food conducted all investigative work for this case. The U.S. Department of Justice, U.S. Attorney's Office District of Nebraska was in charge of the case processing, litigation and negotiation. FDA's Center for Veterinary Medicine and Office of Chief Counsel provided case guidance and assistance. USDA's Animal and Plant Health Inspection Service, Veterinary Services, also cooperated in the case.

Jeff Spykerman is a Special Agent with FDA's Office of Criminal Investigations, Kansas City Field Office.

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FDA FUNDS COOPERATIVE AGREEMENTS FOR FSI RESEARCH

In FY 2000, FDA funded four (4) new cooperative agreements under the President's Food Safety Initiative. These projects may be funded for up to three years depending on progress and the availability of funds. In the February 17, 2000, *Federal Register*, FDA announced the availability of cooperative agreement research funds to study the microbiological hazards associated with the food animal production environment. The newly funded projects are listed in the table below.

Additional information about these agreements is available from Dr. David B. Batson, Center for Veterinary Medicine (HFV-502), Food and Drug Administration, 8401 Muirkirk Road, Laurel, MD 20708, 301-827-8021.

TABLE
New Cooperative Agreements Funded in FY 2000

Project Title	Principal Investigator	Organization	FY 2000 Funds
Does antibiotic usage create drug-resistant *Campylobacter*	Margie D. Lee	University of Georgia	$195,078
Antimicrobial use and resistance in enteric bacteria	Paul S. Morley	Colorado State University	$199,382
Antimicrobial resistance of *Salmonella* isolated from swine	Craig A. Altier	North Carolina State University	$118,535
Livestock feeds as a means of dissemination of antimicrobial resistant organisms and genes	Dale D. Hancock	Washington State University, Pullman	$188,976

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FAXBACK NOW AVAILABLE

by Daryl C. Fleming

CVM is joining FDA's Center for Devices and Radiological Health, and various FDA personnel offices in the use of Fax-on-Demand technology by FaxBack. The FaxBack technology will permit CVM Customers without access to a computer and an internet provider with the ability to obtain some of the documents already available on the CVM Home Page. Only a standard touch-tone telephone and access to a fax machine are required to receive CVM documents.

The procedure is simple, however it may require two phone calls—the first to request one of four current catalogs or lists of documents and their reference numbers, and the second to request a document by entering the reference number. The individual enters the number of the fax machine to receive the document and provides a phone number to identify the requestor.

The CVM system will include more catalogs in the near future and new documents will be added to the various catalogs as they are produced. Some existing documents will also be added. Currently the four available catalogs are:

Updates, Forms, Consumer Information, and the *FDA Veterinarian*.

To obtain a document, for example a *CVM Update*, the following procedure must be followed:

1. Dial 301-827-6635 or 6636
2. Follow the prompts to receive an *Updates* catalog
3. After receiving the catalog and selecting the document of interest
4. Dial 301-827-6635 or 6636 again
5. Follow the prompts to enter the reference number of the document(s) desired
6. Enter the number of the fax machine to receive the document(s)
7. Enter a phone number to identify the requestor
8. Wait for the fax to be received

If another type of document is desired, the two-call procedure must be repeated.

Daryl Fleming is an Industry Compliance Analyst in CVM's Communications Staff.

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NEW ANIMAL DRUG APPROVALS

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Alpharma, Inc. (NADA 141-148)	Decoquinate, Monensin, (Deccox®), (Rumensin®)	Cattle. For the prevention of coccidiosis and improved feed efficiency.	**MEDICATED FEED**—The NADA provides for use of approved, single-ingredient decoquinate and monensin Type A medicated articles to make two-way combination drug Type B and C medicated feeds. The medicated feeds are used for prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii* and improved feed efficiency in cattle fed in confinement. A limitation is that the feed is not to be fed to cattle producing milk for food. *Federal Register* 12/29/00
Schering-Plough Animal Health Corp. (NADA 141-177)	Gentamicin Sulfate, Mometasone Furoate, Clotrimazole, (Mometamax™ Otic Suspension) Rx	Dogs. For the treatment of otitis externa in dogs.	**OTIC**—The NADA provides for use as an ear canal drop for the treatment of otitis externa associated with yeast (*Malassezia pachydermatis*) and/or bacteria susceptible to gentamicin in dogs. The approval qualifies for 3 years of marketing exclusivity. *Federal Register* 01/04/01

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NEW ANIMAL DRUG APPROVALS (Continued)

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Alpharma, Inc. (NADA 141-149)	Decoquinate, Monensin, Tylosin, (Deccox®), (Rumensin®), (Tylan®)	Cattle. For prevention of coccidiosis, improved feed efficiency, and reduction of the incidence of liver abscesses.	**MEDICATED FEED**—The NADA provides for use of approved, single-ingredient decoquinate, monensin, and tylosin Type A medicated articles to make three-way combination drug Type B and Type C medicated feeds for use in growing-finishing cattle fed in confinement for slaughter. The medicated feeds are used for the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*, improved feed efficiency, and reduction of incidence of liver abscesses caused by *Fusobacterium necophorum* and *Actinomyces pyogenes*. *Federal Register* 01/10/01
Blue Ridge Pharmaceuticals, Inc. (NADA 141-174)	Ivermectin (Acarexx™) Rx	Cats and kittens. For the treatment of adult ear mite infestations.	**OTIC**—The NADA provides for the treatment of adult ear mite (*Otodectes cynotis*) infestations in cats and kittens 4 weeks of age and older. Effectiveness against eggs and immature stages has not been proven. This approval qualifies for 3 years of marketing exclusivity. *Federal Register* 01/24/01

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ABBREVIATED NEW ANIMAL DRUG APPROVALS

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Med-Pharmex, Inc. (ANADA 200-292)	Ivermectin (Iversol) Rx	Horses. For treatment and control of internal and cutaneous parasites.	**ORAL**—The ANADA is a generic copy of Merial Ltd's Eqvalan Oral Liquid for Horses NADA 140-439. *Federal Register* 01/24/01
Blue Ridge Pharmaceuticals, Inc. (ANADA 200-281)	Pyrantel Pamoate (Wormexx)	Dogs and Puppies. For the removal of certain gastrointestinal parasites and the prevention of reinfection.	**ORAL**—The ANADA is generic copy of Farnam Co.'s D-WORM Dog Wormer Chewable Tablets NADA 139-191. *Federal Register* 02/09/01

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FDA Veterinarian Subscription Price Increase

The Government Printing Office has informed us that the subscription price for the *FDA Veterinarian* has been increased to $17.00 per year domestic and $21.25 per year for foreign subscriptions. These price increases are due to increased costs of printing and mailing. Subscription order forms are available through the *FDA Veterinarian*. In addition, credit card subscription orders may be placed by telephone (202) 512-1800 or by fax (202) 512-2250. VISA, MasterCard, and Discover cards are accepted.

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