



FDA VETERINARIAN

Center for Veterinary Medicine

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New Law Provides User Fees to Improve Animal Drug Review

On November 18, 2003, President Bush signed legislation that provides user fees to FDA for its animal drug review work. Known as the Animal Drug User Fee Act (ADUFA), this law establishes a funding system for the new animal drug review process that is similar to that established for the human drug review process over a decade ago.

"We expect that the new resources that ADUFA provides will greatly strengthen FDA's animal drug review capabilities, in much the same way that user fees improved our ability to more quickly and efficiently review human drugs," said FDA Commissioner Mark B. McClellan, M.D., Ph.D. "Thanks to the hard effort of the Administration and Congress, as well as HHS Secretary Tommy Thompson's strong support, we have a funding system that assures that FDA's Center for Veterinary

Medicine can meet the challenges of the 21st Century." "The passage of ADUFA marks the beginning of a new era in CVM history just as the Prescription Drug User Fee Act beneficially altered the review of human drugs," said Stephen Sundlof, D.V.M., Ph.D., Director of FDA's Center for Veterinary Medicine (CVM). "The resources provided by this law will help CVM scientists keep pace with the rapid advances in science and medicine that drive the quality of health care for our animals. We view this legislation as a vital component in our commitment to promote and protect public and animal health."

FDA is authorized to collect \$5 million in fiscal year 2004, which began October 1, 2003, \$8 million in fiscal year 2005, and \$10 million in each fiscal year 2006 through 2008.

ADUFA establishes four fees: 1) a sponsor fee, 2) an establishment fee, 3) a product fee and 4) an application fee. About 25% of the total amount to be collected will



Photo by Karen A. Kandra

be received through each fee type. So, in the first fiscal year, FDA expects to receive \$1,250,000 from sponsor fees and the same amount from establishment fees, product fees and application fees.

The fees collected for these services will be directed toward the FDA Center for Veterinary Medicine (CVM) and will be used to provide additional resources for its animal drug review program. The goal is to achieve shorter, more predictable review times by increasing the review staff at CVM and building better management systems. As a result, FDA anticipates substantial savings to the industry in regulatory review and
(Continued, next page)

Farewell

It is with mixed feelings that I inform you that this is my last issue as Editor of the *FDA Veterinarian*. After 26½ years with the Food and Drug Administration, I am taking an early retirement, effective January 2, 2004. Over the past five years, first as Managing Editor, then as Editor, I tried to bring you news of CVM in a format that would be reader-friendly, and informative, and I was pleased that we were able to add a bit of color to the publication two years ago.

After spending half my life at FDA, I plan to enjoy my favorite things, especially horses and foxhunting, and Jack Russell Terriers. I even hope to pursue a second career in photography. Thank you for the opportunity to spread the news of CVM's mission. I was proud to be associated with FDA and CVM. Being able to incorporate my lifelong love of animals into my career was an added bonus.

Karen Kandra

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New Law Provides User Fees (Continued)

developmental expenses—without compromising FDA's high standards for safe and effective products.

The law provides for specific waivers or reductions of fees, including for small businesses and where the fees would present a significant barrier to innovation. FDA is working to prepare guidance and information for the industry regarding the fees, billings and submission of fees, as well as waivers and reduction of fees. Information about this guidance will be included in future issues of the *FDA Veterinarian*. ■

Transcript Available for VMAC Meeting on Animal Cloning

A link to the transcript of the proceedings for the November 4, 2003, FDA Veterinary Medicine Advisory Committee (VMAC) meeting is available on the FDA/CVM Home Page at: <http://www.fda.gov/cvm/index/vmac/VMACFall2003.htm>.

VMAC met to discuss a draft executive summary of a draft risk assessment designed to identify the hazards and characterize the risks of the somatic cell nuclear transfer (SCNT) method of cloning to animal health and food consumption. The draft risk assessment is being prepared by scientists in FDA's Center for Veterinary Medicine (CVM.) Ten

committee members were present at the meeting, and they heard presentations from CVM experts on the subject. At the meeting, FDA posed two questions to VMAC:

1. Based on what we have presented, has the risk assessment adequately identified the hazards and characterized the risks relating to animal health?
2. Based on what we have presented, has the risk assessment adequately identified the hazards and characterized the risks relating to food consumption?

(Continued, next page)

New Deputy Director for Office of Research

CVM is pleased to announce the appointment of Dr. Marleen Wekell as the Office of Research's new Deputy Director. She holds a B.S. degree in Chemistry from Seattle University, an M.S. in Marine Biochemistry and a Ph.D. in Environmental Microbiology and Biochemistry from University of Washington. Dr. Wekell is a published author and international speaker, and holds three patents on a cell assay for marine biotoxins with others in chemistry from the ORA FDA Seafood Products Research Center in Bothell, WA.

Dr. Wekell comes to CVM from New York City, where she was Director of the FDA's North East Regional Laboratory (NRL) for three years. In New York, Dr. Wekell participated on a national committee (with CDC, USDA) for countering food bioterrorism and networking with NYC, counties, states and other Federal agencies to address national emergencies. In addition, she helped increase productivity of the NRL by developing and successfully implementing a rapid food analytical microbiology laboratory utilizing the latest rapid methods (productivity was increased by 100%), and she initiated development



Dr. Marleen Wekell

of a forensic microbiology unit at the NRL to work on criminal cases together with the FDA's Office of Criminal Investigations and the FDA Forensic Chemistry Center.

Previously, Dr. Wekell spent 17 years as Director of FDA's Seafood Products Research Center, in Bothell, Washington. She was responsible for developing a field research center *de novo* in FDA, and developed many methods that were officially collaborated by AOAC International or were incorporated into the Bacteriological Analytical Manual. In addition, Dr. Wekell's group devel-

oped the web-based Regulatory Fish Encyclopedia, and conducted research and methods development on chemical indicators of decomposition, marine toxins, microbial pathogens and parasites in seafood.

Dr. Wekell has held additional FDA positions with the Office of Regional Operations, Office of Seafood, and the Office of Regulatory Affairs, and has served as a Professor at the University of Washington and Seattle University. ■

FDA VETERINARIAN

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BSE Compliance Program Issued

FDA has released a Compliance Program (CP) entitled "BSE/Ruminant Feed Ban Inspections." This Compliance Program is intended to assist both Agency and State investigators in determining compliance with the FDA regulation prohibiting the use of most animal proteins in ruminant feeds (21 CFR Part 589.2000 of the *Code of Federal Regulations*.)

Dr. Stephen F. Sundlof, Director of FDA's Center for Veterinary Medicine, said "FDA issued this CP to help provide guidance and instructions for conducting inspections under the ruminant feed rules. These inspections are extremely important in FDA's efforts to help prevent the establishment and amplification of Bovine Spongiform Encephalopathy (BSE) through feed in the United States, should a case of BSE ever be found in this country."

The success of the inspection program depends on a multitude of State investigators in addition to FDA investigators. In fact, the majority of the inspections have been conducted by State investigators for FDA. This Compliance Program provides comprehensive instructions for FDA and State investigators to help ensure that BSE inspections are

conducted in a uniform manner and are of high quality.

The CP is posted on the CVM Home Page at: http://www.fda.gov/cvm/index/bse/bse_guidance.htm. Single copies of the CP may be obtained from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Ad-

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ministration, 7519 Standish Place, Rockville, MD 20855. Please send one self-addressed adhesive label to assist in processing your request.

The CP represents the FDA's current thinking on the subject. It does not create or confer any rights for or on any person and will not operate to bind FDA or the public. Alternative methods may be used as long as they satisfy the requirements of the applicable statutes and regulations.

This CP is being issued as a Level 1 guidance consistent with FDA's good guidance practices (GGPs) regulation. It is being implemented immediately without prior public comment because of the Agency's urgent need to provide guidance in conducting inspections. However, pursuant to GGPs, FDA requests comments on the guidance and will revise the document, if appropriate. Comments will be considered by the Agency in the development of future policy.

Written comments on the CP may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Electronic comments may be submitted to: <http://www.accessdata.fda.gov/scripts/oc/dockets/comments/commentdocket.cfm>. Comments should be identified with the full title of the guidance document and Docket Number 2003D-0498.

Technical questions about the Compliance Program may be directed to Dr. Neal Bataller, Center for Veterinary Medicine, HFV-230, Food and Drug Administration, 7500 Standish Place, Rm. E441, Rockville, MD 20855, 301-827-0163, nbatalle@cvm.fda.gov. ■

Transcript Available for VMAC Meeting on Animal Cloning (Continued)

Dr. Stephen Sundlof, Director of FDA's Center for Veterinary Medicine, said "I am happy that this transcript is now available to the public. CVM was not looking for simple vote or "yes" or "no" responses to the questions we posed to the Committee. We were asking for the Committee members' thoughts and scientific opinions concerning these two questions. The tran-

script provides important information on their answers."

Individuals who are unable to access the transcript on the Internet may view a copy at: FDA/Division of Dockets Management, 5630 Fishers Lane - Room 1061-HFA-305, Rockville, MD, 20852. Dockets can be contacted by e-mail at: fdadockets@oc.fda.gov, by phone at 301-827-6860, by fax at 301-827-6870, or by

TTY/TDD Users at 1-800-735-2258. If paper copies are needed, there will be a charge for duplicating the transcript.

A draft executive summary of the animal cloning risk assessment is posted on the CVM Home Page at: <http://www.fda.gov/cvm/index/cloning/CLRAES.pdf>. The complete draft risk assessment will be released in the next few months. ■

New VMAC Members

by Aleta Sindelar

Six new members have been selected to join FDA's Veterinary Medicine Advisory Committee (VMAC).

Dr. Corrie C. Brown, D.V.M., Ph.D. is a professor in the Department of Pathology and Coordinator of International Activities at the College of Veterinary Medicine at the University of Georgia. Her expertise is pathology, and the research in her laboratory has focused on the pathogenesis of infectious diseases of food-producing animals.



Dr. Corrie C. Brown

Dr. Arthur L. Craigmill, Ph.D. is a toxicology specialist in the Department of Environmental Toxicology at the University of California at Davis. His area of expertise on the committee is veterinary toxicology. Dr. Craigmill serves as the Western Region Coordinator for the IR-4 Minor Use Animal Drug Program, as well as the Food Animal Residue Avoidance Databank (FARAD).



Dr. Arthur L. Craigmill

Dr. Sherman (Skip) W. Jack, D.V.M. is a professor of veterinary pathology and assistant director in the Department of Pathobiology and Population Medicine within the Diagnostic Laboratory Services of the College of Veterinary Medicine at Mississippi State University (MSU). Dr. Jack also serves as the pathology service chief in the College



Dr. Sherman W. Jack

of Veterinary Medicine at MSU and serves primarily in the fish diagnostic lab at MSU. His area of specialty on the committee is minor use/minor species veterinary medicine.

Dr. John J. McGlone, Ph.D. is a professor of animal and food sciences and cell biology and biochemistry (joint appointment in Texas Tech University Health Sciences Center). He is also the director of the Pork Industry Institute in the College of Agricultural Sciences and Natural Resources at Texas Tech University, and he was certified a Professional Animal Scientist by the American Registry of Animal Science. He currently serves on the Executive Committee of the Board of Trustees of the Association for the Assessment and Accreditation of Laboratory Animal Care, International and the Animal Care, Use and Standards Committee of the Federation of Animal Science Societies. His research focus is on the science of animal welfare, stress physiology and behavior. His specialty on the committee is animal science.



Dr. John J. McGlone

Dr. Lisa K. Nolan, D.V.M., Ph.D. has been recently appointed as professor and Chair of the Department of Veterinary Microbiology and Preventative Medicine at Iowa State University. Her research focuses on bacterial diseases of production animals, including their effects on animal health, public health and food safety. Her specialty on the committee is microbiology.

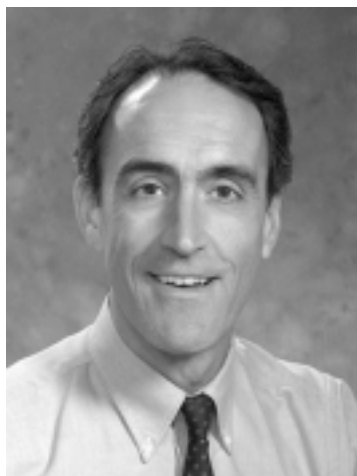


Dr. Lisa K. Nolan

Dr. Mark G. Papich, D.V.M., M.S. is a professor of clinical pharmacology in the Molecular Biomedical Sciences Department of the College of Veterinary (Continued, next page)

... New VMAC Members (Continued)

Medicine at North Carolina State University. He is a past-president and chairman of the Board of the American College of Veterinary Clinical Pharmacology. He also is a fellow in the American Academy of Veterinary Pharmacology and Therapeutics and a member of the American Society of



Dr. Mark G. Papich

Clinical Pharmacology and Therapeutics. His expertise on the committee is pharmacology.

Dr. John Waddell, D.V.M. whose expertise is food animal medicine, replaces Dr. Vernon C. Langston as current Chair of the Committee. Dr. Waddell joined the committee in November 2000. He is a Managing Partner of the Sutton Veterinary Clinic, in Sutton, Nebraska.

The Center is seeking nominations for vacancies in the areas of Biostatistics and Companion Animal Medicine, as well as a consumer representative to replace retired consumer representative, Richard R. Wood. Written nominations should be directed to the Executive Secretary, Aleta Sindelar at 7519 Standish Place, Rockville, MD 20855, and may be emailed to asindela@cvm.fda.gov. ■

Comings and Goings

New Hires

OFFICE OF RESEARCH (OR)

- Dr. Marleen Wekell, Deputy Director
- Jason Abbott, Microbiologist
- Ruby Singh, Staff Fellow

Departures

OFFICE OF THE DIRECTOR (OD)

- Barbara Indech, Regulatory Counsel

OFFICE OF MANAGEMENT (OM)

- Melissa Starinsky, Management Analyst

OFFICE OF SURVEILLANCE AND COMPLIANCE (OSC)

- Dr. Gillian Comyn, Consumer Safety Officer

Retirements

OFFICE OF THE DIRECTOR (OD)

- Daryl Fleming, Industry Compliance Analyst

OFFICE OF SURVEILLANCE AND COMPLIANCE (OSC)

- Patsy Gardner, Industry Compliance Analyst

Consent Decree Against New York Dairy

On October 17, 2003, a Consent Decree of Permanent Injunction was signed in U.S. District Court for the Northern District of New York against Anthony DiNitto, Sr., Anthony DiNitto, Jr., and William Nunes for the sale of cows and calves for human consumption whose tissues exceeded FDA's tolerances for residues of penicillin and sulfadimethoxine.

The use of drugs such as penicillin and sulfadimethoxine in livestock and poultry is strictly regulated by the Food and Drug Administration (FDA.) Before any drug intended for use in animals is approved, it must undergo extensive testing to demonstrate that the food from these animals is safe for human consumption. Withdrawal periods for drugs in edible tissues, which are based upon the depletion and elimination of the drug to a safe residue level in those tissues, ensure that the food we eat is safe and healthful. If an illegal drug residue is detected, FDA investigates the matter and takes regulatory action,

if necessary. This is what happened in the DiNitto case.

A series of violative tissue samples from Anthony DiNitto Dairy were collected from December 31, 1998, through February 15, 2002. DiNitto Dairy produces more than 7 million gallons of milk a year. It also ships cull cows (cows that are removed from milking because they are producing too little milk) and calves for human consumption.

Under the terms of the Consent Decree, the defendants must implement systems for identifying animals, record-keeping, drug control, drug accountability, and drug residue withdrawal control.

The FDA's New York District Office conducted the investigation that lead to this Consent Decree. FDA's Center for Veterinary Medicine Division of Compliance and the Office of the Chief Counsel, and the United States Department of Justice's Office of Consumer Litigation were responsible for the case processing and legal procedures. ■

FDA Issues Guidance on Evaluating the Safety of Antimicrobial New Animal Drugs

FDA has released a new guidance document that for the first time outlines a comprehensive evidence-based approach to preventing antimicrobial resistance that may result from the use of antimicrobial drugs in animals.

Antimicrobial drugs, such as antibiotics, are medicines often used to treat bacterial infections in both humans and animals. Their use has been one of the great advances in modern medicine—helping to prevent many of the leading causes of death for most of human history.

Regardless of why bacteria develop resistance to antimicrobials, when bacteria do develop such resistance, human and animal health is at risk because the medicines that we depend on to treat infections become ineffective. There are several important sources of this problem, including inappropriate use of antibiotics in people, that have been the subject of many public health initiatives by the Department of Health and Human Services and other organizations. The guidance released by FDA is, however, the first that addresses, in a comprehensive manner, the issue of the use of antimicrobials in food-producing animals as a contributing factor to the development of antimicrobial resistance.

The guidance provides a scientific process for assessing the likelihood that an antimicrobial drug used to treat an animal may cause an antimicrobial resistance problem in humans consuming meat or other byproducts from that animal. This process can help prevent antimicrobial drugs with a high risk of causing such problems from being improperly used in food-producing animals, and thereby potentially leading to antimicrobial resistance in humans.

The new guidance encourages drug sponsors to use a risk assessment process to demonstrate that an antimicrobial drug used to treat food-producing ani-

mals will not create a risk of antimicrobial resistant bacteria likely to lead to human health problems.

The document, Guidance for Industry #152 (“Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern”), is not a regulation. Instead it explains a science-based process drug sponsors may use when they seek approval of an antimicrobial for use in food-producing animals.

“Resistance to the antimicrobial drugs needed to treat human illnesses is a serious public health threat, and we intend to use the best science-based methods to prevent it,” said FDA Commissioner Mark B. McClellan, M.D., Ph.D.

Sponsors may still use other methods to establish drug safety for these uses, as long as these methods comply with statutory and regulatory requirements. In general, written guidance helps sponsors understand FDA’s process of evaluating whether a proposed product for approval can be used safely and effectively, in this case with respect to risks of creating antimicrobial resistance.

“Resistance to the antimicrobial drugs needed to treat human illnesses is a serious public health threat, and we intend to use the best science-based methods to prevent it,” said FDA Commissioner Mark B. McClellan, M.D., Ph.D.

“There are many factors contributing to the development of resistant bacteria. Attacking the problem on all fronts, including the appropriate use of antimicrobial drugs in veterinary medicine, is the best way to protect the health of the public. It’s also the best way to promote the safe use of antimicrobials to protect the health of animals, including food-producing animals.” Stephen Sundlof, D.V.M., Ph.D., Director of FDA’s Center for Veterinary Medicine, added, “This guidance uses science to develop a risk-

based approach to the issue of antimicrobial resistance. It permits us to help protect human health while giving veterinarians and livestock producers the tools they need to treat animals.”

The pathway suggested in the guidance document establishes a three-part system for determining an antimicrobial drug’s potential risk to humans if used to treat food-producing animals. The system’s three parts are these:

Part One is the “release assessment,” which determines the probability that resistant bacteria will be present in animals as a result of the use of the antimicrobial new drug.

Part Two is the “exposure estimate,” which gauges the likelihood that humans would ingest the resistant bacteria.

Part Three is the “consequence assessment,” which assesses the chances that human exposure to the resistant bacteria would result in adverse human health consequences. In this context, these are situations in which a physician has difficulty treating a person with an antimicrobial drug because the bacteria infecting the person had acquired resistance to the drug and that resistance came from use of the drug in animals.

Under this system, all of these assessment processes are considered and integrated to determine the overall level of human health risk from resistant bacteria associated with an antimicrobial drug’s use in animals.

If the assessments showed that the risks were significant, FDA could deny the application for marketing authorization, thus preventing the use of the drug in food animals, or FDA could approve the drug, but place conditions on its use designed to ensure it would not pose a human health risk.

More information is available online at www.fda.gov/oc/antimicrobial/questions.html.

Tissue Residue Outreach in New York State

by Jerome G. Woyshner

Milk is New York's leading agricultural product and is produced all across the State, making New York the Nation's third largest dairy-producing State. The milk production cycle requires a constant herd of cows that are capable of producing a steady stream of milk. Cows who are no longer capable of producing milk, or become ill, pose a financial drain for the dairy farmer. In order to reduce cost, and also to secure a financial return on their investment, the cull cows are sold for meat production. In order to protect their investment prior to slaughter, farmers often medicate the animals to keep them healthy. This sometimes results in illegal drug residues, since the dairy farmer may not observe correct withdrawal times, may use inappropriate or unapproved drugs, or may neglect to consult a veterinarian in this process. In FY 02, the U.S. Department of Agriculture/Food Safety and Inspection Service reported 177 violative animals (includes 154 dairy cows) in New York State. In FY 03, 130 violative animals (includes 122 dairy cows) were reported. In response to this public health issue, New York District sent several warning letters to producers for introducing violative culled cows into meat production. Currently, it has three dairy farms under injunction and injunctive actions are pending against two more dairy farms.

In an effort to reduce the number of tissue residue violations in the State, the New York District (NYK-DO) in cooperation with FDA's Center for Veterinary Medicine and the New York State Department of Agriculture and Markets/Division of Animal Industries initiated an outreach program to address this public health concern. The State-wide program focused on educating producers, veterinarians, and students about preventing drug residues in dairy animals. The program started with an exhibit at the Empire Farm Days held in Seneca Falls, New York. Approximately 75,000 people, mostly farmers, attended the farm show, which is the largest outdoor farm show in the Northeast. FDA

investigators answered questions about issues related to veterinary medicine and promoted the upcoming tissue residue workshops.

In September 2003, the outreach program went on the road. Representatives from the New York District Office and veterinarians from the Center for Veterinary Medicine and the New York State Department of Agriculture/Division of Animal Industries traveled to five State University of New York (SUNY) agricultural colleges. The attendees listened to a two-hour program that focused on medicating dairy animals and complying with Federal and State requirements. They also learned about an animal medication record system, which was developed by a veterinarian at the New York State Department of Agriculture and Markets/Division of Animal Industries in cooperation with FDA. The project was developed under a partnership agreement between the two organizations. The New York District received \$19,000 from the Center for Veterinary Medicine to directly fund the project. The recordkeeping system was piloted at six farms that had a tissue residue violation and is being revised based on the outcome of the pilot.

Nearly 200 people attended the workshops, including veterinarians and farmers. However, the majority of attendees were university students, who received academic credit for attending the program. A number of students in attendance were from operating dairy farms and were requested to carry the message provided back to their dairy farms. Attendees showed strong interest, asked excellent questions, and provided great feedback comments. In fact, a veterinarian from a large practice located in Perry, New York, requested that FDA present the program at his clinic.



(From left) Dr. Bruce Thomson, V.M.D., N.Y. State Dept. of Agriculture & Markets; Gillian Comyn, D.V.M., FDA/CVM; Edward Thomas, FDA/NYK-DO/Domestic Compliance Director; Jerome G. Woyshner, FDA/NYK-DO District Director.

The tissue residue workshops were sponsored by five SUNY agricultural colleges and presented on the following dates: State University of New York at Cobleskill, September 16; Morrisville State College, September 17; State University of New York at Delhi, September 18; State University of New York at Canton (in conjunction with the Cornell University Veterinary Medicine/Quality Milk Production Services/Northern Laboratory, and the Northern New York Veterinary Medical Society), September 23; and Alfred State College, September 25.

All attendees received a glossy black folder with a color label of the Holstein cow calling out, "Preventing Drug Residues in Dairy Animals." The Holstein cow and slogan became the trademark of the outreach program. For every completed evaluation form, a stress-reliever spongy cow imprinted with the slogan, "Preventing Drug Residues in Dairy Animals" was given to the attendee. The New York District is also working with the agricultural colleges who sponsored this event to initiate a mailing of literature to all of the invited dairy farmers who were unable to attend the workshops.

Jerome G. Woyshner is the District Director in FDA's New York District Office.



International Activities

Dr. Tollefson Participates in Berlin Symposium

Dr. Linda Tollefson, Deputy Director, Center for Veterinary Medicine traveled to Berlin, Germany on November 8-12, 2003, to attend as an invited presenter and session chairperson at an international symposium titled "Towards a Risk Analysis of Antibiotic Resistance."

The German Federal Institute for Risk Assessment sponsored the meeting in cooperation with the Federal Office of Consumer Protection and Food Safety and the Federal Agricultural Research Centre. The development and spread of antimicrobial-resistant microorganisms and the impact of the use of antimicrobial agents in food-producing animals were the main topics. This was the fourth symposium at the Institute for Risk Assessment on the subject of antibiotic resistance, which is considered to be a serious problem all over the world. Previous symposia were held in 1995, 1997, and 2002. The Institute considers the ban on the use of antimicrobial growth promoters in the European Union from 2006 onwards to be the fruit of these efforts and the first step toward controlling antimicrobial resistance. All growth-promoting antimicrobials that are of drug classes also used in human medicine have already been banned in the EU and all remaining growth-promoting antimicrobials will be removed as of January 1, 2006.

The purpose of the symposium was to present the newest research demonstrating adverse health effects on humans from the use of antimicrobial agents in food-producing animals. A secondary purpose was to identify additional risk management strategies that could be implemented to restrict usage of antimicrobials in food-producing animals to only those situations where an infectious disease has been identified. Scientists at the meeting stated that improvement of husbandry conditions, consistent hygiene, and the increased use of vaccines were alternatives to the use of antimicrobials in food-producing animals, particularly when it came to the treatment of entire herds in which only some animals were sick.

Dr. Tollefson presented the Center's Guidance for Industry #152, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern," which uses a risk-based approach to evaluate human food safety with respect to antimicrobial resistance prior to approval of the drug for use in food-pro-

ducing animals. She also co-chaired a session with Dr. Helmut Tschäpe of the Robert Koch Institute on "Hazard Characterization." Drs. Tollefson and Tschäpe also led a working group on the topic and developed a report.

The symposium was attended by approximately 200 scientists from 16 countries. The participants included several representatives of international organizations including the World Health Organisation (WHO), the Food and Agriculture Organization (FAO) and the Office International des Epizooties (OIE). The participants in the symposium advocated taking all possible steps to reduce the risk of resistance development. The focus at this symposium was on reducing the use of antimicrobial agents in animal production and veterinary medicine. The participants expressly pointed out that this recommendation does not apply to treatment; sick animals must be treated. The scientists concurred that actions taken to mitigate resistance will also help maintain the effectiveness of antimicrobial agents used in veterinary medicine.

There was a great deal of discussion on the prophylactic or "metaphylactic" use of antimicrobials involving the treatment of an entire herd or flock as a precautionary measure after individual animals show signs of illness. Because the dosage in this type of treatment varies considerably such that individual animals may receive sub-optimal amounts of the drug, the practice can facilitate the development of resistant organisms. The Scandinavians have shown that there is potential for curtailing the use of antimicrobials for these purposes. They were able to markedly reduce the use of antimicrobials in swine and poultry production and provide evidence of a decline in resistance without the number of sick animals increasing.

More detailed information on this subject can be accessed on the Federal Institute for Risk Assessment home page (www.bfr.bund.de) under Food/Food Safety/Microbial risks or using the search keyword "Resistance."

The Institute for Risk Assessment plans to incorporate the information from this symposium into its overall assessment of risks resulting from the use of antibiotics in food-producing animals.



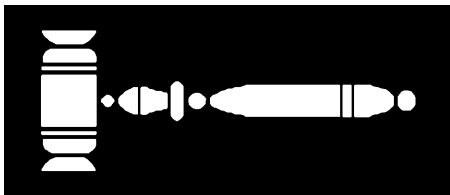
Polish Visitors



Polish veterinarians visited CVM on November 10, and were briefed by CVM officials about the animal drug review process; compliance activities; feed safety including BSE; counterterrorism activities; and CVM's international activities.

Regulatory Activities

by Karen A. Kandra



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

- Tom R. Milius, President, Wilson C. Milius, Inc., Denver, IA
- Jimmy D. Scarrow, Owner, Scarrow Dairy, Wendell, ID
- Thomas O. Leduc, Co-owner, Green Acre Farm, Champlain, NY
- Joe A. and Kimberly L. Sozinho, Owners, Westside Dairy, Caruthers, CA
- Arie Roeloffs, Co-owner, Southfield Dairy, Wendell, ID
- Bernardus H. Amting, Owner, Amting Dairy Farm, Marshall, MI
- Dennis Dirksen, Maria Stein, OH
- John D. Devereaux, Owner, Prague, OK

- Antonio C. Esteves, Dina M. Esteves, Co-owners, Visalia, CA
- Keith E. Lauer, Owner, R & K Livestock, Texhoma, OK

The above violations involved gentamicin in a culled dairy cow; penicillin in a calf; sulfadimethoxine in a cow; oxytetracycline in cows; penicillin in a dairy cow; gentamicin in a dairy cow; and sulfamethazine in a cow;

A warning letter was issued to Robert S. Kopriva, Senior VP, President & CEO, Sara Lee Foods, Cincinnati, OH, for significant deviations from the Current Good Manufacturing Practice (cGMP) regulations for Medicated Feeds. These violations included inability to verify that batch production records were checked by a responsible individual and storing expired and unlabeled product in the mixing area.

A warning letter was issued to Gloria Donaldson, President, Donaldson & Hasenbein, dba J & R Feed Service, Inc., Cullman, AL, for significant deviations from the cGMP regulations for Medicated Feeds, including failure to prop-

erly handle drugs in the mixing area; failure to label all finished feeds; failure to maintain the building in an orderly manner in that water was leaking through a hole in the roof onto raw materials; failure to have a master record file; and, failure of production records to include a written endorsement by a responsible individual.

A warning letter was issued to Francis Guidici, President, LA Heame Company, King City, CA, for significant deviations from the cGMP regulations, including failure to conduct potency assays on representative samples of each feed; failure to assure that all scales and metering devices are tested for accuracy at least once a year; and, failure to prepare and maintain a receipt record for each lot of drug received.

A warning letter was issued to Howard Brown, President, CR Brown Enterprises, Inc., dba CR Brown Feeds, Andrews, NC, for significant deviations from cGMP regulations, including failure to maintain a Master Record File and production records; failure to perform

(Continued, next page)

Regulatory Activities (Continued)

periodic assays for drug components of the medicated feeds whose manufacture requires a medicated feed mill license; and, failure to maintain a daily inventory record for each drug used.

A warning letter was issued to William H. Jenner, President, Lincoln Land Livestock Co., Inc., Mascoutah, IL, for significant deviations from the requirements set forth in Title 21, *Code of Federal Regulations* (CFR), Part 589.2000—Animal Proteins Prohibited in Ruminant Feed. This regulation is intended to prevent the establishment and amplification of Bovine Spongiform Encephalopathy. The inspection revealed that products that contain or may contain prohibited material fail to bear the caution statement—"Do not feed to cattle or other ruminants."

A warning letter was issued to Patrick M. Hunter, President, H & H Feed & Grain, Inc., Vicksburg, MI, for significant deviations from the requirements relating to animal drugs and medicated feeds, including the Veterinary Feed Directive (VFD) regulations. The investigation revealed that the feed mill was manufacturing complete medicated swine feeds containing the VFD drug, Tilmicosin, in a manner that does not conform to the requirements of the agency's regulations. The feed mill failed to use the Type C medicated feed containing Tilmicosin in accordance with labeled mixing directions, which resulted in sub-potent feeds; failed to follow the product's conditions of use by not feeding continuously for a 21-day period; and, failure to print the cautionary statement "Caution: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice," on the VFD medicated feed labeling.

A warning letter was issued to Elton Ray Davis, D.V.M., Owner, Canton Veterinary Clinic, Canton, TX, for dispensing Sterile Penicillin G Procaine in an extra-label manner for two downer cows.

A warning letter was issued to R. Eric Montgomery, President, Oraceutical, LLC, Lee, MA, for selling medicated ear drops with hydrocortisone for veterinary use. These products, "Biotix" and "Clear," are intended for use in the prevention of disease in animals, and they are not covered by an approved new animal drug application, and have not been shown to be safe and effective.

A warning letter was issued to Michael K. Strobush, D.V.M., President/Senior Veterinarian/Co-owner, Grassland Veterinary Service, Granton, WI, for serious deviations from regulations for Extralabel Drug Use in Animals (21 CFR 530), including the compounding and prescribing of sulfamethoxazole and trimethoprim for intramammary infusion to treat mastitis in lactating dairy cattle.

FDA Statement Regarding Glofish

There has been much media attention recently about the marketing of "Glofish." On December 9, 2003, FDA issued the following statement:

Because tropical aquarium fish are not used for food purposes, they pose no threat to the food supply. There is no evidence that these genetically engineered zebra danio fish pose any more threat to the environment than their unmodified counterparts which have long been widely sold in the United States. In the absence of a clear risk to the public health, the FDA finds no reason to regulate these particular fish.

Correction

In the Supplemental New Animal Drug Approvals listed on pages 18 and 19, of the September/October issue of the *FDA Veterinarian*, an incorrect route of administration was listed for Euthanasia Solution (Beuthanasia-D-Special) and Pentobarbital Sodium and Phenytoin Sodium (Euthasol). The indicated routes of administration were listed as subcutaneous or intramuscular, however, the correct routes of administration for both of the drugs is intravenous or intracardiac. We apologize for any confusion.

Alert to Pet Owners—Recall of Petcurean Go! Natural Pet Food

On October 22, 2003, Canadian dog-and-cat food marketer Petcurean Pet Nutrition, Inc. announced an immediate voluntary recall of all Go!

(Continued, next page)



Photo by Karen A. Kandra

If you have fed your dog Petcurean Go! Natural Pet Food, FDA suggests you have your dog checked by your veterinarian for signs of liver disease and anemia.

Alert to Pet Owners—Recall of Petcurean Go! Natural Pet Food (Continued)

Natural pet food manufactured in Texas. The Food and Drug Administration (FDA) continues to receive reports from veterinarians indicating an association between Go! Natural dog food, and dogs being treated for liver disease or liver failure.

FDA suggests owners who have fed their dogs this product during the months of September and October consider having their dogs checked by their veterinarian for signs of liver disease and anemia.

Recalls are actions taken by a firm to remove a product from the market. The

recalled product comes in four, eight, 12 and 30-pound bags, with the recall in effect for all lot codes. Pet owners are urged to return recalled Go! Natural dog food to the place that they purchased it.

New Animal Drug Approvals

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
Fort Dodge Animal Health Division of Wyeth (NADA 141-216)	Moxidectin/Praziquantel (Quest® Plus)	Horses and ponies. For treatment and control of various species of internal parasites.	ORAL —The NADA provides for use of a moxidectin and praziquantel oral gel for the treatment of various species of internal parasites in horses and ponies. <i>Federal Register 08/27/03</i>
Novartis Animal Health US, Inc. (NADA 141-204) (NADA 141-205) (NADA 141-035) (NADA 141-084) (NADA 141-175)	Lufenuron (Program) Milbemycin Oxime and Lufenuron (Sentinel®), Nitenpyram (Capstar®) RX for concurrent use	Dogs and Cats. To kill adult fleas and prevent flea eggs from hatching.	ORAL —An original NADA was filed, 141-204, for the concurrent use in dogs of Sentinel tablets (milbemycin oxime and lufenuron), approved under NADA 141-084, with Capstar tablets (nitenpyram), approved under NADA 141-175, to kill adult fleas and prevent flea eggs from hatching. Another original NADA, 141-205, was also filed for the concurrent use in dogs and cats of Program (lufenuron) Flavor Tabs, approved under NADA 141-035, with Capstar tablets (nitenpyram) to kill adult fleas and prevent flea eggs from hatching. Supplemental NADA's to NADA 141-035, NADA 141-084, and NADA 141-175 were also filed to provide appropriate labeling for the concurrent uses of these products under NADA 141-204 and NADA 141-205, and to NADA 141-035 for use of lufenuron flavor tablets in puppies and kittens as young as four weeks of age. <i>Federal Register 08/29/03</i>
Elanco Animal Health A Division of Eli Lilly & Co. (NADA141-221)	Ractopamine hydrochloride (Optaflexx™ 45)	Cattle. For increased rate of weight gain, improved feed efficiency, and carcass leanness.	MEDICATED FEED —The NADA provides for use of ractopamine hydrochloride Type A medicated articles to make Type B and Type C medicated feeds in cattle fed in confinement for slaughter. <i>Federal Register 09/18/03</i>

(Continued, next page)

New Animal Drug Approvals (Continued)

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
Norbrook Laboratories, Ltd. (NADA 141-143)	Oxytetracycline (Tetradure 300) RX	Cattle, Swine. For treatment of various bacterial diseases and for the control of respiratory disease.	SUBCUTANEOUS OR INTRAMUSCULAR —The NADA provides for veterinary prescription use of Tetradure 300 Injection and over-the-counter use of Oxytetracycline Injection 300mg/ml for the treatment of various bacterial diseases of cattle and swine. Norbrook Laboratories' Tetradure 300 Injection and Oxytetracycline Injection 300mg/ml are approved as generic copies of Pfizer's Liguamycin LA-200, approved under NADA 113-232. Tetradure 300 Injection is also indicated for the control of respiratory diseases in cattle at high risk of developing BRD associated with <i>Manheimia haemolytica</i> . <i>Federal Register</i> 09/19/03
Novartis Animal Health US, Inc. (NADA 141-218)	Cyclosporine (Atopica) RX	Dogs. For the control of atopic dermatitis.	ORAL —The NADA provides for the veterinary prescription use of Atopica for the control of atopic dermatitis in dogs weighing at least 4 pounds body weight. <i>Federal Register</i> 09/19/03
Virbac AH, Inc. (NADA 141-215)	Ivermectin/Praziquantel (Equimax™)	Horses. For the treatment and control of various species of internal parasites.	ORAL —The NADA provides for use of an EQUIMAX paste in horses. <i>Federal Register</i> 09/25/03

Supplemental New Animal Drug Approvals

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
Fort Dodge Animal Health Division of Wyeth (NADA 141-087)	Moxidectin (Quest™ 2.0% Equine Oral gel)	Horses and ponies. For the control of various internal parasites.	ORAL —The supplemental NADA adds an age precaution to labeling for moxidectin gel used for control of various species of internal parasites for oral use in horses and ponies 6 months of age and older. <i>Federal Register</i> 08/27/03
Fort Dodge Animal Health Division of American Cyanamid Co. (NADA 141-108)	Etodolac (Etogesic™) RX	Dogs. For the management of pain and inflammation associated with osteoarthritis.	ORAL —The supplemental NADA provides for a 500-mg tablet size of Etodolac. <i>Federal Register</i> 08/28/03
Pharmacia & Upjohn Co. (NADA 141-200)	Progesterone (Eazi-Breed™ CIDR®)	Dairy cows. For synchronization of the return to estrus.	INTRAVAGINAL —The supplemental NADA provides for use of progesterone intravaginal inserts in lactating dairy cows inseminated at the immediately preceding estrus. <i>Federal Register</i> 10/06/03

Abbreviated New Animal Drug Approvals

<u>Company</u>	<u>Generic and (Brand) Names</u>	<u>Indications</u>	<u>Routes/Remarks</u>
Veterinary Laboratories, Inc. (ANADA 200-315)	Lincomycin hydrochloride	Swine. For the treatment of infectious arthritis and mycoplasma pneumonia.	SUBCUTANEOUS OR INTRAMUSCULAR —The ANADA provides for the use of Lincomycin injectable solution in swine for the treatment of infectious arthritis and mycoplasma pneumonia. Additional action is taken because the concentration of lincomycin solution approved under an ANADA published in the FR on May 14, 2002, was unspecified. Veterinary Laboratories, Inc.'s Lincomycin injection is a generic copy of Pharmacia & Upjohn Co.'s Lincomix approved under NADA 034-025. <i>Federal Register:08/28/03</i>
Pennfield Oil Co. (ANADA 200-357)	Salinomycin, Chlortetracycline (Pennchlor)	Broiler chickens.	MEDICATED FEED —The NADA provides for the use of single-ingredient Type A medicated articles containing salinomycin and chlortetracycline to make two-way combination drug Type C medicated feeds for broiler chickens. Pennfield Oil Co.'s ANADA 200-357 is a generic copy of AlphaPharma, Inc.'s NADA 140-859. <i>Federal Register 09/19/03</i>
Agri Laboratories, Ltd. (ANADA 200-128)	Oxytetracycline (Agrimycin® 200)	Cattle, Swine. For the treatment of various bacterial diseases.	SUBCUTANEOUS OR INTRAMUSCULAR —The ANADA provides for the use of Agrimycin 200. Agri Laboratories Agrimycin 200 is a generic copy of Pfizer's Liquamycin LA-200, approved under NADA 113-232. <i>Federal Register:09/19/03</i>
First Priority, Inc. (ANADA 200-353)	Pyrantel pamoate (Primex Equine) RX	Horses and ponies. For removal and control of various internal parasites.	ORAL —The ANADA provides for Primex Equine Anthelmintic Suspension for oral use in horses and ponies for the removal and control of various internal parasites. First Priority's Primex is a generic copy of Pfizer, Inc.'s Strongid T, approved under NADA 91-739. <i>Federal Register 09/19/03</i>
Altana, Inc. (ANADA 200-330)	Nystatin, neomycin sulfate, thioestrepton, triamcinolone acetonide (Animax Cream) RX	Dogs and Cats. For dermatologic use.	TOPICAL —The ANADA provides for use of Animax Cream Veterinary, a vanishing cream based ointment, for topical dermatologic use in dogs and cats. Altana, Inc.'s Animax Cream is a generic copy of Fort Dodge Animal Health's Panalog Cream, approved under NADA 96-676. <i>Federal Register 09/23/03</i>

(Continued, next page)

Abbreviated New Animal Drug Approvals (Continued)

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
First Priority, Inc. (ANADA 200-352)	Pyrantel pamoate (Primex Canine, Primex Canine-2X)	Dogs. For management of various internal parasites.	ORAL —The ANADA provides for oral use in dogs and puppies of two strengths of pyrantel pamoate suspension for the removal of large roundworms (<i>Toxocara canis</i>) and hookworms (<i>Ancylostomacanthum</i>). First Priority's PRIMEX CANINE and Primex Canine-2X are generic copies of Pfizer, Inc.'s RFD Suspension and Nemex-2 Suspension, approved under NADA 100-237. <i>Federal Register</i> 09/29/03
First Priority, Inc. (ANADA 200-304)	Copper Naphthenate (Pritox™)	Horses and ponies. Used as an aid in treating thrush.	TOPICAL —The ANADA provides for topical use of copper naphthenate solution on horses and ponies as an aid in treating thrush caused by organisms susceptible to copper naphthenate. First Priority's Pritox is a generic copy of Fort Dodge Animal Health's Kopertox, approved under NADA 12-991. <i>Federal Register</i> 09/29/03
Pennfield Oil Co. (ANADA 200-354)	Monensin (Coban®), Chlortetracycline (Pennchlor™)	Broiler chickens.	MEDICATED FEED —The ANADA provides for the use of single ingredient Type A medicated articles containing monensin and chlortetracycline to make two-way combination drug Type C medicated feeds for broiler chickens. Pennfield Oil Co.'s ANADA 200-354 is a generic copy of Alpharma Inc.'s NADA 121-553 for combination use of Aureomycin (chlortetracycline) and Coban. <i>Federal Register</i> 09/29/03
Heska Corp. (ANADA 200-338)	Ivermectin/Pyrantel pamoate (Tri-Heart Plus) RX	Dogs. For treatment and control of certain gastrointestinal parasites.	ORAL —The ANADA provides for veterinary prescription use of Tri-Heart Plus Chewable Tablets for prevention and control of ascarids and hookworms in dogs. Heska Corp.'s Tri-Heart Plus is a generic copy of Merial's Heartgard Plus Chewables, approved under NADA 140-971. <i>Federal Register</i> 09/29/03
Veterinary Laboratories, Inc. (ANADA 200-324)	Dexamethasone RX	Cattle, Horses. For treatment of primary bovine ketosis and as an anti-inflammatory agent.	INTRAVENOUS OR INTRAMUSCULAR —The ANADA provides for use of Dexamethasone injection for the treatment of primary bovine ketosis and as an anti-inflammatory agent in cattle and horses. Veterinary Laboratories, Inc.'s Dexamethasone is a generic copy of Schering-Plough Animal Health's Azium Solution 2 Mg., approved under NADA 012-559. <i>Federal Register</i> 10/02/03

(Continued, next page)

Abbreviated New Animal Drug Approvals (Continued)

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
Phoenix Scientific, Inc. (ANADA 200-265)	Praziquantel	Dogs. For the removal and control of certain cestode parasites.	ORAL —The ANADA provides for the use of Praziquantel Tablets for the removal and control of certain cestode parasites in dogs. Phoenix Scientific, Inc.'s Praziquantel is a generic copy of Bayer HealthCare LLC's Droncit, approved under NADA 111-798. <i>Federal Register</i> 10/03/03

Supplemental Abbreviated New Animal Drug Approvals

<i>Company</i>	<i>Generic and (Brand) Names</i>	<i>Indications</i>	<i>Routes/Remarks</i>
Ivy Laboratories, Division of Ivy Animal Health, Inc. (ANADA 200-221)	Trenbolone acetate and Estradiol (Component® TE-IS)	Feedlot Steers. For increased rate of weight gain and improved feed efficiency.	EAR IMPLANTATION —The supplement provides for an additional dose of trenbolone acetate and estradiol implant for use in steers fed in confinement for slaughter. Ivy Laboratories' Component TE-IS is a generic copy of Intervet, Inc.'s Revalor-IS, approved under NADA 140-897. <i>Federal Register</i> 09/23/03
Ivy Laboratories, Division of Ivy Animal Health, Inc. (ANADA 200-346)	Trenbolone acetate, Estradiol (Component® TE-IH)	Feedlot heifers. For increased rate of weight gain.	EAR IMPLANTATION —The supplement provides for an additional dose of trenbolone acetate and estradiol implant for use in heifers fed in confinement for slaughter. Ivy Laboratories' Component TE-IH is a generic copy of Intervet, Inc.'s Revalor-IH, approved under NADA 140-992. <i>Federal Register</i> 09/23/03
Phoenix Scientific, Inc. (ANADA 200-246)	Pyrantel pamoate (Anthelban V)	Horses and ponies. For removal and control of certain internal parasites.	ORAL —The supplemental ANADA provides for over-the-counter marketing status for pyrantel pamoate suspension, when labeled for oral administration rather than stomach tube, a veterinary prescription procedure. Phoenix Scientific, Inc.'s Pyrantel Pamoate Equine Anthelmintic Suspension is a generic copy of Pfizer, Inc.'s Pamoban horse wormer, approved under NADA 91-739. <i>Federal Register</i> 09/23/03

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