FDA VETERINARIAN

Center for Veterinary Medicine

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CVM APPOINTS THREE NEW MANAGERS

CVM has filled the positions of Deputy Associate Director for Policy and Regulations, Director of the Division of Therapeutic Drugs for Food Animals, and Director of the Division of Surveillance.


Photo by Karen Kandra

Dr. Bill Flynn

Dr. Bill Flynn has been selected as the Deputy Associate Director for Policy and Regulations, and will oversee the Policy and Regulations Staff responsible for developing *Federal Register* documents and guidance documents.

Dr. Flynn joined CVM in 1993 as a reviewer in the Division of Therapeutic Drugs for Food Animals where he also served as acting leader of the Antimicrobial Drugs Team. He later served as a Special Assistant in the Division of Human Food Safety and as Acting Deputy Director of ONADE.


Photo by Karen Kandra

Dr. Lynn Post

Moving to the Office of the Director in 2001, Dr. Flynn concentrated on identifying and assessing emerging complex issues, most notably those dealing with the Center's efforts to define scientifically based criteria for the regulation of antimicrobial drug products.

Most recently, Dr. Flynn successfully led the CVM Antimicrobial Resistance Guidance Group in its efforts to implement the Framework Document, culminating in the publication of draft Guidance for Industry #152, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern."

Dr. Flynn received his D.V.M. and M.S. in Veterinary Preventive Medicine from the Ohio State University.


Photo by Eric Dubbin

Dr. Joan Gotthardt

Dr. Joan Gotthardt has been selected as the Director of the Division of Therapeutic Drugs for Food Animals in the Office of New Animal Drug Evaluation (ONADE), succeeding Dr. Steven Vaughn, now Director of ONADE. In this new capacity, Dr. Gotthardt will direct all activities related to the review of animal safety and effectiveness of therapeutic drugs and feed additives for food animals.

Dr. Gotthardt joined CVM in 1995. She received her D.V.M. from the Virginia Maryland Regional College of Veterinary Medicine. Previously, she worked in ONADE as a reviewer in the Antimicrobial Drugs Team, and as Leader of the Aquaculture Drugs Team. Before

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DISTRIBUTION OF DIOXIN-CONTAMINATED ANIMAL FEED HALTED

FDA recently announced that its dioxin-monitoring program has found elevated levels of dioxin in some mineral components used in animal feeds. In response to notification from FDA about the problem, both the supplier of one of the mineral components (zinc oxide) and the mineral premix blender contacted their customers and urged that they immediately stop further distribution of their products made with this mineral component. The implicated zinc oxide premixes were used in livestock, aquaculture, and poultry feed and feed products.

An additional mineral component (copper oxide) is also being investigated as a possible source of dioxin. Both mineral components currently under investigation are reclamation products from industrial metal production.

Because mineral premixes are diluted greatly in the finished animal feed, it is unlikely that human health effects would occur from this limited exposure. At this point in the investigation, FDA does not believe this poses a human health risk.

Based on present information, FDA has requested the recall of certain animal feed and feed products. The recalled products were distributed to feed manufacturers and suppliers in eleven states (CA, IA, IL, MN, MO, MS, NE, NY, PA, UT and WA) and Canada. The investigation of this incident is continuing and, as further information is learned, additional recalls of other products may be necessary.

One of FDA's public health objectives is to reduce the level of exposure to dioxin in the animal and human foods it regulates. Finding and stopping sources of added dioxin, such as the mineral components, from entering the food supply is one of the primary goals of FDA's dioxin monitoring program. FDA will continue to evaluate this problem and will provide the Agency's findings to the public.

Dioxins are ubiquitous, low level environmental contaminants. With cumulative exposure, they are potential carcinogens and may cause reproductive or

(Continued, next page)

CVM APPOINTS THREE NEW MANAGERS (Continued)

coming to CVM she worked as a supervisor in the Defense Mapping Agency. Dr. Gotthardt is assuming this critical leadership role at a time when ONADE is faced with many challenges including moving to a performance-based environment.

Dr. Lynn Post has been selected as Director of CVM's Division of Surveillance in the Office of Surveillance and Compliance, succeeding Dr. Bill Keller, who retired last summer. In his new role, Dr. Post will direct all activities related to the evaluation of the safety and effectiveness of marketed animal drugs, special dietary feeds, veterinary medical devices, and other veterinary medical products. The Division of Surveillance also reviews product labeling and monitors and evaluates promotion of marketed veterinary drugs, and reports of adverse drug experiences.

Dr. Post received his D.V.M. from Texas A&M University. His graduate education includes an M.S. in veterinary toxicology and a Ph.D. in toxicology from Louisiana State University. He is a Diplomate of the American Board of Veterinary Toxicology and also the Chair of the Exam Committee.

In 1994, Dr. Post came to CVM as a veterinary medical officer in the Division of Production Drugs, ONADE. He transferred to OS&C, Division of Surveillance, as a reviewer in 1998. He was appointed as the Adverse Drug Event Coordinator in 2000, and served as the VICH Chair of the Pharmacovigilance Expert Working Group that met in Tokyo, Japan during October 2002. Dr. Post has been the Acting Director for the Division of Surveillance since July 2002, and has received numerous awards and commendations as a Commissioned Corps Officer of the Public Health Service.

FDA VETERINARIAN

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FDA INVESTIGATES IMPROPER DISPOSAL OF BIOENGINEERED PIGS

FDA and the Center for Veterinary Medicine continue to investigate the improper release of some experimental hogs to a livestock dealer from an experiment in transgenics by the University of Illinois, officials said.

The University has been "very cooperative" during the investigation, reports Mr. John Matheson, Senior Regulatory Scientist at CVM.

An FDA investigation conducted at the end of January revealed that the University had released 386 hogs from the experiment. The University has said that the hogs did not contain the genetic construct of the parent stock.

The Agency believes that, based on present information, this incident poses no public health risk. Nevertheless, if confirmed, it would represent a significant breach of the FDA requirements for this study. To date, this appears to be an isolated incident in which measures already in place to dispose of experimental transgenic animals may not have been followed.

Recent FDA inspections of research facilities at the University of Illinois at Urbana/Champaign indicate that between April 2001 and January 2003 University researchers released 386 pigs from these studies to a livestock dealer. The researchers claim that these pigs, which were the offspring of transgenic animals, did not inherit the inserted genetic material from their parents—that is, they were not themselves transgenic. However, FDA cannot verify this assertion because the researchers did not conduct sufficient evaluation or keep sufficient records for FDA to assess whether the offspring inherited the inserted genetic material.

Because these were experimental animals, FDA had not yet determined the safety or efficacy of the genetic material they contained. The genes were engineered so that the proteins would be produced primarily, if not exclusively, in the mammary glands of lactating sows. None of the pigs sent to slaughter are believed to have been old enough to lactate. Therefore, FDA does not believe that any product derived from these animals would have to be removed from commerce for public health reasons, and USDA concurs.

In collaboration with USDA, FDA is continuing to carefully examine the records and practices of the individual researchers and the University. Under the terms of the study protocols, animals involved in this particular study were to have been destroyed by incineration or rendering to prevent their introduction into the human food supply. Based on its current findings, FDA has issued both the University of Illinois and the individual investigators involved in this case a notice of its inspectional observations. FDA will take further action based on the results of the investigation.

DISTRIBUTION OF DIOXIN-CONTAMINATED . . . (Continued)

developmental health problems. Presently, the primary source of human exposure to dioxins is through food.

Environmental sources of dioxin pollution have been markedly reduced over the past decade. The result has been a significant reduction in overall dioxin exposure to the public. To further reduce public exposure to dioxins, the FDA established food and feed surveillance programs. These programs further our understanding of dioxin levels in FDA regulated foods. It was through these surveillance programs that FDA identified the mineral components as the primary source of dioxins in the affected animal feed.

One of FDA's public health objectives is to reduce the level of exposure to dioxin in the animal and human foods it regulates.

FDA is currently investigating whether similar products are being used in other FDA-regulated feed, and whether other feed products incorporated the mineral components. FDA is working cooperatively with State feed regulators and other relevant Federal agencies to trace the distribution of these products.

FDA ORDER PROHIBITS EXTRA-LABEL USE OF PHENYLBUTAZONE

FDA has issued an order prohibiting the extra-label use of phenylbutazone animal and human drugs in female dairy cattle 20 months of age or older. FDA is issuing this order based on evidence that extra-label use of phenylbutazone in these dairy cattle will likely cause an adverse event in humans. The Agency finds that such extra-label use presents a risk to the public health for the purposes of the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA).

There are currently no approved uses of phenylbutazone in food-producing animals.

AMDUCA amended the Federal Food, Drug, and Cosmetic Act to allow licensed veterinarians to prescribe extra-label uses of approved animal drugs and human drugs in animals. Section 2(a)(4)(D) of the AMDUCA provides that the Agency may prohibit an extra-label drug use in animals if, after affording an opportunity for public comment, the Agency finds that such use presents a risk to the public health.

Phenylbutazone became available for use in humans for the treatment of rheumatoid arthritis and gout in 1949. However, it is no longer approved, and thus not marketed, for any human use in the United States. This is because some patients treated with phenylbutazone have experienced severe toxic reactions, and other effective, less toxic drugs are available to treat the same conditions.

Deborah Cera, a CVM compliance officer, noted that newer animal drugs, such as Banamine, have largely replaced the use of phenylbutazone as a treatment for arthritic or lame cattle. "The level of use on the farm has fallen over the years," Cera said, in an interview with the *FDA Veterinarian*. "We want to ensure that the public is never exposed to residues of this toxic drug."

Phenylbutazone is known to induce blood dyscrasias, including aplastic anemia, leukopenia, agranulocytosis, thrombocytopenia and deaths. Hypersensitivity reactions of the serum-sickness type have also been reported. In addition, phenylbutazone is a carcinogen, as determined by the National Toxicology Program.

For animals, phenylbutazone is currently approved only for oral and injectable use in dogs and horses. Use in horses is limited to horses not intended for food. There are currently no approved uses of phenylbutazone in food-producing animals. Investigation by FDA and State regulatory counterparts has found phenylbutazone on farms and identified tissue residues in culled dairy cattle. In addition, USDA's Food Safety Inspection Service has reported phenylbutazone residues in culled dairy cattle presented for slaughter for human food throughout the U.S. in the past two calendar years. This evidence indicates that the extra-label use of phenylbutazone in female dairy cattle 20 months of age or older will likely result in the presence, at slaughter, of residues that are toxic to humans, including being carcinogenic, at levels that have not been shown to be safe.

FDA is accepting comments on this order until April 29, 2003. Written comments should be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. All comments should include docket number 03N-0024. The order will become effective May 29, 2003, unless FDA revokes or modifies the order or extends the comment period.

Additional information on this prohibition is contained in the February 28, 2003, *Federal Register*. Questions about this prohibition may be directed to: Gloria J. Dunnavan, Center for Veterinary Medicine (HFV-230), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-1168, e-mail: *gdunnava@cvm.fda.gov*.

UPDATE ON FDA INITIATIVE TO IMPROVE REGULATION OF PHARMACEUTICAL MANUFACTURING

FDA recently announced that it has accomplished the initial objectives set in its ongoing initiative to modernize the Agency's regulation of pharmaceutical manufacturing and product quality. CVM was an active participant in the Agency's efforts to modernize its regulations.

This initiative is part of Health and Human Services Secretary Tommy G. Thompson's broader efforts to improve and streamline the regulatory process in order to improve Americans' access to quality health care and services. Two years ago, Secretary Thompson created an HHS-wide initiative on regulatory reform to conduct an ongoing review of HHS regulations and to oversee changes in regulations. He appointed an expert advisory panel that made hundreds of specific recommendations. This action reflects the Secretary's goal of smart regulation.

"Using state-of-the-art approaches in FDA's many critical review and inspection activities will encourage innovation and continuous improvement in drug manufacturing to minimize production problems, and that will make it easier to get safe, high quality medications to patients who need them," said Mark B. McClellan, M.D., Commissioner of Food and Drugs. "These initiatives are part of the Department of Health and Human Services' overall efforts to improve the quality, safety, and cost of medical products. We will focus our attention and resources on the areas of greatest risk, with the goal of encouraging innovation that maximizes public health protection and promotion."

These announcements are a significant interim step in a major agency-wide initiative on "Pharmaceutical Current Good Manufacturing Practices (cGMPs) for the 21st Century: A Risk Based Approach," a two-year program which applies to pharmaceuticals, including biological human drugs and veterinary drugs.

The initiative, announced in August 2002, was designed to evaluate and improve upon the agency's approach to reviews and inspections related to the manufacturing of human and animal drugs and biologics.

Highlights of what's been completed to date include:

- clarifying the scope of FDA's electronic submission and record-keeping requirements and providing for enforcement discretion in certain areas while FDA considers whether to revise the Part 11 regulations to facilitate innovation for modern manufacturing, electronic record keeping, and regulatory submissions;
- facilitating continuous improvement and innovation in manufacturing by allowing manufacturers to make certain types of changes in their processes without prior FDA approval;
- launching a program to identify and address inconsistencies across program areas with respect to all drug cGMP warning letters;
- issuing for public comment a progress report on improving dispute resolution procedures to facilitate early resolution of scientific and technical disputes and allow for greater transparency;
- clarifying the language used to communicate deficiencies observed during cGMP inspections to better describe the purpose and effect of the investigator's observations issued at the conclusion of an FDA inspection;
- planning public workshops on the scientific foundations of the initiative that will help shape the FDA's next steps in its implementation;
- focusing FDA resources on inspections that are likely to achieve the greatest public health impact (e.g., sterile drug manufacturing);
- providing a progress report that considers adding product and technical specialists with relevant expertise to inspection teams that do not yet include such specialists, a promising step for improving the technical quality and consistency of FDA's inspections; and
- enhancing the Agency's expertise in pharmaceutical technologies by hiring a number of additional experts and collaborating actively with academic groups and other outside experts.

The "Pharmaceutical cGMPs for the 21st Century" initiative will include additional intermediate and long-term steps. The major goals of the initiative include:

- ensuring that state-of-the-art pharmaceutical science is utilized in the regulatory review and inspection policies;

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EXTRA-LABEL DRUG USE IN VETERINARY MEDICINE

by Gillian Comyn, D.V.M., M.P.H., D.A.C.V.P.M.

Introduction

Since 1994, when Congress passed the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA), veterinarians in the U.S. have enjoyed legitimate extra-label use (ELU) privileges. Veterinarians can safeguard ELU privileges by following AMDUCA, and by educating clients (particularly food animal producers) on AMDUCA and prudent drug use principles. This article outlines key points of AMDUCA in plain language.

Animal Medicinal Drug Use Clarification Act

Extra-label drug use (ELU) refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. ELU of new animal drugs was considered illegal and permitted only as a matter of enforcement discretion until the passing of AMDUCA. AMDUCA amended the Federal Food, Drug, and Cosmetic Act (the Act), legalizing extra-label drug use by and under the order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship, and became effective in 1996 when implementing regulations (21 CFR Part 530) were published.

AMDUCA allows veterinarians to prescribe extra-label uses of certain approved animal drugs and approved human drugs for animals under specified conditions.

The key components and conditions of AMDUCA[1] are as follows:

- **Veterinarian-Client-Patient Relationship (VCPR)**
- **General Conditions for Extra-Label Use Under AMDUCA**
- **Conditions for Extra-Label Use in Food Animals**
- **Compounding Under AMDUCA**
- **Prohibitions Under AMDUCA**

(Continued, next page)

FDA COMPLETES FIRST STEPS . . . (Continued)

- encouraging the adoption of new technological advances in high quality and efficient manufacturing by the pharmaceutical industry;
- assessing the applicable cGMP requirements relative to the best quality management practices;
- strengthening public health protection by implementing risk-based approaches that focus both industry and FDA attention on critical areas for improving product safety and quality; and
- enhancing the consistency and coordination of FDA's drug quality oversight activities.

"Using state-of-the-art approaches in FDA's many critical review and inspection activities will encourage innovation and continuous improvement in drug manufacturing to minimize production problems, and that will make it easier to get safe, high quality medications to patients who need them," said Mark B. McClellan, M.D., Commissioner of Food and Drugs.

The initiative is being overseen by an agency steering committee with representatives from the Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), Office of Regulatory Affairs (ORA), and the Office of the Commissioner (OC). Janet Woodcock, M.D., Director of CDER, is the chairperson of the steering committee.

According to Dr. Woodcock, "FDA expects to complete and publish a comprehensive implementation plan for this cGMP initiative by mid-year. These initial accomplishments are the first steps toward achieving FDA's goals for a 21st-century regulatory system for pharmaceutical manufacturing designed to protect the public health and to ensure that safe and effective drugs are available to the American public."

Additional information on the initiative can be found online at *www.fda.gov/cder/gmp/index.htm*.

EXTRA-LABEL DRUG USE IN VETERINARY MEDICINE (Cont.)

Veterinarian-Client-Patient Relationship (VCPR)

The regulation defines a valid veterinarian-client-patient relationship as one in which:

(1) A veterinarian has assumed the *responsibility* for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;

(2) There is *sufficient knowledge* of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and

(3) The practicing veterinarian is readily available for *follow-up* in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has *recently seen* and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by *medically appropriate and timely visits* to the premises where the animal(s) are kept.

General Conditions for Extra-Label Drug Use Under AMDUCA

(1) There is no animal drug approved for the intended use;

(2) Or, there is an animal drug approved for the intended use, but the approved drug is not in the required dosage form or concentration;

(3) Or, the approved drug has been found to be clinically ineffective when used as labeled;

(4) Or, if the intended use is in a non-food animal, an approved human drug can be used even if an approved animal drug is available.

(5) In food animals, use of approved human drugs is not permitted if (an) approved animal drug(s) can be used.

(6) RECORDKEEPING: The veterinarian must maintain records with animal identification (in food animal practices, on a group, herd, flock, or per-client basis). The records have to include: established name of the drug and its active ingredient, or if formulated from more than one ingredient, established name of each ingredient; condition treated; species of the treated animal(s); dosage administered; treatment duration; number of animals treated; and withdrawal, withholding, or discard time(s), for meat, milk, eggs, or any food from the animals treated. The veterinarian must keep these records for 2 years or as required by Federal or State law, whichever is greater. The records must be available at any reasonable times to FDA designated personnel, for copying and verifying.

(7) LABELING: The label on a drug dispensed for ELU, whether by a veterinarian or dispensed by a pharmacist on the order of a veterinarian, must have the following information: name and address of the prescribing veterinarian (and the pharmacy if dispensed this way). Also, the labeling must have on it the following:

- animal identification (individual for companion animals, or group or pen if food animal),
- indication (what condition is the drug being used to treat),
- number of animals treated (in the case of food animals),
- dosage, route, and duration of treatment,
- withdrawal intervals, and,
- any cautionary statements (for example: not for use in horses intended for food).

(8) AMDUCA does not allow extra-label drug use in animal feeds.

(9) AMDUCA does *not* permit veterinarians, or pharmacists, to compound unapproved finished new animal drug products from *bulk* drugs

Conditions for Extra-Label Use in Food Animals

(1) *Before prescribing or dispensing an approved new animal or human drug for an extra-label use in food animals*, the veterinarian must:

- make a careful diagnosis and evaluation of the conditions for which the drug is to be used;
- provide an estimated, scientifically-based, withdrawal interval for the milk, meat, eggs, or other edible products from the treated animal (this

(Continued, next page)

EXTRA-LABEL DRUG USE IN VETERINARY MEDICINE (Cont.)

information may be obtained by the veterinarian in context of a VCPR from among other sources, scientific literature, academia, or the Food Animal Residue Avoidance Databank (FARAD)[2];

- make sure that the identity of the treated animal or animals is maintained;
- take measures to assure that assigned timeframes for withdrawal are met and no illegal drug residues occur in any food-producing animal subjected to extra-label treatment.

(2) When considering extra-label use of an approved human drug in food animals:

- the veterinarian must have medical rationale for the use;
- the veterinarian may *not* use an approved human drug *if* an animal drug approved for use in food-producing animals can be used instead for the particular ELU; and
- *if* scientific information on the human food safety aspect of the use of the drug in food-producing animals is not available, the veterinarian must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

Compounding Under AMDUCA

FDA defines compounding as the manipulation of drugs to obtain products that differ from the starting materials in an approved dosage form drug. *Under AMDUCA, compounding is considered to be extra-label drug use, and must be done from approved finished dosage form human or animal drugs only*. Like any extra-label use, compounded drugs should not be used if an approved drug can be used at its approved dose and dosage form. AMDUCA does *not* permit veterinarians, or pharmacists, to compound unapproved finished new animal drug products from *bulk* drugs. *Unless* conditions set forth in 21 CFR 530.13(b) are met, the compounding of a new animal drug from an approved human or animal drug results in an adulterated new animal drug.

AMDUCA does not allow extra-label drug use in animal feeds.

Conditions for Compounding

(1) all relevant portions of the regulation have been complied with;

(2) there is no approved new animal or approved new human drug that when used as labeled or in the available dosage form and concentration, will properly treat the condition diagnosed. Compounding from a human drug for use in food-producing animals will not be permitted if an approved animal drug can be used for the compounding;

(3) the compounding is performed by a licensed pharmacist upon the order of a veterinarian or by a veterinarian within the scope of their professional practice;

(4) adequate procedures and processes are followed that ensure the safety and effectiveness of the compounded product;

(5) the scale of the compounding operation is commensurate with the established need for compounded products (e.g., similar to that of comparable practices); and

(6) all relevant State laws relating to the compounding of drugs for use in animals are followed.

Prohibited Drug Uses Under AMDUCA

As described above, AMDUCA allows FDA to place limits on certain extra-label drug uses in animals. These limits include prohibitions of certain extra-label uses. Though The Act provides a stepwise procedure leading to a prohibition, the Agency does not have to take all the steps before prohibiting an extra-label use if it finds that the extra-label drug use "presents a risk".

When assessing the risk from an extra-label drug use, the Agency may inspect a veterinarian's records. The purpose of the inspection is to document the extent and nature of the extra-label use, not for enforcement reasons. The Agency provides informal public notice when it makes such a finding. If the Agency finds that an extra-label drug use presents a risk, or a required analytical method has not been developed, the Agency

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FDA PROPOSES REGULATIONS FOR REGISTERING FOOD FACILITIES

On February 3, 2003, FDA published a proposed regulation that provided FDA new authority in protecting the nation's food supply against terrorist acts and other threats.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, requires domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States to register with the FDA by **December 12, 2003**. This includes all animal feed, pet food, feed ingredients and additives. To find out more or to see if your facility is required to register, see the FDA Bioterrorism Act of 2002 home page at *http://www.fda.gov/oc/bioterrorism/bioact.html*>.

"Improving the FDA's food safety inspection, detection and monitoring capabilities is and has been a top priority of the Department even before the events of 9/11. Since then we have taken strong steps to enhance the FDA's ability to make our food supply safer," said Secretary of Health and Human Services Tommy G. Thompson. "This FDA effort is the latest in a series of measures we are taking to build stronger safeguards for the American people."

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EXTRA-LABEL DRUG USE IN VETERINARY MEDICINE (Cont.)

may prohibit the use. Any new prohibition ordered by the Agency will be published in the *Federal Register*, with a ninety-day delayed effective date and a sixty-day comment period. The order will be effective in ninety days, unless it is revoked or modified, or the comment period is extended. When a prohibition or any other important regulatory change is codified, the notice is posted immediately on the CVM web site and disseminated through printed media (*FDA Veterinarian*, veterinary and trade journals and other sources).

The Current List of Drugs Prohibited From Extra-Label Use (As listed in 21 CFR 530.41)

These drugs (both animal and human), families of drugs, and substances are currently prohibited for extra-label uses in all *food-producing* animals, (***including horses intended for human food***):

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dimetridazole
- Ipronidazole and other nitroimidazoles
- Furazolidone, Nitrofurazone, other nitrofurans
- Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine)
- Fluoroquinolones
- Glycopeptides

(Editor's note: This list is complete as of press date, see related article ***FDA Order Prohibits Extra-Label Use of Phenylbutazone*** on page 4.)

Conclusion

AMDUCA legalized extra-label use of approved animal and human drugs in animals when that use is under the supervision of a veterinarian and in accordance with FDA regulations. AMDUCA provided veterinarians with privileges comparable to those generally enjoyed by physicians. Veterinarians can protect these privileges by complying with AMDUCA, and understanding the permitted *and* prohibited extra-label drugs and uses (including compounding).

For more information on AMDUCA, other regulations and policies, and to request hard copies, please visit the CVM Home Page, *http://www.fda.gov/cvm/default.html*, and look under Quick Index. Notices of proposed rulemaking and final rules, such as additions to prohibited drug list, are announced by *Federal Register* notices and posted on the CVM Home Page, *http://www.fda.gov/cvm/default.html* and the FDA Dockets Advanced Publication Display website, *http://www.accessdata.fda.gov/scripts/oc/ohrms/index.cfm*.

Dr. Comyn is a Consumer Safety Officer in CVM's Division of Compliance.

[1] http://www.fda.gov/cvm/index/amducca/530.txt

[2] http://www.farad.org/

FDA PROPOSES REGULATIONS FOR REGISTERING . . . (Cont.)

"This measure will bolster our ability to regulate effectively the more than 400,000 domestic and foreign facilities that deal with food within our country," said FDA Commissioner Dr. Mark B. McClellan. "Our ability to efficiently and effectively help protect the nation's food supply is a critical part in our Agency's counterterrorism mission. Thanks to the efforts of Senators Gregg and Kennedy, and Representatives Tauzin and Dingell, the Bioterrorism Act gives FDA this important new authority."

"Improving the FDA's food safety inspection, detection and monitoring capabilities is and has been a top priority of the Department even before the events of 9/11. . . ." —Secretary Thompson

Under the proposal all domestic food facilities would be required to register whether or not food from the facility enters interstate commerce. Except for specific exemptions, the new regulation would apply to all facilities for all foods and animal feed products regulated by FDA.

Photo by Karen Kandra

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, requires domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States to register with the FDA by December 12, 2003.

The proposed regulation would require the owner, operator, or agent in charge of a domestic or foreign facility to submit a registration to FDA, including the name and address of each facility at which, and trade names under which, the registrant conducts business, and the categories of food the facility handles. For a foreign facility, the registration must include the name of the U.S. agent for the facility. The U.S. agent may register a foreign facility if it is authorized to do so by the facility. The proposal also would require facilities to update any changes to the information previously submitted within 30 days of the change.

The proposal specifically excludes farms, restaurants, other retail food establishments, nonprofit food establishments in which food is prepared for or served directly to the consumer, certain fishing vessels, and facilities (such as meat and poultry slaughterhouses) that are regulated exclusively by the U.S. Department of Agriculture. Also exempt are foreign facilities if the food from the facility undergoes further processing or packaging by another foreign facility before it is exported to the U.S. A foreign facility is not exempted from registration, however, if the processing or packaging activities of the subsequent facility are limited to the affixing of a label to a package or other de minimis activity. In that instance, both the facility manufacturing/processing the food and the facility performing the de minimis activity would have to register.

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LEVERAGING EXAMPLES – PART IV: FOOD SAFETY COOPERATIVE AGREEMENTS

by David B. Batson, Ph.D.

Introduction

This is the fourth in a series of articles on leveraging activities in the Center for Veterinary Medicine (CVM). Through the use of a real-life example of a cooperative agreement, this article will describe the cooperative agreement award process and will demonstrate how these agreements can be used as a leveraging tool for addressing important research questions posed by the Center.

A cooperative agreement serves as a mechanism through which collaboration can be established between the FDA and an institution or organization outside FDA. In so doing, substantial technical expertise is contributed by both parties. The FDA provides at least part of the funding for the project.

The FDA initiates the cooperative agreement process by publishing a Request for Application (RFA) in the *Federal Register*. The Grants Management and Program Staff reviews all applications for their responsiveness to the RFA. Those applications found to be noncompliant with the RFA are returned to the applicant without further consideration. An ad hoc panel of experts subsequently reviews applications that are in compliance with the RFA, determining the application's scientific and technical merit. A National Advisory Council provides a second level of review on the scientific merit of the applications. Ultimately, the Director of the Center renders the final judgement regarding FDA funding decisions for that Center.

The responsiveness of cooperative agreement applications is based on the following criteria:

1. Research should be proposed that is within one or more of the objectives listed in the Research Goals and Objectives Section.
2. The proposed study is within the designated budget guideline and costs are adequately justified and fully documented;
3. The rationale for the proposed study is sound and the study design is appropriate to address the objectives of the RFA;
4. Laboratory and associated animal facilities are available and adequate;
5. Support services, e.g., biostatistical, computer, etc. are available and adequate, and;
6. The Principal Investigator and support staff have research experience, training and competence.

Once the agreement is awarded, substantive involvement continues in the research program, including, but not limited to the following:

1. FDA appoints a Project Officer who actively monitors the supported program under each award. This includes annual site visits and the review of quarterly progress reports.
2. FDA establishes a Project Advisory Group that provides guidance and direction to the Project Officer

(Continued, next page)

FDA PROPOSES REGULATIONS FOR REGISTERING . . . (Cont.)

The law requires FDA to notify the registrant of receipt of registration and to assign each facility a unique registration number. The registration may be electronic, via the Internet, or by paper through surface mail. FDA strongly encourages electronic registration, however, as the Internet system FDA plans will be able to accept electronic registration from anywhere in the world 24 hours a day, seven days a week. A registering facility also would receive confirmation of electronic registration and its registration number instantaneously once all the required fields on the registration screen are completed. There is no fee associated with registration.

Written comments on this proposed regulation can be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Comments can be sent electronically through *www.fda.gov/dockets/ecomments* or through the Bioterrorism Act home page. It is important to include the docket number 02N-0276 when providing comments. The deadline for comments is April 4, 2003.

LEVERAGING EXAMPLES . . . (Continued)

with regard to protocol development, data analysis and analytical methods used by the investigator.

3. FDA scientists collaborate with the recipient and have final approval on experimental protocols, data analysis, interpretation of findings, and co-authorship of publications.

A Sample Cooperative Agreement Program: Microbial Hazards Associated with the Animal Production Environment

FDA is mandated to assure the microbiological safety of foods, including those derived from animals. Even though the American food supply is among the safest in the world, millions of Americans are stricken yearly by illnesses caused by the food they consume. Some 5,000 people per year, primarily the very young and elderly, die as a result of these foodborne illnesses. One of the goals of the Agency's Food Safety Research Program is to reduce the incidence of foodborne disease to the greatest extent possible through the recognition of appropriate prevention procedures. CVM's concerns relate to microbial hazards associated with the pre-harvest phases of food animal production, including aquaculture.

In order to address some of the questions associated with the microbial hazards pre-harvest research question, the Center launched a cooperative agreement program with the publication of an RFA. The specific program objective was to stimulate research on microbiological hazards associated with the food animal production environment. It was of particular interest to FDA that this research advance scientific knowledge of human foodborne pathogens, such as *Salmonella*, *Escherichia coli*, and *Campylobacter*. Potential areas of investigation included: (1) selection for and dissemination of antimicrobial resistance in the animal production environment, (2) approaches to mitigate or minimize antimicrobial resistance, and (3) the impact of antimicrobial drug use on the carriage of foodborne pathogens and sentinel microorganisms used for monitoring programs.

Projects that fulfilled any one or a combination of the following specific objectives were considered for funding:

(1) Studies on the development, dissemination, transmission and persistence of antibiotic resistant bacteria and/or genetic determinants from these bacteria in the animal production environment. The horizontal transmission of antimicrobial resistant bacteria and resistance genes in the animal and animal production environment was of special interest. Also, the persistence of antimicrobial resistant foodborne pathogens and/or genes in the animal production environment after withdrawal of antimicrobials was of special interest. FDA/CVM was interested in research in all food-producing animal species, but was especially interested in poultry and the poultry production environment.

(2) Research on the mitigation/intervention strategies to decrease or minimize antimicrobial resistance in the animal production environment through the manipulation of drug use, altering drug dosages (including amount, frequency and duration of drug administration), use of competitive exclusion products, and/or the rotation of antimicrobials administered to beef cattle, dairy cattle, swine, poultry, and aquaculture species.

(3) The effect of antimicrobial use on the carriage and/or shedding of foodborne pathogens (i.e., pathogen load) in the above listed animal species.

This program allowed the Center to leverage and expand its on-going program by partnering with outside organizations, such as, universities. This collaboration permitted the Center to utilize outside microbiological expertise, facilities, and equipment to address significant research questions on microbial hazards associated with pre-harvest phases of food animal production. Additional information on the projects that were funded under this program can be found on CVM's web site: *http://www.fda.gov/cvm/fsi/fsior/FSIOR.htm*.

Concluding Comments

Although this particular cooperative agreement program was initiated by the FDA, it is possible for individuals and organizations to submit proposals based upon projects consistent with the mission of CVM. Therefore, if you have any questions on the Food Safety Cooperative Agreement Program, leveraging in general, or if you have an interest in initiating a collaboration with CVM, please contact Dr. David Batson at 301-827-8021 or David Lynch at 301-827-5337.

Dr. Batson is a Health Science Administrator at CVM's Office of Research.

INTERNATIONAL VETERINARY DRUG ACTIVITIES ENGAGE FDA/CVM SCIENTISTS

by Pamela L. Chamberlain D.V.M., DABT, Ph.D.

Veterinary Drug Residues and the Global Food Supply, Bangkok, Thailand

The National Food Processors Association (NFPA) invited the FDA/CVM to participate in a day-long seminar entitled, "Veterinary Drug Residues and the Global Food Supply" held in Bangkok, Thailand on January 23, 2003. The seminar was part of the NFPAs formal launch activities commemorating the opening of the organization's first international regional office in Bangkok.

Some countries within this region are currently experiencing significant trade difficulties resulting from residues of chloramphenicol in certain exported seafood products. The seminar was designed to address, in a very comprehensive way, veterinary drug development, regulation, residue measurement and monitoring and appropriate use practices. NFPA-Asia will serve the food processors of Southeast Asia. The organization views this region as a key region for current and future food trade. The countries within southeast Asia that NFPA will be focusing on are Thailand, Indonesia, Malaysia, the Philippines, Singapore, Brunei, Vietnam, Laos, Myanmar, and Cambodia and to the extent possible, South Korea, and Japan. For now, their main focus is on Thailand.

Dr. Pamela Chamberlain represented the Center and gave presentations entitled, "Old Veterinary Drugs: Why do Problems Exist," and "Residues in Foods: What are the Limits and Why?" The presentations were designed to deliver a clear message about the rigorous nature of the drug approval process in the U.S. and how tolerances, maximum residue limits and decisions to ban extra-label use of certain drugs are based on sound, scientific principles with protection of the public health being a primary concern. They are not arbitrary decisions designed to serve as barriers to trade.

The seminar was attended by approximately 150 people. Hallway feedback was very positive and complimentary toward all topics and presenters.

The NFPA was grateful for FDA/CVM's participation because it provided an example to the future members of NFPA-Asia of the positive working relationship the organization has with government regulators in the United States.

FAO/WHO Expert Committee on Food Additives, Geneva, Switzerland

Several FDA/CVM scientists participated in the 60th Meeting of the Joint FAO/WHO Committee on Food Additives (JECFA) held in Geneva, Switzerland, February 6-12, 2003. JECFA was convened to evaluate certain veterinary drug residues in food.

JECFA serves as a scientific advisory body to the Codex Alimentarius. The role of JECFA is to evaluate toxicology, residue chemistry and related information and make recommendations for acceptable daily intake (ADI) levels and maximum residue limits (MRLs).

At the 60th meeting, the Committee recommended new MRLs for neomycin in cattle liver, kidney and milk; for imidocarb in cattle muscle, liver, kidney, fat and milk and dicyclanil in sheep muscle, liver, kidney, and fat. In addition, the Committee recommended that the ADI for trichlorfon be lowered from 20 to 2 ug/kg bw per day. The Committee withdrew the MRLs for flumequine and carbadox based on evidence showing both are direct acting genotoxic carcinogens and, therefore the Committee was unable to establish an ADI for human exposure to residues. Previously, the Committee had recommended MRLs for carbadox based on the approach used by the U.S. FDA for its approval of carbadox. The Committee recognized that use of this approach was a risk management decision and will look to the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) for future guidance on this issue.

JECFA's recommendations are first reviewed by the CCRVDF which in turn makes recommendations to the Codex Alimentarius Commission on the advancement and adoption of MRLs as international Codex standards. JECFA is regarded as a risk assessment body while CCRVDF makes risk management decisions on the recommendations it receives from JECFA.

Drs. Pamela Chamberlain, Richard Ellis, Lynn Friedlander, and Kevin Greenlees from CVM attended as working members of the Committee. Dr. Sundlof attended as an observer in his capacity as Chair of the CCRVDF. The summary of the conclusions reached by the Committee on compound evaluations and other matters considered is available on the internet at *http://www.who.int/pcs/jecfa/Summary60.pdf*.

Dr. Chamberlain is a Team Leader in CVM's Division of Epidemiology.

AAFCO FRAMEWORK FOR REGULATORY ACTION ON COMMERCIAL ANIMAL FEEDS CONTAINING COMFREY

CVM supports recent action by the Association of American Feed Control Officials, Inc. (AAFCO) in recommending to State feed control officials that enforcement action be initiated to remove from distribution animal products containing comfrey. AAFCO's guidance to State feed control officials on March 3, 2003, follows the announcement made at AAFCO's Annual Meeting in August 2002, that comfrey, determined to be a health and safety concern in animals, is recommended for removal from all animal feeds.

Comfrey, determined to be a health and safety concern in animals, is recommended for removal from all animal feeds.

This AAFCO-recommended enforcement event follows a lengthy notification period of informing manufacturers and distributors of animal feeds that many of the ingredients they are using may not be in compliance with Federal and State commercial feed laws. The enforcement event provides a uniform time period for States to begin enforcement action against products containing comfrey. AAFCO intends to followup with States to determine the effectiveness of this event and is likely to recommend enforcement events for other ingredients in the future.

AAFCO's Enforcement Strategy for Marketed Ingredients Task Force identified comfrey as the target ingredient. This Task Force based its selection on published scientific information provided by the FDA's Center for Veterinary Medicine, an active member of AAFCO. Comfrey has been shown to cause liver damage in humans and in animals. Due to safety concerns, the FDA advised manufacturers on July 6, 2001, that comfrey should not be used in human dietary supplements.

The enforcement event is recommended to State feed control officials to clarify the regulatory status of ingredients sold for consumption by animals in feed, including livestock feed and pet food. All feed ingredients must be shown to be safe and efficacious for their intended use prior to distribution.

AAFCO has developed a fact sheet that reviews the routes available for gaining approval to include new ingredients in animal feeds including the food additive petitions, generally recognized as safe determinations, and establishing a definition in the Official Publication of AAFCO. More information is available in the fact sheet entitled "Options Available for Acceptance of a Proposed Feed Ingredient", available on the AAFCO web site at *http://www.aafco.org*. Animal feeds are regulated at both the Federal and State level. Feed ingredients not recognized or acceptable for their intended use may be subject to regulatory action by the State feed control officials and the FDA.

For additional information regarding the AAFCO-recommended enforcement activity, please contact Dr. Ali Kashani, AAFCO President, Washington Department of Agriculture, P.O. Box 42589, Olympia, WA 98504-2589, telephone (360) 902-2028.

CVM COMINGS AND GOINGS

In an effort to keep our readers apprised of new personnel developments, we will report new hires, retirements, and resignations of CVM personnel.

JANUARY HIRES

- **Dr. Dong Yan/Chemist/ONADE** – Dr. Yan reviews new animal drug applications in the Residue Chemistry Team, Division of Human Food Safety.
- **Lisa Durphy/Management Analyst/OM** – Ms. Durphy provides the human resource liaison link between CVM and the personnel team.

FEBRUARY HIRES

- **Dr. Alice Weiss/Veterinary Medical Officer/ONADE** – Dr. Weiss reviews new animal drug applications in the Generic Animal Drug Team.

RETIREMENTS

- **Dr. Donald Campbell/ONADE** – Dr. Campbell formerly worked in the Generic Animal Drug Team.

FDA AND AAFCO SPONSOR WORKSHOP

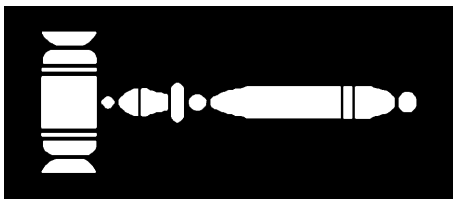
FDA and the Association of American Feed Control Officials (AAFCO) recently sponsored a workshop dedicated to development of tests for detection of prohibited mammalian proteins in animal feed. The workshop, held in Tucson, Arizona, attracted more than a dozen domestic and international presenters along with an audience of approximately eighty. Drs. Dragan Momcilovic, CVM and Larry D'Hoostelaere, FDA Office of Regulatory Affairs (ORA), co-chaired the meeting.

Presenters from government including CVM, academia, and industry covered two general areas: introductory/general interest and specific approaches to test development. Reports on the latter showed that detecting protein by using immunological methods is the most favored approach followed by DNA analysis, and microscopy. The reports also suggested that different developers are at different stages of developing a test for detecting protein. While some speakers claimed that they have tests that are ready for use, others cautioned that significant technical challenges remain to be addressed before a successful test is developed.

Presentations from this workshop are available on the web at *www.aafco.gov*, under "meetings".

REGULATORY ACTIVITIES

by Karen A. Kandra



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

- Scott Blond, D.V.M., Wyoming, NY
- Charles L. Earsing, Owner, Charles L. Earsing Dairy Farm, Alexander, NY
- John Hoogendam Jr. & Marvin L. Hoogendam, Co-owners, Hoogendam Dairy, Merced, CA
- William M. Walk, Sigel, IL
- John E. Gherty, President and CEO, Land O'Lakes, Inc., St. Paul, MN
- Dimas S. Costa, Darryl J. Azevedo, William J. Carr, Laurence M. Pietrowski, Co-owners, Costa View Farms, Madera, CA
- Peter M. Zacharais, Owner, Zacharias Holsteins, Falmouth, ME
- William M. Vargulick, Owner, William M. Vargulick Dairy Farm
- Eric J. Boersma, Owner, Boersma #2 Dairy, Mira Loma, CA
- James P. Reynolds, Co-owner, Reyncrest Farms, Inc., Corfu, NY
- Gerald R. Vukman, D.V.M., Oakfield, NY
- Antonio Azevedo, Owner, Antonio Azevedo Dairy, Filer, ID
- Robert S. Wilcom, Frederick, MD
- Dale C. Devries and Thomas R. Devries, Owners, Devries Family Farm, LLC, Moxee, WA
- Arthur H. Marquez, Owner, Marquez Dairy, LLC, Chino, CA
- Jose L. Lourenco, Owner, Lourenco Dairy #2; Buhl, ID

The above violations involved illegal residues of flunixin meglumine in two cows; sulfadimethoxine and flunixin in cows; penicillin in a calf; sulfadimethoxine in a beef steer; penicillin in a sow; tetracycline in a cow; gentamicin in a dairy cow; oxytetracycline in a cow; penicillin in a culled dairy cow; flunixin in cow; sulfamethazine in a downer cow; sulfadimethoxine in a cow; sulfadimethoxine in a Holstein cow; and sulfadimethoxine in several culled dairy cows.

A warning letter was issued to William Cramer, Owner, Diamond Pacific, Perris, CA for significant deviations from the current Good Manufacturing Practice (cGMP) regulations for licensed medicated feed manufacturers. Violations included failure to conduct the required number of assays of all medicated feeds containing carbadox, chlortetracycline, sulfathiazole, and penicillin, and other drugs; failure

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VMAC SEEKS NOMINATIONS

FDA is requesting nominations for voting members to serve on the Veterinary Medicine Advisory Committee (VMAC) in one of the following specialty areas: Companion Animal Medicine, Chemistry, Biostatistics, and Consumer representative. Information regarding the committee can be found on the CVM home page at *http://www.fda.gov/cvm/index/vmac/vmactoc.htm*.

FDA has a special interest in ensuring that women, minority groups, and the physically challenged are adequately represented on advisory committees and, therefore, encourages nominations of qualified candidates from these groups.

All nominations and curricula vitae with the exception of the consumer representative should be sent to Aleta Sindelar, Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 301-827-4515, e-mail: *asindela@cvm.fda.gov*. The submission deadline will be announced in the *Federal Register* Notice.

Nominations for Consumer representatives should be sent to the attention of Dr. Linda A. Sherman, Advisory Committee Oversight and Management Staff (HF-4), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Persons nominated for membership on the committee shall have adequate specialized training and experience necessary to qualify the nominee as an expert suitable for appointment. The nomination is subject to

(Continued, next page)

REGULATORY ACTIVITIES (Continued)

to adequately sequence feeds, including the manufacture of a horse ration after a feed containing monensin which is toxic to equines; failure to maintain production records for the required length of time; and, failure to comply with Veterinary Feed Directive (VFD) requirements.

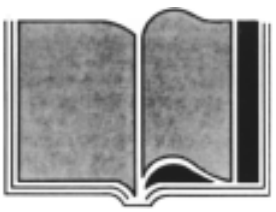
A warning letter was issued to David G. Hoover, President, Hoover Feed Service, Inc., Goshen, IN, for significant violations of the Federal Food, Drug, and Cosmetic Act, in that the use of the new animal drug in feed manufactured did not conform with an approved New Animal Drug Application as required by section 512 of the Act. The feed mill was found to be manufacturing a medicated feed as a complete feed (Type C) for lactating dairy cattle that is not approved for use in lactating dairy cows.

A warning letter was issued to Nyle A. McAnally, General Manager, McAnally Enterprises LLC, Lakeview, CA, for significant deviations from the current Good Manufacturing Practice (cGMP) regulations for licensed medicated feed manufacturers. Some of the violations included failure to conduct the required number of assays for medicated feeds containing amprolium; failure to compare the actual drug inventory with the theoretical drug inventory; failure to maintain production records for the required length of time; and, use of Type A medicated articles in a manner contrary to their approved labeling.

A warning letter was issued to Paul Ramer, Owner, Paul Ramer Construction, Argos, IN, for causing the adulteration of a new animal drug by continuously feeding medicated feed containing an unapproved animal drug to lactating dairy cows, and offering the milk from those cows for human food.

A warning letter was issued to Charles L. VanderPloeg, President/CEO, Vet Pharm, Inc., Sioux Center, IA, for selling prescription drugs for veterinary use that are adulterated and misbranded. The drugs "Amoxil Amoxicillin for Oral Suspension" and "Sulfamethoxazole and Trimethoprim Oral Suspension USP" among others, are human drugs that were being dispensed for animal use without the required labeling, including adequate directions for use.

FDA VETERINARIAN INDEX AVAILABLE



A topical index for the 2002 *FDA Veterinarian* is now available on the CVM Internet Home Page at *http://www.fda.gov/cvm/index/fdavet/2002/02index.pdf*. Readers who wish to obtain a paper copy of the Index may call or write the *FDA Veterinarian*.

VMAC SEEKS NOMINATIONS (Continued)

review, and may include experience in medical practice, teaching, and/or research relevant to the field of activity of the committee. The term of office is four years. Any interested person may nominate one or more qualified persons for membership on one or more of the advisory committees. Self-nominations are also accepted.

Nominations shall include the name of the committee, a complete curriculum vitae of each nominee, current business address, and telephone number, and shall state that the nominee is aware of the nomination, is willing to serve as a member, and appears to have no conflict of interest that would preclude membership. FDA will ask the potential candidates to provide detailed information concerning such matters as financial holdings, employment, and research grants and/or contracts to permit evaluation of possible sources of conflict of interest.

NEW ANIMAL DRUG APPROVALS

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Schering-Plough Animal Health Corp. (NADA 141-206)	Florfenicol (Nuflor®)	Swine. For treatment of respiratory disease.	**ORAL**—The NADA provides for use of a florfenicol concentrate solution to make medicated drinking water for administration to swine for the treatment of respiratory disease associated with several bacterial pathogens. Tolerances for residues of florfenicol in swine liver at 2.5 ppm and 0.2 ppm in muscle are added to the regulation. *Federal Register* 12/24/02
Bayer Corp., Agriculture Division, Animal Health (NADA 141-208)	Imidacloprid, Ivermectin (Advantage® DUO) RX	Dogs. For the prevention of heartworm disease and treatment of flea infestations (*Ctenocephalides felis*).	**TOPICAL**—The NADA provides for veterinary prescription use in dogs of an imidacloprid and ivermectin topical solution for the prevention of heartworm disease caused by *Dirofilaria immitis* and treatment of flea infestations (*Ctenocephalides felis*). *Federal Register* 12/26/02
Pfizer, Inc. (NADA 141-207)	Danofloxacin mesylate (A180®) RX	Cattle. For treatment of bovine respiratory disease	**SUBCUTANEOUS**—The NADA provides for veterinary prescription use in cattle for treatment of bovine respiratory disease associated with *Mannheimia (Pasteurella) haemolytica* and *Pasteurella multocida*. FDA is also amending the regulation to add the acceptable daily intake(ADI) of 2.4 micrograms per kilogram of body weight per day and a tolerance in edible tissues of cattle at 0.2 ppm (parts per million) in liver and 0.2 ppm in muscle. *Federal Register* 12/27/02
RMS Laboratories, Inc. (NADA 141-210)	Triamcinolone (Genesis™ Topical Spray) RX	Dogs. For control of pruritus.	**TOPICAL**—The NADA provides for use of triamcinolone topical spray in dogs for the control of pruritus associated with allergic dermatitis. *Federal Register* 01/31/03

SUPPLEMENTAL NEW ANIMAL DRUG APPROVALS

Company	Generic and (Brand) Names	Indications	Routes/Remarks
Fort Dodge Animal Health, Division of Wyeth (NADA 141-043)	Trenbolone Acetate, Estradiol Benzoate (Synovex® Choice)	Cattle, steers. For increased rate of weight gain.	**SUBCUTANEOUS**—The supplemental NADA provides for an ear only implant containing 100 mg trenbolone acetate and 14 mg estradiol benzoate for increased rate of weight gain in steers fed in confinement for slaughter. Not for dairy or beef replacement heifers. *Federal Register* 12/27/02
Natchez Animal Supply Co. (NADA 137-687)	Formalin	Finfish, shrimp. For control of certain external parasites and fungi.	**TOPICAL**—The supplement provides for the use of formalin in a water bath for the control of certain external parasites on finfish and shrimp and for the control of fungi on finfish eggs. *Federal Register* 02/04/03

ABBREVIATED NEW ANIMAL DRUG APPROVALS

Company	Generic and (Brand) Names	Indications	Routes/Remarks
Ivy Laboratories, Division of Ivy Animal Health (ANADA 200-346)	Trenbolone acetate, Estradiol (Component® TE-H)	Feedlot heifers. For increased rate of weight gain and improved feed efficiency.	**SUBCUTANEOUS**—The product Component TE-H approved under this ANADA is a generic copy of Intervet's Revalor-H approved under NADA 140-992. *Federal Register* 12/24/02
Delmarva Laboratories, Inc. (ANADA 200-291)	Clindamycin liquid (Clinsol®)	Cats, dogs. For the treatment of various bacterial infections.	**ORAL**—The product Clinsol approved under this ANADA is a generic copy of Pharmacia & Upjohn's Antirobe Aquadrops Liquid approved under NADA 135-940. *Federal Register* 12/26/02
Phoenix Scientific, Inc. (ANADA 200-176)	Praziquantel (Prazitech™) RX	Dogs, cats. For the removal of various species of tapeworms.	**INTRAMUSCULAR or SUBCUTANEOUS**—The product Prazitech is a generic copy of Bayer Corp.'s Droncit 5.68% injectable solution approved under NADA 111-607. *Federal Register* 12/31/02
First Priority, Inc. (ANADA 200-340)	Ivermectin (Privermectin™)	Cattle. For treatment and control of various species of external and internal parasites.	**TOPICAL**—The product Privermectin is a generic copy of Merial Ltd.'s Ivomec pour-on for cattle approved under NADA 140-841. *Federal Register* 01/27/03

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ABBREVIATED NEW ANIMAL DRUG APPROVALS (Continued)

Company	Generic and (Brand) Names	Indications	Routes/Remarks
Phoenix Scientific, Inc. (ANADA 200-303)	Lincomycin Hydrochloride	Swine, broiler chickens. For the treatment of swine dysentery or the control of necrotic enteritis in chickens.	**ORAL**—The product Phoenix Scientific's Lincomycin Hydrochloride Soluble Powder is a generic copy of Pharmacia & Upjohn's LINCOMIX approved under NADA 111-636. *Federal Register* 01/27/03
ECO LLC (ANADA 200-348)	Ivermectin (Ecomectin)	Cattle. For treatment and control of various species of external and internal parasites.	**TOPICAL**—The product Ecomectin is a generic copy of Merial Limited's Ivomec pour-on for cattle approved under NADA 140-841. *Federal Register* 01/30/03
Phoenix Scientific, Inc. (ANADA 200-313)	Levamisole (Levamisole Hydrochloride Soluble Pig Wormer)	Swine. For the treatment of various internal parasites.	**ORAL**—The product Phoenix Scientific's Levamisole Hydrochloride Soluble Pig Wormer is a generic copy of Schering-Plough Animal Health's Tramisol approved under NADA 112-049. *Federal Register* 01/31/03

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPROVALS

Company	Generic and (Brand) Names	Indications	Routes/Remarks
Alpharma, Inc. (ANADA 200-189)	Lincomycin Hydrochloride	Swine.	**ORAL**—The supplement provides for reducing the preslaughter withdrawal time to zero days for use of lincomycin soluble powder in medicated drinking water for swine. *Federal Register* 12/24/02
Boehringer Ingelheim Vetmedica, Inc. (ANADA 200-008)	Oxytetracycline (BIO-MYCIN® 200, OXY-TET™ 200)	Lactating dairy cattle. For treatments of various bacterial diseases.	**SUBCUTANEOUS OR INTRAMUSCULAR**—The supplement provides for administration of these oxytetracycline injectable solutions to lactating dairy cattle. *Federal Register* 12/24/02
Alpharma, Inc. (ANADA 200-130)	Neomycin sulfate (Neo-sol® 50)	Turkeys. For the control of mortality.	**ORAL**—The supplement provides for the use of neomycin sulfate soluble powder in the drinking water of growing turkeys for the control of mortality associated with *Escherichia coli* organisms susceptible to neomycin. *Federal Register* 12/27/02

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