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Feed Safety Team Holds Public Meeting on Risk Ranking

by Jon F. Scheid, Editor

The Center for Veterinary Medicine's Animal Feed Safety System (AFSS) team used its fourth public meeting, held in May 2007, to present the concept of exposure scoring for feed contaminants, which will be used as part of the risk-ranking method the team is developing.

The risk-ranking approach is explained in the AFSS team's Framework Document, first drafted in 2005 and revised in December 2006. The Framework presents the directions and goals of the AFSS.

One of the gaps identified in the Framework is the lack of a comprehensive animal feed safety program in the United States. The Food and Drug Administration is addressing that gap by writing process control regulations covering the procurement, receipt, manufacture, and distribution of all animal feed, including pet food, and all ingredients.

The Framework also calls for FDA to develop a risk-based approach to feed safety, which is why the team is developing the risk-ranking method for feed contaminants. The risk-ranking method takes into consideration physical, chemical, and microbiological contaminants. FDA will use the risk-ranking method to help prioritize the use of resources to address the hazards presenting the greatest risk to public and animal health.

The team used the previous public meeting, held September 2006, to identify the hazards of concern (feed contaminants) and to present the concept of health consequence scoring, which considers the likelihood of adverse effects if animals are exposed to a contaminant in feed. The health consequence scores, combined with the results of the exposure scoring, will be used as a method to rank the various risks from feed contaminants.

At the May 22 meeting, the AFSS team used the production of swine diets—nursery, grower, and finisher—to explain how exposure scoring would work. In their presentations, the team

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Recent Pet Food Recall Extremely Complex

by Walt D. Osborne, M.S., J.D., Assistant Editor, and Jon F. Scheid, Editor

The recall of pet food contaminated with melamine and other compounds was one of the most complex recalls FDA has ever dealt with, and it showed how complex our food (including pet food) distribution system is and how interconnected it is with the world market.

Contaminated product sold by just two companies in China ultimately led to a recall of more than 1,000 pet food products, including 200 brands and millions of packages of individual servings.

However, the recall also showed just how quickly and effectively FDA could mobilize in this kind of situation, allocating a significant amount of resources to find the cause of the problem and get information to the consumer.

The problem

On March 15, 2007, Menu Foods, Inc., of Streetsville, Ontario, Canada, notified FDA of a problem involving its dog and cat foods, and the following day the firm initiated a voluntary recall.

Menu Foods is a private label pet food manufacturer that produces pet food products that are sold to consumers by different retail companies. Initially, the recall involved about 60 million packages of dog and cat foods sold by nearly 100

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

...Public Meeting on Risk Ranking *(Continued)*

members discussed the types and levels of contaminants that might be found in the feed ingredients and the complete swine feeds, and explained that feed processing must be considered in determining exposure scoring, because processing could either enhance or mitigate some of the risks from the contaminants.

For the examples presented, the AFSS team members used whatever data were available, but where no data existed they used expert opinions. The AFSS team said it hoped members of the feed industry and other experts would work with CVM to add data on contaminants, especially about the effects of feed processing on the hazards.

Melamine issue demonstrated importance of AFSS

Dr. Dan McChesney, Director of CVM's Office of Surveillance and Compliance, opened the May 22 meeting by describing how the recall of pet food contaminated with melamine had "altered the landscape" of feed (including pet food) safety.

Because of the recall, "animal feed safety" had become a household expression, he said. The recall generated news stories for several weeks following the initial recall announcement in mid-March. It also brought millions of individuals to FDA's pet food recall page on the Web site. Thousands of consumers called FDA offices across the country. The recall also generated interest in Congress, and the Senate passed a bill addressing pet food safety issues, Dr. McChesney said.

This amount of attention to the issue drove home the fact that AFSS is needed, Dr. McChesney said.

He also pointed out that the melamine-contaminated pet food recall, while significant and possibly the largest pet food recall ever, was not the only feed recall. In fact, 33 firms had initiated 118 recalls in fiscal year 2006, he said. For 2007, by the time of the May 22 AFSS meeting, 15 firms had initiated 23 recalls, he said.

Future meeting

The AFSS team will continue to review comments from the May 22 meeting, but is also planning another public meeting for early in calendar year 2008. That meeting is tentatively scheduled for February. That meeting, and possibly other future meetings, will be used to discuss how the risk-ranking method will combine health consequence and exposure scores to rank risks.

Meanwhile, the AFSS docket remains open for comments. Comments should be sent to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Electronic comments may be submitted to *http://www.fda.gov/dockets/ecomments*.

Comments should be labeled with Docket Number 2003N-0312.

The transcript, list of attendees, and presentations from the May 22 meeting are available on CVM's Web site, at *http://www.fda.gov/cvm/AFSS.htm*.

Recent Pet Food Recall Extremely Complex *(Continued)*

companies. The products were produced at Menu's facilities in Emporia, KS, and Pennsauken, NJ, between December 3, 2006, and March 6, 2007. The recalled products were moist (packaged in pouches) and canned foods described as "cuts and gravy" style pet foods.

Menu initiated the recall after receiving complaints from a company that sold products manufactured by Menu and after the death of some animals that made up a palatability panel, which pet food companies, such as Menu, use to make sure pet food is palatable after the company has made a change in the formulation. The company suspected the problem could be related to wheat gluten used to make the food, because the only change in the production of the pet food was a change in the supplier of the wheat gluten. The wheat gluten had been imported by ChemNutra, Las Vegas, NV, from China.

Wheat gluten is a mixture of two proteins obtained when wheat flour is washed to remove the starch. One use of wheat gluten is as a filler and binder in wet-style, cuts-and-gravy-type pet food. It provides a gelatinous consistency and is used to thicken pet food gravy.

On March 30, FDA announced that its labs had discovered melamine in product labeled wheat gluten that was used in pet food. Additionally, Cornell University scientists had found melamine in the urine and kidneys of deceased cats that were part of a taste testing study conducted for Menu Foods. The association between melamine in the kidneys and urine of cats that had died and in the food they ate was undeniable. And even though the health effects of melamine had not been fully documented, the fact that the pet food contained melamine was enough for FDA to take action. The presence of the contaminant, an unapproved food additive, caused the pet food to be adulterated.

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FDA VETERINARIAN

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Recent Pet Food Recall Extremely Complex *(Continued)*

Melamine is used in plastics, glue, fire retardants, and other products. Melamine is not approved by FDA for any food uses. Although it is used in some parts of the world as a fertilizer, it is not registered for such use in the United States. Published research regarding melamine and any effect on the health of cats and dogs is scarce.

In April, the melamine problem grew. On April 15, importer Wilbur Ellis, Co., San Francisco, CA, told FDA that a product it called rice protein concentrate, imported from China, was contaminated with melamine. The company began a recall of 155 metric tons on April 18.

FDA has so far identified two Chinese suppliers as the source of melamine-contaminated products: Xuzhou Anying Biologic Technology Development Co., Ltd., which supplied the contaminated wheat gluten; and Binzhou Futian Biology Technology Co., Ltd., which supplied the contaminated rice protein concentrate.

Food safety

Some of the potentially contaminated pet food scraps, which is waste material from the pet food manufacturing process, was fed to pigs and chickens. The material was used on hog farms in 8 States, at 30 broiler farms, and at 8 breeder poultry farms.

Also, in May, FDA discovered as part of its investigation that contaminated wheat gluten products were used to manufacture fish feed in Canada, and some of that feed was shipped to the United States and fed at fish hatcheries.

The U.S. Department of Agriculture joined FDA in conducting a human food safety risk assessment to determine whether these animals should be kept out of the food supply. The assessment found that any melamine or related compounds fed to animals would be diluted to such an extent in any food taken from the animals that it would not create a human health concern.

The assessment found that, if a person ate only food containing melamine and the related compounds, including cyanuric acid, at levels that were found in meat, exposure would still be 250 times less than what is considered a safe level.

Put another way, a 132-lb. person would have to eat 800 lbs. of pork or chicken per day containing melamine or related compounds to reach an exposure level that would create a human health concern.

FDA working diligently

FDA recognizes that pets are important to the American people, and the agency dedicated significant staff to determining the exact cause of the contamination and to resolving the problem. These efforts included:

- Ensuring that all contaminated product was identified and that retailers removed it from distribution. This effort was FDA's first priority. All the contaminated wheat gluten and rice protein has been traced, and all the pet food manufacturers that had received contaminated ingredients have been identified and have initiated recalls.
- Dedicating each of its 20 district offices to this investigation.
- Assigning more than 400 employees to collect pet food samples, monitor the recall's effectiveness, take consumer complaints, and prepare consumer complaint reports.
- Determining the cause. Veterinarians, toxicologists, pathologists, chemists, and other specialists from CVM and other parts of the agency were involved in researching potential causative agents and analyzing information.
- Working with its regulatory partners in all 50 State agriculture and health agencies to inform them of the status of the investigative and analytical efforts.

FDA and CVM used their Web sites to give consumers the sometimes complex information about the recall in the most straightforward way possible. The information about the pet foods that were recalled was presented in a

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Advice to Pet Owners

Although the recalled pet food should no longer be available, consumers can check the Food and Drug Administration's Web site *(http://www.fda.gov/oc/opacom/hottopics/petfood.html)* to make sure the products they have are not part of the recall.

Listed products should not be fed to animals. Any pet food products not listed can safely be used.

However, should a pet exhibit a sudden onset of symptoms, such as loss of appetite, lethargy, or vomiting, pet owners should stop feeding the pet food and contact a veterinarian.

Any consumers who have any pet foods covered by the recall are advised to return them to the store where purchased and request a refund. In addition, any products affected by the recall should be stored in a secure place—out of reach from children and pets—until the products can be returned.

If a pet owner has fed a recalled product to a dog or cat, the pet should be closely monitored for the signs of illness already mentioned, which would most likely show up within a couple of days of feeding. If renal failure is diagnosed by a veterinarian, pet owners should hold onto the pet food if the brand and lot number are covered by the recall.

Pet owners need to understand that, though there may be financial costs associated with any veterinarian visit, reimbursement for such care does not fall within the agency's regulatory authority.

Recent Pet Food Recall Extremely Complex *(Continued)*

database that consumers could search by species, specific product, packaging, the "best before" dates, size, and product code. FDA also posted all press releases, whether from the pet food companies or from the government agencies, on its Web site.

Several components of FDA, including CVM, worked together to develop and validate analytical methods, which were then posted on CVM's Web site so companies and independent laboratories could conduct their own screening of feed ingredients for melamine and related compounds.

Protecting human health

As a precaution, to make sure melamine was not causing human health problems, FDA asked the Centers for Disease Control and Prevention (CDC) to utilize its surveillance network to monitor for signs of human illness related to the recalled pet food. FDA also initiated an assignment to look at similar ingredients that are used in human food. To date, CDC surveillance has not shown an increase in renal failures in humans, which is the most likely health outcome that would be expected from exposure to wheat gluten contaminated with melamine.

In addition to working with CDC and Cornell University, CVM is receiving reports and data from Banfield Pet Hospital about animals treated for possible ingestion of the affected pet food products. FDA also exchanged information with the American Veterinary Medical Association in order to ensure that it is providing accurate information to its members on how to report adverse events to the agency, and worked with the Veterinary Information Network, and the American Association of Veterinary Laboratory Diagnosticians. In addition, companies that sell pet food have been helpful.

FDA's Regulation of Pet Food

Under the Federal Food, Drug, and Cosmetic Act, pet foods, like human foods, must be pure and wholesome, safe to eat, produced under sanitary conditions, contain no harmful substances, and be truthfully labeled. In addition, canned pet foods must be processed in conformity with the low-acid canned food regulations (21 CFR Part 113) to ensure the pet food is free of viable microorganisms.

With respect to pet food labeling, FDA regulations require proper identification of the product, net quantity statement, name and place of business of the manufacturer or distributor, and a proper listing of all the ingredients in order from most to least, based on weight. Most States also enforce their own labeling regulations, many of which are based on a model provided by the Association of American Feed Control Officials (AAFCO). The Model Bill is included in AAFCO's Official Publication, available in some libraries and available for purchase from AAFCO. (Web site: *http://www.aafco.org*).

AAFCO has posted online a set of questions and answers concerning the regulation of pet foods. It is available at *http://www.aafco.org/Portals/0/Public/Q-AND-A-REGARDING-PETFOODREGS.PDF*.

For more information and filing adverse reaction report

All of the information available for public release was posted to the FDA Web site (*http://www.fda.gov/oc/opacom/hottopics/petfood.html*) and CVM Web site (*http://www.fda.gov/cvm/default.html*).

Consumers and veterinarians who wish to report adverse reactions or other problems can go to FDA's Internet page at *http://www.fda.gov/opacom/backgrounders/complain.html* to obtain contact information for the FDA complaint coordinator in their State, as well as obtain information on what kind of information should be included in such a report. This Web site is also a good point of contact for veterinarians who have case files and post-mortem results related to cases where renal failure is involved and the animal owners were feeding food covered by the recall. ■

U.S. Ingredient Supplier Used Melamine

In a development unrelated to the pet food recall, a feed ingredient supplier that sells binding agents used to make pelleted feed products told the Food and Drug Administration in May that the company had been using melamine, but has since stopped.

FDA reported on May 30 that Tembec BTLSR Inc., Toledo, OH, said it was using melamine to make two aquaculture products, AquaBond and Aqua-Tec II, which Tembec distributed for a second company, Uniscope, Inc., Johnstown, CO.

Uniscope also made a pellet binding ingredient, Xtra-Bond, using ingredients from Tempec that contained melamine.

FDA has advised feed manufacturers to recall finished feed made with AquaBond or Aqua-Tec II, due to the estimated levels of melamine and related compounds in the finished products.

Initial information has led FDA to believe that a recall is not needed for finished feed made with Xtra-Bond, because of the estimated low melamine level in the finished feed. However, as more information is obtained, there may be specific products or circumstances that could require a recall.

Food derived from animals fed these products is unlikely to pose a human health risk, FDA concluded, based on the interim risk assessment FDA and the U.S. Department of Agriculture conducted earlier in May.

On-Line Internet Sales of Animal Drugs: Good or Bad?

by Walt D. Osborne, M.S., J.D., Assistant Editor

No one would disagree that the Internet has changed our lives in countless ways. For many of us, it has become our primary means of research, communication, learning the news, and even shopping. What could be easier than the press of button to bring the world to our fingertips? Through secure Web sites, we freely offer up our e-mail address, personal information, and even our credit card numbers to make a purchase. Clearly, the Internet has become for many Americans the fastest, easiest, and most convenient way to shop, eliminating the need to get in a car, fight traffic, find a parking place, and sift through racks of merchandise only to find the product you want is out of stock.

Purchasing medications on line has become extremely popular in recent years. But along with the convenience, the anonymity, and the ability to shop in the privacy of our own home comes the need for care and attention to the pitfalls of on-line shopping, especially for something that affects our—or our pet's—health. Purchasing approved drugs online through legitimate pharmacy sites on the Internet provides consumers with a convenient way to obtain needed medications for Fido, Fifie, and Flopsy, sometimes at more affordable prices. Many reputable Internet pharmacies allow pet owners to consult with a licensed pharmacist from the privacy of their home, and some of these pharmacies can provide customers with written product information.

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FDA Letter Reminds Feed Manufacturers of Their Obligations

by Walt D. Osborne, M.S., J.D., Assistant Editor

The extensive recall of pet foods that began in March 2007 due to contamination with melamine and its analogs led to the issuance of a letter in May 2007 from CVM Director, Dr. Stephen Sundlof, to feed and feed ingredient manufacturers reminding them of their legal responsibilities.

Specifically, every ingredient used in an animal feed or feed ingredient must be safe for its intended use, whether the product is meant to be used to feed animals intended for human consumption or to feed non-food animals, such as pets. In the letter, manufacturers were encouraged to make sure they have procedures in place that ensure the safety of the products and ingredients in their products, as well as the safety of the packaging and processing supplies they use. In addition, manufacturers should also verify that their suppliers have such procedures in place. Guidance on these requirements is available at *www.cfsan.fda.gov/~dms/alert.html*.

As the letter noted, manufacturers are responsible for taking their own measures to ensure the safety of their marketed products. They should not wait for possible FDA testing of their materials before pursuing the necessary steps to achieve a high level of safety.

Screening procedure

Companies that are interested in performing their own tests for melamine and its analogs can refer to FDA's Web site at *www.fda.gov/cvm/GCMSMelamine.htm*. The methodology used by the Food Emergency Response Network laboratories can be found there. As indicated at the link, this version (2.1, dated May 16, 2007) of the gas chromatography (GC) and mass spectrometry (MS) method for the presence of melamine, ammeline, ammelide, and cyanuric acid should be regarded as interim. This procedure was developed to screen various matrices for the presence of melamine and some related compounds at the established minimum reporting level of 10 micrograms per gram and above, using GC/MS. Samples are extracted using a mixture of acetonitrile/water/diethylamine, and the analytes are subsequently converted to trimethylsilyl derivatives for analysis.

Surveillance

As part of a protein ingredient surveillance assignment FDA issued on May 1, 2007, FDA, in conjunction with State regulatory authorities, has been performing inspections of various food and feed facilities. A variety of protein ingredients commonly used in food and feed manufacturing have been sampled and tested for the presence of melamine and melamine-related compounds, all of which are known as triazines. Protein concentrates such as wheat gluten, corn gluten, corn meal, soy protein, and rice protein concentrate imported from China or transshipped from China will be tested. During these inspections, FDA will point out the importance of ensuring the safety and security of the manufacturers' ingredients and products by knowing their manufacturing and packaging operators, ingredient suppliers, contract manufacturers, and sources for all incoming materials.

On-Line Internet Sales of Animal Drugs… *(Continued)*

Valid prescription required

However, a number of problems with some Internet pharmacies have been reported, such as sales of veterinary prescription medications without valid prescriptions; such sales are illegal and violate Section 512 of the Federal Food, Drug, and Cosmetic Act (FFDCA), as well as 21 Code of Federal Regulations Section 530. These Federal sanctions require that a licensed veterinarian authorize a prescription only pursuant to a "valid veterinarian-client-patient relationship." More importantly, animal drugs sold without a valid prescription could pose a health threat to pets and other animals. Unfortunately, the Internet makes it easy for unscrupulous people to sell human and animal drugs to consumers without Federal safeguards in place. A Web site may appear to be associated with a legitimate pharmacy, when in fact it is not. Web sites that sell prescription drugs without a valid prescription deny pet owners the protection provided by an examination conducted by a licensed veterinarian.

The National Association of Boards of Pharmacy *(www.nabp.net)* has identified approximately 200 domestic Web sites that dispense prescription drugs but do not offer an online prescribing service whereby a prescription would first have to be mailed or FAXed. However, many of the Web sites that do offer both prescription drugs and a prescribing service are located in foreign countries (e.g., Namibia, Sri Lanka, and Thailand), and these pose a major problem for the Food and Drug Administration because it is so hard for the agency to control these overseas operations. Such "rogue" Internet sites think nothing of using deceptive practices to lure purchasers, and they can literally be in business today, close down tomorrow, and reopen the next day in a new location.

So, how does a pet owner identify a quality, legitimate Internet pharmacy? Admittedly, there really is no fool-proof way to ensure such an operation. But the National Association of Boards of Pharmacy has created a voluntary pharmacy certification program called VIPPS (Verified Internet Pharmacy Practice Sites) to help consumers evaluate Internet pharmacies. The VIPPS seal of approval identifies those online pharmacies that are appropriately licensed and prepared to practice pharmacy via the Internet, and that have successfully completed a rigorous criteria review and inspection. Pet owners who experience problems with any online pharmacy should report the pharmacy to the Board of Pharmacy in their home State as well as the pharmacy's State, if it is different. Naturally, any adverse reactions suffered by a pet or other animal should be reported to either the veterinary drug sponsor or FDA (1-888-FDA-VETS).

…the National Association of Boards of Pharmacy has created a voluntary pharmacy certification program called VIPPS (Verified Internet Pharmacy Practice Sites) to help consumers evaluate Internet pharmacies.

On-going Federal efforts

FDA works closely with the States to determine the validity of online prescriptions and to bring enforcement actions under State law, Federal law, or both, as appropriate. FDA has worked with trade associations and the Association of Attorneys General to establish points of contact in all of the States specifically for Internet-related problems. Several States have taken or are thinking about taking action against illegitimate online sellers of prescription drugs. Fourteen States (Arizona, California, Colorado, Connecticut, Illinois, Michigan, Kansas, Nevada, New Jersey, Ohio, Texas, Washington, Wisconsin, and Wyoming) have already taken some action against physicians prescribing drugs over the Internet. Most of these cases involve cease and desist orders, but some States have imposed fines and are contemplating stiffer penalties.

Foreign pharmacies

Pet owners and all consumers need to understand that it is illegal for anyone, including a foreign pharmacy, to ship drugs that are not approved by FDA into the United States, even though the drug may be legal to sell in that pharmacy's country. The FFDCA requires all drugs—including animal drugs—to be proven safe and effective before marketing in this country. U.S. law also requires that products approved for sale in the United States have their formulation approved by FDA, be made in a plant that is registered with FDA, and be produced under quality standards enforced by FDA.

The following categories of products cannot be legally sold in the United States:

- prescription drugs available from a foreign pharmacy that are products not approved by FDA;
- products with similar, but not identical formulations as FDA-approved products;
- products not made under the quality standards required by U.S. law or labeled according to U.S. requirements; and
- products not stored or distributed under the quality conditions required in the United States.

Reporting unlawful sales on the internet

Consumers who believe they have encountered a Web site that is illegally

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New Drug To Treat Heart Failure in Dogs Gets OK

by Walt D. Osborne, M.S., J.D., Assistant Editor

On May 16, 2007, the Food and Drug Administration announced the approval of the first drug to treat congestive heart failure in dogs in over 10 years. The product, Vetmedin® (pimobendan), is approved for managing the signs of mild, moderate, or severe (modified New York Heart Association [NYHA] Class II, III, or IV) congestive heart failure in dogs due to atrioventricular valvular insufficiency or dilated cardiomyopathy. Vetmedin® is indicated for use with concurrent therapy for congestive heart failure as appropriate on a case-by-case basis. The drug, which is sold by veterinary prescription in tablet form, helps alleviate the signs of heart failure by increasing contractility (the force of heart muscle contraction) and by dilating blood vessels (decreasing resistance to blood flow).

Veterinarians classify congestive heart failure according to clinical signs. Class II is mild (fatigue, shortness of breath, and coughing) and is apparent when ordinary exercise is exceeded. Class III is moderate (comfortable at rest, but exercise capacity is minimal). Class IV is severe (no capacity for exercise, and disabling clinical signs are present, even while at rest).

The product, Vetmedin® (pimobendan), is approved for managing the signs of mild, moderate, or severe (modified New York Heart Association [NYHA] Class II, III, or IV) congestive heart failure in dogs due to atrioventricular valvular insufficiency or dilated cardiomyopathy.

The safety and effectiveness of Vetmedin® were evaluated in a 56-day, multi-site, active controlled field study with pivotal success determined at day 29. A total of 355 dogs with modified NYHA Class II, III, or IV congestive heart failure due to atrioventricular valvular insufficiency or dilated cardiomyopathy were randomly assigned to either the Vetmedin® treatment group or the active control, Enacard® (enlapril maleate) treatment group. Treatment success in the first group (80.7 percent) was determined to be non-inferior to the treatment success in the second group (76.1 percent).

Vetmedin® is made by MEDA Manufacturing GmbH, Cologne, Germany, for Boehringer Ingelheim Vetmedica, Inc., of St. Joseph, MO.

Adverse reactions associated with Vetmedin® (and Enacard®) were potentially related to congestive heart failure, the therapy of congestive heart failure, or both, and included poor appetite, lethargy, diarrhea, worsening signs of heart failure, heart failure death, increase in the blood urea nitrogen (azotemia), and mild increases in serum liver enzymes.

FDA's Center for Veterinary Medicine cautions that pimobendan is not intended for use in cats and is only for use in dogs that are diagnosed as explained above. Vetmedin® acts to alleviate the clinical signs of congestive heart failure, rather than to reverse the underlying cardiac pathology. It does not replace the need for other appropriate concurrent heart failure therapy, which includes the use of diuretics and anti-arrhythmic drugs. ■

On-Line Internet Sales of Animal Drugs … *(Continued)*

selling any medical products over the World Wide Web are encouraged to select one of the three options below to report to FDA.

If the report:

- involves a life-threatening situation due to an FDA-regulated product you purchased from a Web site, call 301-443-1240 immediately. (Also contact your health professional/veterinarian for medical advice.)
- involves a serious reaction or problem with an FDA-regulated product, fill out FDA's MedWatch reporting form (*https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm*). (Also contact your health professional/veterinarian for medical advice.)
- involves a problem Web site that does not involve a life-threatening or otherwise serious reaction, fill out the online form located on FDA's Web site at *http://www.fda.gov/oc/buyonline/buyonlineform.htm*. To report e-mails promoting medical products that you think might be illegal, forward the email to webcomplaints@ora.fda.gov.

Caution always urged

The agency cautions pet owners who want to buy their pet's medication over the Internet to proceed cautiously, to talk with their veterinarian, and to insist on the same quality expected from a veterinary clinic or pharmacy. Fido, Fifie, and Flopsy deserve nothing less. ■

CVM Hopes to Keep Pergolide Available for Treating Horses

by Walt D. Osborne, M.S., J.D., Assistant Editor

Peroglide is a drug that was approved for use in humans and was used in an extralabel manner by veterinarians to treat Cushing's syndrome in horses. The Food and Drug Administration is working with sponsors of approved pergolide products and all other interested parties to ensure that the drug remains available to treat Cushing's syndrome in horses until a new animal drug application is approved.

On March 29, 2007, FDA issued a Public Health Advisory detailing the removal of pergolide (brand name, Permax) products from the market by its manufacturer, Valeant Pharmaceuticals; makers of the generic equivalents—Par Pharmaceutical and Teva Pharmaceuticals—also removed their products from the market. Concerns about cardiac side effects in humans (including heart valve damage) led to this action by the firms. Pergolide, a dopamine agonist, had been approved for managing the signs and symptoms of Parkinson's disease in humans.

FDA is aware that veterinarians prescribe pergolide in an extralabel manner to treat Cushing's syndrome in horses. The syndrome usually affects horses in their mid- to late-years of life. Diagnosis is made by a veterinarian using a combination of clinical findings and diagnostic testing. Signs of the equine disease include excessive water-drinking and urination, abnormal hair growth and shedding, pot belly, general malaise, increased appetite and resultant weight gain, chronic laminitis, and a compromised immune system (which can lead to respiratory ailments, skin infections, hoof abscesses, ulcers, and gum disease).

Because of the severity of this disease in horses and the large population of horses affected by the syndrome, FDA is doing what it can to keep the drug available for use in horses. This effort includes trying to make the approved human product available through veterinary distribution channels and exercising enforcement discretion as appropriate with respect to pharmacy compounding of pergolide when done in response to a veterinarian's prescription. Bulk substance used for pharmacy compounding should be labeled "for animal use only," and all pharmacy compounding must be done under a valid veterinary prescription to treat an affected horse. Even though the sponsors of the human drug have stopped marketing pergolide for human use, CVM is working with drug sponsors who are interested in seeking approval of a new animal drug application to treat Cushing's syndrome in horses.

FDA Removes Hydrogen Peroxide From Low-Regulatory Priority List

When the Food and Drug Administration approved 35% PEROX-AID® earlier this year, it removed hydrogen peroxide from a list of "Low Regulatory Priority Aquaculture Drugs." This change means that only the approved product may be legally used, and if an aquaculture producer continues to use any hydrogen peroxide other than the approved product, that use could now result in a citation from an FDA investigator.

FDA maintains a low-regulatory priority list of products that can be used by the aquaculture industry for specified indications without drawing a regulatory enforcement response from FDA.

The list, available at *http://www.fda.gov/cvm/Documents/LRPDrugs.pdf*, is part of the Center for Veterinary Medicine's Policies and Procedures Manual. FDA has reviewed the products and indications on the list and decided that the agency is unlikely to object to the use of these compounds for the indications and levels listed if the compounds are used according to good management practices. Also, producers must be sure the low-regulatory priority products they use are suitable for use in food-producing animals, and that the use is not likely to harm the environment. This list does not affirm the safety or efficacy of these compounds.

FDA had hydrogen peroxide on the low regulatory priority list for controlling fungi on all species and life stages of fish, including eggs.

However, following the approval of 35% PEROX-AID®, aquaculture producers should not use other hydrogen peroxide products. The approved product has undergone FDA review and was found to be safe and effective when used according to label directions.

35% PEROX-AID® was approved for control of mortality in freshwater-reared finfish eggs, due to saprolegniasis; freshwater-reared salmonids, due to bacterial gill disease associated with *Flavobacterium branchiophilum*; and freshwater-reared coolwater finfish and channel catfish, due to external columnaris disease associated with *Flavobacterium columnare (Flexibacter columnaris)*. The sponsor is Eka Chemicals, Inc., Marietta, GA.

FDA's Recall Authority Is Important Arrow in Agency's Enforcement Quiver

by Walt D. Osborne, M.S., J.D.

"Recall" is defined in the Food and Drug Administration's regulations as a firm's removal or correction of a marketed product that the agency considers to be in violation of the laws it administers and against which the agency would initiate legal action, e.g., seizure.[1] There are a few specific exceptions (for products for human use), but for the most part, the enforcement tool of recall for animal products actually amounts to this voluntary action by the product-maker.

The teeth of a recall are revealed in the legal sanctions in place, should a firm not initiate a recall. In such instances, FDA can initiate a court action for removing or correcting violative, distributed products as part of its mandate to protect public health. Typically, these actions take the form of a seizure, which is a judicial civil action against an animal feed, drug, or device in violation of the adulteration and/or misbranding provisions of the FFDCA. The purpose of this action is to remove the offending product or products from the channels of commerce. However, the effect of a seizure can be somewhat limited, in that a separate action is needed for each place where the product is located. The product is in essence "arrested" by means of a Complaint filed in the appropriate U.S. District Court. The Court then orders the U.S. Marshal to seize the goods in question. Seizure, multiple seizure, or other court action is also indicated when FDA has reason to believe that a recall would not be effective, determines that a recall is ineffective, or discovers that a violation is continuing.[2]

On the other hand, with a recall, a firm can retrieve all of the dangerous or illegal products by means of just one action.

FDA has attributed three different categories to product recalls to indicate the relative degree of health hazard posed by the product being recalled:

- Class I involves a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death;
- Class II involves a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote; and
- Class III involves a situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.[3]

FDA determines the recall classification based on an evaluation of the health hazard presented by a product being recalled or considered for recall. This evaluation is carried out by an ad hoc committee of FDA scientists and takes into account the following factors: (1) whether any disease or injuries have already occurred from use of the products; (2) whether any existing conditions could contribute to a clinical situation that could expose humans or animals to a health hazard; and (3) assessment of the hazard to various segments of the population, the severity of the risk to that population, the likelihood or occurrence of the hazard, and the consequences (immediate or long-range) of occurrence of the hazard.[4] If, based on this health hazard evaluation (HHE), the decision is made that the recall should be a Class I, the agency will advise the firm that a press release should be issued; the agency will work with the firm to devise this press release. If the firm refuses to issue one, FDA will prepare a press release for it. But it is always in the firm's best interest to prepare its own release so that it can apply the preferred message about the story being announced. In contrast, Class II and Class III recalls rarely are the subject of a press release, but all recalls are listed in the weekly "FDA Enforcement Report."[5]

Actual examples of Class I recall classifications of veterinary products during Fiscal Year 2006 included animal feeds that contained monensin, excessive salt in chicken feed, and aflatoxin in various pet foods. These recalls were classified as Class I because they all involved animal deaths. Examples of Class II recalls from the FDA Enforcement Report included excessive levels of Vitamin D3 in pet foods, possible metal tags in dog food, and enamel can lining flaking off into pet food. And lastly, examples of Class III recalls included such labeling violations as absent directions-for-use labeling on bulk animal feed, and animal food products in circulation beyond the expiration date.[6]

(Fiscal Year 2007 saw a huge recall of millions of individual servings of pet food manufactured by Menu Foods, Streetsville, Ontario, Canada. See the article, "Recent Pet Food Recall Extremely Complex," on page 1.)

For both a firm-initiated recall and an agency one, a recall strategy must be put together.[7] In addition to including the results of the HHE, the strategy must include the depth of the recall, i.e., the level in the distribution chain to which the recall is to extend:

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FDA's Recall Authority . . . *(Continued)*

the consumer level, the retail level, or the wholesale level. In addition, the recall strategy plan may need to include a public warning (usually in the form of a press release), which is used to alert the public that a product being recalled presents a serious health hazard. These warnings are primarily reserved for urgent situations where other means for preventing use of the recalled product appear inadequate. Ordinarily, FDA issues these, following consultation with the recalling firm. In those situations where the firm decides to issue the warning, FDA will request the opportunity to review and comment on the warning.

Lastly, the recall strategy plan must specify the method or methods to be used and the level of effectiveness checks that are to be conducted by the firm in order to verify that all consignees at the recall depth specified by the strategy have received notification of the recall and have taken appropriate action. There are five levels of effectiveness and audit checks as follows:

- Level A = 100% of the total number of consignees to be contacted;
- Level B = greater than 10% but less than 100% of the consignees;
- Level C = 10% of the total number of consignees;
- Level D = 2% of the total; and
- Level E = no effectiveness checks needed.

An example of this last category would be a recalled food that is no longer on store shelves, such as bagged salad that is 2 weeks past its expiration date.

In Fiscal Year 2006, the Center for Veterinary Medicine was involved in a total of 136 recalls; 40 of these involved violations of the ruminant-to-ruminant feed ban to curtail the transmission of bovine spongiform encephalopathy. Since Fiscal year 1999, CVM has averaged 219 recalls per year.

Conclusion

FDA plays an important public health role by assessing the net benefits and risks of the products it regulates. FDA acts only for the public well-being. When the agency determines that a recall is necessary, it is acting in the best interests of the public. A company has a moral obligation to comply, and most act quickly to protect public and animal health, as well as the reputation of their product. While perhaps not 100 percent effective, product recall continues to play a pivotal role in the effective removal of products that pose a danger to public health or violate the laws that FDA administers. As we have seen, it is but one of FDA's several arrows contained in its enforcement quiver to carry out its public health protection mandate.

Footnotes:

[1] 21 C.F.R. 7.3 (g).

[2] 21 C.F.R. 7.40 (c)

[3] Investigations Operations Manual 2006, FDA.

[4] 21 C.F.R. 7.41 (a).

[5] 21 C.F.R. 7.50.

[6] Fiscal Year 2006 Annual Report, Center for Veterinary Medicine.

[7] 21 C.F.R. 7.42 (b).

Infant Death Demonstrates *Salmonella* Risk From Turtles

The death of a 4-week-old infant in Florida earlier this year demonstrated the risk of salmonellosis from baby turtles.

Scientists were able to match the strain of bacteria that made the infant sick with the strain found in a baby turtle in the house in which the infant had lived. Scientists were able to "fingerprint" the *Salmonella*, and they identified it as *Salmonella* pomona.

The Food and Drug Administration banned the sale of baby turtles, except for certain educational purposes, in the 1970s as a means to prevent children from becoming ill with salmonellosis. The prohibition applies to turtles with shells (carapace) of 4 in. or less. These turtles were often given to children for pets and are small enough so that children often handle them or put them in their mouths, which is how *Salmonella* transfers from the turtles to children.

Baby turtles are a natural source of *Salmonella*, which are a group of bacteria that can cause salmonellosis. *Salmonella* are often found on the shell or skin of the turtles.

The symptoms of salmonellosis include diarrhea, stomach pain, nausea, vomiting, fever, and headache.

Not only infants, but also children, the elderly, and anyone with a lowered resistance to disease (due to pregnancy, cancer, chemotherapy, organ transplant, diabetes, liver problems, or other problems) are at risk of serious disease and even death from salmonellosis.

FDA is reminding consumers not to purchase small turtles as pets. Consumers should thoroughly wash their hands after handling any turtle.

International Activities

Chinese Food Safety, Trade Representatives at CVM

On June 19 CVM hosted the training of 14 food safety and trade specialists from China as part of a 7-week program sponsored by the Joint Institute for Food Safety and Applied Nutrition (JIFSAN). This program is one of several efforts by the U.S. Government to train developing countries in sanitary and phytosanitary requirements as members of the World Trade Organization. The day-long series of presentations by CVM technical experts covered veterinary drug approval procedures and review criteria and food and feed safety controls. Here, the Chinese visitors are listening to a presentation about U.S. regulations designed to prevent the spread of bovine spongiform encephalopathy.

The presentations at CVM were also attended by representatives of the U.S. Department of Agriculture's Food Safety and Inspection Service and the National Pork Producers Council.

CVM Reminds Veterinarians to Correctly Use Flunixin Meglumine

The Center for Veterinary Medicine has investigated several cases of violative residue levels of flunixin meglumine in meat, and in May 2007 it issued a reminder to veterinarians about the proper use of the drug and the requirements veterinarians must meet to use the product in an extralabel manner.

CVM had received reports that flunixin meglumine was being prescribed and/or administered to cattle by an intramuscular route. However, the approved route of administration in cattle is restricted to intravenous administration. Using the drug intramuscularly is an extralabel use of the drug.

Flunixin Meglumine Injection is approved for use in cattle for the control of pyrexia associated with bovine respiratory disease and endotoxemia. It is also indicated for the control of inflammation in endotoxemia.

Intramuscular administration of flunixin meglumine can cause violative drug residues, because the drug takes longer to deplete with this route of administration than with intravenous injections.

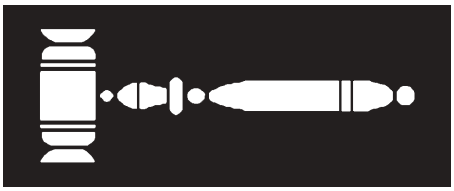
Under certain conditions, extralabel drug use is permitted under the Animal Medicinal Drug Use Clarification Act of 1994, which modified the Federal, Food, Drug, and Cosmetic Act.

Under the law, veterinarians are permitted to use drugs in an extralabel manner, meaning in ways not approved and specified on the label. But the veterinarian must meet certain requirements, including establishing a substantially long withdrawal period, supported by scientific evidence, so that any food from the animal will not contain violative drug residues. (A withdrawal period is the time between when an animal is administered a drug and when food products—meat, milk, eggs, or other edible products—can safely be obtained from the animal.)

Approved uses of drugs have specified withdrawal times. When drugs are used in an extralabel manner, the veterinarian takes on the responsibility of making sure the withdrawal period is adequate to prevent any violative residues in food products.

A veterinarian cannot legally prescribe the use of a drug in an extralabel fashion unless the use is required to avoid animal suffering or death. CVM has discovered, though, that veterinarians have been prescribing the use of flunixin meglumine intramuscularly simply for convenience. Under the law, that reason is not sufficient to permit extralabel use.

Regulatory Activities for April and May 2007



Warning Letters

A WARNING LETTER was issued to Leonard D. Hoekstra, president of Doon Elevator Company, Doon, IA, for significant deviations from the current Good Manufacturing Practice (cGMP) regulations for medicated feeds (21 CFR Part 225). The deviations caused the feeds being manufactured at this facility to be adulterated under Section 501(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA). FDA's investigation revealed the following: medicated feeds had been manufactured containing the combinations of chlortetracycline with carbadox and penicillin with carbadox, and neither of these combinations is approved; the production records are not adequate to facilitate a recall of specific batches of medicated feeds, if necessary; and deliveries of bulk medicated feeds were not adequately labeled to ensure the proper use of the feed (e.g., the labeling accompanying bulk medicated feeds did not contain feeding directions or the indications for use statement).

Residues of the drug, gentamicin, in the kidney tissues of two calves offered for sale as food led to the issuance of a WARNING LETTER to Manuel Carrizales of Hereford, TX. There is no tolerance for residues of this drug in the edible tissues of bovine animals (21CFR 556. 300) and, therefore, the animals were adulterated within the meaning of Section 402(a) of the FFDCA. In addition, Mr. Carrizales was cited for offering for slaughter as food another calf that contained the drug ivermectin in the liver and muscle tissue at concentrations of 0.114 parts per million (ppm) and 0.023 ppm, respectively. By regulation (21 CFR 556.344), the established tolerance for ivermectin in the edible tissue of cattle is 0.1 ppm in the liver and 0.01 ppm in the muscle. As a result, this animal was also deemed adulterated under Section 402(a) of the FFDCA.

Merle W. Young, Jr., owner of the Young View Farm, West Glover, VT, received a WARNING LETTER for offering animals for sale for slaughter as food that were adulterated under Section 402(a) of the FFDCA. Specifically, tissue sampling conducted by the U.S. Department of Agriculture (USDA) revealed the presence of 0.622 ppm of the drug, flunixin, in the liver tissue of one of the slaughtered cows. A tolerance of 0.125 ppm has been established in 21 CFR 556.286 for residues of this drug in the liver tissues of cattle. Tissues taken from a second cow that was offered for slaughter as food revealed the presence of 8.54 ppm of the drug neomycin in the kidney tissue. A tolerance of 7.2 ppm has been established for residues of this drug in kidney tissue of cattle (21 CFR 556.430). Mr. Young was also cited in the WARNING LETTER for using both drugs extralabel in violation of Section 512 of the FFDCA and of 21 CFR 530, in that the use was not by or on the lawful order of a licensed veterinarian within the context of a valid veterinarian/client/patient relationship.

A WARNING LETTER was issued to David Tucker Purchase, co-owner of Fairmont Dairy LLC of Craftsbury, VT, for marketing two animals for sale as food in violation of the adulteration provisions of Section 402(a) of the FFDCA. The investigation by FDA also revealed that the firm caused the new animal drugs penicillin G procaine and flunixin meglumine injection to be unsafe under Section 512(a) and adulterated within the meaning of section 501(a)(5) of the FFDCA. Specifically, a dairy cow offered for slaughter was found to have 0.22 ppm of penicillin in the kidney tissues. Pursuant to 21 CFR 556.510, a tolerance of 0.05 ppm has been established for residues of this drug in the edible tissues of cattle. A second dairy cow offered for slaughter was found to have 0.234 ppm of flunixin in the liver tissue. Pursuant to 21 CFR 556.286, a tolerance of 0.125 ppm has been established for residues of this drug in the liver of cattle. FDA also determined that the firm administered penicillin G procaine without following the dosage level and duration of treatment for cattle set forth in the approved labeling and it did so without the supervision of a licensed veterinarian, in violation of 21 CFR 530.11(a). In addition, the Fairmont Dairy administered flunixin meglumine without following the route of administration for beef and dairy cattle set forth in the approved labeling and did so without the supervision of a licensed veterinarian, in violation of 21 CFR 530.11(a). Furthermore, the dairy's extralabel use of these drugs resulted in illegal drug residues, in violation of 21 CFR 530.11(d). Because the extralabel use of these drugs was not in compliance with 21 CFR Part 530, the drugs were unsafe under Section 512(a) and were adulterated within the meaning of section 501(a)(5) of the FFDCA.

Similar violations were cited in a WARNING LETTER issued to Leonard M. Giglio, owner of Rockland Farm of Bolton, CT, for marketing a dairy cow for slaughter that was adulterated under section 402(a) of the FFDCA. Samples from the animal revealed the presence of residues of the new animal drug, gentamicin sulfate, in the kidney tissue. No tolerance has been established for residues of this drug in the uncooked edible tissues of cattle. The farm was also cited for lacking adequate recordkeeping systems and for not using gentamicin sulfate by or on the order of a licensed veterinarian within the context of a valid veterinarian/client/patient relationship. This violated Section 512(a) of the FFDCA and also 21 CFR 530.

Ferdinand M. Ritsema, owner of the Lakin Dairy of Lakin, KS, received a WARNING LETTER from FDA for violations of the safety and adulteration provisions of Sections 512 and 501(a), respectively, of the FFDCA. Specifically, Mr. Ritsema was cited for extralabel use of penicillin and sulfadimethoxine without following the parameters set forth in the Act. Penicillin was administered without following the dosage level, duration of treatment, and withdrawal period set forth in the approved labeling and without the supervision of a licensed veterinarian, in violation of 21 CFR 530.11(a). In addition, Mr. Ritsema administered

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Albon (sulfadimethoxine) to a dairy cow for a longer period of time than listed on the drug label. This cow was offered for sale for slaughter for human food. The prescription label the firm's veterinarian affixed to the penicillin that was used listed a 10- to 14-day withdrawal time, but Albon is labeled for treatment for 5 days with a 7-day withdrawal time. Company records indicated that the animal was withheld from slaughter for 1 day after stopping treatment with Albon and penicillin. Albon is prohibited from extralabel use in lactating dairy cattle under 21 CFR 530.41(9). In addition, a number of expired new animal drugs were observed by FDA investigators in the firm's storage room.

Violations of Sections 402(a), 512, and 501(a) of the FFDCA have been cited in a WARNING LETTER that FDA issued to the three co-owners of the Thiele Dairy in Clearwater, NE. Specifically, tissue samples collected from a dairy cow that was offered for slaughter revealed the presence of gentamicin in the kidney tissues, but no tolerance for this drug in the kidney tissues of cattle has been established in 21 CFR 556.300. Therefore, the animal was adulterated pursuant to Section 402(a) of the FFDCA. Adequate treatment records and drug inventory system were also found to be lacking. FDA investigators also found that the firm was using gentamicin extralabel without complying with Section 512(a) of the FFDCA. For example, the dairy administered gentamicin without following the veterinarian's written instructions for type of animal and for withdrawal time, and this was done without consulting the veterinarian, i.e., without the supervision of a licensed veterinarian, in violation of 21 CFR 530.11(a). Furthermore, the dairy's extralabel use resulted in an illegal drug residue, in violation of 21 CFR 530.11(c).

A WARNING LETTER was issued to Steve T. Kemp, owner of Kemp Cattle of Fort Worth, TX, for violation of Section 402(a) of the FFDCA. Specifically, the firm offered for slaughter as food a total of four calves that were found to be adulterated due to the presence of certain drugs. Tissue sampling by USDA revealed the presence in one calf of the drug penicillin at 0.45 ppm in the liver tissue and 0.11 ppm in the kidney. A tolerance of 0.05 ppm has been established in 21 CFR 556.510 for residues of this drug in the uncooked, edible tissues of cattle. Tissues samples taken from the other three calves revealed the presence of residues of the drug gentamicin in the liver and kidney of two and in the kidney of the third. There is no tolerance established for residues of this drug in the edible tissues of cattle.

Similar violations were cited in a WARNING LETTER issued to Leonard McDaniel, owner, doing business as L & M Cattle Co., of Dallas, TX. Specifically, Mr. McDaniel offered for slaughter as food three calves that were adulterated under Section 402(a) of the FFDCA because two of them contained residues of the drug gentamicin in the liver and kidney and the third calf contained gentamicin residues in the kidney tissue. As stated earlier, there is no tolerance established for residues of this drug in the edible tissues of bovine animals.

Gentamicin is also the subject of a WARNING LETTER issued to James R. Correa, D.V.M., owner of Bear Creek Veterinary Services of Merced, CA. Specifically, a USDA inspection of a dairy cow and an investigation by FDA revealed that the cow in question was raised at a farm but had been medicated; the farm used the veterinary services of Bear Creek Veterinary Services. The WARNING LETTER noted that the drug gentamicin had been prescribed extralabel for use to treat bacterial scours and septicemia in cattle, but gentamicin is not approved for this use in cattle. In addition, Dr. Correa prescribed penicillin G procaine for use at a dose exceeding the approved dosage of 1 cc per 100 lbs. The FDA investigation revealed that Dr. Correa failed to comply with Section 512(a) of the FFDCA and 21 CFR Part 530 by failing to do the following: make a careful diagnosis and evaluation of the conditions for which the drug is to be used; establish a substantially extended withdrawal period prior to marketing of milk, meat, eggs, or other edible products supported by appropriate scientific information; institute procedures to ensure that the identity of the treated animal(s) was carefully maintained; take appropriate measures to ensure that no illegal drug residues occurred in any food-producing animals subjected to the extralabel treatment; comply with the labeling requirements in 21 CFR 530.12(c) by not providing the route of administration for the drug and failing to correctly identify the animals to be treated; and establish a valid veterinarian-client-patient relationship, as set out in 21 CFR 530.3(i).

A WARNING LETTER was issued to Joe A. Sozinho and Kristy Heldman, partners of Clearview Dairy, LLC, in Jerome, ID, for offering for slaughter as food an animal that was adulterated pursuant to Section 402(a) of the FFDCA. Specifically, a USDA inspection of the slaughtered dairy cow revealed the presence of 17.91 ppm of sulfamethazine in the liver tissue and 21.22 ppm of the drug in the muscle tissue. A tolerance of 0.10 ppm has been established for negligible residues of sulfamethazine in the uncooked edible tissues of cattle, as codified in 21 CFR 556.670. In addition, the firm adulterated the new animal drug sulfadimethoxine (Albon) within the meaning of section 501(a)(5) of the Act when it failed to use the drug in conformance with its approved labeling; the drug was used extralabel but not by or on the lawful order of a licensed veterinarian within the context of a valid veterinarian/client/patient relationship as required by the FFDCA and by 21 CFR Part 530.

Daniel S. VanGrouw, owner of Dan VanGrouw Dairy, Meridian, ID, received a WARNING LETTER for offering for slaughter for food a dairy cow that was adulterated under Section 402(a) of the FFDCA. Specifically, USDA's inspection of the animal's tissues revealed the presence of sulfadimethoxine at 5.69 ppm in the muscle. A tolerance of 0.1 ppm has been established for residues of this drug in the edible tissues of cattle as codified in 21 CFR 556.640. FDA's investigation also found that the dairy held animals under conditions that are so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. The firm lacked

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an adequate system to ensure that medicated animals have been withheld from slaughter for appropriate periods of time to permit depletion of potentially hazardous residues of drugs from edible tissues, which was also a violation of Section 402(a) of the FFDCA.

Recalls

A firm-initiated Class I recall is ongoing by T.W. Enterprises, Inc., of Ferndale, WA, for 12,463 of its Beef Pizzle dog chews in a variety of sizes. The recall was begun because the product is contaminated with *Salmonella*. Distribution was carried out in California, Washington, Pennsylvania, Illinois, and Oregon.

A Class II recall is ongoing by Southern States Frederick Cooperative, Inc., of Frederick, MD, for 101 tons of a variety of animal feeds. The reason for the recall was that a liquid supplement was added to the feed products processed by a feed mill, and the ingredient was not declared on the labels of bulk and bagged feed. The supplement is not intended for use in some animals. Distribution was limited to Maryland.

A Class II recall of 50 50-lb. bags of Excel-R-Ate L Mixer Medicated, containing 177.78 g/ton of lincomycin, made by Suther Feeds, Inc., of Frankfort, KS, has been completed. The feed, which was distributed only in Kansas, was recalled by the firm because it was subpotent.

A firm-initiated Class II recall is ongoing by Schering-Plough Animal Health Corporation, Summit, NJ, for 12,774 syringes of its Phenylzone Oral Paste for horses; each syringe contains 6 grams of phenylbutazone. The products were made in Ireland and were distributed nationwide in the United States. The syringes were recalled because several of them contained plungers incorrectly calibrated in animal weight, rather than in grams of Phenylzone delivered.

A Class III recall has been completed by MFA, Inc., of Columbia, MO, for 131 tons of bulk feed labeled as "Bulk LVO Starter IV CSP Pellet Medicated, A Complete Starter Feed for Baby Pigs, containing 100 g/ton chlortetracycline, 100 g/ton sulfathiazole, and 50 g/ton penicillin (as procaine)." The reason for the recall was that the product was mislabeled as containing sulfathiazole, but it actually contained sulfamethazine. The firm has also completed a Class III recall of 33.7 tons of bulk feed labeled as "Bulk LVO Starter IV CSP Pellet Medicated, A Complete Starter Feed for Baby Pigs, containing 100 g/ton chlortetracycline, 100 g/ton sulfathiazole, and 50 g/ton penicillin (as procaine)." The reason for this recall was that the product was supposed to only contain AureoZol containing sulfathiazole, but Aureomix containing sulfamethazine was also used. Distribution of all of the affected products was limited to Missouri.

A Class III recall is ongoing by Fort Dodge Laboratories, Inc., of Fort Dodge, IA, for 7,476 200-ml. bottles and 44,365 500-ml. bottles of the firm's Cydectin, moxidectin, Injectable Solution for Beef and Nonlactating Dairy Cattle, Antiparasitic, Sterile. The reason for the recall is that the firm cannot ensure validated parameters were met in the aseptic filing room. Distribution of the products was nationwide. The company is also undertaking a Class II recall of 139 62-pouch pails of its Aureomycin Chlortetracycline Soluble Powder, for Veterinary Use in Drinking Water, containing 25 g/lb. chlortetracycline HCl. The reason for this recall was that a 9-month stability sample was out of specification (low) for chlortetracycline HCl. Distribution was nationwide and in Panama.

A Class III firm-initiated recall has been completed by MFA Inc. of Columbia, MO, for 20 50-lb. bags of Muscle Pig IV CSP and 5,840 lbs. of bulk Muscle Pig III CSP that are mislabeled as containing sulfathiazole, when they actually contain sulfamethazine. This firm also completed a Class III recall of 3,900 lbs. of bulk and 235 of its 50-lb. bags of Muscle Pig III and 350 of its 50-lb. bags of Muscle Pig IV for the same reason. Additionally, a Class III recall of 229 of its 50-lb. bags of Muscle Pig IV and of 60 of the firm's 50-lb. bags of Muscle Pig III was completed. This product was supposed to only contain AureoZol containing sulfathiazole, but Aureomix containing sulfamethazine was also used. Distribution of all of the recalled products was limited to Missouri.

Approvals for April and May 2007

CVM has published in the *Federal Register* notice of the approval of these New Animal Drug Applications (NADAs)

VETMEDIN (pimobendan) Chewable Tablets (NADA 141-273), filed by Boehringer Ingelheim Vetmedica, Inc. The NADA provides for the use of VETMEDIN Chewable Tablets in dogs for the management of the signs of mild, moderate, or severe (modified New York Heart Association Class II, III, or IV) congestive heart failure due to atrioventricular valvular insufficiency or dilated cardiomyopathy. VETMEDIN is indicated for use with concurrent therapy (e.g., furosemide, etc.) for congestive heart failure as appropriate on a case-by-case basis. Notice of approval was published May 17, 2007.

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Approvals for April and May 2007 *(Continued)*

New Animal Drug Applications (Continued)

PROTAZIL (1.56% diclazuril) Antiprotozoal Pellets (NADA 141-268), filed by Schering-Plough Animal Health Corp. The NADA provides for the use of PROTAZIL in horses for the treatment of equine protozoal myeloencephalitis caused by *Sarcocystis neurona*. Notice of approval was published April 27, 2007.

WORMXPLUS (praziquantel and pyrantel pamoate) Flavored Chewables and VIRBANTEL (praziquantel and pyrantel pamoate) Flavored Chewables (NADA 141-261), filed by Virbac NH, Inc. The NADA provides for the use of both products in dogs and puppies for the treatment and control of various internal parasites (i.e., *Toxocara canis, Toxascaris leonina*); hookworms (*Ancylostoma caninum, Ancylostoma braziliense, Uncinaria stenocephala*); and tapeworms (*Dipylidium caninum, Taenia pisformis*). Notice of approval was published April 4, 2007.

CVM has published in the *Federal Register* notice of the approval of these Supplemental New Animal Drug Applications (NADAs)

AQUAFLOR (florfenicol) (NADA 141-246), filed by Schering-Plough Animal Health Corporation. The supplemental NADA provides for the use of Aquaflor (florfenicol), a type A medicated article, by veterinary feed directive (VFD) to formulate type C medicated feed for the control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilium*. The single VFD order form for florfenicol includes both catfish and freshwater-reared salmonid indications because each comprises multiple species and is approved in each for use under similar directions and conditions of use. Notice of approval was published April 20, 2007.

CVM has published in the *Federal Register* notice of the approval of these Abbreviated New Animal Drug Applications (ANADAs)

BUTORPHANOL TITRATE INJECTION (2mg/mL) (ANADA 200-408), filed by IVX Animal Health, Inc. The ANADA provides for the use of Butorphanol Titrate Injection (2mg/mL) for veterinary prescription use in cats for the relief of pain. The product is approved as a generic copy of TORBUGESIC-SA (butorphanol titrate, USP), approved under NADA 141-047, held by Fort Dodge Animal Health, a Division of Wyeth. Notice of the ANADA approval was published May 18, 2007.

SUPERIORBUTE (phenylbutazone) Powder (ANADA 200-333), filed by Superior Equine Pharmaceuticals, Inc. The ANADA provides for the use of SUPERIORBUTE Powder administered to horses in feed for the relief of inflammatory conditions associated with the musculoskeletal system. SUPERIORBUTE Powder is approved as a generic copy of IVX Animal Health, Inc.'s Phenylbutazone Tablets, USP, approved under NADA 91-818. Notice of approval was published May 18, 2007.

NOROMECTIN Plus (ivermectin and clorsulon) Injection for Cattle (ANADA 200-436), filed by Norbrook Laboratories Ltd. The ANADA provides for the use of NOROMECTIN Plus Injection for Cattle by subcutaneous injection for the control of various internal and external

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Approvals for April and May 2007 *(Continued)*

Abbreviated New Animal Drug Applications (Continued)

parasites. It is approved as a generic copy of Merial Ltd.'s IVOMEC Plus Injection for Cattle (NADA 140-833). The firm's NOROMECTIN (ivermectin) Injection for Cattle and Swine (ANADA 200-437) was also approved. The ANADA provides for the use of this drug by subcutaneous injection in cattle, swine, reindeer, and American bison for the treatment and control of various internal and external parasites. This ANADA is approved as a generic copy of Merial's IVOMEC Injection for Cattle and Swine, which was approved under NADA 128-409. Notice of both ANADA approvals was published May 17, 2007.

- TETROXY Aquatic (oxytetracycline hydrochloride) Soluble Powder (ANADA 200-460), filed by Cross Vetpharm Group Ltd. The ANADA provides for the use of TETROXY Aquatic for skeletal marking of finfish fry and fingerlings by immersion. Notice of approval was published May 9, 2007.

- CLINDAMYCIN HYRDOCHLORIDE Oral Drops (ANADA 200-418), filed by First Priority, Inc. The ANADA provides for the use of Clindamycin Hydrochloride Oral Drops in dogs and cats for the treatment of various skin and dental infections due to susceptible bacterial pathogens. The newly approved product is approved as a generic copy of Antirobe Aquadrops Liquid, sponsored by Pharmacia & Upjohn Co., a division of Pfizer, Inc., under NADA 135-940. Notice of approval was published April 20, 2007.

- MURICIN (mupirocin) Ointment 2% (ANADA 200-418), filed by Altana, Inc. The ANADA provides for the use of mupirocin ointment 2% for the treatment of bacterial skin infections in dogs. The drug is approved as a generic copy of Pfizer, Inc.'s, BACTODERM Ointment, approved under NADA 140-839. Notice of approval was published April 11, 2007.

- HEIFERMAX 500 (melengestrol acetate) Liquid Premix and BOVATEC (lasalocid sodium) single-ingredient Type A medicated articles to make dry and liquid, two-way combination drug Type B or Type C medicated feeds for heifers fed in confinement for slaughter. ANADA 200-451 was filed by Ivy Laboratories, a Division of Ivy Animal Health, Inc. The ANADA is approved as a generic copy of NADA 140-288, sponsored by Pharmacia & Upjohn Co., a Division of Pfizer, Inc., for combination use of MGA 500 and BOVATEC. Notice of approval was published April 4, 2007.

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