FDA VETERINARIAN
Center for Veterinary Medicine
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CVM Researcher Renate Reimschuessel Nominated for Service to America Medal

For her work to uncover properties of melamine and related chemicals in pet food that were so dangerous to dogs and cats, Center for Veterinary Medicine scientist Dr. Renate Reimschuessel was named in June as one of 29 "Service to America Medal" finalists and is now a contender for one of the eight medals to be awarded in September.

Dr. Reimschuessel is a research biologist at CVM's Office of Research. Through her efforts, the Food and Drug Administration was able to determine how melamine and related chemicals were responsible for kidney damage in dogs and cats.

Partnership for Public Service awards Service to America Medals to federal employees who make significant contributions to the safety, health, and well-being of American citizens.

Dr. Renate Reimschuessel dosing fish with melamine at her aquaculture research facilities in the Center for Veterinary Medicine's Office of Research. Dr. Reimschuessel has been nominated for a Service to America Model for her work in discovering how melamine and related chemical combined to produce harmful crystals in the kidneys of animals.

According to information included in Dr. Reimschuessel's nomination for the medal, scientists were not able to determine the cause of injury and death to dogs and cats, even though the problem had been linked to pet food contaminated with melamine. Scientists generally rejected the idea that melamine was the problem because they thought the chemical was non-toxic.

When she was called in to help the investigation, Dr. Reimschuessel said she felt as though she were pulling together "pieces of a big, complicated puzzle." The information she had available came from researchers in CVM, other parts of FDA, and the U.S. Department of Agriculture, and from private companies, practicing veterinarians, and universities. Even pet owners were able to help.

As she studied the problem, she noticed that the literature she reviewed mentioned small changes to kidneys exposed to melamine, a finding not referenced in the most commonly consulted articles on the topic.

Based on her experience and insight, she formulated the theory that melamine was combining with a similar chemical to form crystals in the kidneys of the dogs and cats, often resulting in death of the animals. She also knew that physicians will sometimes see the development of kidney crystals in human chemotherapy patients. The crystals, if prolific, will cause severe kidney damage that can lead to death.

She ultimately proved she was right. Along with melamine, the pet food causing the injuries also contained cyanuric acid or other, related chemicals. The combination of the two chemicals forms crystals in the kidneys of dogs and cats, leading to kidney damage and failure.

She proved her theory by feeding melamine and cyanuric acid to fish. The fish receiving either the melamine or the cyanuric acid alone did not develop kidney crystals. But fish receiving both chemicals developed crystals similar to those seen in the afflicted cats and dogs.

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IN THIS ISSUE

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

FDA Announces ProHeart® 6 Return to Market

by Jon F. Scheid, Editor

ProHeart® 6 (moxidectin) Sustained Release Injectable for Dogs, a unique heartworm preventive product, is returning to the U.S. market.

The drug's sponsor, Fort Dodge Animal Health, voluntarily removed the product from the U.S. market and ceased production of it in 2004 because of the Food and Drug Administration's concerns about reports of adverse reactions to the drug. The reported reactions, which included numerous deaths, were unanticipated and unexplained. FDA requested that the drug be removed from the market until the company and FDA could further investigate the situation and resolve concerns.

Fort Dodge Animal Health has changed the manufacturing specifications for Proheart® 6 to minimize the inclusion of residual solvents in the final product. Also during this time, the number of adverse event reports from international markets, where the product remained available, has declined.

Fort Dodge Animal Health, a division of Wyeth, is based in Fort Dodge, IA.

In June 2008, FDA approved a Supplemental New Animal Drug Application for ProHeart® 6 that revises the label and client information sheet to include additional warnings, precautions, and adverse reactions. Additionally, FDA concurs with Fort Dodge Animal Health's decision to market ProHeart® 6 under a risk minimization and restricted distribution plan. Only veterinarians who have undergone in-depth training from Fort Dodge Animal Health will be allowed to obtain the drug, which will be available only from the sponsor. After a veterinarian has undergone the training, he or she will be able to purchase ProHeart® 6 as needed.

Heartworm disease is caused by *Dirofilaria immitis* and is transmitted via mosquito bites. Dogs show no signs of the disease until the heartworm larvae mature. The mature larvae gather in the right atrium and pulmonary artery of the dog, which can produce cardiopulmonary effects in the dog. Dogs suffering from heartworm infections can have a cough and can display a low tolerance

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...Service to America Medal *(Cont.)*

At first, scientists remained skeptical of Dr. Reimschuessel's finding, largely because they were not finding sufficient crystals in kidneys to cause the problem. Dr. Reimschuessel solved that puzzle, too. The reason pathologists were not seeing many crystals was because most kidney tissue samples were preserved in formalin, as part of a standard laboratory procedure. Dr. Reimschuessel discovered that formalin dissolves the crystals over time. So, by the time most pathologists reviewed the tissue samples, few crystals remained.

Through Dr. Reimschuessel's work, FDA regulatory officials understood the nature of the problem and knew what they had to do to contain it. Also, Dr. Reimschuessel's work allowed scientists to develop screening techniques that FDA and pet food manufacturers used to detect melamine in pet food and ingredients, thus further preventing harm to the Nation's pets.

For her work, Dr. Reimschuessel was also recognized on the floor of the House of Representatives by Rep. C.A. Dutch Ruppersberger of Maryland.

In a statement that appeared in the June 25, 2008, *Congressional Record*, the official publication of the U.S. Congress, Rep. Ruppersberger said:

"Due to Dr. Reimschuessel's discovery, the United States has increased surveillance for melamine and related compounds in food ingredients. In an effort to identify potential risks to humans, she is continuing to test the effects of melamine in chickens, pigs, and fish. Dr. Reimschuessel's research helped improve the way our government preserves scientific specimens and identified the ability of nontoxic compounds to become toxic when combined. These discoveries helped resolve an immediate crisis, and her continued efforts are helping protect the U.S. food supply from tainted imports and toxic chemical combinations."

According to Partnership for Public Service, the other award finalists includes federal employees with achievements in scientific research, renewable energy, consumer protection, health care, tsunami warning, refugee resettlement, malaria prevention, environmental conservation, human rights, foreign affairs, disaster relief, and border enforcement.

From the 29 finalists, eight winners will be awarded the medals at a September 16 ceremony to be held in Washington, D.C.

FDA VETERINARIAN

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...Return to Market *(Continued)*

for exercise. A dog with severe heartworm disease can die from it.

Veterinarians want heartworm prevention options because treating the disease is more difficult and puts a dog at greater risk than preventing the disease. For example, during treatment, the heartworm could break off, creating risks of clots and possibly killing the dog. Also, drugs approved to treat mature heartworms have low margins of safety.

ProHeart® 6 prevents heartworm disease in dogs for 6 months following injection. It is the only drug approved in the United States with a sustained period of protection. Many veterinarians want ProHeart® 6 available as an option when the dog's owner is unable, unwilling, or unlikely to regularly administer the monthly oral or topical treatments that otherwise must be used.

Fort Dodge Animal Health has revised the product's label. The label warns not to use the drug within a month of the time a dog receives vaccinations and not to use it in dogs with pre-existing allergic disease, including food allergies, skin allergies, and flea allergy dermatitis. In addition, the label states that veterinarians should not administer the drug to dogs that are sick, debilitated, underweight, or have a history of weight loss.

The post-approval section of the label has been updated to include reported adverse reactions, such as liver and blood disorders.

Dog owners will be required to sign a consent form before their dogs are treated and will receive a revised Client Information Sheet that includes updated safety information.

FDA says that owners who think their dogs are suffering from an adverse event from ProHeart® 6 should immediately contact their veterinarians, who can treat the dog for the problem. Under the risk minimization and restricted distribution plan, veterinarians will agree to submit Adverse Experience Reports to Fort Dodge Animal Health.

CVM Releases Its Annual Report for Fiscal Year 2007

The Center for Veterinary Medicine in May released its Annual Report covering Fiscal Year 2007.

The newest report continues the feature CVM started with its first report in FY 2003 of presenting the performance goals established for the Center's Management Team, and then stating whether the goals were met. The complete list of goals is presented in the report's Appendix F, which appears for the first time in this Report.

Also, as with the previous reports, the FY 2007 edition presents a description of CVM's organization, responsibilities, sphere of influence, and stakeholders and partners.

The report presents CVM's activities in the format of "Challenges and Accomplishments," covering areas such as animal drug review, reducing the risk of antimicrobial resistance, controlling the risk from bovine spongiform

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Comings and Goings

New Hires

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Heather Longstaff, Staff Fellow
- Che VanHoose, Legal Instruments Examiner
- Rosalind Price, Legal Instruments Examiner
- Marjorie Lidard, Management Specialist
- Robin Nguyen, Consumer Safety Officer
- Jason Smith, Staff Fellow
- Octavia Weatherspoon, Legal Instruments Examiner
- Schevon Charles, Legal Instruments Examiner
- Karen Ekelman, Supervisory Biologist
- Ron Miller, Staff Fellow

OFFICE OF RESEARCH

- Steven Matthews, Animal Caretaker
- Virginia Mills, Animal Caretaker
- G. Hemakanthi DeAlwis, Staff Fellow

OFFICE OF SURVEILLANCE AND COMPLIANCE

- Christina Wilkes, Consumer Safety Officer
- Martine Hartogensis, Deputy Director

OFFICE OF MINOR USE AND MINOR SPECIES ANIMAL DRUG DEVELOPMENT

- Joan Gotthardt, Supervisory Veterinary Medical Officer

Departures

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Charles Gray, Chemist
- Marina Feric, Biological Aide
- Joan Gotthardt, Supervisory Veterinary Medical Officer

OFFICE OF SURVEILLANCE AND COMPLIANCE

- Mark Hackman, Consumer Safety Officer
- Karen Ekelman, Supervisory Biologist

OFFICE OF RESEARCH

- Michael Scott, Staff Fellow

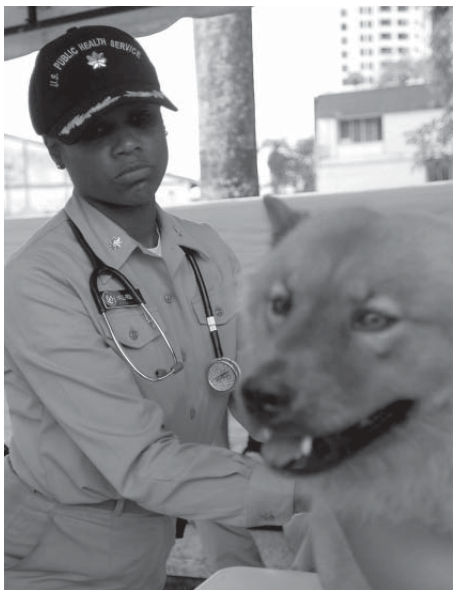
CVM Veterinarian Participates in Latin America Humanitarian Mission

by Jon F. Scheid, Editor

Dr. Elvira Hall-Robinson, a veterinarian who works at the Center for Veterinary Medicine's Office of Research, took a month away from her regular duties to serve on a medical team aboard the U.S. Navy Hospital Ship, *USNS Comfort*, when it made a humanitarian assistance mission to 12 Latin American and Caribbean countries last year.

Dr. Hall-Robinson is a Commander in the Commissioned Corps of the U.S. Public Health Service (PHS). The PHS is one of seven uniform services of the United States that includes personnel with a mission of protecting, promoting, and advancing the health of the Nation.

The PHS Commission Corps is organized under the U.S. Department of Health and Human Services. Members of the Commissioned Corps are deployed to disaster areas and they are capable of carrying out emergency medical and public health operations at remote sites. Dr. Hall-Robinson, for example, volunteered for two deployments to the Gulf Coast following Hurricane Katrina, once as a public health specialist to determine the safety of food supplies, and once as a veterinarian to take care of pets displaced by the storm.



Elvira Hall-Robinson, a veterinarian with CVM's Office of Research, volunteered to spend a month aboard the U.S. Navy Hospital Ship, USNS Comfort, during its 4-month humanitarian mission to Latin American and the Caribbean. Dr. Hall-Robinson is a Commander in the U.S. Public Health Service's (PHS) Commissioned Corps. She was part of a 15-member PHS team that provided medical and veterinary care in rural areas. Here, she is examining a dog at a field treatment site at the Bueanaventura Coliseum in Buenaventura, Colombia. (U.S. Navy photo by Mass Communication Specialist 3rd Class Kelley E. Barnes)

The *Comfort* was deployed on a 4-month mission as part of President Bush's Joint Service Latin American Health Initiative, announced in March 2007, to help improve the health and welfare of people from Latin America and the Caribbean. When President Bush announced the *Comfort's* mission, HHS Secretary Michael Leavitt sent word to the members of the PHS asking for volunteers. PHS members take part in these missions not only to provide humanitarian aid and assistance, but also to train and be prepared for deployments to remote sites and abroad during emergencies.

For the Joint Service Latin American Health Initiative, the PHS personnel were part of the more than 700-person medical team on the *Comfort*. The PHS volunteers were divided into four 15 to 17-person teams, each team serving for 1 month, so no individual member had to spend too much time away from family and regular job. The PHS teams included physicians, nurses, dentists, dental hygienists, environment specialists, and a veterinarian capable of working with large animals.

USNS Comfort (U.S. Navy photo by Mass Communication Specialist 2nd Class Lolita M. Lewis)

The *Comfort* sailed from Norfolk, VA. It visited 12 countries from June to October 2007, spending about a week at each port. Dr. Hall-Robinson joined the ship in August as it visited Peru and continued with it as it visited Ecuador, Colombia, and Haiti. Dr. Hall-Robinson was part of the *Comfort* Preventive Medicine team. Altogether, that team had more than 37,000 preventive health encounters in underserved communities throughout the entire mission.

Field veterinary work

During the mission, Dr. Hall-Robinson treated farm and companion animals. Most of the work was preventive medicine, typically deworming and vaccinating the animals and providing them with vitamin packs. Helping to keep all animals healthy is

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...Latin America Humanitarian Mission *(Continued)*

important for human health, she said. In the countries she visited, all of the animals, not just the pets, are considered a part of the family and live with the people. Many of the rural villages had houses with dirt floors. Pigs were often penned inside the house, which kept the pigs in close proximity to family members. Parasites from the animals infect the people, too, Dr. Hall-Robinson said.

Also, Dr. Hall-Robinson said, the companion animals are just as important to the villagers in Latin America as they are to people in the United States. She described a little girl, probably not 3 years old, who kept her kitten with her at all times. The kitten and the little girl were perfectly comfortable together, she said.

Dr. Hall-Robinson said that treating large farm animals was often difficult, because she did not have restraining equipment available, such as chutes. In one case, to deworm cattle, she had to work with owners who would restrain an individual animal, giving Dr. Hall-Robinson a chance to use a pour-on dewormer.

The mission was well organized, Dr. Hall-Robinson said. Advance teams would visit the department of health or agriculture in each of the countries to obtain information on the type of treatments that would be needed. In most cases, she said, she had the drugs and vaccines she needed to treat the animals. In a few cases, though, she bought supplies locally.

Her typical day would start at 6 a.m. or earlier, depending on how she would be transported to the treatment sites, which were all on shore. In one port, the *Comfort* was able to dock, so the medical staff could easily come and go. In another case, due to security concerns, the *Comfort* was anchored 30 miles off shore. The staff would have to fly to shore in a helicopter, a dozen people at a time, or make the trip aboard one of the *Comfort's* "hospitality" boats.

CVM's Dr. Elvira Hall-Robinson and a local veterinarian provide veterinary care at the Buenaventura Coliseum in Buenaventura, Colombia. (U.S. Navy photo by Mass Communication Specialist 3rd Class Kelley E. Barnes)

The importance of pets: Dr. Elvira Hall-Robinson, during her month-long tour with the U.S. Navy Hospital Ship, USNS Comfort, found that pets are as important as farm animals to many of the residents of the Latin American countries. This young girl and her cat were nearly inseparable.

Most of the time, the medical staff was all back onboard the ship by 6:00 or 7:00 p.m., when they would clean equipment, get ready for the next day, and write reports. They teams worked 7 days a week.

Security was always a concern. In some countries, the medical staff needed only limited protection. In other countries, the local military escorted the teams to the sites and back to the ship, Dr. Hall-Robinson said. The medical staff was fully briefed on the type of work needed at each site visit and on security issues. "We had a lot of briefings," she said.

Lunch in the field was something the military calls "MREs," or Meals Ready to Eat.

When first deployed in a new country, the first day was usually spent setting up; getting equipment and medicines in place, and finding a suitable spot to work. (Occasionally, Dr. Hall-Robinson's veterinary treatment site was simply a table set up in a clearing.) The remaining 6 or 7 days were spent treating animals.

Dr. Hall-Robinson said she found the work highly rewarding. It gave her a chance to help animals that would not otherwise receive treatment. These missions also help her be ready for emergency deployment, she added. Going to these remote areas can lead to "culture shock" for someone who has not done missions like this, which would make it harder to adjust to the environment when deployed on an emergency mission, she said.

Osteoarthritis in Cats: A More Common Disease Than You Might Expect

by Carmela Stamper, DVM, Communications Staff

Thanks to the marvels of modern veterinary medicine, our pets are living much longer lives. With longer lives, however, come chronic diseases such as osteoarthritis. Osteoarthritis is a commonly recognized disease in dogs. However, it is now being recognized as a disease of geriatric cats.

Osteoarthritis is a degenerative condition of the joints in which the normal cartilage cushion in the joint breaks down. Eventually, adjacent bones rub against each other, causing pain, decreased joint movement, and sometimes the formation of bone spurs and other changes around the joint.[1] Osteoarthritis is a progressive disease; however, it can be actively managed so that the course of the disease is slowed and remaining joint function is preserved.

Physical diagnosis of osteoarthritis in cats is difficult even for experienced veterinarians. Cats, unlike most dogs, can tolerate severe orthopedic disease due to their small size and natural agility. Cats generally resent being physically handled or manipulated during clinical examinations. Thus, the examining veterinarian may have difficulty in determining whether a cat is pulling its foot away because of pain or simply because it doesn't want to be touched.[2] Cats are also notorious for cowering on the examination table and remaining immobile. Due to these obstacles in diagnosing osteoarthritis in cats, veterinarians will often simply rely on the cat owner's observations that their pet is not moving around as well as it once did. Veterinarians will rule out osteoarthritis as a diagnosis by actually having the owners treat the cat for osteoarthritis and seeing if the owners note any improvement in their cat's quality of life.

Changes to osteoarthritis-affected joints in cats are usually subtle. Decreased range of joint motion, commonly seen in dogs, is uncommon in cats (in one study by Clarke and Bennett, published in the *Journal of Small Animal Practice*, 5 of 86 cat joints with osteoarthritis had decreased range of motion).[3] Crepitus, a grinding/crunching sound or feeling in a joint, is also common in dogs, but uncommon in cats (no joints of the 86 joints in the same study had crepitus). Thickening of the tissues surrounding affected joints, however, is a common finding (58 of 86 joints in the previously cited study).

Clinical signs of osteoarthritis in cats include weight loss, loss of appetite, depression, change in general attitude, poor grooming habits, urination or defecation outside the litter pan, and inability to jump on and off objects.[4] Surprisingly, lameness is not as commonly reported a clinical sign by owners as one would expect. Because joints are frequently bilaterally affected (meaning that if one elbow is affected, the other elbow is also affected), cats can compensate and appear to be walking normally.[5] In the study by Clarke and Bennett evaluating clinical signs of osteoarthritis in 28 cats, 43 percent (12 cats) were described to be limping, 71 percent (20 cats) were described as unwilling to jump, and 67 percent (19 cats) had reduced height of jumps.[6]

The most frequently affected joints in cats are the elbows and hips, although shoulders and hocks have also been reported.[7] Interestingly, arthritis of the vertebrae and sternum (the axial skeleton) is also common. In one study, 74 of 218 cats were diagnosed with osteoarthritis.[8] Of the 74 cats, 21 (28.4 percent) had osteoarthritis in the limbs and the vertebrae, 24 (32.4 percent) had osteoarthritis in the vertebrae only, and 29 (39.2 percent) had osteoarthritis in the limbs only.

Several studies have been conducted evaluating radiographic changes associated with osteoarthritis in cats. In general, radiographic changes observed in cats with osteoarthritis are less severe than those observed in dogs with osteoarthritis. In many cases, cats with osteoarthritis have no radiographic changes. For example, in one study evaluating 292 cats with osteoarthritis, 229 cats had no radiographic evidence of the disease, while evidence was present in the other 63 cats.[9] In another study published in the *Journal of the American Veterinary Medical Association*, 10 of 100 cats with osteoarthritis had no radiographic changes.[10] In an ongoing feline osteoarthritis study by world-renown veterinary pain expert, B. Duncan X. Lascelles, Assistant Professor of Small Animal Surgery at the North Carolina State University School of Veterinary Medicine, where he also directs the school's Integrated Pain Management Service, 73 percent of enrolled cats had evidence of osteoarthritis on radiographs.[11] The radiographic changes noted in the study were mild, but when the affected joints were examined at necropsy, significant cartilage loss was found. Thus, radiographic changes in cats, if present, may not correspond to the degree of osteoarthritis present in the joints.

A recently published study in the *Journal of Veterinary Internal Medicine* evaluated the association between radiographic and physical examination

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Osteoarthritis in Cats... *(Continued)*

findings in 13 cats with osteoarthritis. A total of 208 joints were evaluated for evidence of pain and/or radiographic changes associated with osteoarthritis. Of these, 110 joints were identified as having osteoarthritis (55 joints were painful and 55 joints had radiographic changes). However, only 18 of the 110 joints had both clinical pain and radiographic changes.[12] Thus, painful joints did not necessarily correspond to radiographic findings.

Treatment options for cats with osteoarthritis are limited. Non-pharmaceutical treatment options include weight loss for overweight cats, increased exercise, and environmental accommodations (e.g., using litter pans with lower sides for ease of entering and exiting, and elevating food and water bowls, and providing soft bedding).[13] With regard to pain relief, steroids have been used in the past; however, they have fallen out of favor due to side effects.[14] The only approved non-steroidal anti-inflammatory drug (NSAID) for use in cats is Metacam® 5mg/mL Solution for Injection. However, it is approved for a one-time dose for the control of postoperative pain associated with orthopedic surgery, ovariohysterectomy, and castration in cats. Metacam® is not approved for any repeat dosing. Thus, no NSAID is currently approved for safe, long-term control of osteoarthritis pain in cats.

Development of pain assessment tool

Because pain relief is an important topic in veterinary medicine, the Center for Veterinary Medicine's Staff College recently hosted a day-long seminar on pain recognition and pain measurement in dogs and cats by Dr. Lascelles (BSc, BVSc, PhD, CertVA, DSAS(ST), DECVS, DACVS). His current research is focused on acute and chronic pain in dogs and cats; namely, the mechanisms of pain, the best methods for clinically measuring both acute and chronic pain, and, once pain is identified, the best methods to alleviate it.

Pain in animals, particularly cats, is difficult to assess, and there are few validated pain assessment tools. Dr. Lascelles discussed efforts to address these problems. He described the various lameness scales and assessment tools used in canine and feline pain studies. Currently, much of the data obtained from canine and feline pain studies are "subjective," meaning that the observer introduces some personal bias when recording pain assessments. An example of a subjective tool is a questionnaire. Researchers, including Dr. Lascelles, are trying to develop more "objective" tools for pain assessment to greatly decrease personal bias. Currently used objective tools include force plate analysis (measures the amount of force a limb generates at one instant in time) and pressure-sensitive walkways (that indirectly measure the amount of force generated at one moment in time).

Dr. Lascelles is developing a new objective tool, a collar-mounted activity monitor, for use in measuring animal activity levels. In general, animals with osteoarthritis have decreased mobility and activity. Therefore, an objective tool that could be used to detect differences in pre- and post-pain-treatment activity would be useful in assessing the effectiveness of new pain drug products for animals. Dr. Lascelles conducted a study using activity monitors to assess the effectiveness of NSAID treatment on 13 client-owned cats with osteoarthritis. During the study he compared the pre-treatment and during-treatment values obtained from the collar-mounted activity monitor with pre-treatment and during-treatment client questionnaire answers regarding cat activity. Overall, the client answers and the activity monitor values generally corresponded. Thus, the study provided some early validation for use of collar-mounted activity monitors to assess pain. Further evaluation and comparison of activity monitors with other currently used assessment tools is needed before activity monitors can be considered fully validated objective pain assessment tools.

Conclusion

Diagnosis of osteoarthritis in cats is difficult even for the experienced veterinarian. Thus the disease remains largely underdiagnosed and undertreated. However, as new methods of pain assessment are developed, osteoarthritis in cats may soon become a readily recognized and actively managed disease, thus alleviating the silent suffering of many geriatric cats.

Endnotes

1 National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health. Handout on Health: Osteoarthritis. May 2006. NIH Publication No. 06-4617.

2 Clarke SP and Bennett D. Feline osteoarthritis: a prospective study of 28 cases. 2006. Journal of Small Animal Practice. 47(8): 439-445.

3 Ibid.

4 Hardie EM. Management of osteoarthritis in cats. 1997. Veterinary Clinics of North America: Small Animal Practice. 27(4): 945-953.

5 Ibid.

6 Clarke and Bennett, pp. 439-445.

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U.S., Japan Science/Technology Cooperation Utilizes, Conserves Natural Resources

by Richard Arkin, J.D., Assistant Editor

The Food and Drug Administration's Center for Veterinary Medicine has taken a leadership role in the U.S.-Japan Cooperative Program in Natural Resources (UJNR), a technology exchange program between the United States and Japan.

A senior official of the Center for Veterinary Medicine is highly involved in this international effort. Dr. Marleen Wekell, Director of CVM's Office of Research (OR) in Laurel, MD, chairs the UJNR Joint Panel on Toxic Micro-Organisms. This panel examines toxic algae, bacterial pathogens and their toxins, and toxigenic fungi that contaminate food and cause human or other animal diseases. The panel also looks for ways to prevent such illnesses. She joined the UJNR panel in 1996. She became the Treasurer of the UJNR Joint Panel on Toxic Micro-Organisms in 1997 and was elected Chair in 1998.

Even before she joined the UJNR panel, Dr. Wekell, as the Director of the FDA Seafood Products Research Center in Bothell, WA, was known as an international expert on marine toxins, several species of bacterial pathogens causing foodborne illness, and development of methods for determining quality of aquatic products.

As a panel member, Dr. Wekell hosted several Japanese scientists to work in the Bothell laboratory. In addition, U.S. scientists have been able to work in their counterpart laboratories in Japan. Other U.S. panel members have also hosted Japanese scientists in their respective laboratories. This exchange of scientists, which continues to this day, has helped the United States and Japan to standardize methods for the detection of bacterial pathogens and toxins produced by bacteria, fungi, and algae and to exchange information.

Dr. Wekell remained Chair when she left Washington State to become the Director of the FDA's North East Regional Laboratory, New York, NY, and continued in 2003 when she joined CVM's OR. As Chair of the UJNR panel on Toxic Micro-Organisms, she has organized and chaired together with the other U.S. panel members three symposia in the United States. Each dealt with the focus of the panel, foodborne bacterial pathogens and their toxins, mycotoxins (fungal toxins), and marine toxins (including toxic dinoflagellates).

Dr. Wekell's duties as chair include lining up speakers, securing a meeting site and hotel, and publishing the results. At present she is working with the other eight U.S. panel members from FDA, U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC) to organize a similar symposium to be held November 2008 in New Orleans, LA.

In recent years, OR has played an important role in representing the United States with the UJNR panel on Toxic Micro-Organisms. Several OR researchers have

(Continued, next page)

Osteoarthritis in Cats... *(Continued)*

[7] Ibid.

[8] Clarke SP, Mellor D, Clements DN, et al. Prevalence of radiographic signs of degenerative joint disease in a hospital population of cats. 2005. Veterinary Record. 157:793-799.

[9] Godfrey DR. Osteoarthritis in cats: a retrospective radiological study. 2005. Journal of Small Animal Practice. 46:425-429.

[10] Hardie EM, Roe SC, and Martin FR. Radiographic evidence of degenerative joint disease in geriatric cats: 100 cases (1994-1997). 2002. Journal of the American Veterinary Medical Association. 220:628-632.

[12] Lascelles BDX, CVM Staff College lecture, March 27, 2008.

[13] Lascelles BDX, Hansen BD, Roe S, et al. Evaluation of client-specific outcome measures and activity monitoring to measure pain relief in cats with osteoarthritis. 2007. Journal of Veterinary Internal Medicine. 21(3): 410-416.

[13] Hellyer P, Rodan I, Downing R, et al. AAHA/AAFP pain management guidelines for dogs and cats. 2007. Journal of the American Animal Hospital Association. 43:235-248.

[14] Caney S. Feline Arthritis. 2007. Veterinary Focus. 2007. 17(3):11-17.

U.S., Japan Science/Technology Cooperation… *(Cont.)*

made presentations, and, in 2006, OR hosted a week-long visit of a *Campylobacter* expert from Japan.

On alternate years, when the meetings are held in Japan, Dr. Wekell has chaired sessions and made presentations. At present, the UJNR panel from Japan on Toxic Micro-Organisms has nine panel members who are senior scientists from the National Institute of Health Sciences, the Department of Food Safety, the National Food Research Institute, the Fisheries Research Institute, and the National Institute of Animal Health. All panel members include international experts on animal and human health, marine toxins, bacterial pathogens, toxigenic fungi, and food safety (both humans and other animals).

In addition to Dr. Wekell, the U.S. panel members include: Dr. Ed Cleveland, from the USDA's Agricultural Research Service (ARS), New Orleans, LA; Dr. Douglas Abbott, USDA's Food Safety and Inspection Service, Athens, GA; Dr. Art Liang, CDC, Atlanta, GA; Dr. Ken Voss, ARS, Athens, GA; Dr. Chris Maragos, ARS, Peoria, IL; Dr. Mariana Miliotis, FDA's Center for Food Safety and Applied Nutrition (CFSAN), College Park, MD; Dr. Jim Hungerford, FDA's Office of Regulatory Affairs, Bothell, WA; and Dr. Morris Potter, CFSAN, Atlanta, GA.

According to Dr. Wekell, "Being a part of the UJNR has been one of the more rewarding experiences of my life. It has enabled me to work closely with other U.S. and Japanese counterparts." She added, "Over the years, all the panel members from both countries have become not only treasured colleagues in research, but also good friends."

The Toxic Micro-Organisms Panel members routinely exchange cultures as well as laboratory reports and various publications on toxic micro-organisms. Other exchanges have included botulism toxins, methods for mycotoxin decontamination in commodities, and toxin standards used in analyses. Some of the toxin standards are not sold commercially and are available only from those engaged in research on the respective toxins.

The panel's work has led to the publication of eight books, most through the sponsorship of international symposia, on topics that have never been covered or summarized in a book or review. One of these landmark publications introduced pioneering Japanese work on the food poisoning bacterium *Vibrio parahemolyticus* to the international scientific community.

Through the panel's collaborative efforts, avian botulism has been identified as the cause of epidemic wild waterfowl poisoning in Japan. Japanese manufacturing processes incorporated into U.S. businesses have increased production efficiency. Also, the panel's efforts have contributed to the identification of seafood poisonings previously unknown to U.S. researchers and the development of bacteria tolerance regulations for use in U.S. and Japanese meat and poultry industries. Through the panel, U.S. scientists have supplied information on the genetics of peanuts and peanut processing methods to Japanese scientists working on development of a peanut that is genetically resistant to toxic fungi.

A Typical Micro-Organism Symposium

A meeting hosted by CVM and CFSAN in November 2006 was typical of Panel symposia. Dr. Wekell served as meeting chair and program coordinator for this "10th International Symposium on Toxic Micro-Organisms: Meeting the Challenges of Toxic Micro-Organisms and Pathogens: Implications for Food Safety and Public Health."

Attendees were welcomed to the symposium by Dr. Wekell, who chaired several sessions, along with then-CVM Director Dr. Stephen Sundlof, then-CFSAN Director Dr. Robert Brackett, and USDA Agricultural Research Service National Program Leader Dr. Jane Robens. A business pre-meeting took place the day before the science and technology sessions.

Sessions at this meeting included presentations and discussions of food safety policy and public health, data thresholds for regulatory or public health response, responses to indications of pathogens in products when there is no evidence of human illness, epidemiology of foodborne disease and in microbial risk assessment, and risk assessment for policy making. Other presentations and discussion included discussions of the National Antimicrobial Resistance Monitoring System (NARMS), development of standardized methods for testing antimicrobial resistance, marine and freshwater toxins and seafood toxin outbreaks, pathogen detection, and other laboratory methods.

A session at this meeting co-chaired by Dr. Wekell focused on microbial resistance. OR scientist Dr. David White gave a presentation on NARMS, and OR scientist Dr. Patrick McDermott presented on the development of standardized methods for testing antimicrobial resistance.

The meeting also included "Poster Session" presentations, covering shorter and more specific research efforts of the type usually presented in peer-reviewed poster form.

The proceedings of this Symposium will soon be published in the *Journal of Food Additives and Contaminants* as part of a dedicated issue later this year.

(Continued, next page)

U.S., Japan Science/Technology Cooperation… *(Cont.)*

Origins of UJNR

The UJNR emerged from a proposal offered by the United States during the third meeting of the U.S-Japan Bilateral Committee on Trade and Economic Affairs in January 1964. The U.S. proposal was for structured "government-level exchanges of technology specialists and research results in the area of human and natural resources that would benefit both countries." The result was a cabinet level agreement to facilitate cooperative efforts and equitable technology exchange in the field of natural resources.

The first meeting of the UJNR took place in May 1964 with the participants' stated purpose of "utilizing cooperation between Japan and the United States, so that both countries can learn from each other to the maximum extent possible the means of effectively utilizing and conserving the world's natural resources and solving problems in human housing environments."

The UJNR, which now functions within the framework of the 1989 U.S.-Japan Agreement in Science and Technology, has enhanced the efficiency of natural resources development and conservation. The UJNR has fostered exploration and adoption of diverse ideas, and has broadened understanding of important scientific issues in both countries. Through this spirit of scientific collaboration, the United States and Japan have made significant progress in understanding natural processes and promoting sound management of natural resources.

The UJNR also acts as a mechanism for implementing policies set forth by the 1993 U.S.-Japan Common Agenda and the U.S.-Japan Science and Technology Agreement.

The United States and Japan agreed to the Common Agenda (Common Agenda for Cooperation in Global Perspective) as a framework for bilateral cooperation, focusing the resources and technical expertise of the world's two largest economies on global challenges. The UJNR has played a key role in two of the four pillars of the Common Agenda: Protecting the Global Environment and Advancing Science and Technology. (The other two are Promoting Health & Human Development and Responding to Challenges to Global Stability.) The Common Agenda has resulted in creation of more than 80 scientific cooperation projects and projects involving cooperative development assistance.

The U.S.-Japan Science and Technology Agreement, which goes back to 1988, offers a similar opportunity for the exchange of scientific ideas, data, and studies.

The UJNR is one of four research exchanges between the United States and Japan. The other three exchanges cover basic science, health/medical affairs, and social/cultural affairs.

UJNR Panels

At present, the UJNR consists of 18 "panels" (committees). Of these, nine deal with marine science and technology. They are:

- Marine Facilities
- Diving Physiology
- Sea Bottom Surveys
- Marine Geology
- Marine Mining
- Aquaculture
- Pacific Observation and Research
- Submersible Research
- Marine Environmental Science and Technology.

The remaining nine are terrestrial or non-marine panels. They are:

- Conservation, Recreation, and Parks
- Earthquake Prediction Technology
- Fire Research and Safety
- Forage Seed Prediction
- Forestry
- Mycoplasmosis
- Protein Resources
- Toxic Microorganisms
- Wind and Seismic Effects.

Each UNJR panel meets as needed, usually once a year, at sites alternating between the United States and Japan. The meetings are primarily for presentation and discussion of research topics, but business sessions at the meetings also evaluate activities and determine if changes are needed.

The U.S. and Japanese governments have primary responsibility for UJNR planning, organization, and control. However, nongovernmental organizations and individuals are often invited to participate as consultants or advisors at panel symposia. Research results are disseminated through professional journals, panel proceedings, technical reports, press releases, presentations, and other media.

In Japan, all UJNR panels are coordinated by the Ministry of Education, Culture, Sport, Science, and Technology, with participation and advice primarily from the Ministry of International Trade and Industry,

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CVM Releases Its Annual Report... *(Continued)*

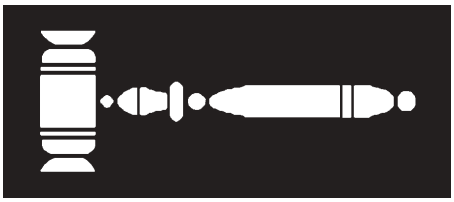
encephalopathy, ensuring feed safety, working with counterterrorism, and avoiding unsafe drug residues in food. These areas are all updated from the previous annual report.

The FY 2007 Report highlights CVM's activities in the area of protecting the health of companion animals. In the section on "Highlights from FY 2007," the report describes in detail the work CVM and the Food and Drug Administration did in response to the melamine contamination of dog and cat food, and it reports on the large number of companion animal health products approved during the fiscal year.

A new feature of this year's report is its look. Under the guidance of Center Director Dr. Bernadette Dunham, the report includes several photographs taken by members of CVM's staff. In a cover letter describing the report, Dr. Dunham said, "We are showcasing the spectacular photographic talents of the CVM staff, to make the report even more attractive and fun to look through."

The report will be made available on CVM's Web site later this year. Meanwhile, printed copies are available from CVM. Contact Shannon Cameron, HFV-12, room 3508, 7519 Standish Place, Rockville, MD 20855; e-mail, shannon.cameron@fda.hhs.gov; or phone phone at 240-276-9301.

Regulatory Activities – March-July 2008



Recalls

Hartz Mountain Corporation of Secaucus, NJ, is carrying out a firm-initiated Class I recall of 888 bottles of Hartz Vitamin Care for Cats and Kittens chewable tablets. The product, which was distributed nationwide, tested positive for the presence of *Salmonella*.

Purina Mills LLC d/b/a Land O'Lakes Purina Feed LLC, Camp Hill, PA, is carrying out a Class II, firm-initiated recall of 100,450 bags of 68 different animal feed products for horses, cattle, dear, lambs, and pigs that were distributed nationwide. The products are being recalled because they contain elevated levels of aflatoxins.

A Class II firm-initiated recall is ongoing by Smiths Medical PM, Inc., Waukesha, WI, for 16 units of the SurgiVet V6004 NIBP Monitor. The tantalum capacitor located at C5 on the V64004 display board of the Smith Medical PM, Inc., BCI® Mini-Torr Plus® NIBP Monitor with SpO2 Built-In Printer, may be reverse polarized. As a result the monitor might turn off or the monitor might immediately reset. The affected units were distributed in Alabama, Louisiana, New Mexico, Pennsylvania, Texas, Wisconsin, Canada, Ecuador, and Hong Kong.

A Class III firm-initiated recall has been completed by Cargill, Inc., of Billings, MT, for more than 34 tons of lamb, sheep, cattle, and llama feed because the products contained excessive and undeclared amounts of chlortetracycline. Distribution had been in Montana and Wyoming.

Milbank Mills, Inc., of Chillicothe, MO, is carrying out a firm-initiated Class III recall of two of its medicated feeds under its Silver Moon Feeds label. The products in question involve 73 10-lb. bags, 47,760 lbs. in bulk, and 2,219 50-lb. bags. The products, which were distributed in Missouri and Iowa, are being recalled because the incorrect bag tag was used.

IVX Animal Health, Inc., of St. Joseph, MO, is conducting a firm-initiated Class III recall of approximately 19,500 bottles of sterile aqueous solution products for animal use under the VetTek brand. The products, which were distributed only in Missouri, are being recalled due to a lack of sterility assurance.

A Class III firm-initiated recall has been completed by CP Medical of

(Continued, next page)

U.S., Japan Science/Technology Cooperation... *(Cont.)*

the Ministry of Agriculture, Forestry, and Fisheries; the Ministry of Public Management, Home Affairs, Posts, and Telecommunications; the Land, Infrastructure, and Transport Ministry; the Ministry of Foreign Affairs, and the Environmental Agency. The U.S. Embassy in Tokyo and the Japanese Embassy in Washington, DC, also play vital roles in program coordination and implementation.

In the United States, the overall UJNR is coordinated by the Bureau of Oceans and International Environmental and Scientific Affairs, U.S. Department of State. The National Oceanic and Atmospheric Administration of the Department of Commerce coordinate the committee's marine panels under the Marine Resources and Engineering Coordination Committee. The U.S. Department of Agriculture (USDA) coordinates the non-marine panels of the UJNR. The U.S. Departments of Commerce, Defense, Energy, Interior, and Transportation, the Environmental Protection Agency, the National Aeronautics and Space Administration, the National Institutes of Health, and the National Science Foundation also participate extensively in the program.

Regulatory Activities *(Continued)*

Portland, OR, for 878 boxes (12 packages in each box) of Polydioxanone (PDO) Monofilament Synthetic Absorbable Sterile Sutures. The recall was carried out because the package is labeled for a 37 mm 1/2 circle cutting needle, but may contain a 37 mm tapered needle. Distribution took place in Arizona, Michigan, Missouri, Nebraska, Nevada, Texas, and Israel.

Qualis Group LLC of Des Moines, IA, is carrying out a firm-initiated Class III recall of approximately 900 containers of Dionne Foot Rot Treatment Topical Antiseptic. The reason for the recall was that the active ingredient, iodine, failed stability testing. Distribution of the products took place in Illinois, Missouri, Washington, Oklahoma, North Carolina, Iowa, Tennessee, and South Dakota.

More than 61 million units of non-domestic bird food and other wild animal feed are the subject of an ongoing, firm-initiated Class III recall by Scotts Miracle Gro, Canal Winchester, OH. The products were distributed nationwide and are being recalled because the food and feed products were found to have been treated with pesticides that were not labeled with instructions for approved use only on wild bird or wild animal products or on all of the individual components that might be present in such stored grain mixtures.

Central Connecticut Cooperative Farmers Association, Manchester, CT, has completed a Class I firm-initiated recall of 5,870 lbs. (bulk and 50-pound bags) of 12% Equinator Integrity Horse Pellets that were distributed in the state. The reason for the recall was that the horse feed was contaminated with medication not approved for use in horses.

A total of 44,675 units of DVMax Ointment, Gentamincin Sulfate, USP, Betamethasone Valerate, USP, and Clotrimazole, USP Ointment, packaged in 10-gm, 20-gm, and 215-gm containers are the subject of a firm-initiated, ongoing Class II recall by IVX Animal Health Inc., St. Joseph, MO. The products, which were distributed nationwide, may not meet homogeneity specifications.

A Class III firm-initiated recall is ongoing by Southern States d/b/a Cooperative Milling, Inc., Gettysburg, PA, involving 1,142 bags of pelleted horse and sheep feeds. The products, which were distributed in Delaware, Maryland, New Hampshire, New Jersey, New York, Pennsylvania, and Virginia, were recalled due to elevated aflatoxin levels.

Warning Letters

FDA has sent a WARNING LETTER to Barry J. Paskewitz, Redwood Falls, MN, for violations of the adulteration provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA). Specifically, Mr. Paskewitz's cattle operation consigned a livestock hauler to transport 36 cows for slaughter as food. Inspection by the U.S. Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS) yielded the presence in one of the cows of residues of penciling in the kidney tissue at 0.21 parts per million (ppm). A tolerance of 0.05 ppm has been established for residues of penicillin in the uncooked edible tissues of cattle (21 CFR 556.510). This excess amount of the drug in the tissues caused the animal to be adulterated under section 402(a) of the FFDCA. FDA's investigation also found that this firm held animals under conditions that are so inadequate that medicated animals bearing potentially harmful drug residues could enter the food supply. The WARNING LETTER also cited Mr. Paskewitz for lacking a system to ensure that animals he buys, feeds, and then sells for slaughter as food have not been medicated or, if they have been medicated, to allow the firm to withhold the animals from slaughter for an appropriate period of time to deplete potentially hazardous residues of drugs from edible tissues.

John D. Johnson, owner of the Johnson Dairy of Eaton, CO, received a WARNING LETTER for violations of the same adulteration provision of the FFDCA involving the sale of four different animals. Specifically, this firm sold a Holstein cow for slaughter as food that was found to have flunixin in the muscle tissue at 0.061 ppm and in the liver tissue at 0.570 ppm. A tolerance of 0.025 ppm has been established for residues of this drug in the edible muscle tissues of cattle and 0.125 ppm in the edible liver tissue of cattle (21 CFR 556.286). The presence of these excess levels of flunixin in the animal tissues caused the animal to be adulterated under section 402(a) of the FFDCA. A second Holstein cow was found to have residues of sulfadimethoxine in the liver tissue 0.12 ppm, thereby exceeding the established tolerance of 0.10 ppm as codified in 21 CFR 556. 640. A third Holstein cow was found to have residues of flunixin in the liver tissue at 0.341 ppm, exceeding the established tolerance of 0.125 ppm set forth in 21 CFR 556.286. A fourth Holstein cow was found to have residues of flunixin in the muscle tissue at 0.270 ppm and in the liver tissue at 4.912 ppm, exceeding the established tolerances of 0.025 ppm and 0.125 ppm, respectively (21 CFR 556.286). Adequate treatment records were also found to be lacking.

A WARNING LETTER has been sent by FDA to Frank and Mary Arburua, co-owners of the Pyrenees Dairy in Chino, CA, for violations of the adulteration provisions of the FFDCA. Specifically, the dairy sold three cows on three different dates and all were found to contain residues of penicillin in the kidney and liver tissues, respectively, as follows: 0.44 ppm in the kidney, 0.24 ppm in the liver; 0.28 ppm in the kidney, 0.17 ppm in the liver; and 0.19 ppm in the kidney, and 0.07 ppm in the liver. A tolerance of 0.05 ppm has been established for residues of penicillin in the edible tissues of cattle (21 CFR 556. 510), thus rendering the three cows adulterated under section 402(a) of the FFDCA. In addition, the firm was found to lack adequate animal treatment records and was also found to be in violation of the extralabel use provisions of the Act (sections 512(a) and 501(a)).

Violations of the adulteration provisions in the FFDCA also led to the issuance of a WARNING LETTER by FDA to Richard Van Dyk, owner of the Van Dyk Dairy #1, Jerome, ID. Specifically, the company sold a dairy cow for slaughter as food that was found to contain residues of the drug sulfadimethoxine at 0.14 ppm in the liver tissue. A tolerance of 0.1 ppm has been established for residues of this drug in the edible uncooked liver tissue of cattle (21 CFR 556.640). USDA's sampling also revealed the presence of the drug sulfamethazine in the same animal at 0.46 ppm in the liver tissue and 0.19 ppm in the muscle tissue; there is no established tolerance for sulfamethazine in lactating dairy cows. The presence of these drugs at inappropriate levels rendered them adulterated under section 402(a) of the FFDCA. In addition, the firm was found to have adulterated the drug Sustain III (sulfamethazine) Bolus within the meaning of section 501(a) of the FFDCA by failing to use the drug in conformance with

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Regulatory Activities *(Continued)*

its approved labeling. Treatment records were also found to be lacking.

FDA issued a WARNING LETTER to John and Maria Nunes, co-owners of the John and Maria Nunes Dairy, Turlock, CA, for violations of the adulteration provisions of the FFDCA. Specifically, the dairy consigned a dairy cow for slaughter as food that contained residues of the drug, gentamicin, in the kidney tissue. No tolerance for residues of this drug has been established by FDA (21 CFR 556.300), thereby rendering the animal adulterated under section 402(a) of the Act. In addition, because the firm provided a signed certification that no animal would be supplied containing any illegal drug residues, it was found in violation of section 301(h) of the FFDCA (providing a false guaranty). In addition, the dairy adulterated the new animal drugs, Legacy Gentamicin Sulfate Solution, Duramycin 100 Oxytetracycline Hydrochloride Injection, Sulfadimethoxine Injection 40%, Albon Sulfadimethoxine Boluses, and PEN-AQUEOUS Penicillin G Procaine, Injectable Suspension U.S.P., within the meaning of section 501(a) of the FFDCA by failing to use the drugs in conformance with their approved labeling.

John and Jolene Schoneveld and Martin and Alice Bouma, co-owners of the Lakeview Dairy Farms, Bakersfield, CA, have received a WARNING LETTER from FDA for violations of the adulteration provisions of the FFDCA. Specifically, the dairy consigned a dairy cow for sale at auction for slaughter as food. FSIS sampling revealed the presence of the drug flunixin in the liver at 0.448 ppm and in the muscle tissue at 0.063 ppm. A tolerance of 0.125 ppm in the liver and 0.025 ppm in the muscle tissue has been established for residues of this drug (21 CFR 556.286). The excess levels thereby rendered the animal adulterated pursuant to section 402(a) of the Act. The firm was also found to have adulterated Flunixin Meglumine Injectable Solution under section 501(a) of the FFDCA by failing to use the drug in conformance with its approved labeling. The firm also failed to maintain complete treatment records for the operation.

A WARNING LETTER has been issued to Gerald L. Gilbert, president of Country Morning Farms, Warden, WA, for violations of the adulteration provisions of the FFDCA. Specifically, the farm consigned one dairy cow for slaughter as food that contained residues of the drug sulfadimethoxine in the liver tissue at 14.45 ppm. A second dairy cow that was also consigned for slaughter as food contained residues of the same drug in the liver tissue at 5.81 ppm. A tolerance of 0.1 ppm has been established by FDA for residues of sulfadimethoxine in the edible tissues of cattle (21 CFR 556.640(b)), rendering both cows adulterated under Section 501(a)(5) of the FFDCA. The dairy was found to have not used the drug in conformance with its approved labeling. The drug was administered at a higher dosage than indicated on the approved label, and the dairy did not observe the pre-slaughter withdrawal period required by the label.

FDA has sent a WARNING LETTER to Neil and Paul Chelton and Chad Keeler, co-owners of Pal-Nel Farms, Corry, PA, for violations of the adulteration provisions of the FFDCA. The farm consigned two bob veal calves for slaughter as food. FSIS samples taken of them revealed the presence of 272.43 ppm neomycin in the kidney tissue of one animal and 134.44 ppm neomycin in the kidney tissue of the other one. A tolerance of 7.2 ppm has been established by FDA for residues of this drug (21 CFR 556.430), thereby rendering the two animals adulterated under Section 402(a) of the Act. Failure to follow drug withdrawal times and violations of the extralabel use provisions as set forth in 21 CFR 530 were also cited in the WARNING LETTER.

Violations of Section 402(a) of the FFDCA were also cited in a WARNING LETTER issued by FDA to Chris Cole, owner of the A.B. Cole Dairy Farm, Meshoppen, PA. Specifically, the dairy consigned a bob veal calf to be slaughtered for food. Sampling revealed the presence of the drug sulfamethazine in the muscle tissue of the calf at 46.18 ppm and in the liver tissue at 36.41 ppm. A tolerance of 0.1 ppm has been established by FDA for residues of this drug in the uncooked edible tissues of cattle (21 CFR 556.670), thereby rendering the animal adulterated. 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. An adequate system to ensure that animals medicated by the dairy have been withheld from slaughter for appropriate periods of time to permit depletion of potentially hazardous residues of drugs from edible tissues was lacking.

Jonathan J. Glick, owner of a dairy operation in Howard, PA, has received a WARNING LETTER from FDA for violations of the adulteration provisions of the FFDCA. Specifically, the dairy sold a cow for slaughter as food that was found to contain residues of the drug sulfadimethoxine in liver tissue at 3.05 ppm and in the muscle tissue at 1.41 ppm. A tolerance of 0.1 ppm has been established by FDA for residues of this drug in the uncooked edible tissues of cattle (21 CFR 556.640), rendering the animal adulterated under Section 402(a) of the Act. FDA's investigation also found that the firm held animals under conditions that were so inadequate that medicated animals bearing potentially harmful drug residues were likely to enter the food supply.

FDA has issued a WARNING LETTER to Phil G. Mlsna, president of Mlsna Dairy Supply, Inc., Cashton, WI, for violations of the adulteration provisions of the FFDCA. Specifically, the dairy consigned to a hauler a dairy cow that was found to have 0.128 parts per million (ppm) of the drug, flunixin, in the liver tissue. A tolerance of 0.125 ppm has been established for residues of this drug in the liver of cattle (21 CFR 556.286(b)(1)(i)). The presence of the excess amount of flunixin caused the cow to be adulterated under Section 402(a) of the FFDCA. The dairy was also found to adulterated sulfadimethoxrine and flunixin meglumine within the meaning of section 501(a)(5) of the FFDCA when it failed to use these drugs in conformance with their approved labeling. Specifically, the extralabel use requirements were not followed appropriately.

Ronald P. St. John, managing partner of Alliance Dairies, Trenton, FL, has received a WARNING LETTER from FDA for offering for slaughter an adulterated animal. Specifically, the dairy sold a cow for slaughter as food that was later found to contain residues of penicillin in the kidney tissue at 0.17 ppm. A tolerance for this drug of 0.05 ppm has been established (21 CFR 556.510), rendering the animal adulterated under Section 402(a) of the FFDCA. The firm was also found to have adulterated the new animal drugs penicillin and tylosin within the meaning of Section 501(a)(5) of the Act when it

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Regulatory Activities *(Continued)*

failed to use them in accordance with their approved labeling. The firm was also found to have provided a false guaranty in violation of Section 301(h) of the FFDCA.

Adulteration violations were also cited in a WARNING LETTER from FDA to Jerry Harris, owner of Harris Dairies, Rising Star, TX. The firm sold a Holstein dairy cow for slaughter as food that was later found to have residues of the drug sulfadimethoxine at 0.13 ppm in the liver tissue. A tolerance of 0.1 ppm has been established for residues of this drug in the edible tissues of cattle (21 CFR 556. 640(b)(1)), thus rendering the animal adulterated under Section 402(a) of the FFDCA. In addition, the firm adulterated a brand of sulfadimethoxine antibacterial soluble powder within the meaning of section 501(a)(5) of the FFDCA when it failed to use the drug in conformance with its approved labeling with respect to extralabel uses.

Daniel Logue, president of the Central Connecticut Cooperative Farmers Association, Manchester, CT, has received a WARNING LETTER for violations of the safety and adulteration provisions of the FFDCA. Specifically, samples of the firm's equine feed, 12% Equinator Integrity Horse Pellets, BH716, were found to contain the new animal drugs lasalocid sodium and salinomycin, neither of which is approved by FDA for use in equine feed. The presence of the drugs rendered the equine feed unsafe under Section 512(a)(2) of the Act and adulterated under Section 501(a)(6) of the Act.

A WARNING LETTER has been issued to Gary Domina of Enosburg Falls, VT, for violations of the adulteration provisions of the FFDCA. According to the letter, he offered an animal for slaughter for sale as food that contained residues of the drug dihydrostreptomycin in the kidney tissue at 9.78 ppm. A tolerance of 2.0 ppm has been established for residues of this drug in the kidney of cattle (21 CFR 556.200)). In addition, FDA's investigation found that Mr. Domina adulterated the new animal drug dihydrostreptomycin within the meaning of section 501(a)(5) of the Act when he failed to use this drug in conformance with its approved labeling. The approved application for this drug, Quartermaster brand of dihydrostreptomycin, restricts this drug to use by or on the order of a licensed veterinarian. The use of this drug was not by or on the order of a licensed veterinarian, and because the use of this drug deviated from its approved application, the drug was unsafe under section 512(a)(1)(A) of the FFDCA and the use caused it to be adulterated within the meaning of section 501(a)(5) of the Act.

Approvals for March-July 2008

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

- PANACUR PLUS (ivermectin, fenbendazole, and praziquantel) Soft Chews (NADA 141-286), filed by Intervet, Inc., Millsboro, DE. The approved NADA provides for the veterinary prescription use of PANACUR PLUS (ivermectin, fenbendazole, and praziquantel) Soft Chews for the treatment and control of various internal parasites and for the treatment of canine heartworm disease in adult dogs. Notice of approval was published June 13, 2008.

- CONVENIA (cefovecin sodium) Injectable (NADA 141-285), filed by Pfizer, Inc., New York, NY. The approved NADA provides for the veterinary prescription use of CONVENIA (cefovecin sodium) Injectable in cats and dogs by subcutaneous injection for the treatment of skin infections. Notice of approval was published May 22, 2008.

- NUFLOR GOLD (florfenicol) Injectable Solution (NADA 141-265), filed by Schering-Plough Animal Health Corp., Summit, NJ. The approved NADA provides for the use of NUFLOR GOLD (florfenicol) Injectable Solution by subcutaneous injection in beef and non-lactating dairy cattle for the treatment of bovine respiratory disease. Notice of approval was published April 18, 2008.

- ZILMAX (zilpaterol hydrochloride) RUMENSIN (monensin USP), TYLAN (tylosin phosphate), and MGA (melengestrol acetate) Type A medicated articles (NADA 141-280), filed by Intervet, Inc., Millsboro, DE. The approved NADA provides for the use of ZILMAX (zilpaterol hydrochloride), RUMENSIN (monensin USP), TYLAN (tylosin phosphate), and MGA (melengestrol acetate) Type A medicated articles to make dry and liquid four-way combination Type B and Type C medicated feeds used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness; for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*; and for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes*; and suppression of estrus (heat) in heifers fed in confinement for slaughter during the last 20 to 40 days on feed. Notice of approval was published April 8, 2008.

- ZILMAX (zilpaterol hydrochloride) and MGA (melengestrol acetate) Type A medicated articles (NADA 141-284), filed by Intervet, Inc., Millsboro, DE. The approved NADA provides for the use of ZILMAX (zilpaterol hydrochloride) and MGA (melengestrol acetate) Type A medicated articles to make dry and liquid two-way combination Type B and Type C medicated feeds used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness; and for suppression of estrus (heat) in heifers in confinement for slaughter during the last 20 to 40 days on feed. Notice of approval was published March 31, 2008.

- BMD (bacitracin methylene disalicylate) and NICARB (nicarbain) Type A medicated articles (NADA 141-279), filed by Alpharma, Inc., Bridgewater, NJ. The approved NADA provides

(Continued, next page)

Approvals for March-July 2008 *(Continued)*

New Animal Drug Applications (Continued)

for the use of BMD (bacitracin methylene disalicylate) and NICARB (nicarbazin) Type A medicated articles to formulate two-way combination drug Type C medicated feeds for broiler chickens. Notice of approval was published March 26, 2008.

- ZILMAX (zilpaterol hydrochloride) and RUMENSIN (monensin USP) Type A medicated articles (NADA 141-278), filed by Intervet, Inc., Millsboro, DE. The approved NADA provides for the use of ZILMAX (zilpaterol hydrochloride) and RUMENSIN (monensin USP) Type A medicated articles to make dry and liquid, two-way combination Type B and Type C medicated feeds for increased rate of weight gain, improved feed efficiency, and increased carcass leanness; and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 20 to 40 days on feed. Notice of approval was published March 18, 2008.

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

- VETISULID (sulfachlorpyridazine sodium) Powder (NADA 33-373), filed by Fort Dodge Animal Health Corp., Fort Dodge, IA. The NADA is approved for the oral use of VETISULID (sulfachlorpyridazine sodium) Powder in calves and swine for the treatment of diarrhea caused or complicated by *Escherichia coli* (colibacillosis). The supplemental NADA provides for a revised food safety warning statement for oral use of sulfachlorpyridazine in the milk replacer of ruminating calves. Notice of approval was published June 24, 2008

- TYLAN 40 SULFA-G (tylosin phosphate and sulfamethazine) Elliptical Pellets (NADA 041-275), filed by Elanco Animal Health, a Division of Eli Lilly & Co., Indianapolis, IN. The approved supplemental NADA provides for revision of an effectiveness claim and pathogen nomenclature on TYLAN 40 SULFA-G (tylosin phosphate and sulfamethazine) Elliptical Pellets, a Type A medicated article. Notice of approval was published June 17, 2008.

- DERAMAXX (deracoxib) Chewable Tablets, (NADA 141-203), filed by Novartis Animal Health US, Inc., Greensboro, NC. The approved supplemental NADA provides for the addition of a 50-milligram size of DERAMAXX (deracoxib) Chewable Tablets used for the control of pain and inflammation in dogs. Notice of approval was published June 13, 2008.

- PROHEART 6 (moxidectin) Sustained Release Injectable for Dogs (NADA 141-189), filed by Fort Dodge Animal Health, Division of Wyeth, Fort Dodge, IA. The approved original NADA provides for veterinary prescription use of PROHEART 6 (moxidectin) Sustained Release Injectable for Dogs, used for prevention of heartworm disease and treatment of existing hookworm infections. The approved supplemental NADA updates the warning, precaution, adverse reactions, and post-approval experience sections of the product labeling. Notice of approval was published June 9, 2008.

- BAYTRIL 100 (enrofloxacin) injectable solution (NADA 141-068), filed by Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, KS. The approved supplemental NADA provides for the use of BAYTRIL 100 (enrofloxacin) injectable solution in swine for the treatment and control of swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*. Notice of approval was published April 23, 2008.

- VETSULIN (porcine insulin zinc) Suspension (NADA 141-236), filed by Intervet, Inc., Millsboro, DE. The approved supplemental NADA provides for the veterinary prescription use of VETSULIN (porcine insulin zinc) Suspension for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in cats with diabetes mellitus. The application also provides for a lower initial dosage of insulin for dogs. Notice of approval was published April 18, 2008.

- BAYTRIL 100 (enrofloxacin) injectable solution (NADA 141-068), filed by HealthCare, LLC, Animal Health Division, Shawnee Mission, KS. The approved NADA provides for the use of Baytril 100 (enrofloxacin) injectable solution for the treatment of bovine respiratory disease associated with several bacterial pathogens. The supplemental NADA provides for the use of the product in female dairy cattle less than 20 months of age. Notice of approval was published April 2, 2008.

- PEN BP-48 (penicillin G benzathine and penicillin G procaine) injectable suspension (NADA 65-498), filed by IVX Animal Health, Inc., St. Joseph, MO. The approved NADA provides for the use of PEN BP-48 (penicillin G benzathine and penicillin G procaine) injectable suspension for the treatment of animal diseases associated with several bacterial pathogens. The supplemental NADA provides for changing a bovine pathogen name from *Corynebacterium pyogenes* to *Actinomyces pyogenes* on product labeling. Notice of approval was published March 31, 2008.

- TETRADURE 300 (oxytetracycline) Injection (NADA 141-143), filed by Norbrook Laboratories, Ltd., Newry, Northern Ireland. TETRADUE 300 (oxytetracycline) Injection is approved for use to treat various bacterial diseases of cattle and swine. The supplemental NADA provides for changing a bovine pathogen genus from *Haemophilus* to *Histophilus* on product labeling. Notice of approval was published March 20, 2008.

- PEN-G MAX (penicillin G procaine) Aqueous Suspension (NADA 65-110), filed by IVX Animal Health, Inc., St. Joseph, MO. PEN-G MAX (penicillin G procaine) Aqueous Suspension is used for the treatment of animal diseases associated with several bacterial pathogens. The supplemental NADA provides for changing the pathogen name from *Erysipelothrix insidiosa* to *Erysipelothrix rhusiopathiae* on product labeling. Notice of approval was published March 17, 2008.

(Continued, next page)

Approvals for March-July 2008 *(Continued)*

Supplemental New Animal Drug Applications (Continued)

- TOMORROW (cephapirin benzathine) Intramammary Infusion (NADA 108-114), filed by Fort Dodge Animal Health, Division of Wyeth, Fort Dodge, IA. The supplemental NADA revises labeling for TOMORROW (cephapirin bezathine) Intramammary Infusion administered to dairy cows entering their dry period for the treatment of mastitis. Notice of approval was published March 7, 2008.

- VALBAZEN (albendazole) Oral Suspension (NADA 110-048), filed by Pfizer, Inc., New York, NY. The supplemental NADA provides for the use of VALBAZEN (albendazole) Oral Suspension for the treatment of liver flukes in nonlactating goats. The approval of this supplemental NADA relied on publicly available safety and effectiveness data contained in Public Master File 5582, which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for the use of new drugs in minor animal species and special uses. Notice of approval was published February 29, 2008.

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

- BUTORPHIC (butorphanol tartrate) Injection (ANADA 200-332), filed by Lloyd, Inc., Shenandoah, IA. The ANADA provides for the veterinary prescription use of BUTORPHIC (butorphanol tartrate) Injection in horses for the relief of pain associated with colic and postpartum pain. Lloyd's BUTORPHIC Injection is approved as a generic copy of TORBUGESIC, sponsored by Fort Dodge Animal Health, Division of Wyeth, under NADA 135-780. Notice of approval was published June 2, 2008.

- PETREM (sevoflurane) (ANADA 200-438), filed by Minrad, Inc., Buffalo, NY. The ANADA provides for the use of PETREM (sevoflurane) inhalant anesthetic in dogs. The product is approved as a generic copy of SEVOFLO, sponsored by Abbott Laboratories, under NADA 141-103. Notice of approval was published May 7, 2008.

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

- BIMECTIN (ivermectin) Paste 1.87% (ANADA 200-326), filed by Cross Vetpharm Group Ltd., Dublin, Ireland. The approved supplemental ANADA provides for the addition of effectiveness claims against various species of internal parasites of horses on the labeling of BIMECTIN (ivermectin) Paste 1.87%. Notice of approval was published June 17, 2008.

- FLUNIXIN MEGLUMINE INJECTION (ANADA 200-124), filed by IVX Animal Health, Inc., St. Joseph, MO. The supplemental ANADA provides for veterinary prescription use of FLUNIXIN MEGLUMINE INJECTION intravenously in lactating dairy cattle for the control of pyrexia associated with acute bovine mastitis. Notice of approval was published May 15, 2008.

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