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Center for Veterinary Medicine
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FDA Releases Final Guidance on Genetically Engineered Animals

by Jon F. Scheid, Editor

The Food and Drug Administration issued a final guidance in January 2009 to clarify FDA's approach to the regulation of genetically engineered (GE) animals and to provide industry and other stakeholders an overview of how producers of these animals can meet their responsibilities and obligations as they develop these animals. This guidance, and accompanying information, including a series of question and answer documents can be found at *www.fda.gov/cvm/GEAnimals.htm*.

According to the Federal Food, Drug, and Cosmetic Act (FFDCA), the "recombinant DNA (rDNA) construct" that is engineered to introduce a new trait into an animal fits the legal definition of a new animal drug because it is an article other than food intended to affect the structure or function of an animal. When scientists introduce a new rDNA construct into an animal, the animal is then often referred to as a GE animal.

FDA's Center for Veterinary Medicine has the authority under the FFDCA to regulate the commercialization of new animal drugs. The guidance says that CVM will continue to use this authority to review animals carrying the genetically engineered constructs.

According to Dr. Randall Lutter, FDA's Deputy Commissioner for Policy, FDA has been using this approach since producers of GE animals began to approach the Agency. "This draft guidance should clarify for all of our stakeholders the approach the FDA has been using to regulate GE animals for some time," he said. "The goal of the guidance is to explain to producers of GE animals how to meet their obligations under the existing laws and regulations," Dr. Lutter said. FDA issued the guidance at this time because the technology has evolved to a point where commercialization of these animals is rapidly approaching reality.

In addition, the guidance should help consumers understand how FDA is overseeing the commercialization of GE animals and what protections are in place, Dr. Lutter added.

CVM is in the best position to provide oversight for this technology, according to CVM Director Dr. Bernadette Dunham. "CVM is comprised of a dedicated staff of professionals trained to examine the impact of new science on the health of humans and other animals," Dr. Dunham said during a January 15, 2009, media teleconference about the final GE animal guidance. "We have assembled a multi-disciplinary group of individuals from across the Center who work together to address the complex and often novel issues that this technology can pose. That group includes molecular biologists, veterinarians, environmental specialists, animal scientists, professors, and board certified toxicologists," she said.

What is a GE animal?

GE animals "are simply animals such as cattle, pigs, fish, and goats that have had a piece of DNA added to them to introduce a desirable trait," according to Dr. Larisa Rudenko, CVM's Senior Advisor for Biotechnology. She added, "The GE animals themselves are not drugs; rather they contain new animal drugs."

GE animals were first produced in the 1980s, and since then the technology has expanded. Some animals were developed to produce pharmaceuticals for human use in their milk or blood, or provide cells, tissues, or organs for human transplantation. Some GE animals will be better able to resist disease, possibly including bovine spongiform encephalopathy, also known as "mad cow disease." Other animals are being developed so that they can produce high-value products for industrial use or for consumers. Some are being developed because they will have less of an effect on the environment. And others will produce food products with desirable attributes, such as pork with higher levels of Omega-3 fatty acids.

Oversight

As with any review of a new animal drug, CVM will be considering the safety of the gene construct to the animal, the safety of any food derived

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In This Issue

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

New NARMS Retail Meat Report Streamlined, More User Friendly

by Jon F. Scheid, Editor

The most recent National Antimicrobial Resistance Monitoring System (NARMS) Retail Meats report, containing data from 2006, was posted on the Center for Veterinary Medicine's Web site in October 2008 (*http://www.fda.gov/cvm/2006NARMSAnnualRpt.htm*).

The report's authors have improved the document's readability by eliminating duplicative information to reduce its complexity and by highlighting key information.

NARMS is a national monitoring program operated jointly by CVM, the U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC). Through the program, public health specialists collect data to monitor changes in antimicrobial drug susceptibilities of certain bacteria collected from humans, animals, and retail meats. They publish the data for wider use.

The report's authors had received some feedback from users that said the previous reports were difficult to navigate, which led to the revision. As an indication of the streamlining that took place, the latest report is 90 pages, down from the 240 pages of the previous report.

The NARMS program began in 1996. Since 2002, the program includes surveillance of retail cuts of meat. Each month, officials from 10 sites across the United States each collect 10 chicken breasts, ground turkey, ground beef, and pork chops samples from retail operations.

The samples are purchased by personnel at "FoodNet" (Foodborne Diseases Active Surveillance Network) sites. FoodNet is a joint effort by the Department of Health and Human Services, State health departments, and USDA. The FoodNet program was created to capture a more accurate and complete picture of trends in the occurrence of foodborne illness.

Under the NARMS retail meat program, the 10 FoodNet sites analyze the samples for *Campylobacter* and *Salmonella* using standard methods. In addition, four sites

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FDA Releases Final Guidance... *(Cont.)*

from the animal (if it is intended to enter the food supply), the effectiveness of the construct, and any possible threat to the environment.

Transparency is a frequently cited concern about the approval of GE animals. In the final version of the guidance, the Agency announced its intent to hold public advisory committee meetings prior to approving any GE animal. These meetings are open to the public and will aid in informing the public about the product that FDA is reviewing and how the Agency has conducted its review. Once an animal drug is approved and notice of the approval appears in the *Federal Register*, CVM publicly releases key information about the approval, which is posted on its Web site.

Addressing environmental concerns will be an important part of the pre-approval process, Dr. Rudenko said. The pre-approval process that will apply to GE animals "is really quite rigorous," she said. "We are very concerned about appropriate record keeping, and that the appropriate studies be conducted to determine safety to the animal, food safety if the GE animal is intended for food, and making sure that the GE animal exhibits the traits that the sponsor intends them to exhibit." GE animal sponsors also will have to perform an environmental assessment including providing sufficient information for CVM to be able to examine the possibility of a GE animal escaping, potentially interbreeding with wild populations, and assessing the risk(s) that may pose.

If a food produced from a GE animal is materially different from food derived from non-GE animals, it will have to be labeled. Dr. Eric Flamm, Senior Science Policy Advisory at FDA, said that, if a GE pig produces meat with more omega-3-fatty acids than is contained in meat from non-GE animals, the meat would have to be labeled as containing the higher levels. "If you have changed the food in a material way, that change has to be indicated in labeling," he said. Labeling would not be required, though, to indicate only that a food was derived from GE animals.

Dr. Rudenko added that, based on risk, the Agency might decide to apply enforcement discretion to some GE animals. For instance, animals of species not traditionally consumed as food, used for laboratory research, and kept in highly contained conditions would not need to be approved. In addition, some other non-food animals, once subject to a risk-based review, might also be marketed without a formal approval (e.g., GloFish).

However, she added, any sponsor developing a GE animal, no matter what the use, should discuss the development with CVM to determine what requirements the sponsor will have to follow.

FDA VETERINARIAN

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BSE Rules

CVM Releases Draft Guidance on New BSE Rule

by Jon Scheid, Editor

The Food and Drug Administration has developed a draft compliance guide for renderers to answer questions raised by the rendering industry about a rule written to enhance protections against bovine spongiform encephalopathy (BSE).

The draft compliance guide includes topics such as the requirement for removing certain materials from cattle that can no longer be rendered for feed use, methods for determining the age of cattle, liability issues, and requirements for recordkeeping.

The final rule was announced in April 2008. The rule defines "cattle material prohibited in animal feed," or CMPAF, and prohibits it from any animal feed or pet food. (Text of the rule can be accessed at *www.fda.gov/cvm/bsetoc.html*.)

Cattle material prohibited from all animal feed as defined by this rule includes brains and spinal cords from cattle 30 months of age or older. Therefore, properly removing the brain and spinal cord and carefully determining the age of cattle are key steps for complying with the rule.

Also included in the definition of cattle material prohibited from all feeds are the carcasses of any BSE-positive cattle, and carcasses of cattle defined as "not inspected and passed for human consumption" (commonly referred to as "deads") that do not have the brain and spinal cord removed or are not demonstrated to be less than 30 months of age.

The rule also prohibits tallow (defined as fat from cattle) for use in ruminant feed that contains more than 0.15 percent insoluble impurities. And it prohibits the use of

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New NARMS Retail Meat Report... *(Continued)*

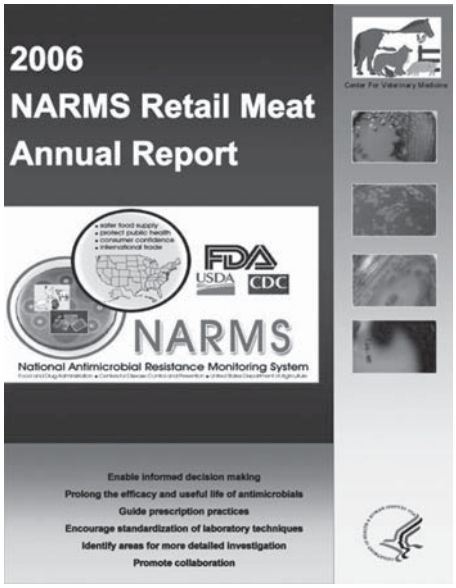
culture samples they collect for the presence of *Enterococcus* and *E. coli*, using FDA-described methods.

Bacterial isolates are sent to FDA/CVM for confirmation of species and serotypes, antimicrobial susceptibility testing, and genetic analysis.

Changes to the report

Earlier reports presented fairly extensive information by State, but those data were useful only to the individual States, according to Dr. Patrick McDermott, acting NARMS Director. Also, previous reports combined some data from different types of meat, "which did not offer insight into sources of resistance," Dr. McDermott said. In addition, previous reports contained some redundant information, which was removed for the most recent report.

The newer report also provides more usable information on *Campylobacter*. "We removed the tables for overall data on *Campylobacter* and added tables and figures that show specifics for



C. jejuni and *C. coli*," Dr. McDermott said. Those two *Campylobacter* species account for more than 90 percent of all isolates, and they show "important and substantial difference in their rates of resistance," he said. "Because *C. jejuni* causes more than 90 percent of human infections, resistance by species provides an added layer of information needed to estimate public health consequences of resistance," he added.

Another significant improvement in the report about 2006 data is that it contains revised information on multidrug resistance patterns for *Salmonella* and *E. coli*. This information highlights patterns of public health interest, such as ACSSuT (ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline), ACT/S (ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole), and ACSSuTAuCf (ACSSuT, amoxicillin-clavulanic acid, and ceftiofur).

Although no further changes are currently planned, Dr. McDermott said he continues to seek feedback from users so he can make improvements in the future. But for now, he said, "We believe the changes make the report more concise and user-friendly, and thus more accessible by stakeholders."

BSE Rules

...Draft Guidance on New BSE Rule (Continued)

mechanically separated beef derived from material that falls under the definition of CMPAF.

The rule places significant responsibility on renderers, who in most cases are the first handlers of animal protein used in feed. Since the rule was published, rendering companies have asked for guidance to make sure they know how to be in compliance, especially with the provisions about adequate removal of the brain and spinal cord. Renderers are also concerned with liability issues, because they receive material, including dead cattle, from many sources over which they have no direct control.

Representatives of the rendering industry have met with Center for Veterinary Medicine officials to discuss the requirements of the rule, according to Shannon Jordre with CVM's Division of Compliance. In those meetings, and through an ongoing series of e-mail messages and phone calls, the rendering industry has presented its questions and concerns.

CVM initially addressed the industry's concerns in July 2008 when it issued a document presenting a series of questions and answers about implementing the rule. (*www.fda.gov/cvm/bse_QA.htm*)

The new draft guidance (#195, "Small Entities Compliance Guide for Renderers – Substances Prohibited From Use in Animal Food or Feed," *www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0597-gdl.pdf*), issued on November 25, 2008 offers more information.

The approaches presented in the draft guidance are only suggestions. FDA encourages the industry to be innovative in developing better alternatives, according to Dr. Burt Pritchett, a member of CVM's animal feed safety team and a specialist in BSE.

The guidance was published as draft and represents FDA's current thinking on the topic. Interested parties may comment on the guidance document before it is finalized.

The draft guidance defines CMPAF and states that if "you (i.e., renders) receive, manufacture, blend, process, or distribute any of these materials, you must comply with the provisions of this regulation."

Removing brain, spinal cord

The draft guidance says that no single method is best for removing the brain and spinal cord, saying instead that companies can select the method that would work the best based on the layout of their plant, the cost of equipment, the skill level of employees, and the availability of alternative means of disposing of tissue surrounding the brain and spinal cord.

Some options for brain removal include using suction equipment to remove the brain through the *foramen magnum*, which is a large hole at the base of the skull through which the spinal cord passes; opening the skull and removing the brain; or leaving the brain in the skull and treating the entire head as CMPAF.

Options for removing the spinal cord include removing the hide, eviscerating the carcass, and using a saw to split the carcass down the midline to expose the spinal canal; cutting out the spinal cord with surrounding vertebral column; or removing the skeletal muscle or other parts and leaving the remaining carcass—which would contain the spinal cord in place—and treat it as CMPAF.

The approaches presented in the draft guidance are only suggestions. FDA encourages the industry to be innovative in developing better alternatives, according to Dr. Burt Pritchett, a member of CVM's animal feed safety team and a specialist in BSE.

Cattle aging

Because material taken from cattle under 30 months of age will not be considered CMPAF, the draft guidance explains what methods are acceptable for determining the age of (or "aging") cattle. The best evidence of age, according to the guidance, is documentation from the current owner, which should include the owner's name and address and the date and location of the animal's birth. This documentation should be linked to a marking on the animal, such as an ear tag, implant, or tattoo.

Renderers can also rely on an examination of the animal's teeth (dentition) to determine age. In cattle, the third and fourth permanent incisors come through the gum line between ages of 24 and 30 months. "Therefore," the draft guidance says, "cattle would be considered to be less than 30 months of age if the third permanent incisor has not yet come through and grown above the gum line." The draft guidance includes diagrams of teeth in the mouth of an animal to show what to look for.

Recordkeeping, liability

The draft guidance says renderers can rely on certification from the livestock producer about the age of the animals, or about the fact that CMPAF was separated from other material at a slaughter facility, for example. It further states that the government considers the "knowing

(Continued, next page)

Regulatory Activities: August – November 2008

Warning Letters

Jerald D. and Jeremy D. Visser, co-owners of Viacres LLC and Natural Milk, LLC, Sumas, WA, have received a Warning Letter for violations of the adulteration provision of the Federal Food, Drug, and Cosmetic Act (FFDCA). Specifically, the dairies sold three dairy cows for slaughter as food that were found to contain excess levels of the drug sulfadimethoxine in the edible tissues. In the first instance, an analysis of tissue samples revealed the presence of sulfadimethoxine at 6.47 parts per million (ppm) in the muscle tissue and 5.40 ppm in the liver tissue. In the second instance, the dairy cow in question was found to contain residues of the same drug in the muscle tissue at 7.73 ppm and in the liver tissue at 4.12 ppm. In the third instance, the dairy cow was found to contain sulfadimethoxine in the muscle tissue at 0.41 ppm and in the liver tissue at 0.42 ppm. FDA has established a tolerance of 0.1 ppm for residues of this drug in the edible tissues of cattle. In addition, the firms' treatment records were found to be so inadequate that medicated animals bearing potentially harmful drug residues were likely to enter the food supply. The dairy operation failed to maintain complete treatment records, the Warning Letter said.

A Warning Letter has been issued to John E. Shrock, owner of a dairy farm in Middlefield, OH, for violations of the adulteration provision of the FFDCA. Specifically, Mr. Shrock sold a bob veal calf that was subsequently found to contain residues of the drug sulfamethazine in the liver tissue at 19.94 ppm and in the muscle tissue at 22.94 ppm. FDA has established a tolerance for this drug in the edible tissues of cattle at 0.1 ppm. Mr. Shrock was also found to have violated the extralabel use provision of the FFDCA and implementing regulations because the dairy operation did not use sulfamethazine as directed by its approved labeling.

Violations of the new animal drug provisions of the FFDCA were cited in a Warning Letter issued to Dr. Race L.

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BSE Rules ...Draft Guidance on New BSE Rule *(Continued)*

and willful making of any false, fictitious or fraudulent statements or representations" about such matters covered by the regulation potentially a criminal offense.

Under the rule, recordkeeping requirements apply to any company that renderers cattle material. In general, the records must indicate that CMPAF was not used to produce animal feed. Often, normal business records are sufficient, the draft guidance said.

Renderers can use third-party certification to verify that a supplier effectively kept CMPAF out of material shipped to the renderer.

Records must be kept for 1 year after they were created. The draft guidance urges renderers to tell their suppliers about the recordkeeping requirement and the requirement to keep the records for 1 year.

Compliance, implementation

The requirement for compliance with the rule begins when the rule goes into effect.

CVM has been taking other steps besides developing the draft guidance to help industry get ready. For example, CVM had participated in two "Webinars" (a seminar held using the Internet and a conference call) with industry to explain the requirements for compliance by the end of 2008. One of the Webinars was for members of the National Renderers Association (NRA) and the American Meat Institute, the National Meat Association, and the American Association of Meat Processors. It was sponsored by the NRA. Another Webinar was with and for members of the NRA, the National Cattlemen's Beef Association, and the National Milk Producers Federation. This Webinar was also sponsored by the NRA.

The draft guidance is not "prescriptive" in its requirements for compliance, Mr. Jordre said. Instead, it gives companies the flexibility to comply with the intent of the rule.

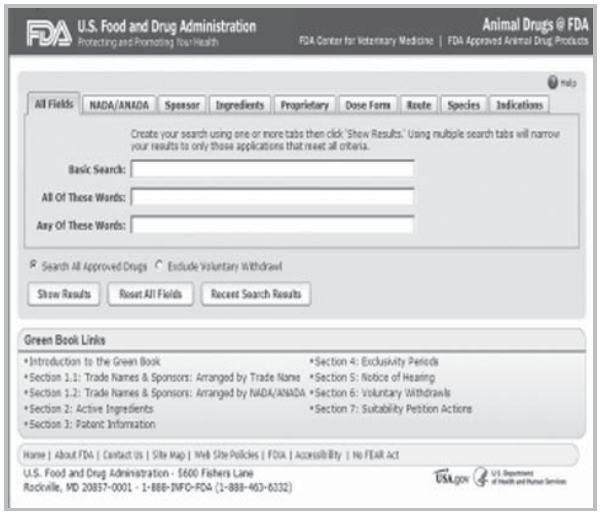
An important aspect of being in compliance is the documentation of procedures a company uses to keep CMPAF out of animal feed, Mr. Jordre said. Companies should have written procedures they use to determine the age of cattle, remove the brain and spinal cord, and sample tallow for the level of impurities. Companies will also be expected to show that they are following their own written procedures.

State and Federal inspectors have received some preliminary information about the requirements of the rule, Mr. Jordre said. CVM will conduct additional training for inspectors before the rule goes into effect, explaining in detail what to look for during an inspection. Although inspections under the new rule will not begin until after the rule goes into effect, State and Federal inspectors doing inspections at rendering facilities this winter will likely be asking those firms if they are aware of the rule and if they have begun to plan how it will affect their operations.

CVM Lists Approved Animal Drugs on Easy to Use Web Site

On October 1, 2008, the Center for Veterinary Medicine launched a new Web site, "Animal Drugs @FDA," an easily accessible link to a database of all approved animal drugs.

The new Web site provides an easy to use search capability. For example, the user can use simple word searches, or search by species, indications, ingredient, the New Animal Drug or Abbreviated New Animal Drug Application number, or dose form. The user can type in the information or use the "drop down" menu to make a selection.



Information presented about the drugs includes sponsor name and address, ingredient, species, routes of administration, dosage form, indications, and withdrawal time.

Information about approved drugs had previously been available through the "Database of Approved Animal Drugs (DAAD)," a database and Web site maintain for the past 20 years by the Virginia Polytechnic Institute and State University, Blacksburg, VA. All of the data on approved animal drugs assembled by the university has been incorporated into a database that links to Animal Drugs @ FDA.

The new Web site is also home for the electronic files of listed drugs commonly known as the Green Book. FDA is required to make those files available under the Generic Animal Drug and Patent Term Restoration Act.

The development of the new database and Web site took approximately 2 years, according to Dr. Jeff Punderson, project coordinator for CVM.

The Animal Drugs @ FDA database will be maintained by CVM's Office of New Animal Drug Evaluation. Dr. Charles Andres, a supervisor in ONADE, will be responsible for the database.

The current plan is to update the database monthly, Dr. Andres said. At some point, the Center expects to update the database as soon as a drug approval is publicly announced.

Regulatory Activities... *(Continued)*

Foster and Dr. Martin R. Smith, of Drs. Foster and Smith, Inc., of Rhinelander, WI. The two men marketed via the Internet such products as "Joint Care Primary 1," "Joint Care Primary Plus 1," "Joint Care-Advanced 2 with MSM," "Joint Care Premium 3, " "Joint Guard Treats," and "Premium Plus Omega-3, Gel Caps." Based on statements made on the company's Web site, the products were found to be drugs under Section 201(g) of FFDCA and new animal drugs under Section 201(v) of FFDCA because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in dogs and cats without being the subject of approved new animal drug applications. Samples of the statements included, "help manage the crippling effects of osteoarthritis," "work by actually healing the damage that has been done," "builds cartilage," "reduce pain," "reduce the signs of feline arthritis," "treat arthritis in dogs," and "decrease inflammation in arthritic dogs and cats."

FDA has issued a Warning Letter to Douglas L. Richards, a dairy farmer in Rome, NY, stating that he offered for sale an animal for slaughter as food that was adulterated. A U.S. Department of Agriculture Food Safety and Inspection Service (USDA/FSIS) analysis of tissue samples collected from the animal found levels of sulfamethazine at 9.58 ppm in liver tissue and 8.79 ppm in muscle tissue. FDA has not established a tolerance for residues of sulfamethazine in lactating dairy cattle. The presence of sulfamethazine in edible tissues from this animal in these amounts causes the food to be adulterated under FFDCA. The investigation also found that the animals were held under conditions that were so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. Mr. Richards had failed to maintain complete treatment records, according to the Warning Letter. Food from such animals is considered adulterated under FFDCA. The letter also said that Mr. Richards administered a sulfa drug to the dairy cows as directed by approved labeling.

FDA has sent a Warning Letter to Rudolf P. DeJong, Jr., president, Red Arrow Dairy, LLC, Coopersville, MI, for sale of an animal for slaughter

(Continued, next page)

Regulatory Activities... *(Continued)*

as food that was adulterated under FFDCA. An investigation revealed that Mr. DeJong sold a bob veal calf and told the buyer that it was intended to be raised as a steer by the purchaser, but did not tell the purchaser that it should not be slaughtered for use as food. The animal was subsequently slaughtered for use as food, and a USDA/FSIS inspection found 0.13 ppm penicillin in the kidney and 0.151 ppm flunixin in the liver. FDA has not set a tolerance for residues of those drugs in edible tissues of calves to be processed as veal. The presence of the residues in edible tissues causes food from the animal to be considered adulterated under FFDCA. The investigation also found that the animals were held under conditions that were so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. Mr. DeJong had failed to maintain complete treatment records.

FDA has sent a Warning Letter to Paul W. Rothermel, owner, Paul Rothermel Livestock, Hartville, OH, because an investigation found that Mr. Rothermel sold an animal for slaughter as food that was adulterated under FFDCA. He had sold a bob veal calf as food that was adulterated. A USDA/FSIS analysis of tissue samples from the animal found the presence of flunixin at 0.425 ppm in liver tissues and 0.035 ppm in muscle tissue. FDA has not established a tolerance for residues of flunixin in edible tissues of calves. The presence of the drug in edible tissues from the animal in the amounts cited causes the food to be adulterated within the meaning of FFDCA. FDA's investigation also found that Mr. Rothermel held animals under conditions so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. The Warning Letter said his operation lacks a system to ensure that the animals he buys and sells for slaughter for food have not been medicated or have been properly withheld from slaughter long enough to deplete the potentially hazardous drug residues in edible tissue.

FDA has sent a Warning Letter to Andrew J. Miller, owner of a dairy operation in Big Prairie, OH, because an investigation found that he offered for sale an animal for slaughter as food that was adulterated under FFDCA. An investigation revealed that he had sold a bob veal calf for slaughter for food that a USDA/FSIS analysis revealed the presence of 26.27 ppm of penicillin in the muscle tissue, 0.86 ppm in the liver tissue, and 0.42 ppm in the kidney tissue. FDA has established a tolerance of 0.05 ppm residues of penicillin in edible tissues of cattle. The presence of this drug in edible tissues from the animal in amounts found causes the food to be adulterated within the meaning of FFDCA. In addition, the FDA investigation found that Mr. Miller held animals under conditions so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. The letter said that Mr. Miller failed to maintain treatment records, failed to establish a system to control the administration of drug treatments to his animals, failed to establish an adequate inventory system for determining the quantities of drugs used to medicate the animals, and fed milk from treated cows to calves intended for slaughter. Food from such animals is considered adulterated.

FDA has not established a tolerance for residues of flunixin in edible tissues of calves. The presence of the drug in edible tissues from the animal in the amounts cited causes the food to be adulterated within the meaning of FFDCA.

FDA has sent a Warning Letter to Bradley D. Bouma, senior partner, Legacy Dairy Farms LP, Plainview, TX, because an investigation found that animals the dairy operation had offered for sale for slaughter as food were adulterated. The investigation revealed that the dairy operation sold a dairy cow for slaughter as food, and tissues from that animal that were tested by USDA/FSIS were found to have the presence of oxytetracycline at 14.30 ppm in the kidney tissue and the presence of flunixin at 0.184 ppm in the liver. The tolerance level set by FDA is 12 ppm for residues of oxytetracycline in the kidney of cattle and 125 parts per billion for residues of flunixin in the liver of cattle. Also, the Warning Letter said, the operation sold another dairy cow for slaughter as food that a USDA/FSIS analysis of tissue samples from the animal revealed that the tissue had flunixin at 3.427 ppm in the liver tissue. The presence of oxytetracycline and flunixin in edible tissues from these animals in these amounts causes the food to be adulterated under the FFDCA. The investigation also found that the dairy operation held animals under conditions that were so inadequate that medicated animals bearing potentially harmful drug residues are likely to enter the food supply. The operation, for example, failed to maintain complete treatment records. Food from animals held under such conditions is adulterated under the FFDCA. The investigation also found that the operation adulterated the new animal drug oxytetracycline, because the operation did not used it as directed by its approved labeling.

CVM Staff College: The Learning Resource Center for Excellence

The Center for Veterinary Medicine strives to be a high-performance organization. An important aspect of high performance is a highly educated and informed staff. To that end, the Center has established a Staff College that offers scientific training, as well as courses in management and in leadership, to all of its employees.

In a recent interview with *FDA Veterinarian*, **Connie R. Mahon**, Director of CVM's Staff College, presented an overview of the College and the CVM's plans for it.

Q: How would you describe the role of the Staff College in CVM's structure?

A: The Staff College provides learning opportunities for us to grow and develop, foster our Center's stewardship philosophy, discover what it means to each of us to be a leader and to be a part of something spectacular, an essential member of this organization.

Carl Sagan once wrote about how as civilization progressed we moved ourselves away from the stars by building the walls of the cities around us. Children would grow and mature completely unaware of what was beyond those walls. The CVM Staff College ensures that we (at CVM) have a clear view of the stars, and it strives to remove barriers that may keep us from finding what is ours to find.

Q: You mentioned individual leadership. Under its High Performance Organization approach to management, the Center stresses the leadership role each employee has. How does the Staff College enhance that role?

A: The Staff College offers CVM employees learning opportunities for career and leadership development. The competency-based curricula enhance and reinforce individual skills, promote personal growth as well as organizational performance in support of the CVM mission.

CVM, like many other parts of the government, faces the need to prepare and develop new leaders as the Federal government continues to experience a retirement wave with approximately 60 percent of the Federal workforce eligible to retire over the next 10 years. As CVM deals with developing global events, new threats, from bioterrorism, for example, and emerging science and technology, the requirement for effective leaders becomes even more critical. Leaders of the future will need to be knowledgeable in order to lead global and technological initiatives.

(The Staff College is part of CVM's Office of Management.) CVM Office of Management's theme is "leadership belongs to everyone." It is a reflection of CVM's philosophy of stewardship and unique culture. We at the Staff College have created leadership development programs for all who aspire to enhance their leadership skills. Our leadership development programs consist of mentoring, coaching, and other development activities; all of which serve as powerful catalysts for our continuous learning, advancement, and growth.

Q: You mentioned that the Federal government, which of course includes CVM, will see a wave or retirements over the next decade. Exactly how can the Staff College help address that issue?

A: In support of the CVM Succession Plan, which was created because of the large number of employees expected to retire over the next 10 years, and to ensure the development of a cadre of talented and ready employees for CVM, we focus on strengthening the talent and skills of everyone in the organization, regardless of the person's job, role, or position. We believe in developing our employees as they enter the organization, rather than starting their development near the peak of their career.

Distance learning and the virtual classroom

Q: You bring a unique background and a highly developed interest in distance learning to CVM's staff college. Can you tell us about your background?

A: My interest in and passion for designing distance learning began when the first cholera outbreak in 100 years was reported in South America in 1991. As the outbreak spread across South and Central America including the Mexican states, transmission of the infectious agent among the Texas Border town population was predicted by public health officials. The faculty at the University of Texas Health Science Center at San Antonio, where I was a member at the time, immediately recognized the urgent need to develop continuing education programs to enhance the knowledge and skills of clinicians and clinical laboratory practitioners in the rapid diagnosis and identification of the cholera agent.

With limited State funding, we traveled hundreds of miles on weekends and delivered continuing education programs along the Texas-Mexico border towns such as Brownsville, Laredo, and Eagle Pass.

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CVM Staff College . . . *(Continued)*

Participants in these programs included clinicians from interior Mexico, who rarely had such educational opportunities. This experience provided the stimulus to develop continuing education and academic programs via distance education.

Since that time, the availability and capability of virtual/Internet technology in providing distance education have tremendously improved. Today, the ability to provide learners with access to learning at any time and from anywhere is more important than ever.

CVM Learning Resource Center

Q: That explains your interest in distance training. How does that relate to CVM's public health mission?

A: With emerging molecular technology innovations, scientific discoveries, and gene-based techniques, methods in animal drug development as well as animal food safety have undergone dramatic changes.

At the same time, pathogens and infectious diseases continue to be recognized. The resurgence of "classic" pathogens (those pathogens we have known about for years) continues to occur and microorganisms that previously were treated empirically have expanded their scope of infections so they cause more and different types of infections. These pathogens have also become more virulent and resistant to antimicrobials.

To address the need for continuous professional development in these highly specialized and rapidly advancing areas of new science and biotechnology, we at the Staff College constantly look for innovative ways to effectively deliver program contents that would be easily accessible, available, appropriate, absorbable, and applicable.

Because of improvements in communication technology, we have been able to deliver course offerings that can be accessed at any time from anywhere using virtual technology. We implemented on-demand collaboration applications technology from WebEx Communications, Inc., to provide individuals with access to the CVM curriculum via online training and "e-learning." Offering on-demand and live online classrooms eliminates the time and distance constraints and increases employee productivity and opportunities to participate. The recording feature of the technology allows us to record presentations and archive them in a reference library for individuals to view at their convenience or look for information pertinent to CVM application reviews. Using this delivery method, we have been able to enhance collaboration across the Agency and external organizations in the exchange of scientific information.

A collaborative MPH program

Q: Under your leadership, the Staff College has brought a Masters of Public Health (MPH) program to CVM. What prompted that, and how will it help CVM do its job?

A: The constant interactions of humans, animals, and the environment have a tremendous impact on public health. Current and evolving health threats include infections transmitted through animals, insects, food, and water, as well as illnesses resulting from environmental toxins, antimicrobial resistance, and bioterrorism. Because of zoonotic diseases and the fact that animals are the major source of the pathogens involved in foodborne illnesses, the need for veterinary scientists who are trained in public health issues continues to increase.

Veterinary public health professionals understand the interaction of human and animal health and have knowledge of the epidemiology and ecology of zoonotic diseases.

In order to address the need for expertise in veterinary public health, the CVM Staff College and the University of Maryland, Baltimore, (UMB) have come together to create opportunities for qualified and eligible CVM employees to pursue a Veterinary Public Health specialization as an option within the MPH degree program.

We offer the MPH courses at the CVM Staff College and design them to allow flexibility and accessibility (via online) to CVM employees, while still allowing maximum class interactions. We delivered the first course, "Principles in Epidemiology," in the fall of 2006. The course was designed in a "blended-learning" format, a combination of Web-based technology, through which students are able to access course lectures and materials via the Internet, and traditional classroom meetings for interactive class discussion.

Other courses in public health that we have recently offered include "Applied Epidemiology," "Pharmacoepidemiology," and "Exposure, Risk, and Public Health." This fall, we offered new courses "Biostatistical Methods" and "Foundations of Public Health." These courses were delivered via our virtual classroom using the synchronous live on-line collaboration tool provided by WebEx.

We are now extending our collaborative efforts with UMB to other centers in the Food and Drug Administration. We anticipate that our MPH program

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BSE INSPECTION UPDATE

CVM Reports BSE Inspection Figures as of November 15, 2008

As of November 15, 2008, the Food and Drug Administration had received more than 66,000 reports of inspections done under the ruminant feed rule designed to prevent the establishment and spread of bovine spongiform encephalopathy (BSE) in the United States.

Approximately 71 percent of the inspections were conducted by State officials under contract or other arrangement with FDA, with the remainder conducted by FDA officials.

Inspections conducted by State and FDA investigators are classified to reflect the compliance status at the time of the inspection, based upon whether objectionable conditions were documented. Based on the conditions found, inspection results are recorded in one of three classifications:

- OAI (Official Action Indicated) when inspectors find significant objectionable conditions or practices and believe that regulatory sanctions are warranted to address the establishment's lack of compliance with the regulation. An example of an OAI classification would be findings of manufacturing procedures insufficient to ensure that ruminant feed is not contaminated with prohibited material. Inspectors will promptly reinspect facilities classified OAI after regulatory sanctions have been applied to determine whether the corrective actions are adequate to address the objectionable conditions.
- VAI (Voluntary Action Indicated) when inspectors find objectionable conditions or practices that do not meet the threshold of regulatory significance, but warrant an advisory to inform the establishments that inspectors found conditions or practices that should be voluntarily corrected. VAI violations are typically technical violations of the 1997 BSE Feed Rule. These violations include minor recordkeeping lapses or conditions involving nonruminant feeds.

(Continued, next page)

CVM Staff College . . . *(Continued)*

will be the model for other collaborative academic and leadership development programs in CVM.

Q: What do you see for the future of CVM's Staff College?

A: As Yogi Berra once said, "The future ain't what it used to be."

The world has changed. CVM's Staff College aims to take on the opportunity of becoming a high-impact learning organization. The high-impact factors that we need to address include the multigenerational workforce, alignment of learning and talent management strategies, and the organization's learning culture.

- **Addressing the multigenerational workforce:** We need to consider the impact of employees from "Generation X" and "Generation Y" in our learning development and delivery methods, recognizing that their learning styles are immensely different than those in other generations. We have to be prepared to meet the needs of our younger employees and be able to reach them with our learning development programs.
- **Alignment with talent management:** Our career and leadership development programs encourage internal career mobility, assist in recruiting, hiring, and retaining employees as well as facilitate our leadership pipeline. We therefore plan to improve our learning and development programs' alignment with talent management strategies.
- **Organization's learning culture:** In his editorial, "Best practices for high-impact learning," (*CLO*, August 2008), Josh Bersin cited the organization's learning culture as the greatest predictor of impact in learning environments. He also emphasized that the consistent reinforcement of professional development by management is what drives remarkable results. We are continuing to enjoy the Center Leadership Team's support and engagement in our efforts, and the encouragement of the Center's employees in their career development. Collaborative learning, discussion groups, communities of practice and on-demand learning have become as essential as formal lectures and seminars. We need to understand and learn how to develop not just content but also context, and how changes in technology, CVM's demographics, and organizational structures affect our best practices.

Where are we going from here? How about toward "second star to the right and straight on until morning."

CVM Reports BSE Inspection Figures... *(Continued)*

- NAI (No Action Indicated) when inspectors find no objectionable conditions or practices or, if they find objectionable conditions, those conditions are of a minor nature and do not justify further actions.

(Note: The following figures are as of November 15, 2008.)

Renderers

These firms are the first to handle and process (i.e., render) animal proteins. After they process the material, they send it to feed mills and/or protein blenders for use as a feed ingredient.

- **Number of active firms whose initial inspection has been reported to FDA** – 267
- **Number of active firms handling materials prohibited from use in ruminant feed** – 155 (58 percent of those active firms inspected)

  Of those 155 firms:

  - ❖ 0 firms were classified as OAI
  - ❖ 3 firms (2.0 percent) were classified as VAI

Licensed feed mills

In the inspection report database, FDA lists medicated feed licensed feed mills separately from non-licensed feed mills. But the licensing has nothing to do with handling prohibited materials under the feed ban regulation. FDA requires feed mills to have medicated feed licenses to manufacture and distribute feed using certain potent drug products, usually those requiring some pre-slaughter withdrawal time, to produce certain medicated feed products.

- **Number of active firms whose initial inspection has been reported to FDA** – 1,075
- **Number of active firms handling materials prohibited from use in ruminant feed** – 494 (46 percent of those active firms inspected)

  Of those 494 firms:

  - ❖ 0 firms were classified as OAI
  - ❖ 4 firms (0.8 percent) were classified as VAI

Feed mills not licensed by FDA

These feed mills are not licensed by FDA to produce medicated feeds.

- **Number of active firms whose initial inspection has been reported to FDA** – 5,290
- **Number of active firms handling materials prohibited from use in ruminant feed** – 2,685 (51 percent those active firms inspected)

  Of the 2,685 firms:

  - ❖ 0 firms were classified as OAI
  - ❖ 29 firms (1.1 percent) were classified as VAI

Protein blenders

These firms blend rendered animal protein for the purpose of producing feed ingredients used by feed mills.

- **Number of active firms whose initial inspection has been reported to FDA** – 387
- **Number of active firms handling materials prohibited from use in ruminant feed** – 196 (51 percent of those active firms inspection)

  Of those 196:

  - ❖ 0 firms were classified OAI
  - ❖ 0 firms were classified VAI

Renders, feed mills, protein blenders

This category includes only those firms that manufacture, process, or blend animal feed or feed ingredients using prohibited materials.

- **Number of active renderers, feed mills, and protein blenders whose initial inspection has been reported for FDA** – 6,712
- **Number of active renders, feed mills, and protein blenders processing with prohibited materials** – 506 (7.5 percent)

  Of those 506 firms:

  - ❖ 0 firms were classified OAI
  - ❖ 11 firms (2.2 percent) were classified VAI

Other firms inspected

Examples of such firms include ruminant feeders, on-farm mixers, pet food manufacturers, animal feed salvagers, distributors, retailers, and animal feed transporters.

- **Number of active firms whose initial inspection has been reported to FDA** – 21,865
- **Number of active firms handling materials prohibited from use in ruminant feed** – 7,295 (33 percent of those active firms inspected)

  Of those 7,295:

  - ❖ 0 firms were classified OAI
  - ❖ 113 firms (1.5 percent) were classified VAI

Total firms

(Note that a single firm can be reported under more than one firm category; therefore, the summation of the individual OAI/VAI firm categories will be more than the actual total number of OAI/VAI firms, as presented below.)

- **Number of active firms whose initial inspection has been reported to FDA** – 24,065
- **Number of active firms handling materials prohibited from use in ruminant feed** – 7,876 (33 percent of those active firms inspected)

  Of those 7,876:

  - ❖ 0 firms were classified OAI
  - ❖ 121 firms (1.5 percent) were classified VAI

Approvals for September–November 2008

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

REBALANCE (sulfadiazine/pyrimethamine) Antiprotozoal Oral Suspension (supplement to NADA 141-240), filed by Animal Health Pharmaceuticals, LLC, St. Joseph, MO. The NADA is approved for the treatment of equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*. The supplemental NADA provides for a revised human food safety warning on the labeling. Notice of approval was published September 17, 2008.

SAFE-GUARD (fenbendazole) 20% Type A medicated article (supplement to NADA 131-675), filed by Intervet Inc., Millsboro, DE. The supplemental NADA provides for manufacture of a fenbendazole free choice, liquid Type C medicated feed for use in dairy and beef cattle for the removal and control of various internal parasites. Notice of approval was published October 8, 2008.

EXCEDE (ceftiofur crystalline free acid) Sterile Suspension (supplement to NADA 141-209), filed by Pharmacia & Upjohn Co., a Division of Pfizer, Inc., New York, NY. The supplemental NADA provides for veterinarian prescription use of ceftiofur crystalline free acid injectable suspension for the treatment of bovine foot rot (interdigital necrobacillosis) in beef, non-lactating, and lactating dairy cattle. Notice of approval was published October 8, 2008.

DRAXXIN (tulathromycin) Injectable Solution (supplement to NADA 141-244), filed by Pfizer, Inc., New York, NY. The supplemental NADA provides for treatment of bovine foot rot (interdigital necrobacillosis) associated with *Fusobacterium necrophorum* and *Porphyromonas levii* in beef and non-lactating dairy cattle. Notice of approval was published October 8, 2008.

PREVICOX (firocoxib) Chewable Tablets (supplement to NADA 141-230), filed by Merial Ltd., Duluth, GA. The supplemental NADA provides for the veterinary prescription use of firocoxib chewable tablets in dogs for the control of postoperative pain and inflammation associated with orthopedic surgery. Notice of approval was published October 31, 2008.

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

Phenylbutazone Tablets (ANADA 200-433), filed by First Priority, Inc., Elgin, IL. The ANADA provides for the veterinary prescription use of Phenylbutazone Tablets in horses for the relief of inflammatory conditions associated with the musculoskeletal system. The product is approved as a generic copy of First Priority, Inc.'s, PRIBUTAZONE Tablets, approved under NADA 048-647. Notice of approval was published November 12, 2008.

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