FDA VETERINARIAN

Center for Veterinary Medicine

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CVM Adopts Updated Process for Accepting Drug Sponsor Information Electronically

by Jon F. Scheid, Editor

The Center for Veterinary Medicine can now accept certain information from drug sponsors through an improved electronic submission system that includes an "Electronic Submission Gateway" (ESG) developed by the Food and Drug Administration.

CVM officially moved to the improved electronic submission system on June 29 and announced the change in a series of revised "Guidance for Industry" documents posted to CVM's Web site. The key guidance is #108, "Guidance for Industry: How to Submit Information in Electronic Format to CVM Using the FDA Electronic Submission Gateway." It describes the new electronic submission process, which includes using the FDA gateway, and explains what drug sponsors need to do before they can begin providing electronic submissions to CVM.

CVM has been accepting data from sponsors electronically since 1997 using an e-mail system. Over the years, that system became outdated. FDA modernized its e-mail system in 2006, giving CVM an opportunity to modernize its electronic submission process to include the newer FDA gateway interface.

FDA developed its ESG system to accept information from all FDA stakeholders, including sponsors of human drugs and medical devices, as well as veterinary drug sponsors. The ESG process was initiated as a collaborative effort between CBER and CDER and has been leveraged to other Centers to aid in providing a single point of entry for all electronic submissions to the Agency.

(Continued, next page)

CVM Approves Use of Selenium Yeast in Beef Cattle Supplements

by Jon F. Scheid, Editor

The Center for Veterinary Medicine has changed its regulations to permit the use of selenium yeast in feed supplements for limit-feeding of beef cattle and in salt mineral mixes for free-choice feeding of beef cattle.

Due to selenium's toxicity at certain levels, the regulation limits use to 3 mg per head per day when used in feed supplements for limit-feeding, and up to 120 parts per million (ppm) in salt-mineral mixtures for free-choice feeding, at a maximum rate of intake of 3 mg of selenium per head per day.

CVM's action is based on a food additive petition filed by Alltech Biotechnology Center, Nicholasville, KY. Approval of the petition allows any firm to market selenium yeast for these uses if the product meets the conditions specified in the regulation.

This approval is the first to allow selenium yeast supplementation other than through its addition to complete feed. In complete feeds, an animal's exposure to selenium is limited by how much feed the animal can consume. The use of selenium yeast in something other than a complete feed requires the livestock producer to be sure to limit the amount of the selenium-containing feed supplement the animals consume.

The American Feed Industry Association petitioned FDA in 1986 to permit the addition of inorganic selenium

(Continued, next page)

In This Issue

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

CVM Adopts Updated Process... *(Continued)*

Veterinary drug sponsors who want to use the ESG need to first register with the ESG and CVM. As part of CVM's registration process, drug sponsors identify one individual in the company to serve as the point of contact for CVM. That individual will file a digital signature with CVM, which will be used to verify the authenticity of any electronic submission from that company.

Once a company is registered with CVM and the gateway, the company can use it to send six types of submissions associated with new animal drug reviews (Notice of Claimed Investigational Exemptions, Final Disposition of Animals Not Intended for Slaughter, Notice of Intent to Slaughter for Human Food Purposes, Request for Meeting or Teleconference, Protocol for Non-Clinical Laboratory and Effectiveness Studies, and Electronic Submission System Participant Management Form) via the ESG.

Before it could accept these submissions electronically, CVM had to develop electronic formats for each of them. The electronic submissions must have a specific structure. They cannot be as loosely organized as paper submissions, according to Dr. Margaret Zabriski, project coordinator for CVM. Developing the standardized format for each submission type took a significant amount of time and effort on the part of the reviewers of CVM's Office of New Animal Drug Evaluation, she added.

More electronic submission types will be added later, after CVM drug review experts have decided what information they need on the submission and how the information should be organized. However, she added, the largest amount of work was the develpment of the gateway interface. Now that the gateway interface is in place, CVM can focus on developing other electronic submission for drug application information. The process will be like adding "more cars to the train," according to Howard Conrad, with Booz Allen Hamilton, the contracting company that is creating the programs necessary for use on the gateway.

Companies can still submit this information in a paper format. However, documents submitted electronically will be organized in a manner CVM developed, which will permit efficient review by CVM staff.

According to Mr. Conrad, a longer-term goal is to have all documents associated with drug applications available electronically, which will permit rapid and easy search, compared with paper-document searches.

He added that one key improvement CVM sponsors will notice in using the ESG will be the amount of information they can submit electronically. As an example, drug sponsors frequently request meetings with CVM officials who are or will be reviewing their drug applications so the sponsors can be sure what information CVM will want. Under the previous system, a sponsor's request for a meeting came with not much more than an agenda. By using the new electronic submission system, drug sponsors can send significantly more information. For instance, they can send copies of presentations, including slides, and as much data as needed for the discussion.

...Use of Selenium Yeast in Beef Cattle Supplements *(Continued)*

sources, sodium selenite and sodium selenate to feed at 0.3 ppm in complete feed, up from the 0.1 ppm FDA was allowing. The Association argued that the increase was needed because selenium is an essential trace element for animal nutrition, and the level FDA was permitting was not sufficient to meet the needs of many animals.

The regulation permitting inorganic selenium sources in complete feed for chickens, swine, turkeys, sheep, cattle, and ducks at levels up to 0.3 ppm was finalized in 1997. The final regulation also permitted a proportional increase in the limit-feeding consumption rates for sheep to 0.7 mg per head and for beef cattle to 3.0 mg per head; and it permitted an increase in the selenium fortification levels for salt-mineral mixtures for sheep to 90 ppm and for cattle to 120 ppm. The regulation also allowed more flexibility in certain manufacturing controls.

Subsequently, CVM approved the use of selenium yeast, which contains an organic form of the trace element, in complete feeds for turkeys, swine, beef and dairy cattle. No selenium source has been approved for addition to the drinking water of animals.

Notice of the Food Additive approval permitting the use of selenium yeast in feed supplements for limit-feeding of beef cattle and in salt mineral mixes for free-choice feeding of beef cattle published in the *Federal Register* on July 19.

FDA VETERINARIAN

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FDA Publishes MUMS Designation Rule

On July 26, the Food and Drug Administration issued a final regulation implementing the animal drug "designation" provisions of the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act).

MUMS designation of a new animal drug will allow drug sponsors to be granted 7 years of exclusive marketing rights for these limited-demand new animal drugs to encourage the development of drugs for minor uses or in minor animal species. (Major animal species are cattle, swine, chickens, turkeys, horses, dogs, and cats. All other species are considered minor.)

The MUMS Act amended the Federal Food, Drug, and Cosmetic Act by, among other things, establishing section 573 to establish new regulatory procedures that provide incentives intended to make more drugs legally available to veterinarians and animal owners for the treatment of minor animal species and uncommon diseases in major animal species. This Act parallels the Orphan Drug Act for human drugs.

FDA has evaluated all public comments received in response to the September 27, 2005, proposed rule that described the procedure for designating a new animal drug as a minor use or minor species drug. The regulation defines content and format requirements for designation requests, as well as provisions for amending requests changing designation ownership, and annual reporting requirements.

The rule, which becomes effective October 9, 2007, describes the criteria CVM will use for granting or denying these requests. Specific sections of the rule address such topics as verifying MUMS status in a request, granting MUMS designation, and revoking MUMS designation.

Additional information about the final rule is included in the July 26, 2007, Federal Register, *http://www.fda.gov/OHRMS/DOCKETS/98fr/E7-14444.htm*. Questions may be directed to Dr. Bernadette Dunham, CVM, FDA, 7519 Standish Pl., Rockville, MD 20855, 240-276-9090, Bernadette.Dunham@fda.hhs.gov.

Recent Changes to Veterinary Feed Directive Guidance Highlighted

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

On June 26, 2007, the Food and Drug Administration's Center for Veterinary Medicine replaced "Guidance for Industry #120 – Veterinary Feed Directive Regulation" with an updated version to reflect some recent clarifications and changes.

The new version of the guidance can be found on FDA's Web site at *http://www.fda.gov/cvm/Guidance/guide120.htm*.

Readers are reminded that, by regulation (21 CFR 558.3(b)(7)), a veterinary feed directive (VFD) is a written statement issued by a licensed veterinarian that orders the use of a VFD drug in or on an animal feed. The VFD authorizes the animal owner or caretaker to obtain and use the VFD drug in the animal feed in accordance with FDA's approved directions for use.

A VFD drug refers to a new and specific category of drugs, and a licensed veterinarian may write a VFD order only for drugs approved by CVM in that category. To date, two drugs have been approved under this category: (1) tilmicosin for use in the control of swine respiratory diseases; and (2) florfenicol for use in the control of swine respiratory diseases and for control of certain bacterial diseases in aquaculture.

A VFD [veterinary feed directive] drug refers to a new and specific category of drugs, and a licensed veterinarian may write a VFD order only for drugs approved by CVM in that category.

The revised guidance also explains the term "appropriately licensed veterinarian" as it pertains to the VFD regulation. Specifically, the term refers to a veterinarian who has a valid license to practice veterinary medicine in the State in which the animals are located and that he/she is treating within the parameters of a valid veterinarian-client-patient relationship.

Also covered in the revised guidance document is CVM's position on VFD orders that are distributed by means of the Internet. The Center considers the Internet an acceptable electronic means of transmitting VFD orders, provided that the system is shown to be in compliance with FDA's regulations governing electronic records and signatures (21 CFR Part 11). The other requirement is that a feed distributor receive an original, signed VFD order within 5 working days of receipt of the VFD order by means of the Internet.

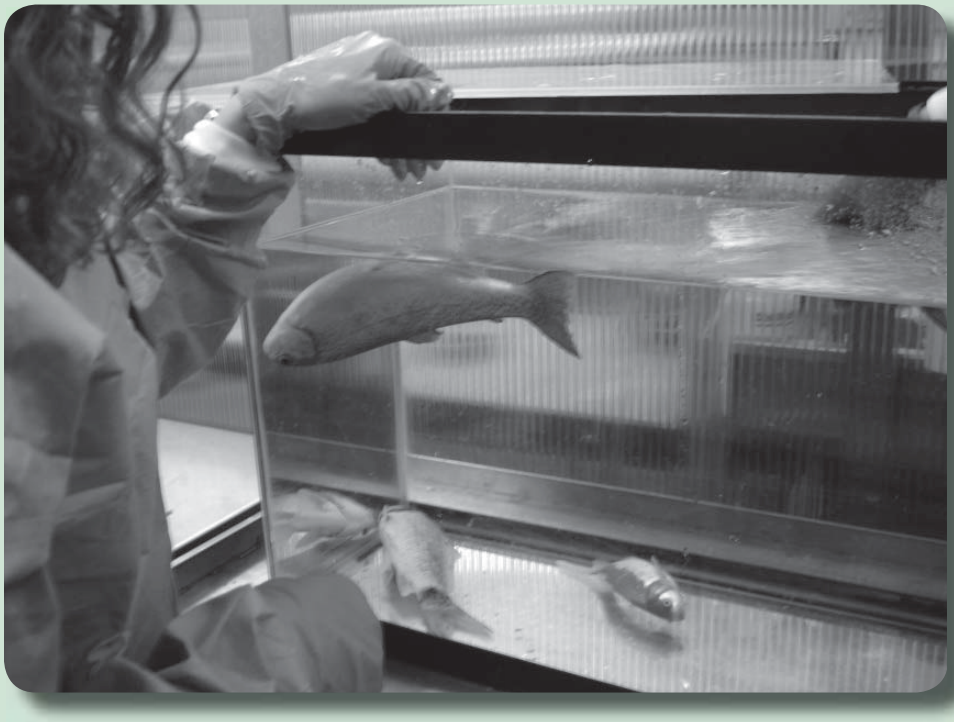
Lastly, the contact information has been updated in the revised guidance, and readers are encouraged to visit the Web site above to obtain that information. All other provisions of Guidance #120, dated March 1, 2001, remain in effect and are unchanged.

AVMA Members Participate in Interactive Aquaculture Lab at CVM

The aquaculture research staff at the Center for Veterinary Medicine's Office of Research conducted a veterinary interactive lab July 17 for members of the American Veterinary Medical Association (AVMA), who were in nearby Washington, DC, attending the association's annual convention. The lab was held at the CVM's research facilities in Laurel, MD.

Here, the AVMA members are touring the research facilities.

A demonstration of fish anesthesia techniques during the veterinary interactive lab.



Photographs courtesy of Craig Harms, D.V.M., Ph.D., Diplomate ACZM, North Carolina State University, College of Veterinary Medicine.

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AVMA Members Participate in Interactive Aquaculture Lab at CVM *(Continued)*

CVM's interactive lab showed the visiting veterinarians practical techniques used in aquatic animal medicine. Here, Dr. Renate Reimschuessel (right), director of aquatic animal research at CVM, demonstrates a necropsy exam to AVMA member Dr. Kathye Kerwan.

AVMA members participating in the veterinary interactive lab at CVM's aquaculture research facilities try out what they have learned about conducting a fish necropsy exam. Workshop faculty member Dr. Lester Khoo (right) is assisting Dr. Paul Gibbons.

CVM Improves Drug Review, Other Activities Through Project Management "Lessons-Learned" Process

The Center for Veterinary Medicine is using project management for several projects, including new animal drug reviews. A key part of project management is the analysis of the project, usually conducted after it is complete, to see what went well and what could be improved for future project performance. The analysis is called the "lessons-learned" process, and it is one of the best ways to ensure that good practices are repeated and bad practices are eliminated. It is also instrumental in making CVM a learning organization and helps build the Center's intellectual capital.

by Madeline Vanhoose, PMP, Director, CVM Project Management Staff, and Petra Garosi, PMP, Supervisory Project Manager, Office of New Animal Drug Evaluation

Lessons learned is a process of documenting the experience gained during a project. Lessons-learned meetings are typically part of the project plan and are conducted near the end of the project as part of the project close-out process. Although lessons-learned meetings are usually held at or near the end of a project, they can also be useful at key interim points during longer projects.

Lessons learned for a project are documented in one or more meetings that involve the project team and may include other stakeholders, including other CVM organizations and executive management when appropriate. The goal is to document the "wins" and the "challenges" by discussing what worked well during execution of the project, what problems were encountered, and what the project manager and the team did to resolve those problems. The lessons learned part of the project can also show where the team deviated from the project plan during plan execution and help the team document the reasons for the deviations.

Lessons learned from projects

The CVM Project Management Staff has conducted lessons-learned exercises on many of CVM's completed projects and conducted an interim lessons-learned exercise on an ongoing project of longer duration. The lessons learned identified the successes and challenges of the team's practices in the following major categories.

Project team

The project team's size, mix of skills, and the team members' roles will all have an impact on the ability of the team to create the project's deliverables efficiently and effectively, and to work together smoothly.

The processes that the project team establishes for managing meetings, handling issue escalation, and communicating within the team can impact how smoothly the team works together and the effectiveness of its interactions with stakeholders, especially the internal CVM organizations represented by project team members.

Documentation of the project team's composition and processes should be incorporated into a project team charter at the beginning of the project, so that the team knows what is expected of it and of each team member.

Project scope

Definition of the scope (i.e., goals, objectives, deliverables, timeline, assumptions, constraints, risks) of a project will help project teams avoid conflict later in the project over what should be in the final deliverable and avoid unnecessary work or rework. The scope of a project also includes the environment in which a project is implemented. For project management purposes, the environment of the project is the other organizations or teams with similar goals and objectives, as well as other external factors that could impact the project.

A project's scope and environment should be incorporated into a project definition document at the beginning of a project.

Project management

Project management tools have helped project leaders and project managers to efficiently and effectively initiate a project, manage the activities of the project against a plan, and support efforts to deal with the ever present challenges created by interactions among the project team members and the stakeholders.

Project planning software tools at CVM (Microsoft Office Project® and Microsoft Office Excel®) have been used to plan projects of different priority, complexity, duration, and scope. Excel has been used to plan smaller, shorter projects with limited scope,

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. . . Lessons-Learned Process *(Continued)*

while Microsoft Project has been used for larger, complex projects of longer duration.

Project planning template tools created for projects repeated often throughout the Center (e.g., writing standard operating procedures, developing guidance documents, or producing annual reports and *FDA Veterinarian*) have been used to increase the efficiency of project planning for similar projects.

Project management communication tools (e.g., a project's charter, project definition document, project plan and schedule) for use in interfacing with stakeholders and internal organizations can support the resolution of conflicts around scope, schedule, and performance of plans.

Project management high-level monitoring tools (e.g., Microsoft Office Project®, Microsoft Office Excel®) can be used to develop "milestone" reports for management. (A milestone represents the achievement of a significant part of the project. When a project milestone is achieved, it is an important step in the progress of the project.) Operational level monitoring tools (e.g., checklists and action item tables) can be used to help track action items for the project team.

Project management process tools for meeting management, decision-making, and team-membership management have been identified as important for smooth operation of project teams and as a way to support conflict resolution in these areas.

Public meetings

Public meetings are used by CVM project teams to communicate with their external stakeholders on issues of common interest and to gain stakeholder feedback. (For example, CVM's project team that is developing an Animal Feed Safety System has held four public meetings.)

Public meeting preparation requires detailed planning and careful management of numerous activities and is facilitated by the use of checklists and a logistics coordinator.

If the public meeting incorporates special features, such as breakout sessions, which the Animal Feed Safety System Team used for its first two meetings, it is important to conduct training of facilitators to define roles and ensure adherence to the timeline and agenda during the meeting.

Sponsors, ONADE benefit from lessons-learned meetings

One of the more exciting new areas of lessons learned at CVM is the Office of New Animal Drug Evaluation (ONADE's) use of lessons-learned meetings to evaluate the processes used for recent approvals granted to animal drug sponsors. The lessons-learned process is one of the project management tools that ONADE is bringing to bear on submissions to improve the quality of the submissions and to enhance the abilities of the team leaders and review staff to manage them. It is also a significant communications tool between ONADE reviewers and application sponsors.

Lessons-learned meetings can be held for any significant approvals (new chemical entities, or for supplements for new indications, species, or routes of administration).

ONADE has developed a procedure that outlines the project manager's role for scheduling, preparing for, and holding lessons-learned meetings with sponsors. The meetings are voluntary. Upon completion of a significant approval, the project manager works with the sponsor and the CVM/ONADE team that reviewed the drug product to determine an appropriate date and time for the lessons-learned meeting. These meetings do not require the sponsors to make official meeting request submissions to the file. A meeting date is selected that provides at least 30 days' advance notice. The project manager then schedules the meeting (which lasts 2 hours or so) and notifies the sponsor and the review team.

Approximately 3-4 weeks in advance, the sponsor sends an overview of the points it wants to make during the lessons-learned meeting. Sponsors are encouraged to organize their points into two categories—what went well, and what needs improvement for next time.

The project manager schedules a CVM/ONADE-only pre-meeting prior to the lessons-learned meeting, giving the review team time to review the sponsor's points and discuss any additional items to bring up at the lessons-learned meeting.

The project manager serves as the facilitator for the lessons-learned meeting.

Recently, sponsors of three significant approvals have volunteered to conduct lessons-learned sessions with CVM staff. Discussions at the meetings focused on the areas of protocols, conduct of studies, summarization of statistical analyses (the data package), communication, and best practices for the future.

ONADE, along with the sponsors, has benefited from these discussions. The biggest area of future best practices identified during these meetings has been communication (e.g., best way to communicate during protocol development, best time to come in for

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. . . Lessons-Learned Process *(Continued)*

meetings, how to handle e-mails, etc.). Other areas are the best ways to handle analyses and the best format for submissions. ONADE encourages sponsors of significant submissions to use this format to help ONADE manage its workload in order to enhance its ability to get safe and effective drugs to market faster.

Lessons learned – the future

In these cases, the lessons learned applied to only one or a few projects, but not across the board to all projects. However, as more key lessons are collected, patterns will emerge. As that happens, some of these lessons can be raised to the level of what, in project management, is called a "best practice." A best practice statement implies that the benefit can be gained for all projects, not just the few that reported it.

CVM's and ONADE's project management staffs will establish processes for converting lessons learned into best practices for the benefit of all staff and project teams and, if appropriate, for incorporating them into CVM's and ONADE's project management methodologies.

Project Management Terms

Project managers sometimes speak their own language that others may not fully understand at first. They use several terms that have specific project management meanings. To help non-project managers better work with the project managers, here is a list of terms and their meanings.

Project Management Glossary

Project charter: A document that gives the project team the authority to use organizational resources for project activities and that formally recognizes the existence of the project. The document includes the goals and objectives of the project and lists the members of the project team and their roles. The document is approved by Center or Office Management.

Project close out: A process to provide for completion and retention of essential project and project management records.

Project deliverable: Any measurable, tangible, verifiable outcome, result, or item that must be produced to complete a project or part of a project and is subject to customer approval.

Project documentation: All documents developed and maintained during the project that are placed in storage for retrieval and access as historical data that can be used for future project estimating and planning activities. These documents may include the project plan, project schedule, project progress reports, meeting agendas and minutes, lessons learned, and archived e-mails.

Project environment: The combined internal and external influences, both individual and collective, that assist or restrict attainment of the project objectives. These influences may be either business or project related or may be a result of political, economic, technological, or regulatory conditions. Everything outside the project that delivers input or receives output from the project is considered part of the environment.

Project issue escalation: A process used by a project leader or manager to raise an issue to the next higher level of decision-making authority to ensure that a problem does not linger in the hands of any one individual or group without resolution. The process ensures critical issues or problems are raised soon enough to prevent impacts to the project, and it ensures the appropriate parties are informed and involved in critical decision-making. The project should always strive to make decisions and address issues at the lowest possible level.

Project management best practices: Techniques or methodologies that, through experience and research, are proven to reliably lead to the desired project outcome. A project leader or manager's commitment to best practices is a commitment to using all the knowledge and technology at his or her disposal to ensure project success.

Project management lessons learned: A review and evaluation of the successes and failures recently experienced during the execution of a project, upon completion of the plan or one of its major milestone, to learn what worked and did not work. The lessons learned results of the review are documented and made accessible to all interested parties as a reference and guide for future project planning and implementation.

(Continued, next page)

Mysterious Honeybee Deaths Leave Sting on Agriculture

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

Scientists and researchers across the Nation are working diligently to try to understand why the number of honeybees has been declining recently at an alarming rate. As many as 35 U.S. States, as well as Canada and countries in Europe and Asia, have witnessed this mysterious decline this past winter (2006-2007). Experienced beekeepers are finding their once-thriving hives empty and abandoned. Investigations suggest that outbreaks of unexplained colony death of honeybees have been ongoing since 2004, and historical reports of similar losses indicate that such losses have occurred as far back as 100 years or more. The cause could be a parasite, a virus, a fungus, a bacterium, a toxin, or other stress; but for now, no one cause has been isolated. The phenomenon has been termed Colony Collapse Disorder (CCD).

Symptoms of CCD

A colony with CCD is generally characterized by all of these conditions occurring simultaneously: (1) complete absence of adult bees in colonies, with little or no build-up of dead bees in or around the colonies; (2) presence of capped brood (cells capped with wax over pupae) in colonies—bees normally will not abandon a hive until the capped brood have all hatched; (3) presence of food stores, both honey and bee pollen, which are not immediately robbed by other bees and which, when attacked by hive pests such as wax moth and small hive beetle, the attack is noticeably delayed. Precursor symptoms that may arise before the final colony collapse are the following: insufficient workforce to maintain the brood that is present; workforce seems to be made up of young adult bees; the queen is uncharacteristically evident outside the hive; and the colony members are reluctant to consume provided feed.

Importance of honeybees

Bees are vital for the pollination of more than 90 fruit and vegetable crops worldwide, including

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. . . Lessons-Learned Process *(Continued)*

Project management templates: A document or file that describes a preset format for a particular type of project or project management activity, used so that the format does not have to be recreated each time a similar project or project activity is undertaken. Microsoft Project templates for frequently repeated project types can be useful for accelerating project planning. Templates can be annotated with instructions to facilitate their use.

Project management: Application of common or specialized knowledge, skills, tools, and techniques to effectively and efficiently carry out project activities to achieve the project goal and objectives within the planned timeframe and budget.

Project milestone report: A report consisting of key events or milestones (critical accomplishments planned at time intervals throughout the project) that is used to monitor overall project performance. The reports usually contain minimal detail and are presented at a highly summarized level.

Project monitoring: Acquiring and analyzing project data on an ongoing basis to determine that the project is on track for timely completion, or so action can be taken when progress fails to match plans and meet objectives.

Project plan: A formal, approved set of documents used to guide both project execution and control. Documents usually include a project definition document, a project team charter, and a project schedule. The project plan documents planning assumptions and decisions, facilitates communication among stakeholders, and documents approved scope, cost, and schedule.

Project schedule: Time-sequenced plan of activities that project managers use to direct and control project execution. Usually shown as a milestone report, a Gantt (a time-related horizontal bar chart) or other bar chart, or a tabular listing of dates.

Project stakeholder: An individual or organization actively involved in the project or that has interests that may be affected, either positively or negatively, as a result of project execution or successful project completion.

Mysterious Honeybee Deaths... *(Continued)*

almonds, peaches, soybeans, apples, pears, cherries, raspberries, blackberries, cranberries, watermelons, cantaloupes, cucumbers, and strawberries. The economic value of these agricultural commodities is somewhere in the area of almost $15 billion in the United States alone. Aside from agricultural crops, many native plants are also pollinated by honeybees, thereby illustrating how the entire ecosystem is being affected by this serious malady.

What is killing the bees?

According to *Feedstuffs Newspaper*, up to 1 million out of a total 2.4 million honeybee colonies in the United States have died out this past winter. Both tracheal mites (*Acarapis woodi*) and varroa mites (*Varroa destructor*) have threatened the bee industry since the 1980s, with significant colony die-offs in the winters of 1995-1996 and 2000-2001. The mites feed on U.S. honeybees and act as a vector for a number of bee viruses. Miticides have been used to combat these pests, but over time, the mites develop resistance. Also, miticides can only be used at certain times of the year because, if used during a nectar flow, they could contaminate the honey crop. In addition, there is evidence that miticides can accumulate in the bees' wax combs to levels that could be harmful to the bees themselves. Tracheal mites do not appear to be a factor in the current die-off. Varroa mites are still a problem, but bees appear to be equally affected in both weak and strong colonies.

Such things as genetically modified foods, mites, pathogens, pesticides, and electromagnetic radiation from cell phones have all been suggested as possible causes of the bees' demise, but the actual causes remain a mystery.

In the spring of 2007, a team of scientists from Edgewood Chemical Biological Center and the University of California, San Francisco, identified both a virus and a parasite that could be behind the die-offs of honeybee colonies. Using a new technology called the Integrated Virus Detection System, which was designed for military use to rapidly screen samples for pathogens, the scientists isolated the presence of viral and parasitic pathogens. The extent of the problem is unknown and is still being studied, as are other detection activities.

Another possible culprit is a class of insecticides known as neonicotinoids, which have been widely detected on pollen at low concentrations in other countries experiencing die-offs of honeybees. Neonicotinoids are systemic pesticides used on plant seeds. When the seeds mature, the pesticide manifests itself throughout the plant. When an insect ingests any part of the plant, it gets a dose of the neurotoxin that can cause a quick and lethal breakdown of the insect's nervous and immune systems. As a result, a bee's ability to learn can become impaired, leading some scientists to suggest that exposed bees may leave the hive and literally not be able to find their way back. One of the chemicals in this class, imidacloprid, is marketed in the United States for use as an insecticide on food crops, as well as to control termites and fleas. Imidacloprid was banned in France in 1999 as a suspected cause of drastic and mysterious die-offs in honeybees. Differences of opinion abound in bee circles, and a direct causal link between the chemical and bee mortality has not been made.

But this said, there seems to be no one singular disease acting as a causal agent of colony deaths, and approximately 25 percent of the bee deaths cannot be attributed to mites or any other known pest. Such things as genetically modified foods, mites, pathogens, pesticides, and electromagnetic radiation from cell phones have all been suggested as possible causes of the bees' demise, but the actual causes remain a mystery.

The Colony Collapse Disorder Working Group, a collaboration of researchers from around the country, including Pennsylvania State University, the U.S. Department of Agriculture (USDA), the Mailman School's Greene Lab, the Florida Department of Agriculture and Consumer Services, the University of Illinois, the University of Delaware, North Carolina State University, and others are working to identify potential causal factors common to CCD colonies and devise preventive measures to disrupt the disorder, with the ultimate goal of ensuring strong honeybee colonies for pollination and honey production.

The role of FDA

Honey is regulated by FDA as a food, and as such, it cannot be marketed in this country unless it is shown to be safe, sanitary, wholesome, and labeled in a truthful manner. So, FDA's interest in the bee industry is basically two-fold: ensuring the quality and purity of honey and ensuring the health of honeybees. Honey is different from most food products that may

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Mysterious Honeybee Deaths... *(Continued)*

contain animal drug residues. Unlike seafood, meat, and milk that contain large amounts of protein and fats, honey contains mostly sugars. It also has natural antimicrobial properties. As a result, many of the traditional approaches used to isolate drug residues do not work for honey. In 2006, researchers from FDA's Center for Veterinary Medicine developed a provisional multi-residue method for 17 drugs in honey. The method uses liquid chromatography-tandem mass spectrometry, both to confirm the identity of the drug and to determine the amount of drug residue present. The USDA Beltsville Bee Laboratory, in an ongoing collaboration with CVM, is generating needed biologically incurred residue samples for the drugs in the multi-residue method.

CVM's Office of Research was also involved in analyzing protein supplements fed to some honeybee colonies to determine whether they could have been contaminated with melamine. Melamine was involved in a recent large-scale pet food recall. Preliminary results found no evidence of melamine in any of the samples tested. Again, this work was done in cooperation with the Beltsville Bee Lab.

The Pollinator Protection Act would authorize $89 million in Federal funding for research and grant programs at the USDA over 5 years for work related to maintaining and protecting bees and native pollinator populations. This bill not only addresses CCD in honeybees, but also the decline of native pollinators in North America.

Other CVM offices are following this problem closely and are ready to assist the country's beekeepers however they can when the causative agent of this syndrome is identified. If a medical need is identified, recent legislation will enable the Office of Minor Use and Minor Species (MUMS) Animal Drug Development and the Office of New Animal Drug Evaluation to encourage pharmaceutical sponsors to obtain approvals for new treatments. The MUMS Health Act was enacted into law on August 2, 2004. It helps make more medications legally available to veterinarians and animal owners to treat minor animal species and uncommon diseases in the major animal species. Some animals of agricultural importance are also minor species, and these include honeybees.

American Foulbrood (AFB) is an infectious brood disease caused by the spore-forming bacterium *Paenibacillus larvae*. Although it is not believed to be responsible for CCD, it is the most widespread and destructive of the brood diseases, afflicting queen, drone, and worker larvae alike. Adult bees, however, are not affected by AFB. To date, FDA has approved two drugs to prevent and/or control AFB in honeybees: Terramycin® (oxytetracycline) Soluble Powder (for prevention and control) and Tylan® (tylosin tartrate) Soluble (for control). This latter drug is used only in cases of AFB that have been identified as resistant to Terramycin® by the State apiary inspection service.

FDA's Office of MUMS and incentives from the MUMS Act could be helpful if it turns out that the cause of CCD could be addressed through a new animal drug approval.

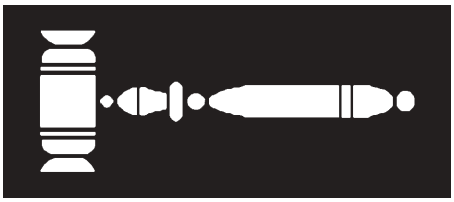
Possible Funding for research

On June 26, 2007, Senators Barbara Boxer, John Thune, and Bob Casey introduced legislation to help research, protect, and maintain America's bee and native pollinator population and ensure the viability of crops that rely on them for pollination. The Pollinator Protection Act would authorize $89 million in Federal funding for research and grant programs at the USDA over 5 years for work related to maintaining and protecting bees and native pollinator populations. This bill not only addresses CCD in honeybees, but also the decline of native pollinators in North America. This bill would enhance funding for research on the parasites, pathogens, toxins, and other environmental factors that affect honeybees and native pollinators. It supports research into the biology of native pollinators and their role in crop pollination, diversifying the pollinators upon which agriculture relies.

Conclusion

As the reader can see, the importance of honeybees cannot be taken for granted. Equally important are the collaborative efforts by government, academia, and the bee industry to try to determine the cause or causes of CCD and how best to tackle this mysterious problem as a means to ensure the continued health of the honeybee and, in turn, the health of the food supply so dependent on these amazing insects. While many of us may fear a bee's sting, even scarier may be the "sting" on our Nation's food supply if the honeybee population continues to decline.

Regulatory Activities for June and July 2007



Warnings Letters

A WARNING LETTER was issued to Janet Cunningham, regulatory affairs consultant at Bayer Health Care LLC (Animal Health Division), Shawnee Mission, KS, for a violation of the misbranding provisions of section 502(n) of the Federal Food, Drug, and Cosmetic Act (FFDCA). Specifically, the firm's 60-second direct-to-consumer TV ad entitled, "Field Trip" for its Advantage Multi™ (imidacloprid/moxidectin) for Dogs, NADA 141-251, minimizes risks associated with use of the drug and fails to reveal material facts about the product in violation of the FFDCA and its implementing regulations (21 CFR 202.1(e)). By omitting and minimizing the risks associated with Advantage Multi™ for Dogs, the TV ad misleadingly suggests that Advantage Multi™ for Dogs is safer than has been demonstrated by substantial evidence or substantial clinical experience. FDA also reviewed certain conference exhibit booth materials for the company's Advantage Multi™ (imidacloprid/moxidectin) products for dogs and cats. The promotional piece for the products, produced by Bayer Health Care LLC, was located in the exhibit booth at the conference. FDA considers the exhibit booth materials to be misleading because they fail to reveal relevant risk information. Therefore, the Agency determined that the drugs are misbranded within the meaning of sections 502(a) and 201(n) of the FFDCA.

Steve M. Hand of Ocilla, GA, received a WARNING LETTER from FDA because dairy cows offered by him for slaughter as food were found to be adulterated within the meaning of section 402(a) of the FFDCA. Specifically, tissue samples taken of one animal revealed the presence of gentamicin in the liver and kidney, although the level was not quantified. Nevertheless, there is no tolerance established for residues of this drug in the edible tissues of cows (21 CFR 300). Tissue samples taken from another cow revealed the presence of penicillin at 18 parts per million (ppm) in the kidney tissue and 12 ppm in the liver. A tolerance of 0.5 ppm has been established for residues of this drug in the edible tissues of cows (21 CFR 556.510).

FDA has sent a WARNING LETTER to Dr. Marilyn M. Porter, regulatory affairs associate/animal testing, Heska Corporation of Des Moines, IA, and to Nancy Thompson-Brown, senior regulatory compliance specialist, Schering-Plough Animal Health Corporation, Union, NJ, regarding their Web site for Tri-Heart® Plus (ivermectin/pyrantel) that was deemed to cause the drug to be misbranded under sections 502(n) and 201(n) of the FFDCA. Specifically, the promotional piece on the Web site was misleading because it presented an unsubstantiated claim about how Tri-Heart® Plus is effective in treating whipworm infections in dogs; however, this product was not approved for

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FDA Announces FY 2008 Animal Drug User Fee Rates

The Food and Drug Administration has announced the animal drug user fee rates for Fiscal Year 2008.

The fees are authorized under the Federal Food, Drug, and Cosmetic Act, as amended by the Animal Drug User Fee Act of 2003. The funds collected support the new animal drug review activity of FDA's Center for Veterinary Medicine.

The FY 2008 fees are:

- Animal drug application – $172,500
- Supplemental animal drug application, for which safety or effectiveness data are required – $86,250
- Annual product fee – $4,125
- Annual establishment fee – $52,700
- Annual sponsor fee – $43,900

The application fees apply to applications submitted to FDA on or after October 1, 2007, to September 30, 2008.

FDA will issue FY 2008 invoices for product, establishment, and sponsor fees by December 30, 2007. The invoices will be due and payable by January 31, 2008. FDA will not accept any animal drug applications for review until the sponsor has paid all the fees it owes.

Comings and Goings

New Hires

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Marina Feric, Biological Aide
- Debra Offenbacker, Biological Aide
- Dr. Gerald Scott Melton, Staff Fellow
- Urvi Desai, Regulatory Counsel

Departures

OFFICE OF RESEARCH

- Patricia Cullen, Animal Feed and Research

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Suzanne Wolcoff, Regulatory Review Officer

Regulatory Activities . . . *(Continued)*

removing or controlling whipworms. Both officials were advised to correct the promotional materials on the Web site concerning Tri-Heart® Plus and any other materials that may contain similar information. They were also warned that future promotional materials should adequately address the claims of heartworm and other intestinal parasite prevention, described in the currently approved labeling, without overstating the effectiveness.

Adulterated medicated feed has led to the issuance of a WARNING LETTER by FDA to Gary L. Grossnickle, president of Southern States Frederick Cooperative, Inc., of Richmond, VA. An inspection of the firm revealed that it was manufacturing and distributing an animal feed mixed with a liquid supplement that contained lasalocid sodium, which is neither approved as a food additive nor considered generally recognized as safe. As a result, the animal feed is considered adulterated under section 402(a) of the FFDCA. Mr. Grossnickle was also cited for redistributing animal feed without a label that had been returned because it contained lasalocid sodium; this amounted to misbranding under section 403 of the FFDCA.

A WARNING LETTER was sent by FDA to Kevin A. Sharpe, owner of Kevin Sharpe Farm of Cortland, NY, for violations of the adulteration provisions in sections 402(a) and 501(a) of the FFDCA. Specifically, the dairy operation had offered for slaughter as food one dairy cow that was found to have residues of penicillin in the kidney tissue at 0.15 ppm and another animal that was found to have residues of the same drug at 0.33 ppm in the kidney tissue. A tolerance of 0.05 ppm has been established by regulation (21 CFR 556.510(a)) for penicillin in kidney tissue. Therefore, both animals are considered adulterated under section 402(a). In addition, Sterile Penicillin G Procaine Injectable Suspension was found to be adulterated under section 501(a) because it was administered without following the dosage level and it was done so without the supervision of a licensed veterinarian in violation of 21 CFR 530.11.

Adulterated pet treats were the subject of a WARNING LETTER issued to Ian W. McCauley, president of T.W. Enterprises, Inc., of Ferndale, WA. Specifically, an analysis of a sample of the firm's American Bullie A. B. Dog Chew, 6" Medium, revealed the presence of *Salmonella muenster*. *Salmonella*, including *Salmonella muenster*, is a micro-organism that is known to be pathogenic to animals and humans. Dog chews bearing or containing *Salmonella* are adulterated within the meaning of section 402(a) of the FFDCA. FDA's inspection also revealed the firm's use of bleach in animal feeds, which was in violation of the agency's food additive petition requirements (21 CFR 571).

Liubov Skibo, director of regulatory affairs at Merial Limited, Duluth, GA, received a WARNING LETTER for making unsubstantiated claims in the firm's advertisement for the canine heartworm drug, Heartgard® Plus. The advertisement, which appeared in the *Journal of the American Veterinary Medical Association*, caused the product to be misbranded under section 502(n) of the FFDCA. Heartgard® Plus is an oral chewable formulation containing ivermectin and pyrantel and is approved for the prevention of canine heartworm disease by eliminating the tissue stage of heartworm larvae for a month after infection and for the treatment and control of ascarids and hookworms. Statements in the advertisements imply the drug is effective for controlling and treating zoonotic diseases generally, not only ascarids and hookworms. These statements thus overstate the demonstrated effectiveness of Heartgard® Plus. In addition, other statements in the ads accompanying a photo gave the overall impression that the use of Heartgard® Plus in dogs will prevent zoonotic transmission of toxocariasis and subsequent ocular larval migrans in humans. FDA is not aware of substantial evidence or substantial clinical experience to support the effectiveness of Heartgard® Plus for the prevention of toxocariasis, ocular larval migrans, or any other zoonotic disease in humans.

A WARNING LETTER was issued to Stanley H. Wilson, owner of S & W Farms, Cave City, KY, for violations of the adulteration provisions contained in section 402(a) of the FFDCA. Specifically, this dairy and beef operation offered one dairy cow for slaughter as food that was found to contain 0.10 ppm penicillin in the kidney tissue and 0.09 ppm penicillin in the liver tissue. A second dairy cow offered for slaughter as food was found to contain 0.19 ppm penicillin in the kidney tissue. A tolerance of 0.05 ppm has been established for residues of this drug in the edible tissues of cattle (21 CFR 556.510(a)). Other violations cited in the WARNING LETTER included inadequate treatment records and an inadequate drug inventory system.

Margaret Gillis, regulatory associate at Elanco Animal Health, Greenfield, IN, has received a WARNING LETTER because of various promotional items associated with the firm's product, Reconcile™ (fluoxetine hydrochloride). Reconcile™ is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of canine separation anxiety in conjunction with a behavior modification plan. The four items in question involved an article entitled, "Separation Anxiety: A Brief Overview," the "reconcile.com" Web site, a consumer brochure, and a print advertisement in the May issue of *Veterinary Forum Magazine*. The pieces and the Web site suggested that the product was more effective than had been demonstrated. Therefore, the drug was found to be misbranded under sections 502(n) and 201(n) of the FFDCA.

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Regulatory Activities . . . *(Continued)*

Noncompliance with the current Good Manufacturing Practice (cGMP) regulations (21 CFR Parts 210 and 211) for the manufacture of finished pharmaceuticals was the basis of a WARNING LETTER issued to Lawrence F. Schneider, president of First Priority, Inc., of Elgin, IL. The firm's noncompliance caused the finished products to be adulterated under section 501(a)(2)(B) of the FFDCA. An FDA inspection also revealed that the firm's "Purple Lotion Wound Dressing" was adulterated because it contained gentian violet and was, therefore, unsafe within the meaning of section 512(a) of the FFDCA. Gentian violet is not generally recognized as safe and effective for any veterinary drug use in food animals. The WARNING LETTER followed the issuance by FDA of a Form 483 (findings of inspection) and a subsequent response to those findings by First Priority, Inc. FDA maintained that many of the firm's explanations and data submissions were incomplete or insufficient. Among the products covered by the FDA inspection were Pyrantel Pamoate Suspension Canine-2X, Povidone Iodine Shampoo, Ivermectin Equine Oral Liquid, Povidone Iodine Shampoo, Iodine Tincture, Cort-Astrin (Hydrocortisone Solution 1%, 1 oz.), Phenylbutazone raw material, and Levoxine Powder. FDA urged prompt corrective action with respect to all of the violations outlined in the letter.

A WARNING LETTER was issued to John M. Nauta, owner of the J & T Dairy, Buhl, ID, for violations of the adulteration provisions of section 402(a) of the FFDCA. Specifically, the firm sold a dairy cow for slaughter as human food that contained sulfadimethoxine in both the liver at 3.53 ppm and the muscle at 1.38 ppm. A tolerance of 1.0 ppm has been established for residues of this drug in the edible tissues of cattle, as codified in 21 CFR 556. 640. In addition, the firm adulterated sulfadimethoxine within the meaning of section 501(a) of the FFDCA when it failed to use the drug in conformance with its label, in that it was used extralabel. The extralabel use of this drug in lactating dairy cattle is prohibited by 21 CFR 530.41(a)(9). The WARNING LETTER also listed a variety of administrative violations.

Nancy Thompson-Brown, senior regulatory compliance specialist with Schering-Plough Animal Health Corporation, Union, NJ, has received a WARNING LETTER regarding a promotional piece (product bulletin) for Nuflor® (florfenicol) Type A Medicated Article for Swine. This piece makes unsubstantiated claims of effectiveness and thus misbrands the drug within the meaning of sections 502(a) and 201(n) of the FFDCA. Additionally, the piece promotes Nuflor® for a new intended use that is not the subject of an approved NADA. When promoted for this new, unapproved intended use, Nuflor® is unsafe within the meaning of section 512(a)(1). Specifically, the promotional piece presents six bulleted points under the heading "Advantages." Three of them are false or misleading because they present claims that go beyond those approved and have not otherwise been substantiated. These three bullet points are: (1) "Fast acting – Reaches therapeutic concentrations in serum and lungs within 4-5 hours"; (2) "Highly palatable – Ensures intake of full dose"; and (3) "VFD status ensures long-term effectiveness." An additional bullet in the promotional piece claims the drug "(s)ignificantly…increased average daily gain compared to untreated controls." Nuflor® is not approved to increase average daily gain.

Offering an adulterated animal for slaughter as food in violation of section 402(a) of the FFDCA was the basis for a WARNING LETTER issued to Robert C. Zieroth, co-owner of KZ Dairy of Raymond, WA. Specifically, an analysis of tissues by the U.S. Department of Agriculture revealed the presence of 23.56 ppm of the drug sulfamethazine in the liver and 48.27 ppm in the muscle tissue of the cow in question. 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). The dairy was also advised that complete treatment records were not being maintained as required by section 402(a) of the FFDCA. In addition, FDA's investigation revealed that the firm failed to use sulfamethazine and lincomycin hydrochloride in conformance with their approved labeling and approved drug applications. The dairy was also warned that both drugs were being used extralabel in violation of 21 CFR Part 530 and were, therefore, unsafe within section 512(a) of the FFDCA and adulterated under section 501(a) of the Act.

FDA has issued a WARNING LETTER to Michael F. Stubbs, owner of the Diamond S Dairy, Hazelton, ID. Specifically, the dairy offered for slaughter as food a dairy cow that contained 0.69 ppm of the drug tilmicosin in the muscle. A tolerance of 0.1 ppm has been established for residues of this drug in the muscle tissue of cattle (21 CFR 556.735(b)(ii)). The presence of the drug in the muscle tissue exceeding the tolerance rendered the animal adulterated within the meaning of section 402(a) of the FFDCA. Furthermore, the firm administered tilmicosin to a lactating dairy cow when the drug is indicated for use in cattle, withdrawal periods set forth in the approved labeling were not followed, and administration of the drug was not done with the supervision of a licensed veterinarian, in violation of 21 CFR 530.11(a). In addition, complete treatment records were lacking.

Mitchell K. Visser, owner of the Par 5 Dairy, Dexter, NM, received a WARNING LETTER from FDA for a violation of section 402(a) of the FFDCA. Specifically, the firm offered for slaughter as food a cow that contained 14.0 ppm of the drug sulfadimethoxine in the liver and 11.34 ppm in the muscle. A

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Regulatory Activities . . . *(Continued)*

tolerance of 0.1 ppm has been established by FDA for residues of this drug in the uncooked edible tissues of cattle, as codified in 21 CFR 556.640. FDA's investigation also revealed that the firm administered sulfadiemethoxine without following the dosage level and withdrawal period set forth in the approved labeling and without the supervision of a licensed veterinarian in violation of 21 CFR 530.11(a). As a result, the drug was found to be unsafe under section 512 of the FFDCA and adulterated under section 501(a)(5) of the Act.

Similar violations were cited in a WARNING LETTER from FDA to Michael W. Copeland, owner of the Madera Calf Ranch, Madera, CA. Specifically, an analysis by USDA of tissue samples collected from an animal raised by the firm as a calf identified the presence of gentamicin (amount not quantified) in the kidney. There is no tolerance for gentamicin in the tissues of cattle (21 CFR 556.300), thus the animal was adulterated within the meaning of section 402(a) of the FFDCA. The firm was also warned that it lacked treatment records for the calves raised on its ranch, as well as an adequate inventory system for determining the quantities of drugs used to medicate the animals in the ranch's care. The WARNING LETTER also noted that the facility adulterated the drugs gentamicin sulfate, penicillin G procaine, tylosin, and ceftiofur hydrochloride within the meaning of section 501(a) of the FFDCA when the facility failed to use these drugs in conformance with their approved labeling.

Recalls

A Class II firm-initiated recall is ongoing by the Springer Magrath Co. of McCook, NE, for approximately 13,255 bottles of "O-NO-MORE" Calf Claimer Powder, packaged in 11-oz. bottles. The recall was undertaken because the finished product was manufactured with bovine blood meal that contained an excess of hair and bone and did not bear the cautionary BSE statement that the product should not be fed to ruminants. Distribution of the recalled product was nationwide.

Altana, Inc., of Meville, NY, is carrying out a Class III recall of 7,092 units of its Muricin (mupirocin) Ointment 2% for dermatologic use on dogs. The reason for the recall is that the product in question is subpotent. Altana had out-of-specification results in three lots of a similar product, Mupirocin Ointment USP, 2%, for human use. The product was also distributed for use on dogs under the trade name Muricin Ointment 2%, sold under Altana's Pharmaderm Animal Health label. Distribution occurred in Massachusetts, Pennsylvania, South Carolina, Alabama, Indiana, Mississippi, Missouri, Texas, Colorado, Arizona, and Washington.

A nationwide, Class III firm-initiated recall is ongoing by Fort Dodge Laboratories, Inc., of Fort Dodge, IA, for more than 33,500 tubes of its Fort Doge Panolog Cream, Nystatin-Neomycin Sulfate-Thiostrepton-Triamcinolone Acetonide Cream USP, for topical use on dogs and cats. The affected products are packaged in 7.5- and 15-g aluminum tubes. The reason for the recall is that one of the active ingredients in the product (triamcinolone acetonide) was from an unapproved manufacturer.

Darling International, Inc., of Irving, TX, has completed a firm-initiated Class II (three different codes) recall and a Class III recall (four different codes) of 682,600 lbs. of its dry rendered tankage (also known as Crax), because the product contained melamine. Distribution was limited to Kansas and Nebraska.

Approvals for June and July 2007

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

PAYLEAN (ractopamine hydrochloride) and TYLAN (tylosin phosphate) (NADA 141-172), filed by Elanco Animal Health, a Division of Eli Lilly & Co. The original NADA provides for the use of two-way combination Type B and Type C medicated swine feeds formulated with PAYLEAN (ractopamine hydrochloride) and TYLAN (tylosin phosphate) single-ingredient Type A medicated articles. The supplement provides for revised indications for the use of Type C medicated feeds used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness; and for the control of swine dysentery associated with *Brachyspira hyodysenteriae* and porcine proliferative enteropathies (ileitis) associated with *Lawsonia intracellularis* in finishing swine, weighing not less than 150 lbs., fed a complete ration containing at least 16 percent crude protein for the last 45-90 lbs. of gain prior to slaughter. Notice of approval was published July 31, 2007.

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Approvals for June and July 2007 *(Continued)*

Supplemental New Animal Drug Applications (Continued)

IVOMEC (ivermectin) (NADA 140-974), filed by Merial LTD. The supplemental NADA provides for the use of IVOMEC (ivermectin) Premix for Swine, a Type A medicated article, for the treatment and control of various internal and external parasites. The supplement revised the approved concentration of ivermectin in Type C medicated feed administered as a top dress to adult and breeding swine. Notice of approval was published July 10, 2007.

DERAMAXX (deracoxib) (NADA 141-203), filed by Novartis Animal Health US, Inc. The supplemental NADA provides for the addition of a 75-mg size of DERAMAXX (deracoxib) Chewable Tablets, used for the control of pain and inflammation in dogs. Notice of approval was published July 10, 2007.

LINCOMIX 20 (lincomycin hydrochloride) and LINCOMIX 50 (NADA 97-505), filed by Pharmacia & Upjohn Co., a Division of Pfizer, Inc. The supplemental NADA provides for the use of LINCOMIX 20 and LINCOMIX 50 Feed Medications in single-ingredient Type B and Type C medicated feeds for swine weighing greater than 250 lbs. and for the addition of a reproductive caution statement to the labeling. Notice of approval was published June 18, 2007.

ADSPEC (spectinomycin sulfate) Sterile Solution (NADA 141-077), filed by Pharmacia & Upjohn Co., a Division of Pfizer, Inc. The original NADA was approved for the use of ADSPEC (spectinomycin sulfate) for the treatment of bovine respiratory disease associated with several bacterial pathogens. The supplemental NADA provides for revising nomenclature for two bacterial pathogens on product labeling for spectinomycin sulfate injectable solution. Notice of approval was published June 6, 2007.

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