FDA VETERINARIAN
Center for Veterinary Medicine
2006 Vol. XXI, No. V

FDA Releases Animal Cloning Draft Risk Assessment; Finds Food as Safe as Conventionally Produced Foods

On December 28, 2006, the Food and Drug Administration (FDA) released a draft risk assessment that concluded meat and milk derived from adult cattle, pig, and goat clones or their progeny are as safe to eat as food already available.

During a 90-day comment period concluding April 2, 2007, FDA is encouraging comments from the public regarding the science of the cloning process. Until it has reviewed all comments, FDA is continuing to ask producers and breeders to voluntarily refrain from introducing food products from animal clones or their progeny into commerce, according to Dr. Stephen Sundlof, Director of FDA's Center for Veterinary Medicine (CVM). CVM initiated the voluntary moratorium in 2001, when the livestock industry started to investigate the use of a type of cloning that appeared to have commercial applicability.

FDA's conclusion about the safety of meat and milk from animal clones and progeny came after FDA scientists reviewed many studies that compared food from adult cattle, pig, and goat clones and their progeny to food from conventionally bred animals, and found no differences in safety. FDA did not make a recommendation regarding the safety of food from sheep clones, due to the limited information currently available.

Dr. Sundlof noted that, even without the voluntary moratorium, the overwhelming majority of meat and milk in the food supply would still come from conventional means, rather than through cloning. The value of these relatively expensive animal clones will be in their genetics, not in the food they produce. Instead, animal clones will be bred by conventional means to produce animals for food. Some animal clones may be used for milk production if the moratorium is lifted. (See the related article in this issue, "A Primer on Cloning and its use in Livestock Operations.")

In addition to food safety, the draft risk assessment also addressed the health of the animals involved in cloning. Scientists consider animal cloning to be an "assisted reproductive technology," like others that are widely used today, such as artificial insemination, embryo transfer, and *in vitro* fertilization. Like these other technologies, and even natural breeding done through mating, cloning can carry risks to the animals involved. No new risks were noted as a result of cloning, however.

The draft risk assessment is approximately 800 pages long and contains data FDA scientists reviewed in reaching their conclusions about food safety and animal health with regard to cloning. Scientists outside FDA examined the draft risk assessment in a peer-review process before the document was publicly released.

FDA's findings echo the National Academy of Sciences' conclusions on animal biotechnology, published in 2002. FDA has reviewed extensive studies and data that have become available since the NAS review and reached similar conclusions.

Risk management plan and draft guidance for industry

FDA released a proposed risk management plan with the draft risk assessment. The proposed risk management plan outlines measures FDA might take to address any risks, such as working with scientific and professional societies that have expertise in animal health and reproduction to develop standards of care for animals involved in the cloning process. FDA also proposed utilizing international scientific organizations to develop a database of information about the health of animal clones and their offspring, as well as the composition of meat and milk derived from the animals.

FDA also released a draft Guidance for Industry that contains FDA's

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In This Issue

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

FDA Reminds Horse Owners of Fumonisin Danger

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

The Food and Drug Administration (FDA) recently issued a reminder to owners of horses that corn and corn products can contain fumonisins, a group of mycotoxins which is extremely harmful for horses. More than 10 types of fumonisins have been isolated and characterized, and of these, the most prevalent in contaminated corn is fumonisin B1, which is believed to be the most toxic. The dangers are dose-related, and horses and rabbits are the most susceptible of the domestic species. Fumonisins can produce a serious neurologic disease in horses known as leukoencephalomalacia.

Each year, a number of horses die from eating corn or corn byproducts containing fumonisins, which are produced from a mold that resides in corn kernels while still on the corn plant. Typically, fumonisin levels are highest in damaged corn kernels and these damaged corn kernels most often end up in the screenings that separate out when corn is handled. FDA recommends that corn screenings not be used in horse feed since many of the investigated cases of fumonisin poisoning in horses have involved the feeding of corn screenings.

Fumonisins are frequently found in varying amounts in corn and corn byproducts, and they can increase under improper storage conditions. Thus, corn and feed containing corn needs to be kept dry and protected from moisture when stored.

In November 2001, FDA's Center for Veterinary Medicine (CVM) and the Center for Food Safety and Applied Nutrition jointly issued a final guidance for industry on fumonisin levels in human food and animal feeds. CVM recommended that corn and corn byproducts used in horse feed should contain less than 5 parts per million (ppm) of fumonisins and comprise no more than 20 percent of the dry weight of the total ration. This guidance for industry can be viewed on FDA's Web site at: *http://www.cfsan.fda.gov/~dms/fumongu2.html*. Additional information about fumonisins is also available at: *http://www.fda.gov/cvm/fumonisin.htm*.

FDA Releases Animal Cloning Draft Risk Assessment *(Continued)*

recommendations on the use of clones and their progeny for human and animal food.

Although FDA is a science-based Agency and has no authority to address ethical issues with regard to animal cloning, it has offered to provide scientific expertise to interested parties working on ethics issues.

FDA is seeking comments from the public for 90 days following the release of the documents. To submit electronic comments, visit *http://www.accessdata.fda.gov/scripts/oc/dockets/comments/commentdocket.cfm?AGENCY=FDA*. Written comments may be sent to: Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD, 20852. Comments must be received by April 2, 2007, and should include the docket number 2003N-0573.

Pet Owners Cautioned About Internet Drug Sales

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

In its November-December 2006 issue of *FDA Consumer*, the Food and Drug Administration (FDA) cautioned pet owners about the potential dangers associated with purchasing animal drugs on the Internet.

The problem arises when unsuspecting consumers purchase these drug products online from enterprises that are fronts for unscrupulous businesses. In these cases, the consumer can end up with products not approved by FDA. While many of the unapproved products are considerably cheaper, they may also pose a health threat to pets and put their lives in danger.

FDA's Center for Veterinary Medicine (CVM) regulates the manufacture and distribution of animal drugs; the dispensing of prescription veterinary drug products falls under the jurisdiction of State pharmacy boards.

There are also some foreign Internet pharmacies that advertise the

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FDA VETERINARIAN

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Pet Owners Cautioned... *(Continued)*

availability of veterinary prescription drugs to U.S. citizens without a prescription. Others state that one of its veterinarians on staff will evaluate a pet after reviewing a questionnaire filled out online by the pet owner. However, this sales technique sidesteps the valid veterinarian-client-patient relationship that is created when a veterinarian physically examines the animal. This physical examination provides the only means for a veterinarian to make a proper diagnosis and determine what therapy is required.

Two of the most commonly used animal prescription drugs that pet owners buy over the Internet are nonsteroidal anti-inflammatory drugs (NSAIDs) and heartworm prevention products. The use of both of these products should be preceded by a blood test and thorough examination of the animal, which cannot be done online. NSAIDs are prescribed for pain relief in dogs with osteoarthritis or for pain following surgery. NSAID therapy needs to be monitored by the treating veterinarian. FDA/CVM has developed an informative brochure on the use of NSAIDs in dogs; it is discussed elsewhere in this issue.

Dogs, cats, ferrets, and some other mammals can get heartworm disease, which exists in all 50 States and is spread by mosquitoes. The heartworm larvae can enter the bite wound, migrate through the animal's tissue, and then grow into adult worms that live in the arteries of the lungs. Heartworm preventives kill the larvae before they become adult worms. The heartworm test involves drawing blood from the animal, so it cannot be done by an Internet pharmacy veterinarian. If the test is not performed, a pet owner could be giving heartworm preventives to a pet that has heartworms, leading to potentially severe reactions in the pets.

Manufacturers of heartworm medications do not sell to Internet pharmacies unless the pharmacies are licensed and are owned by a veterinarian. Nevertheless, a pet owner's own veterinarian is really the best source for obtaining heartworm medication. This way, should a cat or dog that is on heartworm medication contract the disease, the manufacturer will work with the veterinarian directly. At the end of the day, there is no better assurance for your pet's health than a valid veterinarian-client-patient relationship.

NSAIDs Brochure Developed

As mentioned elsewhere in this issue, the Food and Drug Administration (FDA)/Center for Veterinary Medicine (CVM), will make available a brochure about the use of veterinary non-steroidal anti-inflammatory drugs (NSAIDs) entitled, "Treating Pain in Your Dog." Included in the brochure is a description of NSAIDs, as well as answers to the following questions:

- "What should you discuss with your veterinarian?"
- "What should you know before giving your dog an NSAID?"
- "What side effects should you watch for?" and
- "What do I do if a side effect is suspected?"

The brochure is available on CVM's Web site at: *www.fda.gov/cvm* or by writing to FDA at:

Communications Staff/NSAIDs Brochure
FDA/Center for Veterinary Medicine
7519 Standish Place, HFV-12
Rockville, MD, 20855
Ph: 240-276-9300

The Role of CVM's Ombudsman

The Center for Veterinary Medicine (CVM), like most government agencies, has an ombudsman function assigned to a key staff member. The ombudsman helps stakeholders who may have a complaint or concern, and has broader responsibilities for serving as a confidential channel for communications to the Center. This article explains the functions, the legal underpinnings for the job, and the limits of the authority of CVM's ombudsman.

by Marcia K. Larkins, D.V.M., Ombudsman

The term "ombudsman," Scandinavian in origin, and sometimes referred to as "ombud" or "ombudsperson," is a special kind of grievance-handling official—one who investigates citizens' complaints against administrative agencies. It describes a person authorized to receive and investigate complaints, report the findings, and help to achieve equitable settlements.

The basic types of ombudsmen are the classical ombudsman, the advocate ombudsman, and the organizational ombudsman. Classical ombudsmen are created by law and appointed by legislative bodies, do formal investigations, have subpoena power, and can publish public reports. Advocate ombudsmen (American Bar Association Standards) are established by legislation, serve a designated population, and can initiate action in formal forums. Organizational ombudsmen function by informal processes, conduct independent and impartial investigations, and issue reports, but do not publish public reports on the details of their investigations. CVM has an organizational ombudsman.

Knowledge, skills of the organizational ombudsman

An organizational ombudsman requires skills that include being able

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The Role of CVM's Ombudsman *(Continued)*

to listen impartially to a complainant, being sensitive to fairness, and being able to work with others to resolve a dispute. The ombudsman should also have a good working knowledge of the regulations, guidance documents, and administrative policies and procedures relevant to the organization and its customers, as well as those that specifically involve dispute resolution.

The role of an ombudsman within an organization will depend on the culture of that organization. In order to be effective, the ombudsman must:

- Have the support of top management;
- Have access to any individual manager within the organization;
- Act and be perceived as neutral; and
- Be able to offer confidentiality and anonymity to those who contact him or her for informal problem resolution.

Due to the protection provided by the practice of confidentiality, the organizational ombudsman may also serve an important role in receiving information from callers that is useful to an organization. Typically, organizational ombudsmen do not answer questions or voluntarily disclose information regarding anyone that they may have spoken to, and they maintain that privacy unless they have permission to disclose information for the purpose of informal dispute resolution.

The ombudsman enhances his or her skills and knowledge through personal experience in an organization and from training courses, conferences, and workshops sponsored by professional organizations. The International Ombudsman Association is a non-profit organization that provides a forum for practicing organizational ombudsmen. CVM's Ombudsman is a member. The knowledge and experiences shared in discussions with other ombudsmen can also provide valuable information, insight, and professional support. The Coalition of Federal Ombudsmen is based in Washington, DC, and meets every 2 months. The membership includes ombudsmen from FDA and many other Federal organizations.

CVM Ombudsman

CVM's Ombudsman not only handles complaints and helps to resolve disputes, but also serves as a communications channel, a confidential and informal information resource, and a person who helps the organization work for change.

The CVM Ombudsman serves both its employees and customers, assisting in resolving disputes with affected persons and groups both inside and outside the Center. The CVM Ombudsman investigates complaints involving science and science-based policy decisions made by individuals inside and outside the organization, reports the findings, and helps to achieve equitable solutions. The ombudsman also handles complaints concerning the way in which the Center's science-based regulatory policies and certain administrative policies and procedures are implemented, and works to ensure that these are being applied fairly and equitably. The objective is to help find solutions to problems and concerns expressed by customers that meet the needs of both the customer and the organization.

Dispute resolution by the CVM Ombudsman is generally accomplished through informal investigation, shuttle diplomacy, or third-party intervention and informal mediation. Rather than choosing for a complainant how a dispute will be handled, the CVM Ombudsman provides options or helps the complainant develop new options.

The CVM ombudsman knows the values, ethics, policies, and procedures of the organization and understands the structure, processes, and resources within CVM. That knowledge helps the ombudsman to resolve issues and to work toward avoiding recurrence of the same problems.

The FDA dispute resolution procedures for employees and customers requesting review of a scientific controversy is found under 21 *Code of Federal Regulations* (CFR) 10.75 "Internal agency review of decisions." *http://www.washingtonwatchdog.org/documents/cfr/title21/part10.html#10.75*

In addition, CVM has a process for employees to bring critical information that may be controversial or precedent-setting to the ombudsman and ultimately to the CVM Leadership Team, outside of normal supervisory channels. Procedures for Internal CVM Review of Science or Policy Issues Related to Significant Decisions of High Impact can be found at *http://www.fda.gov/cvm/Policy_Procedures/2115.pdf*.

Consistent with typical organizational ombudsmen, the CVM ombudsman does not conduct formal investigations for adjudication, nor does she adjudicate. However, the ombudsman can advise its stakeholders on fair process and assist in facilitating appeals related to regulated products effectively and fairly. The ombudsman's role in CVM's formal appeal process is described in Guidance #79 "Dispute Resolution Procedures for Decisions on Products Regulated by the Center for Veterinary Medicine" (*www.fda.gov/cvm/Guidance/fguide79.htm*).

The CVM's Ombudsman also:

- Provides feedback to the organization on systemic issues;
- Acts as a safety net for those issues that are not addressed through normal channels; and
- Serves as an "early warning" channel for new issues by identifying trends, thus allowing the organization to be proactive.

The CVM Ombudsman is also a point of contact that provides information about an organization to callers by:

- Advising them on how the system works and how they can best access it;
- Clarifying the meaning of and/or providing a copy of a policy; and

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CVM Produces BSE Video About Importance of Cleaning Trucks

The Center for Veterinary Medicine (CVM), in cooperation with three national feed industry trade associations, has produced a video that explains the importance of cleaning out trucks that carry certain feed ingredients in preventing the spread of bovine spongiform encephalopathy (BSE).

The video offers recommendations to truckers for ways to comply with the requirements of the 1997 BSE feed rule concerning cross-contamination of feed for cattle and other ruminants with prohibited material.

Truckers are responsible for making sure their trucks are cleaned between shipments of feed ingredients containing prohibited material and shipments of feed for cattle and other ruminants. Prohibited material includes meat and bone meal and certain other materials from mammals that can carry the infectious agent for BSE.

The recommendations presented in the video are consistent with those listed in Guidance for Industry #68, "Small Entities Compliance Policy Guide for Protein Blenders, Feed Manufacturers, and Distributors," which is available at *http://www.fda.gov/cvm/Guidance/guidance68.htm*.

Instrumental in the development of the video were the American Feed Industry Association (AFIA), the National Grain and Feed Association (NGFA), and the National Renderers Association (NRA). These associations represent most of the animal feed and feed ingredient industry in the United States.

The video is about 11 minutes long. It was kept short on purpose so it could be shown to a truck driver waiting for the truck's feed or ingredients to be loaded or unloaded at the feed or feed ingredient manufacturing facility or rendering plant.

CVM will provide access to the complete video through its Web site (at *www.fda.gov/cvm*). The video is free of copyright and can be downloaded and used by anyone.

AFIA, NGFA, and NRA said they are distributing complimentary single copies on CD to member companies to be used by commercial feed mills, feed ingredient manufacturers, integrators, and others as part of an ongoing educational outreach to trucker-haulers.

The Role of CVM's Ombudsman *(Continued)*

- Providing or helping to find information (names, phone numbers, etc.) that enables callers to go directly to the person who can best address their concern or resolve their problem.

Current issues unique to Federal ombudsmen

Confidentiality, whether communication with an ombudsman constitutes notice to an organization, and record retention are three issues that are ongoing with regard to the rights and responsibilities of organizational ombudsmen. These issues have been discussed in the International Ombudsman Association training courses and annual conferences as to how they apply to all ombudsmen and in Coalition of Federal Ombudsmen meetings with specific regard to Federal ombudsmen in light of current Federal regulations.

Confidentiality, and notice: One of the ombudsman's most important tools is the ability to ensure the confidentiality of any dispute resolution communication. In order to safeguard both the practice and appearance of neutrality and confidentiality, organizational ombudsmen do not do formal investigations or keep formal case records. Simply contacting an ombudsman generally does not constitute legal notice to the organization.

One of the ombudsman's most important tools is the ability to ensure the confidentiality of any dispute resolution communication.

Records retention: Under 21 CFR §10.70, documentation of significant FDA decisions on any matter under Federal law must be provided in an administrative file. However, communications that are made with regard to an informal dispute resolution are not "records" within the meaning of 44 U.S.C. 3301 and are, therefore, not submitted to or received by an ombudsman under Federal law. An ombudsman does not keep case records containing identifying information on behalf of the organization.

Summary

Like most Federal ombudsman, the CVM ombudsman is available to investigate problems and provide options, and also to follow up on resolutions to determine if they were effective. In addition, the ombudsman tracks and monitors issues to determine if repetitive patterns exist and advises CVM's Center Management Team on possible preventative measures.

Finally, the ombudsman at CVM works hard to foster an environment in the organization of fairness, equity, and respect.

Contact the CVM Ombudsman at: *Marcia.larkin@fda.hhs.gov*; 7519 Standish Place, Rockville, MD 20855; (240) 276-9015.

A Primer on Cloning and Its Use in Livestock Operations

by Siobhan DeLancey, Consumer Safety Officer, and Dr. Larisa Rudenko, Senior Advisor for Biotechnology, Office of New Animal Drug Evaluation; and John Matheson, Senior Regulatory Review Scientist, Office of Surveillance and Compliance

Imagine the perfect dairy cow. For eight years she has gotten pregnant on the first try, given birth easily, and produced gallon upon gallon of the best milk. Even when others in the herd got sick, she stayed healthy. She is ideally suited to the climate in which she lives. The farmer has depended on this cow and her daughters in lean times to carry the farm through, but now she is at the end of her reproductive life.

Although the farmer may have this cow's daughters to carry on the line, he also has another alternative: copying her. Biological copying is referred to as cloning. By cloning his prize cow, breeding the clones, and keeping their offspring, the farmer can introduce the natural positive characteristics into the herd quickly. It would take several more years to achieve these same improvements by conventional breeding.

Farmers can also clone animals to produce more uniform quality meat. Take, for example, a male pig (boar) who time after time sires piglets that mature quickly and provide lean meat. If a farmer has several of these boars he could quickly produce an entire herd with consistent, high quality meat.

Researchers have been cloning livestock since 1996. In 2001, when it became apparent that cloning could become a commercial venture, the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) asked that food from clones and their offspring be voluntarily kept out of the food chain. FDA then began an intensive evaluation that included examining the safety of food from these animals.

What is cloning, really?

Cloning is a complex process that lets one exactly copy the genetic, or inherited, traits of an animal (the donor). Livestock species that scientists have successfully cloned are cattle, pig, sheep, and goats. Scientists have also cloned mice, rats, rabbits, cats, mules, horses, and one dog. Chickens and other poultry have not been cloned.

Most people think of livestock breeding taking place through traditional mating, in which males and females physically get together to reproduce. In fact, this type of mating is not often the case.

Traditional mating is not that efficient, if the goal is to produce as many offspring as possible. For example, a male has enough sperm to produce many more offspring than would be possible by traditional mating. Traditional mating also has certain risks: one or both of the animals may be injured in the process of mating. The female may be hurt by the male because he is often so much larger, or an unwilling female may injure the male. There is also a risk of infection or transmission of venereal disease during traditional mating.

Because of these factors, many farmers use assisted reproductive technologies for breeding. These include artificial insemination, embryo transfer, and *in vitro* fertilization. Artificial insemination was first documented in the breeding of horses in the 14th century. The first successful embryo transfer of a cow was in 1951, and the first *in vitro* fertilization (IVF)-derived animal was a rabbit born in 1959. Livestock production in the United States now uses all these methods regularly. For example, most dairy farms don't have bulls, so more than 70% of the Holstein cows bred in the United States are artificially inseminated. The frozen semen can come from a bull many miles, or even many States, away.

Cloning is a more advanced form of these assisted reproductive technologies. Much of the public perception of cloning likely comes from science fiction books and movies. Some people incorrectly believe that clones spring forth fully formed, or are grown in test tubes. This is just not the case. Clones are born just like other animals. They are similar to identical twins, only born at different times. Just as twins share the same DNA, clones have the same genes as the donor animal. A clone is not a mutant, nor is it a weaker version of the original animal. It's just a copy.

In all of the other assisted reproductive technologies, the male and female parents each contribute half of their genes to their offspring. Farmers have worked for years to choose animals with the best traits and breed them together, which increases the chance these good traits will be passed on and become more common in livestock herds. Even though farmers have been able to improve their herds over time, they still can't absolute predict the characteristics of the offspring, not even their sex. Cloning gives the farmer complete control over the offspring's inherited traits. Thus, a farmer who clones an especially desirable, but aging or injured animal knows in advance that the clone will have the genetic potential to be

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…Cloning and Its Use in Livestock Operations *(Cont.)*

an especially good, younger animal. He can then use that animal to further reproduce by traditional mating or other assisted breeding.

How do you make clones?

Most cloning today uses a process called somatic cell nuclear transfer (SCNT). Just as with *in vitro* fertilization, scientists take an immature egg from a female animal (often from ovaries obtained at the slaughterhouse). But instead of combining it with sperm, they remove the nucleus (which contains the egg's genes). This leaves behind the other components necessary for an embryo to develop. Scientists then add the nucleus containing the desirable traits from the animal the farmer wishes to copy. After a few other steps, the donor nucleus and egg fuse, start dividing, and an embryo begins to form. The embryo is then implanted in the uterus of a surrogate dam (again the same as with *in vitro* fertilization), which carries it to term. ("Dam" is a term that livestock breeders use to refer to the female parent of an animal). The clone is delivered just like any other baby animal.

The main use of clones is to produce breeding stock, not food. Clones allow farmers to upgrade the overall quality of their herds by providing more copies of the best animals in the herd.

What can go wrong with cloning?

There are no complications that are unique to cloning. These problems are also seen in animals born from natural mating or assisted reproductive technologies. They seem to happen more often in clones for a number of reasons that probably have to do with parts of the procedure that occur outside the body. The embryo may fail to develop properly during the *in vitro* stage or early on after transfer to the surrogate and may be flushed out of the uterus. If it does develop, the embryo may not implant properly into the uterus of the surrogate dam. Alternatively, the placenta may not form properly, and the developing animal won't get the nourishment it needs.

Large Offspring Syndrome (LOS) is seen in pregnancies of cattle and sheep that come from both assisted reproductive technologies and cloning. With LOS, the fetus grows too large in the uterus, making problems for the animal and its surrogate dam. LOS has not been observed in goats and swine.

As a group, livestock clones tend to have more health problems at birth, and may die more often right after birth than conventionally bred animals. If clones survive the first few days after birth, they seem to become just as healthy and strong as other animals of the same age. By the time clones are young adults, it's not possible to tell them apart from other animals of the same age, even if you conduct a detailed examination. Scientists at FDA and research institutions have looked at blood work for clones that's similar to what people get when they have physicals. These results show that the clones are perfectly healthy, and walk, wean, grow, mature, and behave just like conventional animals.

Why clone?

The main use of clones is to produce breeding stock, not food. Clones allow farmers to upgrade the overall quality of their herds by providing more copies of the best animals in the herd. These animals are then used for conventional breeding, and the sexually reproduced offspring become the food-producing animals. Just as farmers wouldn't use their best conventionally bred breeding animals as sources of food, they are equally unlikely to do so for clones.

Some examples of desirable characteristics in livestock that breeders might want in their herds include the following:

- **Disease resistance:** Sick animals are expensive for farmers. Veterinary bills add up, and unhealthy animals don't produce as much meat or milk. A herd that is resistant to disease is extremely valuable because it doesn't lose any production time to illness, and doesn't cost the farmer extra money for veterinary treatment.
- **Suitability to climate:** Different types of livestock grow well in different climates. Some of this is natural and some results from selective breeding. For instance, Brahma cattle can cope with the heat and humidity of weather in the southwestern United States, but they often do not produce very high grades of meat. Cloning could allow breeders to select those cattle that can produce high quality meat or milk and thrive in extreme climates and use them to breed more cattle to be used for food production. Similarly, pork production has traditionally been centered in the eastern United States, but is moving to different regions of the United States

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(e.g., Utah). Cloning could allow breeders to select those pigs that naturally do well in the new climate, and use them to breed more pigs to be used for food production.

- **Quality body type:** Farmers naturally want an animal whose body is well suited to its production function. For example, a dairy cow should have a large, well-attached udder so that she can produce lots of milk. She should also be able to carry and deliver calves easily. For animals that produce meat, farmers breed for strong, heavy-muscled, quick-maturing animals that will yield high quality meat in the shortest time possible. The most desirable bulls produce offspring that are relatively small at birth (so that they are easier for the female to carry and deliver), but that grow rapidly and are healthy after birth.
- **Fertility:** Quality dairy cows should be very fertile, because a cow that doesn't get pregnant and bear calves won't produce milk. Male fertility is just as important as that of the female. The more sperm he can produce, the more females a bull can inseminate, and the more animals will be born. Beef cattle or other meat-producing animals such as pigs need to have high fertility rates in order to replace animals that are sent to slaughter. Cloning allows farmers and breeders to clone those animals with high fertility rates so that they could bear offspring that would also tend to be very fertile.
- **Market preference:** Farmers or ranchers may also want to breed livestock to meet the changing tastes of consumers. The traits the producers are looking for include leanness, tenderness, color, and size of various cuts. Preferences also vary by culture, and cloning may help tailor products to the preferences of various international markets and ethnic groups.

How does cloning help get these characteristics into the herd more quickly? As we've previously said, cloning allows the breeder to increase the number of breeding animals available to make the actual food production animals. So, if a producer wanted to introduce disease resistance into a herd rapidly, cloning could be used to produce a number of breeding animals that carry the gene for disease resistance, rather than just one. Likewise, if a breeder wants to pass on the genes of a female animal, cloning could result in multiples of that female to breed, rather than just one.

Is it safe to eat food from clones?

It's important to remember that the purpose of clones is for breeding, not eating. Dairy, beef, or pork clones will make up a tiny fraction of the total number of food producing animals in the United States. Instead, their offspring will be the animals actually producing meat or milk for the food supply.

Dairy clones will produce milk after they give birth, and the dairy farmers will want to be able to drink that milk or put it in the food supply. Once clones used for breeding meat-producing animals can no longer reproduce, their breeders will also want to be able to put them into the food supply.

In order to determine whether there would be any risk involved in eating meat or milk from clones or their offspring, in 1999 FDA asked the National Academy of Sciences (NAS) to identify science-based concerns associated with animal biotechnology, including cloning. The NAS gathered an independent group of top, peer-selected scientists from across the country to conduct this study. The scientists delivered their report in the fall of 2002. That report stated that theoretically there were no concerns for the safety of meat or milk from clones. On the other hand, the report expressed a low level of concern due to a lack of information on the clones at that time, and not for any specific scientific reasons. The report also stated that the meat and milk from the offspring of clones posed no unique food safety concerns.

Meanwhile, FDA itself began the most comprehensive examination of the health of livestock clones that has been conducted. The evaluation has taken more than four years. This examination formed the basis of a Draft Risk Assessment to determine whether cloning posed a risk to animal health or to humans eating food from clones or their offspring (*http://www.fda.gov/cvm/cloning.htm*). FDA conducted a thorough search of the scientific literature on clones, and identified hundreds of peer-reviewed scientific journal articles, which it then reviewed. They were also able to obtain health records and blood samples from almost all of the cattle clones that have been produced in the United States and data from clones produced in other countries. FDA compared these health records, and the independently analyzed blood results with similar samples from conventional animals of the same age and breed that were raised on the same farms.

After reviewing all this information, FDA found that it could not tell a healthy clone from a healthy conventionally bred animal. All of the blood values, overall health records, and behaviors were in the same range for clones and conventional animals of the same breed raised on the same farms. FDA also saw that milk from dairy clones does not differ

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significantly in composition from milk from conventionally bred animals.

In the Draft Risk Assessment, FDA concluded that meat and milk from cattle, swine, and goat clones would be as safe as food we eat from those species now. It did not have enough information to make a decision on the safety of food from sheep clones.

For another study similar to the one conducted on cow clones, the Agency also evaluated the health of offspring sexually derived from swine clones, as well as the composition of their meat. After reviewing this very large data set, the Agency concluded that all of the blood values, overall health records, and meat composition profiles of the progeny of clones were in the same range as for very closely genetically related conventionally bred swine. Based on these results, other studies from scientific journals, and our understanding of the biological processes involved in cloning, the Agency agreed with NAS that food from the sexually reproduced offspring of clones is as safe as food that we eat every day. These offspring animals will produce almost all of the food from the overall cloning/breeding process.

In the Draft Risk Assessment, FDA concluded that meat and milk from cattle, swine, and goat clones would be as safe as food we eat from those species now.

What's next?

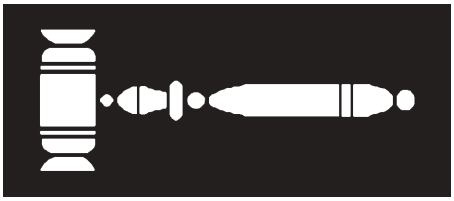
FDA's Draft Risk Assessment includes data collected or published before early 2006. FDA will continue to closely monitor the development of clones and their progeny as a source for food as further data become available.

FDA encourages public comments on the Draft Risk Assessment, Proposed Risk Management Plan, and Draft Guidance for Industry. We will review these comments and evaluate any additional data that may be shared with us during the comment period. We will then issue a Final Risk Assessment, Risk Management Plan, and Guidance for Industry.

Comments and suggestions regarding any of these documents should be sent to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Comments may also be submitted electronically on the Internet at *http://www.fda.gov/dockets/ecomments*. All written comments should be identified with Docket No. 2003N-0573. Please specify which document your comments address.

Copies of the Draft Risk Assessment may be requested from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at *http://www.fda.gov/cvm/cloning.htm*

Regulatory Activities for October and November 2006



Significant deviations from the requirements from the regulations setting forth the animal proteins that are prohibited in ruminant feed (21 CFR 589.2000) were noted in a WARNING LETTER issued to Christopher V.B. Smith, corporate president and CEO of H.J. Baker & Bro., Inc., Westport, CT. Failure to follow the requirements set forth in these regulations resulted in the manufacture and distribution of products adulterated under section 402(a)(4) of the Federal Food, Drug, and Cosmetic Act (FFDCA) and misbranded under section 403(a)(1). The action followed an investigation that showed that the firm failed to establish and use cleanout procedures or other means to prevent carry-over of products that contain or may contain protein derived from mammalian tissues into animal protein or feeds that may be used for ruminants. Specifically, the firm used a screw auger to convey both prohibited and non-prohibited material to bulk storage bins. In addition, the firm failed to label all prohibitive or potentially prohibitive products with "Do not feed to cattle or other ruminants."

A WARNING LETTER was issued to Miriam E. Harthill, president of Churchill Veterinary Supply Company, Inc., Irvine, CA, because an inspection

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Regulatory Activities... *(Continued)*

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of this animal drug manufacturing facility revealed serious violations of the FFDCA. Specifically, the following products were being manufactured without an approved new animal drug application (NADA) on file with FDA to verify safety and effectiveness: Butecort Sweat, Fur-A-Sweat, Foot Freeze, Tie-Up Powder, After Firing Paint, Blue Splint Blister, Liquid Blister, and Soluble Iodine, Nascent. The drugs were adulterated because they are deemed unsafe in the absence of an approved NADA. In addition, two of the products—Blue Splint Blister and Liquid Blister—contain mercury bichloride (mercuric chloride), a chemical that FDA believes is not safe and effective; the Agency has reports of adverse drug reactions, including deaths in animals, resulting from the use of mercury-containing blistering products. FDA also has safety concerns for people who handle these products. As unapproved products, they were found to be misbranded under Section 352(f)(1) of the FFDCA because their labeling failed to bear adequate directions for use. The products are also misbranded under Section 352(o) of the Act because they were manufactured in a facility not registered with FDA.

…two of the [unapproved manufactured] products—Blue Splint Blister and Liquid Blister—contain mercury bichloride (mercuric chloride), a chemical that FDA believes is not safe and effective.

Extralabel use of gentamicin sulfate in violation of 21 CFR Part 530 led to the issuance of a WARNING LETTER to Dr. Richard Price of Dairy Veterinary Services, P.A., Monroe, NH. Specifically, an investigation by FDA revealed that the firm had prescribed the intramammary infusion of the liquid form of gentamicin sulfate to treat coliform mastitis in lactating dairy cattle. The firm's prescription for the extralabel use of gentamicin sulfate solution did not meet the requirements of 21 CFR 530.20, which require that the company: establish a substantially extended withdrawal period prior to marketing of edible products; institute procedures to ensure that the identity of the treated animal is carefully maintained; and take appropriate measures to ensure that assigned timeframes for withdrawal are met and that no illegal drug residues remain in any food-producing animal subjected to extralabel treatment.

Penicillin residues in the kidney tissues of a cow offered for sale as human food exceeding the established tolerance set forth in 21 CFR 556.510 resulted in the issuance of a WARNING LETTER to Gerald C. Thompson, owner of Gerald Thompson Farm, LaFargeville, NY. The presence of 0.17 parts per million penicillin in kidney tissue caused the animal to be adulterated within the meaning of section 402 of the FFDCA. An investigation of the farm also revealed that animals were being held under conditions so inadequate that medicated animals bearing potentially harmful drug residues were likely to enter the food supply. Mr. Thompson also failed to maintain written treatment records to document the identity of the animal, treatment dates, drugs administered, dosage administered, route of administration, and withdrawal times for milk and beef. In addition, Mr. Thompson adulterated Quartermaster penicillin-dihydrostreptomycin in oil because it was being used extralabel, since it was not being administered by a licensed veterinarian.

Penicillin residues in the kidney tissue of a dairy cow offered for sale as food exceeding the established tolerances set forth in 21 CFR 556.510 resulted in the issuance of a WARNING LETTER to Michael H. Vermeer, general manager and co-owner of Vermeer Dairy, Caldwell, ID. The presence of penicillin G procaine at higher levels than authorized caused the animal to be adulterated under section 402 of the FFDCA. In addition, the firm adulterated the drug within the meaning of section 501 of the FFDCA because it was used extralabel and not administered in the presence of a licensed veterinarian. Adequate treatment records were also lacking.

Comings and Goings

New Hires

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Elizabeth Voneiff, Staff Fellow
- Daniel Burnette, Staff Fellow
- Annette Hiss, Staff Fellow
- Gregory Shaw, Project Manager

OFFICE OF SURVEILLANCE AND COMPLIANCE

- Julie Gariner, Veterinary Medical Officer

OFFICE OF MANAGEMENT

- Patricia Carr, Management Officer

Departures

OFFICE OF SURVEILLANCE AND COMPLIANCE

- Elsie Hill, Application Examiner (deceased)

OFFICE OF RESEARCH

- Robert D. Walker, Division Director

Retiring Compliance Director's Mantra Was Consumer Protection

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

Ask Gloria Dunnavan, the Center for Veterinary Medicine's retiring Director of Compliance, who she works for, and her answer is, "I work for the consumer. It's my mantra, and at the end of each day, I ask myself whether I did the very best today for the consumer. If I can say 'yes,' then I accomplished my goal." Ms. Dunnavan's mantra and many other topics were covered recently when I had a chance to sit down and talk with this delightful person about her 37 years in the Federal Government, which came to an end January 4, 2007, when she retired. "It was not an easy decision," she confided, "because I love my job and all of the people I have worked with. Not coming to work will be very difficult for me."

Gloria Dunnavan

Ms. Dunnavan not coming to work as CVM's chief compliance official will also be difficult for the many FDA employees whose lives were touched by her in so many ways over the years. Her departure will leave a gaping hole and shoes not easily filled. What you see is what you get: no pretense, no façade, no airs, no double-talk, and all public service. Strong in her convictions about protecting consumers and animals, Ms. Dunnavan's expertise and dedication to her craft were pivotal features of her 10 years as Compliance Director, as well as her 27 years of government service before that.

A Kentucky native, Ms. Dunnavan (or "Glo" as all her friends and colleagues call her) started out as a school teacher, imparting to young minds the intricacies of chemistry and the physical sciences. But after about a year of this, she realized she wanted to spend her days with something other than chalk dust and test tubes, so she applied for—and was hired—as an entry-level clerk at the Census Bureau in Jeffersonville, IN, just across the Kentucky state line. Her name was put on an availability roster, and in short order, she was notified of an open position for an inspector at FDA. She sent in her application (even though, back in 1972, "male applicants only" actually appeared on the form!), and a week later was interviewed. Another week passed, and she learned that she was hired and should report to the Nashville District office. She worked there as an investigator for 5 years, plus another 1-1/2 years at the resident post, handling several important compliance matters. Then the opportunity for a job as a compliance officer at CVM opened up and she landed it. It was in that role that she developed a sincere interest in reducing the incidence of illegal residues in meat and poultry.

After several years, the position of Director of the Division of Compliance opened, and Ms. Dunnavan, telling it like it is, said she applied for two reasons: to make a real difference; and to make sure that a qualified person took the reins of this important position, which had been vacant for 3 years. She spoke of her realization one day that so much of our daily life's routine involves some aspect of FDA intervention, whether it's ensuring our contact lenses are safe, our cereal is pure, our pet food is safe and labeled correctly, or our prescription drug is safe and effective. "FDA is indeed a consumer protection agency," Ms. Dunnavan said, "and staying focused on that realization helps us make the right decisions." She lamented that some battles cannot be won but stressed that limited time and resources need to be channeled to the ones that can be.

Accomplishments

When asked about changes at CVM, Ms. Dunnavan remarked that one of the most notable changes over the years has been the Center's heightened visibility, both internally and to the public as well. She said there was a time when CVM was more the outlier, operating

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Retiring Compliance Director… *(Continued)*

in the shadow of some of the more news-generating Centers at FDA, such as the Center for Drug Evaluation and Research and Center for Food Safety and Nutrition. But that has changed, especially in the advent of such high-profile areas as drug residues in edible animal tissues, antibiotic resistance, and veterinary drug compounding. Probably the single most significant issue that brought CVM to center stage was BSE, Ms. Dunnavan commented. This issue generated huge public interest, both in terms of public and animal health and safety, but in terms of economic and global impacts as well. Ms. Dunnavan regards the 1997 ruminant feed rule to prevent the spread of BSE as her biggest accomplishment at CVM, especially since the Center can boast that the animal feed industry is more than 99 percent compliant. Ms. Dunnavan's eyes light up when she mentions that the BSE work led to CVM being presented with a coveted "Hammer Award." (The Hammer Award was established by Al Gore, when he was Vice President, to recognize Federal Government teams that made significant contributions to building a government that works better, costs less, and yields results that Americans care about.) This accomplishment that brought about the recognition did not come about easily, however. It took a concerted effort on the part of CVM staff, State and local counterparts, the regulated industry, and others to attain the level of cooperation and shared goals to prevent the spread of BSE in this country. Ms. Dunnavan said she and her staff spent countless hours training, giving speeches, doing interviews, attending meetings, and much more to make the BSE initiative a success. A total of 14,000 inspections have taken place, including inspections of non-licensed feed mills for which no inventory was available. Ms. Dunnavan developed a strategy to locate these facilities and include them on the inspection schedule.

Another source of great pride for Ms. Dunnavan is the marked reduction in drug residues in meat and poultry. She attributes this reduction to such things as the cooperative work with the U.S. Department of Agriculture and other agencies, the design of education and training programs, liaison with veterinarians, and the development of an appropriate policy to address the various cases of noncompliance. Getting the bad apples out of the barrel has been a top priority for this compliance director, and the list of violators is probably pretty long. "Consumers shouldn't have to worry about illegal drug residues in their hamburger; my best customers are sitting in jail," said Ms. Dunnavan with a smile.

Ms. Dunnavan regards the 1997 ruminant feed rule to prevent the spread of BSE as her biggest accomplishment at CVM, especially since the Center can boast that the animal feed industry is more than 99 percent compliant.

A strong advocate of the "High Performance Organization" (HPO) philosophy used at the Center, Ms. Dunnavan has lived and breathed the concept every day on the job. She thanks CVM Director, Dr. Stephen Sundlof, for embracing HPO, building it into the Center's culture, and ensuring that positive changes have been realized over the past several years. Ms. Dunnavan herself provides her team with the necessary tools to get the job done, enough guidance to help them learn and adapt, but then relies on them for help and direction each step of the way. "We all help each other and contribute to each other's work product, confident that in the end, we're all here to help the consumer, and I'm very proud of that," Ms. Dunnavan commented. This team effort was dramatically illustrated by the work to withdraw poultry fluoroquinolones approval. (The FDA Commissioner announced in July 2005 a decision to no longer allow distribution or use of the antimicrobial drug enrofloxacin for the purpose of treating bacterial infections in poultry.) The project was huge and beset with electronic documentation problems that necessitated manual processing to ensure that the deadline to complete the docket was met. "We worked nights and weekends, sometimes till 1:00 a.m., to get that done." Not one to merely shout the commands and have the troops advance, Ms. Dunnavan was right there with the team burning the midnight oil. She runs team meetings the same way: the roles of facilitator, scribe, and timekeeper all rotate. This opera obviously has no "prima donnas," but lots of "spear-carriers" (think "important extras"), and when the curtain call is taken, Ms. Dunnavan stands to the side.

When questioned about a successor, Ms. Dunnavan offered that she hopes the new Director of Compliance will espouse the HPO philosophy, emphasizing cooperation and working together, with the continuous focus on consumer protection. "Hopefully, the successor will build on what has been established here, creating a pleasant working environment, which means less internal strife and a higher quality work product," she said. "And you really need to have a good sense of humor, because laughing every day is a good thing," she added. She also believes strongly in encouraging people to be multi-talented so that co-workers

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Retiring Compliance Director… *(Continued)*

can chip in and help out in areas other than their primary expertise.

Retirement

Ms. Dunnavan has had her share of drama in her personal life, and only now is taking her doctor's orders to put her health ahead of her job—something she resisted doing for far too long. Those 10- to 12-hour days took their toll, and then a fall in her home about 1-1/2 years ago landed Ms. Dunnavan in a wheelchair for 6 months. A 10-week stint at the Duke University Diet and Fitness Center helped her get her life back and lose 189 pounds so far this year—an amazing accomplishment. The process continues, and regular swimming and water exercise have had a dramatic effect on her quality of life and have enabled her to walk so much better and get to the places that she hadn't been able to reach for so many months.

No retirement interview would be complete without questions about the future. "Well, it won't involve a rocking chair on the porch," Ms. Dunnavan quipped when asked. But it does involve a newly purchased home in Wilmington, NC, that has a "snow-free zone" sign in front of it. The house was a recent birthday present to herself. A lover of antiques and the "thrill of the hunt," Ms. Dunnavan will again pursue this long-neglected hobby. Other plans include photography of old churches and possibly a book describing them. Another project involves Pumpernickel. No, not the bread, but the lovable Dachshund she once owned that may be her inspiration for a compilation of short stories. Porcelain painting, rug-hooking, embroidery, and water-color painting may be added to the list. All of this leaves very little time for that rocking chair, doesn't it?

Our interview was ended by a knock on the door, summonsing Ms. Dunnavan to an important meeting. Industry representatives? Senior CVM leadership? Congressional staffers? No, not even close. This was a planning meeting for her upcoming retirement party in February, which will be a big deal. "I'd better get to this meeting," Ms. Dunnavan apologetically stated, "because I want to make sure that everyone who comes has a really good time." And if you know "Glo" like I now know "Glo," you know we'll all have a wonderful time indeed!

Approvals for October and November 2006

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

NUFLOR (florfenicol) (NADA 141-264), filed by Schering-Plough Animal Health Corp. The NADA provides for the Veterinary Feed Directive use of this antibiotic, a Type A medicated article to formulate Type C medicated feeds used for the control of swine respiratory disease (SRD) associated with several bacteria. These bacteria consist of *Actinobacillus pleuropneumoniae, Pasteurella multocida, Streptococcus suis,* and *Bordetella bronchiseptica* in groups of swine in buildings experiencing an outbreak of SRD. Notice of approval was published December 4, 2006.

IVERHART MAX (ivermectin, pyrantel, pamoate, praziquantel) Chewable Tablets (NADA 141-257), filed by Virbac AH, Inc. The NADA provides for veterinary prescription use for dogs of chewable tablets containing ivermectin, pyrantel pamoate, and praziquantel for the treatment and control or prevention of various internal parasites. Specifically, the new product prevents canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for 1 month (30 days) after infection and is approved for the treatment and control of roundworm (*Toxocara canis, Toxascaris leonina*), hookworm (*Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense*) and tapeworm (*Dipylidium caninum, Taenia pisiformis*) infections. Notice of approval was published November 7, 2006.

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Approvals for October and November 2006 *(Continued)*

Abbreviated New Animal Drug Applications (Continued)

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

LINCOMYCIN-SPECTINOMYCIN (lincomycin hydrochloride and spectinomycin dihydrochloride pentahydrate) (ANADA 200-407), filed by Agri Laboratories, Ltd. The ANADA provides for use of Lincomycin-Spectinomycin (lincomycin hydrochloride and spectinomycin dihydrochloride pentahydrate) Water Soluble Powder to create a solution administered in the drinking water of chickens as an aid in the control of airsacculitis caused by either *Mycoplasma synoviae* or *M. gallisepticum* susceptible to lincomycin-spectinomycin and complicated chronic respiratory disease (air sac infection) caused by *Escherichia coli* and *M. gallisepticum* susceptible to lincomycin-spectinomycin. The ANADA is approved as a generic copy of L-S 50 Water Soluble Powder, sponsored by Pharmacia & Upjohn Co., a Division of Pfizer, Inc., under NADA 046-109. Notice of approval was published December 8, 2006.

PRIMEX (Prantel pamoate) ANADA 200-445), filed by First Priority, Inc. The ANADA provides for the oral use of pyrantel pamoate Horse Wormer in horses and ponies as an OTC animal drug product for the removal and control of various internal parasites. First Priority, Inc.'s, PRIMEX Horse Wormer is approved as a generic copy of Pfizer, Inc.'s, PAMOBAN Horse Wormer, approved under NADA 91-739. Notice of approval was published December 4, 2006.

SMZ-MED 454 (ANADA 200-434), filed by Cross Vetpharm Group Ltd. The ANADA provides for the use of (sulfamethazine sodium) Soluble Powder to create a solution administered as a drench to swine or cattle, or in the drinking water of chickens, turkeys, swine, or cattle for the treatment of coccidiosis or various bacterial diseases. The new product is approved as a generic copy of Fort Dodge Animal Health, a Division of Wyeth Holdings Corp.'s, SULMET Soluble Powder, which was approved under NADA 122-272. Notice of approval was published December 4, 2006.

GLYCOPYRROLATE INJECTABLE (ANADA 200-365), filed by IVX Animal Health, Inc. The ANADA provides for veterinary prescription use of Glycopyrrolate Injectable as a preanesthetic agent in dogs and cats. The new product is approved as a generic copy of Fort Dodge Animal Health's (a Division of Wyeth) ROBINUL-V (glycopyrrolate), approved under NADA 101-777. Notice of approval was published November 2, 2006.

CVM has published in the *Federal Register* notice of the approval of these Supplemental NADAs

TYLAN (tylosin) (supplement to NADA 12-491), filed by Elanco Animal Health, a Division of Eli Lilly & Co. The supplement provides for the use of tylosin phosphate Type A medicated articles and provides for an alternate feeding regimen for the control of swine proliferative enteropathies (ileitis) associated with Lawsonia intracellularis. In addition, Elanco Animal Health revised the names on labeling of other enteric pathogens of swine

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Approvals for October and November 2006 *(Continued)*

Supplemental New Animal Drug Applications (Continued)

to reflect changes in the scientific nomenclature for these bacteria. Notice of approval was published December 12, 2006.

BOVATEC 91 (lasalocid) (supplement to NADA 96-298), filed by Alpharma Inc. The supplement provides for the use of lasalocid Type A medicated article (20 percent lasalocid activity per pound) to make free-choice Type C medicated feeds used for increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers). Notice of approval was published November 21, 2006.

PAYLEAN (ractopamine hydrochloride) (supplement to NADA 141-863), filed by Elanco Animal Health, A Division of Eli Lilly & Co. The supplement provides for the use of ractopamine hydrochloride Type A medicated articles in Type B and C medicated feeds used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine. The supplement revises the concentrations of ractopamine hydrochloride fed to finishing swine, weighing not less than 150 pounds, fed a complete ration containing at least 16 percent crude protein for the last 45 to 90 pounds of gain prior to slaughter. Elanco Animal Health also filed a supplement to NADA 141-172 that provides for use of two-way combination Type C medicated swine feeds formulated with ractopamine hydrochloride and TYLAN (tylosin phosphate) single-ingredient Type A medicated articles. The supplement revises the concentrations of ractopamine hydrochloride in Type C medicated feeds used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness; and for the prevention and/or control of porcine proliferative enteropathies (ileitis) associated with Lawsonia intracellularis and for the prevention of swine dysentery (vibrionic) in finishing swine weighing not less than 150 pounds, fed a complete ration containing at least 16 percent crude protein for the last 45 to 90 pounds of gain prior to slaughter. Notice of approval for both supplements was published November 21, 2006.

ULCERGARD (omeprazole) Paste (NADA 141-227), filed by Merial Ltd. The supplemental NADA provides for the administration of omeprazole paste to horses for 8 or 28 days for the prevention of gastric ulcers. The drug is available for over-the-counter lay use because a diagnosis of gastric ulcer disease is not required for use of the drug to prevent the disease. Notice or approval was published October 10, 2006.

CVM has published in the *Federal Register* notice of the approval of these Supplemental ANADAs

OXYTETRACYCLINE HCl Soluble Powder-343 (ANADA 200-247), filed by IVX Animal Health, Inc. The supplemental ANADA provides for the use of Oxytetracycline HCl Soluble Powder-343 in several species. The supplement revises labeling of generic oxytetracycline soluble powder with the current scientific names of the causative bacteria of foulbrood of honeybees. Approval of this supplemental ANADA did not require review of additional safety or effectiveness data or information. Notice of approval for the supplement was published December 8, 2006.

DEPARTMENT OF
HEALTH & HUMAN SERVICES

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Rockville MD 20857

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07-0208