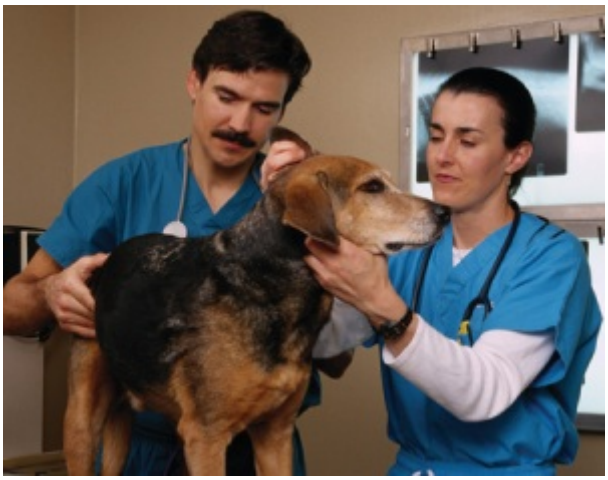
Animal Health and Consumer Protection

FDA Consumer magazine
The Centennial Edition/January-February 2006

By Linda Bren

Nearly a century ago, farmers had a medicine chest of products to "cure" their animals, with names such as Lee's Gizzard Capsules, Liquid Hog Medicine, and Kow-Kure.
The gizzard capsules, made with nicotine, were advertised to get rid of worms in turkeys. Liquid Hog Medicine, which contained lye, was for treating diarrhea in pigs. And Kow-Kure, whose exact ingredients remain a mystery, purported to prevent miscarriages in cows
No one knew whether these products were actually safe or effective, but all were allowed on the market under the federal drug laws at the time.

Such products went by the wayside as Congress passed stronger drug laws, and today, the regulation of animal drugs closely parallels the regulation of human drugs. Like human drugs, all animal drugs must be approved by the Food and Drug Administration before being allowed on the market. The FDA's Center for Veterinary Medicine (CVM) is responsible for regulating drugs and food additives used for animals--both food-producing animals and family pets.



Getty Images
The FDA has approved more than 700 drug products
to help veterinarians treat America's 60 million pet dogs,
75 million pet cats, and 5 million horses.

To date, the CVM has approved nearly 700 drug products for use in 97 million cattle, 59 million pigs, 8.8 billion chickens, 272 million turkeys, 7 million sheep, and millions of other food-producing animals in the United States. In addition, more than 700 approved drug products are available to maintain the health of America's 60 million pet dogs, 75 million pet cats, and 5 million horses.

The FDA employs more than 100 veterinarians, most of them within the CVM. These animal experts--plus chemists, animal scientists, toxicologists, microbiologists, and other professionals--are committed to protecting animal and human health throughout the United States. They evaluate the benefits and risks of proposed veterinary products before permitting them to be marketed; monitor the use of products after they are on the market; take legal action, if necessary, to enforce laws; and conduct research to support the FDA's science-based decisions.

The Evolution of Animal Drug Law

Animal feed and drugs have been regulated for as long as human food and drugs. When Congress passed the Pure Food and Drugs Act in 1906, it introduced the regulation of food and drugs in interstate commerce for "man or other animals."

But the 1906 act gave the FDA limited powers to protect consumers against adulterated and misrepresented food and drugs, says FDA Historian John Swann, Ph.D. "It was against the law to make a false or misleading claim for a product, but it could be difficult to prosecute offenders, especially after the law was amended in 1912 to require that fraudulence be proven to establish misbranding," he says. "And violations of the law were misdemeanors with fines that could be as high as $300 along with jail terms, but more often these were considerably lower. However, the violative products could be seized and destroyed."

The 1906 law did not give the FDA authority to approve products before they were marketed. When the Federal Food, Drug, and Cosmetic Act (FD&C Act) was passed in 1938, it strengthened the FDA's powers. For the first time, manufacturers were required to show evidence that their products were safe before they could sell them.

The decades after the new law went into effect brought the development of many new animal drugs and medicated feeds. The veterinary regulatory arm of the FDA evolved from a small branch in 1953 to a larger division in 1959. Government officials, recognizing the importance of food–producing animal health to the welfare of the country, elevated the division to the bureau level in 1965. In 1984, the Bureau of Veterinary Medicine (BVM) changed its name to the Center for Veterinary Medicine.

Cancer-Causing Chemicals in Food Animals

Congress amended the Federal FD&C Act to include a series of laws addressing food additives in 1958 and color additives in 1960. These laws gave the FDA tighter control over the growing list of chemicals entering the food supply and gave manufacturers the responsibility to establish the safety of their products. The laws included a provision, known as the "Delaney Clause," which established that no food or color additive could be deemed safe--or given FDA approval--if found to cause cancer in humans or animals.

In 1962, the Delaney Clause was modified to permit the FDA to approve the use of carcinogenic compounds in food-producing animals if certain conditions were met. "The FDA felt that food-producing animals could be exposed to carcinogenic drugs and not necessarily pass cancer-causing chemicals on to humans," says Woodrow Knight, Ph.D., director of the CVM's Division

of Production Drugs.

The modification to the Delaney Clause is known as the "Diethylstilbestrol (DES) Proviso," named for a hormone approved in 1954 to promote growth in cattle and sheep. DES had also been approved much earlier in humans. It was thought to prevent miscarriages in women, but the hormone later was linked to vaginal cancers in the daughters of women who were treated with the drug during pregnancy.

Under the DES Proviso, the FDA could approve a carcinogen for food animal use if the concentration of any residue remaining in the edible tissues was so low that it presented an insignificant risk of cancer to consumers.

But measuring drug residues was a problem. Standard tests at that time were not very sophisticated, and regulators were concerned that drug residues in foods might exist in dangerous levels and just couldn't be measured.

Using advances in analytical chemistry, FDA scientists developed techniques to measure minute concentrations of residues, says Knight. "They were able to measure parts per billion or even per trillion." These techniques led to a 1987 regulation called the Sensitivity-of-Method procedures, or SOM. The regulation defines an insignificant risk of cancer as a 1 in 1 million increase in risk, and spells out how to measure the residue concentration.

Although DES was banned for use in people and animals in the 1970s, the DES Proviso remains in effect. SOM procedures are used to determine acceptable residue concentrations of new animal drugs in food produced from animals.

Safety and Effectiveness

Under the Federal FD&C Act of 1938, manufacturers of human or animal drugs only had to show that their products were safe. In 1962, amendments to the act required them to show that their products were also effective. The 1962 amendments generally did not distinguish between human and animal drugs; in 1968, Congress passed legislation to strengthen provisions of the act that pertained to the regulation of animal drugs. Animal drugs, medicated feeds, and food additives were required to be safe for the animal they were intended to be used in and, in the case of food-producing animals, safe for human consumption and safe for the environment. Effectiveness was required to be shown by substantial evidence from one or more adequate and well-controlled studies.

Contaminants and Residues

Every year, infections occur as a result of people ingesting animal products that have been contaminated with various kinds of germs such as salmonella. Furthermore, animal-derived foods can be contaminated by industrial chemicals such as dioxin, natural toxins produced by molds and fungi, and residues of drugs such as antimicrobials. Antimicrobials include antibiotics and other drugs to combat bacteria, viruses, fungi, and certain parasites.

Public health officials were concerned about antibiotic residues in food-producing animals as early as the 1950s, just a few years after penicillin became widely used, says FDA Historian Suzanne White Junod, Ph.D. The government used "milk check stuffers" to remind farmers to pull their cows off antibiotics for a few days before milking them, she says. "The government paid farmers to produce milk then, and the reminder was stuffed in an envelope with the milk check, knowing it would get their attention. That was their way of educating farmers about the need to prevent drug residues in food and to get their voluntary compliance

Today, the CVM's efforts to keep the food supply safe from contaminants and harmful residues include conducting educational programs for industry and farmers, sending Warning Letters to veterinarians and industry, giving guidance to industry, requiring drug labeling changes, and establishing stringent requirements for new drug approval. In some cases, such as with the antibiotic chloramphenicol, the CVM has withdrawn approval to protect public health.

Chloramphenicol was a best seller in the United States in the 1950s. The FDA approved the antibiotic to treat people with meningitis, typhoid fever, and other serious infections. But in some people, this "wonder drug" had a horrible side effect: aplastic anemia, a bone marrow disorder that could be fatal.

The CVM had approved chloramphenicol to treat infections in dogs and cats, but it had never approved it to treat food-producing animals because of the fear that harmful residues would remain in food products. During the early 1980s, testing of American meat samples showed potentially dangerous residue levels of chloramphenicol, indicating that veterinarians and farmers were using the drug illegally to treat cattle and pigs.

This practice presented a danger not only to consumers, but also to those administering the drug. Getting the oral solution into the animal was a messy procedure, and farmers could easily get the drug on themselves. In 1981, a feedlot owner in Kansas used chloramphenicol in hundreds of cattle with pneumonia. The drug seeped into a cut in his hand, and he died later that year from aplastic anemia.

The CVM sent warning letters to thousands of veterinarians nationwide, stating its intent to eliminate all use of chloramphenicol in food-producing animals. In 1986, the CVM banned the oral solution of chloramphenicol for pets to prevent it from being diverted to use in food-producing animals.

Today, chloramphenicol is not found in domestically produced food, but the CVM continues to fight the drug in imported food. Low levels of chloramphenicol have been detected in shipments of imported honey, shrimp, and crayfish from Asia. The FDA has increased its sampling of imported food and works with importers, the FDA's Office of Regulatory Affairs, and the FDA's Center for Food Safety and Applied Nutrition to prevent foods contaminated with chloramphenicol from entering the United States.

CVM scientists also are developing new methods to test for the presence of the drug with greater sensitivity, says CVM Director Stephen F. Sundlof, D.V.M., Ph.D. "In fact, we're working with other laboratories in Europe to make sure that our methods are similar."

"Chloramphenicol is just one of many potentially harmful substances that CVM is developing methods to detect for," adds Sundlof. Because the FDA never approved many of the drugs that it has found in some imported food, we don't have methods to check for residues, he says. "Now we have to go back and develop them."

The CVM continues to monitor drugs that may potentially contribute to antibiotic-resistant strains of pathogens in people. In 2003, the CVM announced a regulatory pathway it had developed so that pharmaceutical sponsors could seek approval of antimicrobial drugs while ensuring that their use would not create drug-resistant bacteria harmful to public health.

The CVM is working with other countries to reach consensus on food and drug standards, says Sundlof. Through organizations such as the Codex Alimentarius Commission, an international food standard-setting group based in Rome, the CVM works with its counterparts in foreign nations to harmonize veterinary drug residue requirements among Codex's more than 160 member countries.

"We have made substantial progress without lowering the high standards of product safety and efficacy that consumers and industry expect from FDA," says Sundlof.

Recent History and Achievements

Improvements to the Federal FD&C Act continue. Within the past 20 years, Congress has passed five major laws that make the CVM even more effective in protecting human and animal health.

In 1988, a generic animal drug act allowed the FDA to approve generic versions of drugs for animals without requiring companies to duplicate research done to prove the safety and effectiveness of the drugs. This law enables companies to offer lower-cost alternatives to brand-name animal pharmaceuticals to the public.

In 1994, the Animal Medicinal Drug Use Clarification Act (AMDUCA) gave veterinarians more flexibility in using their professional judgment to treat animals. The AMDUCA makes it legal for veterinarians, under certain circumstances, to prescribe drugs "off-label," or "extra-label." This means they can legally treat animals with drugs that have been approved for people but not for animals, or with drugs approved for other species, for other diseases and conditions, or at different dosage levels from those listed on the drug label.

In 1996, the enactment of the Animal Drug Availability Act (ADAA) gave the CVM the flexibility to streamline the requirements for approving animal drugs and medicated feeds without compromising public health.

In 2003, the Animal Drug User Fee Act (ADUFA) authorized the FDA to collect fees from sponsors of new animal drugs, and obligated the FDA to meet specific deadlines. "ADUFA helps FDA expedite and improve its review of applications, so that safe and effective products will be available more quickly," says Sundlof.

In 2004, Congress passed the Minor Use/Minor Species (MUMS) Animal Health Act to make more medications legally available to veterinarians and animal owners to treat minor animal species and uncommon diseases in major animal species. A minor species is any animal species other than cattle, horses, pigs, chickens, turkeys, dogs, and cats, which are classified as major species. "Before passage of MUMS, drug companies could rarely afford to bring to market drugs for minor species because the markets were too small to generate an adequate financial return," says Andrew Beaulieu, D.V.M., director of the CVM's Office of MUMS. "The new law provides flexibility and incentives to drug companies to get these limited-use drugs to market."

The MUMS Act is expected to benefit agricultural groups such as fish farmers, sheep and goat producers, and beekeepers, says Beaulieu. "It will also help people who own pets such as guinea pigs or ornamental fish, and it will likely be a great help to zoo veterinarians."

In October 2005, the FDA approved the first minor species drug that was designated under the MUMS Act and thus qualified for seven years of exclusive marketing rights. Aquaflor (florfenicol) is an antibiotic to treat enteric septicemia, a bacterial disease that kills catfish. The disease results in significant economic losses to the U.S. catfish industry. Aquaflor is the first new antimicrobial approved for fish in over 20 years.

Preventing Mad Cow Disease

As the regulators of animal feed, the CVM is a key player in protecting U.S. cattle from bovine spongiform encephalopathy (BSE), also called mad cow disease, and protecting the health of people who consume cattle products. BSE is believed to be caused by abnormal proteins called prions in animal feed, and cattle may contract the disease by eating feed that contains these infectious proteins. People may get a human form of the disease, variant Creutzfeldt-Jakob disease, by eating foods from BSE-infected cows.

In 1997, the CVM adopted a BSE feed regulation that prohibits the feeding of certain mammalian proteins to cattle and other ruminants, such as sheep and goats. Since the feed regulation was established, the CVM and state inspectors have conducted more than 37,000 inspections involving more than 15,000 firms that handle animal feed. More than 99 percent of these facilities are in compliance with the regulation.

After 2003, when federal officials diagnosed the first BSE-infected cow in the United States, the CVM worked to further strengthen the feed regulation. In October 2005, the FDA proposed an amendment to the regulation that requires the removal of certain high-risk materials from all animal feed--not just ruminant feed--to prevent accidental access by cattle to potentially infectious feed.

Counterterrorism

There is widespread concern that terrorists could introduce toxic agents in the food chain to harm human and animal health. In addition, natural disasters or human error could result in contaminated food. The CVM is working with other parts of the FDA and with other federal

agencies to help the nation prepare for a biological emergency, natural disaster, or terrorist attack by making sure there are safe and adequate supplies of animal drugs and animal feeds.

CVM scientists are developing rapid tests to detect contaminants and threat agents in animal feed. "CVM is also working with laboratories that have the capabilities to identify and measure levels of anthrax and other select agents that might be used in an agricultural terrorist attack," says Sundlof.

A Look Ahead

CVM regulators must keep pace with scientific advances that will affect animal and consumer health. One of the CVM's biggest challenges, says Sundlof, is preparing to regulate animal products developed through genetic engineering and through new assisted reproductive technologies such as cloning.

Animal clones, such as prime beef-producing cattle, and genetically engineered animals, such as fast-growing salmon, are part of a growing global effort to produce less expensive, high-quality food.

Researchers also are looking to animal cloning as a means to expand populations of livestock with naturally occurring desirable characteristics such as the ability to thrive in harsh climates, or spread natural resistance to animal diseases through herds rapidly. Genetic engineers are investigating broader ranges of applications in animals--from developing BSE-resistant cattle, to producing pigs as sources of organ transplants, and making animals that can produce human drugs and vaccines.

"There is a revolution unfolding before us," says Sundlof. "I think that in the future we'll be seeing changes in animal agriculture to benefit both animal and human health."

The FDA continues to work toward gaining a thorough understanding of the scientific and risk issues that the field of animal biotechnology presents, and to develop the expertise, regulations, and guidance needed to ensure that products derived from these animals are safe and effective, and that food from these animals is safe, nutritious, and wholesome.

While breeders and genetic engineers are focusing on animals as sources of food, other veterinary researchers continue to develop products to improve the health of pets. In 2004, the CVM approved Vetsulin, the first FDA-approved veterinary insulin for the treatment of dogs with diabetes mellitis. "We expect progress in disease and drug research to generate new drugs for our companion animals," says Sundlof. "We're seeing the same type of research to develop drugs for pets as for humans, such as treatments to improve the quality of life for older dogs and cats."