January/February 2001
Vol. XVI, No. I

FDA VETERINARIAN

ADDITIONAL DAY ADDED TO MEETING ON ESTABLISHING REGULATORY THRESHOLDS ON ANTIMICROBIAL RESISTANCE

An additional day has been added to the Center for Veterinary Medicine (CVM) public meeting to discuss the establishment of regulatory thresholds on antimicrobial resistance. This meeting, originally titled "Establishment of Resistance and Monitoring Thresholds in Food-Producing Animals" and scheduled for October 10-11, 2000, was postponed until January 23-24, 2001. Most recently, the meeting has been expanded to include an additional day and has been re-titled, "Use of Antimicrobial Drugs in Food Animals and the Establishment of Regulatory Thresholds on Antimicrobial Resistance."

The new dates for the meeting are **January 22 - 24, 2001**. The meeting will be held from 8:30 a.m. to 5:00 p.m. at the DoubleTree Hotel, 1750 Rockville Pike, Rockville, MD, 20852.

Individuals who have already registered for the January meeting need not re-register. Individuals who have not registered may find the registration form on the CVM Home Page at *http://www.fda.gov/cvm/antimicrobial/arregis4.doc.*

For general inquiries about the meeting and registration, please contact Lynda W. Cowatch, CVM (HFV-100), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-5281. Technical inquiries should be directed to Aleta Sindelar, CVM (HFV-6), at 301-827-4515. When making reservations with the DoubleTree Hotel (1-800-222-8733), please refer to the "CVM Antimicrobial Resistance Public Meetings" to receive the group discount rate. Individuals who have already reserved rooms may wish to reserve additional day(s) at the hotel to include the earlier start date for the meeting. If you need special accommodations for a disability, please contact the DoubleTree Hotel at least 7 days in advance.

Written comments about the meeting should be submitted by March 24, 2001. Comments should be directed to Docket #98D-0969 and submitted to: Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852; or faxed to (301) 827-6870 with the appropriate identification number. Questions about your submission of comments may be directed to HFA-305 at (301) 827-6860.

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AAFCO INTERNET SURF DAY

The Food and Drug Administration (FDA) participated in a nationwide Surf Day sponsored by the Association of American Feed Control Officials (AAFCO) on October 11, 2000. The purpose of the initial Surf Day was to identify Internet vendors selling equine feeds and equine feed supplements that may not be in compliance with Federal and State commercial feed regulations. This coordinated effort was aimed at informing the out-of-compliance firms of the regulations and bringing them into compliance. The potential animal health issues and economic impact were the driving concerns of the animal feed regulators Surf Day.

Individual State and Federal regulators observing the electronic marketplace have seen an increasing number of non-traditional, unapproved feed additives and ingredients offered for sale. Firms who conduct sales and distribution of commercial feed products via the Internet may not necessarily be aware of the Federal and State regulatory requirements, or may feel that they are not subject to the requirements. The pace of electronic marketing development suggests that circumvention of the commercial feed regulatory and compliance systems may be occurring and must be addressed.

Information gathered from the AAFCO Surf Day will be used to develop an educational response for those firms found to be out of compliance with State and Federal commercial feed regulations. Firms who choose not to comply as a result of the educational effort may be faced

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U.S DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION CENTER FOR VETERINARY MEDICINE

2 ANTIBIOTIC RESISTANCE FROM DOWN ON THE CHICKEN FARM

by Linda Bren

This article appeared in the January/February 2001 issue of the ***FDA Consumer****.*

Chicken wings and turkey drum sticks are almost as ingrained in American culture as apple pie and baseball. But the lip-smackin', finger-lickin' good taste is less palatable when the poultry makes people sick. Even harder to swallow are germs that don't respond to drugs that may be prescribed to fight the sickness.

New evidence that drugs used in poultry can cause antibiotic-resistant infections in consumers spurred the Food and Drug Administration's Center for Veterinary Medicine (CVM) to take action. On October 31, CVM proposed to withdraw the approval of an antibacterial, Baytril (enrofloxacin), used to treat disease in chickens and turkeys. CVM approved Baytril in 1996. Made by the Bayer Corporation of Shawnee Mission, Kan., Baytril belongs to a class of antibacterials called fluoroquinolones, which have been used in humans since 1986.

Shortly prior to CVM's announcement, Abbott Laboratories of North Chicago, Il., requested withdrawal of the approvals for its poultry fluoroquinolone products. This means that Abbott will voluntarily remove these products, trade name SaraFlox, from the market.

The Bayer Corporation has requested a hearing to present safety data to try to keep Baytril on the market. The company must submit all data and analysis to support consideration for a hearing.

Poultry growers use fluoroquinolone drugs to keep chickens and turkeys from dying from *Escherichia coli* (*E. coli*) infection, a disease that they could pick up from their own droppings. But the size of flocks precludes testing and treating individual chickens—so when a veterinarian diagnoses an infected bird, the farmers treat the whole flock by adding the drug to its drinking water. While the drug may cure the *E. coli* bacteria in the poultry, another kind of bacteria—*Campylobacter*—may build up resistance to these drugs. And that's the root of the problem.

People who consume chicken or turkey contaminated with fluoroquinolone-resistant *Campylobacter* are at risk of becoming infected with a bacteria that current drugs can't easily kill.

Campylobacter is the most common bacterial cause of diarrheal illness in the United States, according to the Centers for Disease Control and Prevention. It's estimated to affect over 2 million persons every year, or 1 percent of the population.

Commonly found in chickens, *Campylobacter* doesn't make the birds sick. But humans who eat the bacteria-contaminated birds may develop fever, diarrhea, and abdominal cramps. In people with weakened immune systems, *Campylobacter* can be life-threatening. Eating undercooked chicken or turkey, or other food that has been contaminated from contact with raw poultry, is a frequent source of *Campylobacter* infection. Not washing utensils, countertops, cutting boards, sponges, or hands after coming into contact with raw poultry can also spread the bacteria and cause infection. People infected with *Campylobacter* may be prescribed a fluoroquinolone—which may or may not work.

But the damage doesn't stop there. "Cross-resistance occurs throughout this class of drugs," says Stephen F. Sundlof, D.V.M., Ph.D, director of CVM. "So resistance to one fluoroquinolone can compromise the effectiveness of all fluoroquinolone drugs."

Considered one of the most valuable drug classes available to treat human infections, fluoroquinolones are used to treat a wide range of diseases, including the gastrointestinal illness caused by *Campylobacter* infection.

The use of antibiotics in food animals has been a human health

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AAFCO INTERNET SURF DAY (Continued)

with follow-up regulatory action through the feed regulatory authorities having jurisdiction over the operations concerned.

The AAFCO Surf Day concentrated on identifying issues under the statutory authority of the individual State's feed laws with respect to licensing, registration, adulteration, misbranding, and false or misleading claims. Comprehensive educational efforts will be extended following the evaluation process. Compliance monitoring and follow-up activities will be conducted as needed.

Thirty-seven States and Canada participated in this initial AAFCO Surf Day. Additional information about FDA's participation in the Surf Day may be obtained from Ms. Isabel Pocurull, FDA/CVM, Division of Animal Feeds, 7500 Standish Place, HFV-226, Rockville, MD 20855, telephone 301-827-0175, or e-mail *ipocurul@cvm.fda.gov*. Additional information about AAFCO participation may be obtained from Ms. Sharon Senesac, AAFCO, P.O. Box 478, Oxford, IN 47971, telephone 765-385-1029, or e-mail *<sharon@localline.com>*. □

FDA Veterinarian

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Published bi-monthly.

Home Page: http://www.fda.gov/cvm/

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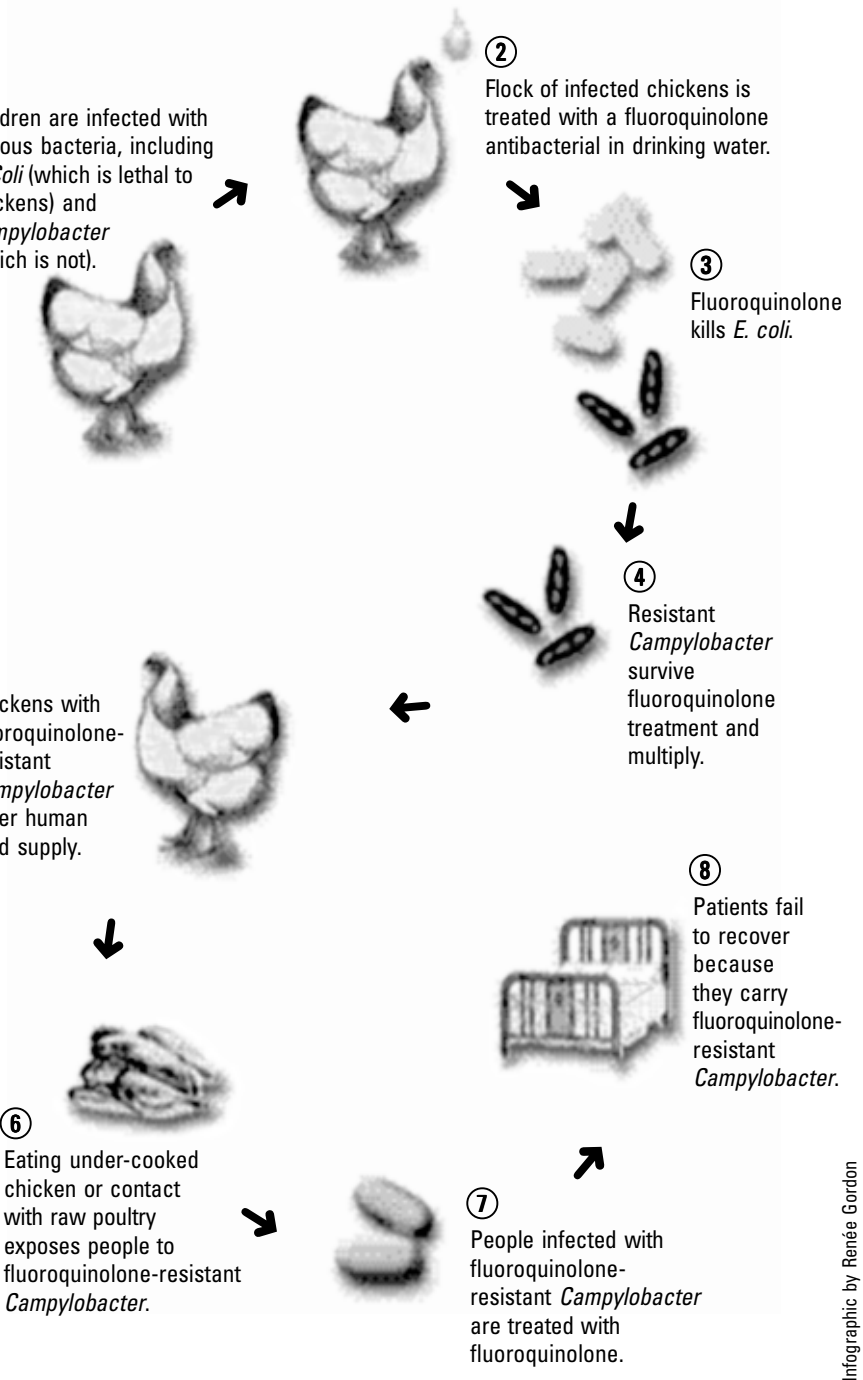
Rockville, MD 20855

How People Get Antibiotic-Resistant Bacteria From Chickens



Infographic by Renée Gordon

concern since the 1970s when FDA first called for restrictions on antibiotics used in animal feed. Prior to 1995, when fluoroquinolones were first approved to treat poultry, very few fluoroquinolone-resistant *Campylobacter* were found in people with foodborne diseases in the United States. After the approval, however, many more fluoroquinolone-resistant bacteria were found in humans and in poultry from slaughter plants and retail stores.

The data to support these findings came from a study by the Minnesota Department of Health and a computerized system called NARMS—the National Antimicrobial Resistance Monitoring System. Created in 1996 as a joint effort by CVM, CDC, and the U.S. Department of Agriculture, NARMS monitors human and animal resistance to 17 antimicrobials. Antimicrobials include antibacterials, antivirals, antifungals, and antiparasitics.

Data provided by NARMS and other sources were used to develop a risk assessment. This assessment, along with other data, supported CVM's decision to propose the withdrawal of approval of Baytril for use in poultry. The risk assessment quantified, for the first time, the magnitude of the dangers to humans eating chicken contaminated with fluoroquinolone-resistant *Campylobacter*.

The risk assessment, completed in October, is only one action CVM has taken to address the antimicrobial resistance problem over the years, says Sundlof. Another part of CVM's proactive program is its proposal to take a stronger regulatory approach when approving new antimicrobial drugs for use in food animals. A "Framework document" (A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals) lays out a plan for evaluating the safety of these drugs based on their importance to human health. If the plan is implemented, the drugs of highest importance—those used to treat a serious or life-threatening disease in humans for which there is no effective alternative treatment—would be subject to the strictest criteria for approval for animal use. Among the studies that would be required by drug sponsors are tests to show their product's potential to induce antibiotic resistance.

CVM has invited input from outside experts on the principles in the Framework document. Two public

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ANTIBIOTIC RESISTANCE FROM DOWN ON THE CHICKEN FARM (Continued)

meetings have been held in the past year and a half, and a third is scheduled for January 22–24 to discuss establishing regulatory thresholds on antimicrobial resistance in food-producing animals. For more details on the meeting and the Framework document, see the CVM Home Page at www.fda.gov/cvm/.

"FDA and CVM will continue to work to put in place a regulatory system that addresses the dangers of antimicrobial resistance and offers better protection to public health," says Sundlof. "At the same time, CVM will strive to assure the safe use of antimicrobial drugs in food-producing animals."

Linda Bren is a Writer-Editor with the FDA Consumer. □

RISK ASSESSMENT ON FLUOROQUINOLONES AVAILABLE

The finalized quantitative risk assessment entitled "The human health impact of fluoroquinolone resistant *Campylobacter* associated with the consumption of chicken" is available on FDA/Center for Veterinary Medicine's Home Page on the Internet at:

http://www.fda.gov/cvm/antimicrobial/Risk_asses.pdf.

In addition, an updated working @RISK model of the analysis described in the report of "The human health impact of fluoroquinolone resistant *Campylobacter* associated with the consumption of chicken" — has been posted on CVM's Home Page. Please note that despite the *.xls extension, this file will not be functional and will not have numeric values printed in all the cells unless the user opens it with @RISK 4.0. If the user does not have this software available, opening the file in Excel will allow the user to see input data values and the functions that were used to generate intermediary and final outputs of the model. The output cells, however, will contain "#NAME?" because the @RISK 4.0 functions will be unknown to Excel.

Individuals interested in this Risk Assessment who do not have access to the Internet may obtain a copy by calling or writing the *FDA Veterinarian*. In addition, they may receive a computer disk with the @RISK working model by calling or writing the newsletter.

Questions about the @RISK model may be addressed to Ms. Mary Bartholomew, FDA/Center for Veterinary Medicine, 7500 Standish Place, HFV-124, Rockville, MD 20855, 301-827-0230, e-mail: *mbarthol@cvm.fda.gov*. □

SCIENTIST DISCUSSES REVIEW OF CLINICAL PATHOLOGY DATA

by Eric S. Dubbin, D.V.M.

Michael Carakostas, D.V.M., Ph.D., Board Certified Pathologist, recently visited CVM's Office of New Animal Drug Evaluation (ONADE) to update reviewers on strategies to assess clinical pathology data for safety studies. Dr. Carakostas is currently director of Corporate Scientific and Regulatory Affairs for the Coca-Cola Company. He taught at Louisiana State University, Tufts, and University of Pennsylvania. He has worked in industry for DuPont, SmithKline Beecham Animal Health.

When CVM requires drug sponsors to test a new animal drug for target animal safety, a major portion of the study includes a battery of blood tests. The two standard categories are hematology (the blood cells) and clinical chemistries (serum enzymes, electrolytes, and other analytes). Dr. Carakostas pointed out the strengths and weaknesses of these blood tests as he spoke and answered questions on the topic. He said that clinical pathology test results can be one of the best ways of judging the effect of the test article on the animal during the in-life phase for the study, but they are often not very specific. A test's reliability is based on its accuracy and precision. Accuracy is defined as how close the test can get to a standard value. Precision is how repeatable is the test.

Another key to a blood test's usefulness is its sensitivity and specificity. Sensitivity is how well a test can detect a true positive. Specificity is how well a test can detect a true negative. A test with high sensitivity will likely be correct when it yields a positive result; whereas a test with a high specificity will likely be correct when it yields a negative result. However, the actual "diagnostic efficiency" of a test can depend more on the "pre-test" probability of disease (or toxicity) than any performance characteristic of a test. Dr. Carakostas used the example of "sink" testing. That is pouring the sample down the sink. He used the example of screening for Feline Leukemia among a population of clinically healthy cats, and assuming that most cats are negative. If one pours the serum sample down the sink and calls them all negative, one will never have a false positive and only occasionally have a false negative result. So a sink test will have 100 percent sensitivity and 0 percent specificity. This was compared to actually running the test with a very good assay. The number of false positives and negatives will be nearly the same if the pre-test probability of disease is low. It was a tongue and cheek example which demonstrated that we must understand the strengths and weaknesses of the tests and the pre-test probability of disease that we run in order to interpret them properly.

Reference ranges are considered the higher and lower acceptable limits of what is normal. Dr. Carakostas pointed out that these ranges are determined by taking samples from

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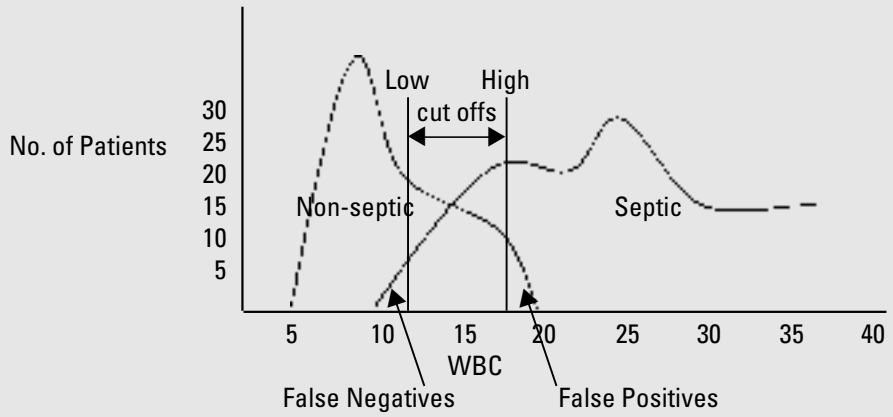
a defined population, determining the mean, and then adding and subtracting 2 standard deviations (+/- 2 S.D.). Reference ranges, therefore, have usefulness in determining cut-off points. However, there is a chance that a normal animal will have a value outside the reference range. This would be a false positive. The test's specificity and sensitivity would come into play here. He then pointed out that these batteries of clinical pathology tests were designed for and work best for a practitioner who knows he/she is often screening for disease. The practitioner might still have to run confirmatory tests as well. Using clinical pathology as a screening technique "to test the healthy population for disease that we cannot see" must be weighed against the potential for false positives. If one was to run a health screen with 20 variables, there is a 40% chance that one of those values would fall outside of the normal range just based on probability.

Dr. Carakostas defined "Diagnostic Efficiency" as the percent of subjects correctly classified by the test result as positive (affected) or negative (non-affected). Since no test is perfect, scientists and practitioners should interpret the test probabilistically. A good screening test should have a high sensitivity (allow for some false positives). A good confirmatory test should have a high specificity. The high specificity is necessary in this instance because the population is enriched with subjects who have a higher probability of being positive. Therefore, the high specificity will have a better chance of finding the *true* negatives.

Dr. Carakostas used the example of the total white blood cell count (WBC or leukocytes) to predict sepsis. Non-septic patients might have a WBC of 5,000 to 20,000. Septic patients might have a WBC of 10,000 to 40,000+. If the cut-off for the diagnosis of sepsis is 18,000, then some non-septic patients would be called septic (false positive). If the cut-off is 12,000, then some septic patients would be called non-septic (false negative). If the cut-off is set midway at 15,000, there would be a mix of false positive and false negatives. When using continuous variables (like multiple samples for WBC) setting cut-off values is a compromise between sensitivity and specificity. (See Figure 1 above.)

FIGURE 1



Another concept that Dr. Carakostas discussed during his lecture is "what is the probability that a variable is significant?" Quite simply the higher the percent change the higher the probability that the variable is significant. Put another way, the farther the value is out of the "normal range" the more likely it is to be truly diseased or abnormal. For example, if a group is running blood urea nitrogen (BUN) values at about 28 mg/dl and another group is running values around 50 mg/dl, the second group is more likely to be truly "affected." Figure 2 below relays this concept.

Dr. Carakostas then discussed the difference between the Scientific Method and Diagnosis within the realm of a Safety Study (see Figure 3 on next page).

All blood tests exhibit normal variation in their results from "the normal population (or control groups)". There are three types of variation:

1. ANALYTICAL – which involves the precision and repeatability of the test.
2. INTRA-ANIMAL – which is variation *within an animal over time.*

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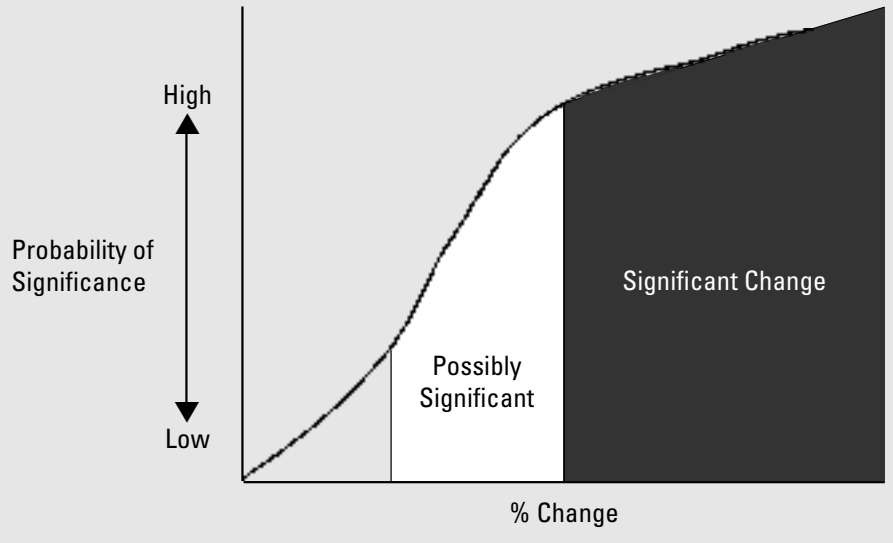
FIGURE 2

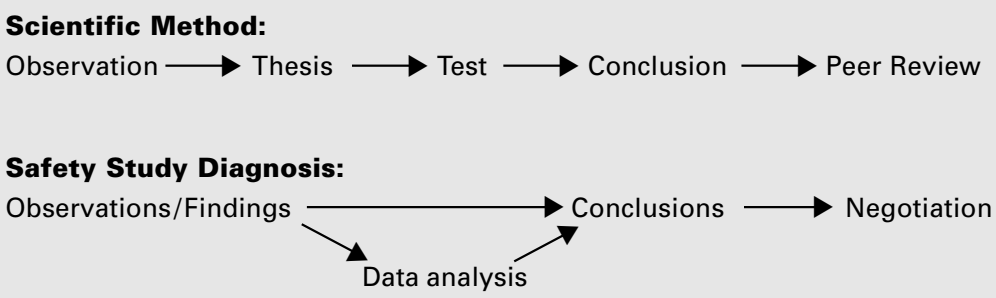


SCIENTIST DISCUSSES REVIEW OF CLINICAL PATHOLOGY DATA (Contin.)

3. INTER-ANIMAL – which is the difference *between* animals.

For example, the variation between animals (inter-animal variation) for an analyte like Sodium (Na^+) is small. That is in healthy animals, there is a tight grouping of Na^+ values. So in this instance, if you had a group of say 100 animals (e.g., rats in a safety study), you could pick 10 at random and run their Na^+ levels and be confident that you had an accurate representative picture. The liver enzyme, alanine aminotransferase, (ALT) has a wider amount of intra-animal variation and using the same study design (for collecting clinical pathology samples as for Na^+) will introduce more "normal variation" into the ALT results. However, because increases in ALT activity are not usually considered to be significant unless the results are 2x or more than the upper normal limit (or control group value), this usually is not a problem. Finally he referred us to the Clinical Pathology Guidelines in the new (FDA) Red Book.

FIGURE 3



Dr. Carakostas concluded his talk with some examples. One was from a cattle study where the WBCs were in the 70, 000 - 80,000 range. Cows with a WBC this high would likely be suffering from Bovine Leukosis Virus. The odds that every cow in the study would have this infection are remote. After looking at a direct stained smear of the blood sample, he determined that there could not be that many WBC in the sample. He was able to determine that the cause of the high WBC was an artifact of the product used to lyse the red blood cells (RBC). Incomplete lysis of the RBC caused the cell counter to erroneously count whole red cells as white cells. Other examples also dealt with the erythron and different types of anemia.

Dr. Carakostas ended his discussion with a challenge to CVM and all scientists to be aware of the importance of these scientific tenets. He warned there are many ways to manipulate scientific studies. It is only when armed with valid scientific data and valid scientific review that we can interpret what the study appropriately concludes.

Dr. Dubbin is a Biologist in CVM's Division of Biometrics & Production Drugs, Office of New Animal Drug Evaluation.

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HIGH PLAINS DRIFTERS?

by Amey L. Adams, Ph.D.

On August 13, 2000, seven members of CVM's Division of Biometrics and Production Drugs arrived in Amarillo, Texas for a 2-day mini-sabbatical to learn more about the cattle feeding industry. This sector of the animal agriculture industry, although concentrated mainly in one geographical area of the United States, represents a significant part of the work of this division at CVM. Most feeder cattle, except for those destined to be labeled "all-natural," receive production enhancing drugs such as ionophores and hormonal implants. These drugs have been approved by FDA.

We were greeted early Monday morning, August 14, by our host, Dr. David Hutcheson, Animal–Agricultural Consulting, and professor emeritus of Texas A&M University. Dr. Hutcheson is a ruminant nutritionist who now resides in Amarillo. Dr. Hutcheson was accompanied by John Keaveny, General Manager, Feedlots for Australia Meat Holdings. The Australian feedlot industry is small but growing, and Mr. Keaveny had come to the U.S. to learn more about how the industry works in this country. Dr. Hutcheson had selected three yards for us to visit, each having different approaches to management, which he considered to be representative of the industry. He also scheduled a visit at the Conservation and Production Research Lab, an experiment station of Texas A&M University (TAMU), which is engaged in research on feeder cattle and feedlot management.

The cattle feeding industry is mostly concentrated in four states: Kansas, Nebraska, Colorado and Texas. Texas is the largest contributor to the U.S. beef market, which marketed 6,065,000 head in 1999, better than 25% of the total U.S. market for fed cattle last year (Cattle Feeders Annual, Texas Cattle Feeders Association, 2000). Cattle generally enter the feedyard weighing approximately 750 lbs. (steers) and 650 lbs. (heifers) and finish at weights of 1250 and 1050 for steers and heifers, respectively. The majority of animals sent to feed lots are steers. The ratio of steers to heifers in the Amarillo

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area is approximately 2:1. Animals generally spend 120 to 150 days on feed, consuming 25-30 lbs. of feed daily, and typically gain between 3 and 4 lbs. per day.

Amarillo, the largest population center in the panhandle, lies in the middle of the Texas feeder cattle industry. It is also the home base of the Texas Cattle Feeders Association (TCFA), which represents interests of the feedlot industry both regionally and nationally.

In order to reduce environmental impact, cattle yards tend to be far-flung enterprises. They also tend to be located well away from population centers to prevent conflicts with urban populations. The area is flat, with only occasional circles of green, corn or milo irrigated by center pivot, growing beneath a cloudless blue sky. The weather was typical for August on the High Plains. Temperatures were above 100°F through most of the day, but dry with a light breeze. We were informed that total rainfall in the area for the year was approximately half normal (about 6 inches).

Our first stop on the tour was Cactus Feedyard, Cactus, TX. Cactus was one of the largest feedyards we were to visit, with more than 60,000 head of cattle. Cactus is an employee-owned independent yard, with approximately one-third of the cattle they feed sent to them on contract, and the remaining two-thirds belonging to the yard. Jim Lookingbill, manager, and Spencer Swingle, nutritionist for Cactus Feedyard, met with us to answer questions and discuss the challenges they face. Mr. Lookingbill also accompanied us on our tour of the yard and the feed processing facility. The managers expressed a strong interest in research, cooperating with various pharmaceutical companies. They maintain an area of the feedyard specifically for animals on trial, which is separated from the rest of the yard.

The next stop was Caprock #4 in Dalhart, TX. Caprock is owned by the Cargill Co., and all 60,000 cattle are owned by Cargill. Bo Kizzar, manager, and Laphe LaRue, cattle manager for Caprock, escorted us on our tour of the facilities.

Photo by Dan Benz

At both these yards the cattle appeared healthy; showing only minor signs of heat stress despite high temperatures, and their good body condition clearly showed they had been eating and drinking. At both feedyards cattle are fed at least three times per day, usually twice in the morning and once in the late afternoon to take advantage of greater appetites during the cooler part of the day. Both yards have their own steam-flaking facility in the feed mill. Steam flaking breaks the seedcoat and gelatinizes the starch in grain, making it more digestible and enhancing its feeding value. Both Cactus and Caprock rely heavily on steam-flaked corn, as well as high-moisture corn as sources of dietary energy. Protein is provided mainly as a commercial pellet, and corn silage was the principal source of dietary fiber.

Young cattle arriving at the feedyards go through a process of ear tagging, implantation, and vaccination. Mr. LaRue stated that they typically finished processing new animals by 10:00 a.m. Some of the contract cattle at Cactus belong to "all-natural" beef growers, who do not allow use of hormone implants, antibiotics or other drugs. If one of these animals becomes ill, and requires treatment with antibiotics, it can no longer be sold as "all-natural", and becomes part of the regular herd.

Cowboys ride the yards throughout the day on the lookout for sick animals. Sick cattle are removed from their pens to a treatment facility where they receive appropriate care. At Cactus, two small "field hospitals" are located at different points in the yard. At Caprock, there is one centrally located hospital barn, to facilitate management of records and drugs. Both feedyards reported that death loss was less than one percent.

The second morning dawned much like the first—cool, dry and breezy, but with the promise of hot weather to come. Dr. Hutcheson met us as he had the previous day. Mr. Keavney, however, had left for Colorado the night before. Another long drive brought us to Tristate Cattle Feeders in Hereford, TX. Tristate was a considerably smaller yard compared to the two operations we had observed the day before. They keep approximately 15,000 head on the premises, all of which are on contract from growers. Mr. Sam Kirk, one of the owners of Tristate, invited us for coffee in his office and a brief presentation. We were shown a short promotional video for Tristate, which explained the philosophy of the owners and the advantages of feeding cattle in a smaller yard. Mr. Kirk explained that each incoming calf received an ear tag. One side of the tag identified the calf's lot or pen, the other side has a unique number for the calf itself. This allowed management to track individual animals throughout their stay at the yard,

(Continued, next page)

information which then could be provided to the cattle owners.

As part of the tour of the feedyard, we were taken to the hospital barn, where we observed several calves as they were moved through a chute to receive health checks and medication, if indicated. Two workers recorded body temperature and other pertinent observations, and entered the information into the calves' health record. Some of these calves belonged to a grower wanting to sell them as "all-natural" beef. Due to the limitations this contract imposed, the calves could only be monitored and administered vitamins and electrolytes.

Photo by Dan Benz

Tristate also uses steam flaking to prepare its grain. However, unlike Cactus and Caprock, they were using sorghum (milo) rather than corn. We had asked the managers at Caprock why they did not use sorghum, which is more drought-tolerant than corn. They informed us that sorghum required processing at higher pressure in order to break the hard seedcoat. This meant more time needed for the process, as well as more frequent replacement of rollers and other equipment. We discussed this with Mr. Kirk, who responded that they had "all the time in the world" to process sorghum, and he had not noticed any increase in wear. This, then, was another advantage of maintaining a smaller yard.

These large, concentrated animal feeding operations (CAFOs) face stiff environmental challenges. Texas has some of the strictest regulations in the country regarding waste management from CAFOs. Each facility in the region is required to have a catch-pond capable of holding the maximum amount of rainfall recorded in a 24-hour period in a 20-year period. Liquid effluent is mixed with water and sprayed as fertilizer on crops by center-pivot irrigation. Dry manure is scraped from cattle pens and spread on cropland to increase organic matter in the soil. The state of Texas has provided guidelines to CAFO managers regarding the amount of cropland required to utilize animal waste effectively and minimize environmental impact of these operations.

After our visit with Tristate and a brief lunch, we started back toward Amarillo. We stopped in Bushland to tour the Conservation and Production Research Lab, experiment station of Texas A&M University. We met with Dr. Andy Cole of USDA's Agricultural Research Service (ARS), who works in cooperation with TAMU in the area of beef cattle nutrition and management. Dr. Cole showed us the facilities, which included a small teaching/experimental feedyard. A key area of research interest is nitrogen flow and volatilization from CAFOs. At the back of each animal pen a monitoring device had been placed to record effluent runoff from the pens. Dr. Cole explained that they also were currently researching means of reducing nitrogen volatilization from animal waste. Volatilized nitrogen (ammonia) combines with other pollutants in the atmosphere that may contribute to acid rain. Although ammonia emissions from CAFOs are not yet a major source of concern in the U.S., they are the subject of great concern and extensive research in Europe. Dr. Cole expressed the hope that the research he and others were performing would prevent ammonia emissions from becoming a problem in North America.

The last stop on our tour was the headquarters of the Texas Cattle Feeders Association in Amarillo. We met with Dr. Richard McDonald, President and CEO of TCFA. Dr. McDonald explained the role of TCFA as a representative of the interests of the cattle feeding industry to legislators and regulatory agencies, as well as providing support to cattle feeders in Texas, Oklahoma and New Mexico with information, promotional materials, public relations and numerous other services.

At the conclusion of our tour, we thanked Dr. Hutcheson for taking the time and trouble to select sites and arrange visits with such a diverse group of individuals. We feel that this brief mini-sabbatical provided us with a broader understanding of a large sector of the food animal industry, and a unique opportunity to meet with key stakeholders in the regulatory process and discuss their challenges and concerns.

Dr. Adams is a Biologist in CVM's Division of Biometrics and Production Drugs, Office of New Animal Drug Evaluation. Other CVM attendees included Dr. Woodrow Knight, Dr. Jack Caldwell, Dr. Dan Benz, Dr. Eric Dubbin, Dr. Brian Garthwaite, and Ms. Patricia Ryan.

□

NARMS SCIENTIFIC MEETING SCHEDULED

FDA announced in the November 28, 2000, *Federal Register* (*http://www.fda.gov/OHRMS/DOCKETS/98fr/112800f.htm*) that a National Antimicrobial Resistance Monitoring System (NARMS) Scientific Meeting will be held on March 15 and 16, 2001. The topic to be discussed at the meeting, that will be held at the DoubleTree Hotel, 1750 Rockville Pike, Rockville, MD, is the results from NARMS and related antimicrobial resistance research. The public meeting and poster session will be held from 8:30 a.m. to 5:00 p.m. on both days. An early evening poster session and social hour will be held on March 15, 2001, from 5:30 p.m. to 7:30 p.m.

NARMS was established in 1996 as a collaborative effort among the FDA, U.S. Department of Agriculture (USDA), and Centers for Disease Control and Prevention (CDC). The NARMS program prospectively monitors changes in susceptibilities of human and animal enteric bacteria to 17 antimicrobial drugs. Bacterial isolates are collected from human and animal clinical specimens, from healthy farm animals, and raw product from food animals. The objectives of the system are: (1) to provide descriptive data on the extent and temporal trends of antimicrobial susceptibility in Salmonella and other enteric organisms from human and animal populations, (2) to facilitate the identification of resistance in humans and animals as it arises, and (3) to provide timely information to veterinarians and physicians. The ultimate goal of these activities is to prolong the lifespan of approved drugs by promoting prudent and judicious use of antimicrobial drugs and to identify areas for more detailed investigation.

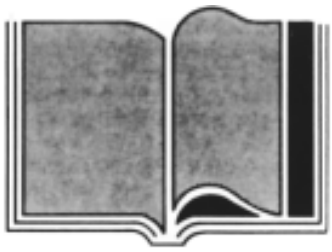
There is no registration fee for the meeting, but registration is required. Limited space is available, and early registration is encouraged. Logistics for the meeting and the registration form is on the CVM Home Page at: *http://www.fda.gov/cvm/index/narms/NARMSPM.htm*. The registration form should be sent to Kathy Hemming, Center for Veterinary Medicine (HFV-250), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-0184, (FAX) 301-827-7625.

Abstract preparation and submission information for posters is available on the CVM Home Page at the location listed above. Instructions and submission forms may be downloaded in MSWord or WordPerfect. Poster abstracts should be submitted to Dr. Charlotte A. Spires, Center for Veterinary Medicine (HFV-250), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-6853, e-mail: *cspires@cvm.fda.gov* by January 15, 2001.

Additional information about the meeting and the agenda will be available on the CVM Home Page before the meeting. If you need special accommodations due to a disability, please contact the DoubleTree Hotel at least 7 days in advance, 800-222-8733.

Interested persons may submit written comments regarding this meeting to FDA's Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852, by January 29, 2001. Comments may also be submitted by fax to 301-827-6870. Comments should be identified with Docket No. 00N-1620. □

NARMS PUBLICATION NOW AVAILABLE



The United States has a system in place that allows the Food and Drug Administration to monitor resistance to antimicrobials used in humans and food animals. The system is called the National Antimicrobial Resistance Monitoring System-Enteric Bacteria (NARMS-EB). This system combines the activities of FDA, the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA) to create a nationwide monitoring system. NARMS was started and expanded because of human health concerns related to the use of antimicrobials in food animals. The NARMS program is a major component of the Surveillance portion of the Food Safety Initiative.

As part of the Food Safety Initiative, CVM published a booklet entitled *National Antimicrobial Resistance Monitoring System–Enteric Bacteria: A program to monitor antimicrobial resistance in humans and animals*, to explain the NARMS system. The booklet describes how resistance develops in bacteria and gives an overview of how NARMS data are collected in the human and animal parts of the program. It also describes what this data can tell us, and what additional steps are being taken to ensure that significant human antimicrobial therapies are not lost due to the use of antimicrobials in animals.

According to Jon Scheid, Director of CVM's Communications Staff, "This booklet is a valuable educational tool that will help to increase understanding of this important program." The NARMS booklet is being distributed to the veterinary community, consumers and the general public. It has been prepared as part of a broad effort to educate the public on the subject of antimicrobial resistance, and the activities targeted at monitoring and controlling this public health threat.

To obtain a copy of the NARMS booklet, contact the *FDA Veterinarian* at 301-594-1755. □

10 NRSP-7 HOLDS SEMI-ANNUAL COMMITTEE MEETING

by Meg Oeller, D.V.M.

The USDA's Minor Use Animal Drug Program, National Research Support Project #7 (NRSP-7) held its semi-annual meeting of the technical committee on October 23 and 24 in Rockville, MD. The spring meeting is hosted each year by one of the four regions, but the fall meeting is always held in Rockville to provide an opportunity for input from members of FDA's Center for Veterinary Medicine (CVM).

The purpose of the NRSP-7 Minor Use Animal Drug Program is to address the shortage of minor use animal drugs by funding and overseeing the efficacy, animal safety, and human food safety research and environmental assessment required for drug approval. The scope of the program includes minor species of agricultural importance, and generally excludes companion animals.

Attendance and Membership Changes

The technical committee is made up of a National Coordinator, 4 Regional Coordinators, 4 regional Administrative Advisors, and liaisons from USDA and FDA. The National Coordinator is Dr. John Babish (Cornell University). The Regional Coordinators are Dr. Arthur Craigmill (University of California, Davis), Dr. Alistair Webb (University of Florida), Dr. Robert Holland (Iowa State University), and Dr. Paul Bowser (Cornell University). The Administrative Advisors are Dr. Kirklyn Kerr (University of Connecticut), Dr. John Nielson (University of Florida), Dr. David Thawley (University of Nevada), and Dr. Don Robertson (Kansas State University). The USDA representative is Dr. Larry Miller (Washington, DC) and the FDA liaison is Dr. Meg Oeller (Rockville, MD). This meeting was also attended by the National NADA coordinator for Aquaculture, Rosalie Schnick and Dr. Guy Stehly of the USGS, as well as by reviewers and managers from FDA/CVM.

This meeting marked the first attendance of 2 new administrative advisers. Dr. David Thawley has replaced Dr. Donald Robertson as the administrative advisor for the Western Region. Dr. Robertson moved to Kansas State from the Western Region and replaced retiring Dr. Gerald Beuning as the North Central administrative advisor. Dr. Beuning served the program for over 5 years and will be missed. Dr. Kirklyn Kerr replaced Dr. William Saylor as the advisor for the Northeast Region. Dr. Saylor resigned from the program under the weight of other work responsibilities. He was an invaluable asset to the program for many years and will be sorely missed. The committee welcomes its new members and looks forward to a long and successful association.

Reports to the Committee

The committee heard reports from the administrative advisors and the USDA liaison. These centered on budget considerations for USDA and the NRSP-7 program itself.

Rosalie Schnick gave an overview of the progress of the Federal-State Aquaculture Drug Approval Partnership Program. She distributed her semi-annual report which describes the activities of the program and the progress made in each of the eight ongoing projects. She notified the committee that the rights to some of the compounds being investigated for approval have been sold to other companies. Commitments to pursue approvals of these products for aquaculture use will be sought once the transactions are complete.

New Plans to Improve Communication

The committee decided to institute monthly teleconferences between the National Coordinator, the Regional Coordinators, and the FDA Liaison to improve communication about projects and emerging issues of concern. This should improve the efficiency of the program and allow more prompt response to requests.

New Brochures Coming

Dr. Babish shared proofs of the layout of the new NRSP-7 brochure that will be printed soon. This brochure describing the program and supplying contact information will be made available at professional meetings and conventions concerned with animal health.

NRSP-7 Website

Dr. Webb provided an overview of the new and improved NRSP-7 website: *http://www.nrsp7.org* . The website currently provides links to minor species group websites, updated names and addresses of committee members, interactive Animal Drug Request Forms for new project requests, and a "Frequently Asked Questions" section. Plans are underway to implement features including "Breaking News", feature articles, a searchable database of animal drugs, and a searchable database of NRSP-7 activities. Please visit the site and give us your opinion.

Spring 2001 meeting

The NRSP-7 Spring meeting will be hosted by the Northeast Region and will be held in Groton, Connecticut.

Workshop 2001

The NRSP-7 program traditionally hosted a workshop on a minor species concern every 2 years. The last workshop was held in 1996 on the topic of "Drug Approval for Minor Species in the 21st Century". After 1996, resources were directed towards activities other than the sponsorship of workshops. The program is now planning to hold a workshop next September or October at a hotel in the Dulles airport area. The discussion will probably center on species

(Continued, next page)

grouping. Input from producers, veterinarians, and pharmaceutical companies will be important to help guide future research and projects.

Regional Reports

The Regional Coordinators reported on the progress of the active projects in their respective regions. NRSP-7 currently has 22 active projects underway. These are summarized in Table 1. There are 8 additional projects pending.

New Animal Drug Requests continue to come in, so the program remains very busy with active projects.

Species grouping

The attendees had a lively discussion of species grouping. This concept involves demonstrating, usually through pharmacokinetics, that similar species may be grouped for the purposes of demonstrating effectiveness, target animal safety, and human food safety. One outcome could be that a representative species could be studied to provide data to support the inclusion of similar species on the label of a new animal drug. This is probably most needed in aquaculture where there are literally hundreds of species and it is not practical to test the drug on them all. Other groups also could benefit from such research. This includes gamebirds (pheasants, partridges, and quail), deer (white tail, red deer, elk, etc.), and ratites (ostriches, emus, and rheas). It must be emphasized that the research may show that the species are not similar, or are not similar for some classes of drugs. Learning what is and is not suitable for grouping will be very valuable in making drug approval for minor species more efficient.

The researchers who were present summarized the work that they are doing in this area and their plans for future studies. This provided an opportunity for discussion of areas that need to be explored and methods that are being used to do so.

TABLE 1.
Active NRSP-7 Projects

	Drug	*Route of Administration*	*Species*	*Indication*
1.	Amoxicillin trihydrate	injection	dairy goats	bacterial pneumonia
2.	Oxytetracycline	injection	dairy goats	bacterial pneumonia
3.	Oxytetracycline	injection	sheep	bacterial pneumonia
4.	Ivermectin	injection	rabbits	ear mites
5.	Tylosin	soluble powder	honey bees	American foulbrood
6.	Lasalocid	oral (feed)	pheasant	coccidiosis
7.	Clopidol	oral (feed)	pheasant	coccidiosis
8.	Tilmicosin	injection	veal calves	respiratory infections
9.	Progesterone	CIDR	sheep	estrus synchronization
10.	Hydrogen peroxide	topical	various fish	bacterial gill disease
11.	Carp Pituitary	injection	various fish	spawning aid
12.	Sulfadimethoxine/ ormetoprim	oral (feed)	pheasants	bacterial infections and coccidiosis
13.	Nitarsone	oral (feed)	partridge	blackhead
14.	Zoamix	oral (feed)	pheasants	coccidiosis
15.	Fenbendazole	oral (feed)	pheasants, partridges & quail	gapeworm, capillaria
16.	MGA/GnRH	feed/injectable	sheep	estrus synchronization
17.	Oxytetracycline	oral (feed)	finfish	bacterial infections
18.	Lasalocid	oral (feed)	deer	coccidiosis
19.	Strontium chloride	immersion	fin fish	otolith marking
20.	Lasalocid	oral (feed)	goats	coccidiosis
21.	Pirlimycin	intramammary	goats	mastitis
22.	Lincomycin	soluble powder	honey bees	American foulbrood

The day-and-a-half meeting was an excellent opportunity to provide an update on the status of all aspects of the program as well as an opportunity to expand partnerships with other organizations.

For more information about NRSP-7, please visit our website http://www.nrsp7.org or call Dr. Meg Oeller (301) 827-3067.

Dr. Oeller is a Veterinary Medical Officer in CVM's Office of the Director. □

12 PROPER LABELING OF ANIMAL DRUGS—THE VETERINARIAN'S REQUIREMENTS

by Michael R. Talley, D.V.M.

Why is drug labeling important? Drug residues in milk, meat, and other food derived from animals occur on the farm, not later in the processing channels. Labeling requirements exist as part of the overall efforts employed by Federal and State agencies, veterinarians, the animal industry, and producers to avoid drug residues in our food supply. The requirements are intended to ensure that the producer has adequate directions for use of the product in hand every time the drug is administered. Great emphasis is placed on proper drug labeling in an attempt to heighten the producer's awareness of proper drug use and residue avoidance.

The requirements for proper labeling* of veterinary prescription drugs and extra-label use (ELU) drugs by veterinarians exist in three general areas. The first includes requirements under State veterinary practice acts and/or the board of pharmacy regulations. The second set of regulations exists under the Federal Food, Drug, and Cosmetic Act (the Act). The third set of requirements for proper drug labeling is in the Grade A Pasteurized Milk Ordinance (PMO). The PMO is a model ordinance that has been adopted into many State laws. The PMO governs the shipment of Grade A milk in interstate commerce in the U.S.

What do State practice and boards of pharmacy acts require for animal drug labeling? The requirements vary from State to State. It is up to the individual veterinary practitioner to be familiar with their State requirements. In general, States require that all veterinary prescription and ELU drugs be properly labeled when dispensed. A complete label should include the information set forth in the table below, but more may be required.

REQUIRED BY:	***State laws***	***AMDUCA***	***PMO***
Name and address of the prescribing veterinarian	Yes	Yes	Yes
Active ingredient(s)	Yes	Yes	Yes
Directions for use	Yes	Yes	Yes
Cautionary Statements	Yes	Yes	Yes
Withdrawal, withholding, or discard time for meat, milk, eggs of other food	Yes	Yes	Yes
Vet's phone number	Some States	No	No
Client name	Some States	No	No
Animal identification	Some States	No	No
Expiration date	Some States	No	No

What is required under the Federal Food, Drug, and Cosmetic Act? The Animal Medicinal Drug Use Clarification Act (AMDUCA) 21 CFR Part 530 applies to the extra-label use in an animal of any approved new animal drug or new human drug by or on the lawful order of a licensed veterinarian within the context of a valid veterinary-client-patient relationship. Any human or animal drug prescribed and dispensed for extra-label use by a veterinarian or dispensed by a pharmacist on the order of a veterinarian shall bear or be accompanied by labeling information adequate to assure the safe and proper use of the product. The specific required information is found in the table.

What about the PMO? The PMO requires specific labeling information to be included on all drugs stored on dairy farms (see table). This includes prescription drugs, ELU drugs, and drugs sold over-the-counter. The Grade A Pasteurized Milk Ordinance (PMO) was not produced by the Public Health Service/Food and Drug Administration alone. The PMO was developed with the assistance of milk sanitation and regulatory agencies at every level of Federal, State, and local government including both health and agriculture departments; all segments of the dairy industry including producers, plant operators, equipment manufacturers, and associations; many educational and research institutions; and helpful comments from many individual sanitarians and others. The finding on a dairy farm of an improperly labeled animal drug may result in that farm failing a compliance inspection and possible loss of their permit to ship Grade A milk.

What about drugs sold over-the-counter (OTC)? All FDA-approved OTC drugs bear adequate directions when used in accordance with their labeling (on label use). If an OTC drug is dispensed by a veterinarian for an ELU, its label must comply with State, Federal, and PMO requirements.

Dr. Talley is a Veterinary Medical Officer in CVM's Office of Surveillance and Compliance. □

* The State and PMO labeling requirements discussed in this article are in addition to the approved labeling or the general labeling provision of the Federal FD&C Act.

FDA PUBLISHES FINAL VETERINARY FEED DIRECTIVE RULE

In the December 8, 2000, *Federal Register*, the FDA published the final regulation to implement the Veterinary Feed Directive (VFD) drugs section of the Animal Drug Availability Act of 1996 (ADAA). This new regulation states the requirements for distribution and use of a VFD drug and animal feed containing a VFD drug. A VFD drug is a drug approved by FDA for use in animal feeds which is limited to use under the professional supervision of a licensed veterinarian. No extra-label use of a VFD drug is permitted.

A veterinary feed directive is a written statement that authorizes the client (the owner of the animal or animals or other caretaker) to obtain and use animal feed containing a VFD drug to treat their animals only in accordance with the FDA-approved directions for use. A veterinarian may issue a VFD only if a valid veterinarian-client-patient relationship exists, as defined in Title 21, Part 530.3(i) of the *Code of Federal Regulations*. The information needed on a VFD is stated in the final rule.

Although statutory controls on the distribution and use of VFD drugs are similar to those for prescription animal drugs, the implementing VFD regulations are tailored to the unique circumstances relating to the distribution of animal feeds containing a VFD drug. This rule helps ensure the protection of public health while enabling animal producers to obtain and use needed drugs as efficiently and cost-effectively as possible.

A copy of the final regulation published in the *Federal Register* is available on CVM's Internet Home Page, at: <*http://www.fda.gov/cvm/index/vfd/vfd.html*>. A copy of this rule may also be obtained by calling or writing the FDA VETERINARIAN. Please include a self-addressed adhesive label to assist in processing your request.

Additional information on the final rule may be found in the December 8, 2000, *Federal Register*, and from Zoe Gill, Center for Veterinary Medicine (HFV-226), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-6667, e-mail: zgill@cvm.fda.gov. □

REGULATORY ACTIVITIES

The following firms/individuals received warning letters for offering animals for slaughter that contained illegal drug residues:

- Kenneth B. Becker, Sr., Carlyle, IL
- John Reitsma & Jesus M. Hurtado, Co-owners, Rotary Dairy, Hollister, ID
- Dale L. Moreland, Anna, IL
- I. W. Ward, Waco, TX
- Frank F. Miranda, Miranda Livestock, Hanford, CA

These violations involved illegal residues of penicillin in a dairy cow; sulfadimethoxine in a dairy cow; oxytetracycline in a cow; streptomycin in a horse; and sulfamethoxazole in a calf.

In addition, a warning letter was issued to Josua W. Reyneveld, J. W. Reyneveld Dairy Farm, Inc., Bakersfield, CA, for a tissue residue violation in a calf containing streptomycin and sulfamethoxazole. Mr. Reyneveld has a history of offering animals for sale for human food use, which have been found to be adulterated with drug residues, dating back to 1992.

A warning letter was issued to Anthony W. DeGroot, Tony DeGroot Dairy, Hanford, CA, for a tissue residue violation in a calf containing sulfamethoxazole. Mr. DeGroot is a repeat violator with a history of offering several animals for sale for human food use, which have been found to be adulterated with drug residues, dating back to 1993.

Warning letters were sent as a result of violative conditions found during investigations of the following medicated feed manufacturing facilities:

- Wenck Feeds, Inc., Lidderdale, IA
- Pan American Grain Mfg. Co., Inc., Guaynabo, PR
- Crumbaker Pork, LLC, Salina, KS

These violations included failure to perform the required three drug potency asays on batches of medicated feeds; failure to calibrate production weighing scales; failure to match master formulas with the actual rations being produced; failure to show accurate drug inventory record with appropriate drug lot number used on days when lot number changes; failure to include name and quantity of drug component use in each batch on production record; and use of illegal drug levels in the feed.

□

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Elanco Animal Health, a Division of Eli Lilly & Co. (NADA 141-170)	Narasin, Tylosin Phosphate, (Monteban®), (Tylan®)	Broiler chickens. For use as an aid in the prevention of coccidiosis, for increased rate of weight gain, and improved feed efficiency.	**MEDICATED FEED**—The NADA provides for use of approved, single ingredient narasin and tylosin phosphate Type A medicated articles to make two-way combination Type C medicated feeds. The Type C medicated feeds are used as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati*, and *E. maxima*, increased rate of weight gain, and improved feed efficiency. For broiler chickens only. Feed continuously as sole ration. Do not allow turkeys, horses or other equines access to formulations containing narasin. *Federal Register* 11/01/00
Bayer Corp. Agriculture Division, Animal Health (NADA 141-176)	Enrofloxacin, Silver Sulfadiazine Emulsion (Baytril® Otic Emulsion) Rx	Dogs. For the treatment of otitis externa.	**OPHTHALMIC and TOPICAL**—The NADA provides for use as an eye drop in dogs depending on weight (5 - 10 drops, 35 pounds or less; and 10 -15 drops, more than 35 pounds). To be applied twice daily for up to 14 days. This approval qualifies for 3 years of marketing exclusivity. *Federal Register* 11/07/00
Alpharma, Inc. (NADA 141-147)	Decoquinate, Chlortetracycline (CTC), (Deccox®), (ChlorMax®)	Calves, beef cattle and non-lactating dairy cattle. For the prevention of coccidiosis, treatment of bacterial enteritis and bacterial pneumonia.	**MEDICATED FEED**—The NADA provides for use of approved decoquinate and chlortetracycline (CTC) Type A medicated articles to make two-way combination Type B and Type C medicated feeds. The Type C medicated feeds are used for prevention of coccidiosis caused by *Eimera bovis* and *E. zuernii*, for treatment of bacterial enteritis caused by *Escherichia coli,* and for treatment of bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to CTC. Do not feed to calves to be processed for veal. Do not feed to animals producing milk for food. *Federal Register* 11/07/00
Novartis Animal Health US, Inc. (NADA 141-175)	Nitenpyram (Capstar)	Dogs, puppies, cats, kittens. For the treatment of flea infestations.	**ORAL**—The NADA provides for an OTC oral tablet for the treatment of flea infestations in dogs, puppies, cats, and kittens that are 4 weeks of age and older and 2 pounds of body weight or greater. One tablet given as needed. This approval qualifies for 5 years of marketing exclusivity. *Federal Register* 11/27/00

(Continued, next page)

NEW ANIMAL DRUG APPROVALS (Continued)

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Alpharma, Inc. (141-136)	Salinomycin, Bacitracin Methylene Disalicylate, (BIOCOX), (BMD®)	Broiler, roaster, and replacement (breeder and layer) chickens. For prevention of coccidiosis and as an aid in the prevention and control of necrotic enteritis, increased rate of weight gain, and improved feed efficiency. Roaster and replacement chickens. For prevention of coccidiosis, increased rate of weight gain, and improved feed efficiency. ADIs for bacitracin and salinomycin are codified.	**MEDICATED FEED**—The NADA provides for use of approved, single ingredient salinomycin and bacitracin methylene disalicylate Type A medicated articles to make two-way combination Type C medicated feeds. The Type C medicated feeds containing 40 to 60 g/ton salinomycin and 4 to 50 g/ton bacitracin methylene disalicylate are used for prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina*, *E. maxima, E. brunetti, and E. mivati*, and for increased rate of weight gain and improved feed efficiency in roaster and replacement chickens. The Type C medicated feeds containing 40 to 60 g/ton salinomycin and 50 g/ton bacitracin methylene disalicylate are used for prevention of coccidiosis caused by *E. tenella, E. necatrix, E. acervulina, E. maxima, E. brunetti* and *E. mivati*, and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium spp.* or other organisms susceptible to bacitracin in broiler, roaster, salinomycin and 100 to 200 g/ton bacitracin and replacement chickens. The Type C medicated feeds containing 40 to 60 g/ton methylene disalicylate are used for the prevention of coccidiosis caused by *E. tenella, E. necatrix, E. acervulina, E. maxima, E. brunetti*, and *E. mivati*, and as an aid in the control of necrotic enteritis caused or complicated by *Clostridium spp.* or other organisms susceptible to bacitracin in broiler, roaster, and replacement chickens. An acceptable daily intake (ADI) for bacitracin residues of 0.05 milligram per kilogram of body weight per day (mg/kg/day) is added. A tolerance for bacitracin residues in uncooked edible tissue of cattle, swine, chickens, turkeys, pheasants, and quail of 0.5 part per million (ppm) is established. An ADI for salinomycin residues of 0.005 mg/kg/day is added. *Federal Register* 11/28/00 □

ABBREVIATED NEW ANIMAL DRUG APPROVALS

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Farnam Companies, Inc. (ANADA 200-282)	Pyrantel Tartrate (Continuex™)	Horses. For the prevention and control of various species of internal parasites.	**MEDICATED FEED**—The ANADA is a generic copy of Pfizer Inc.'s NADA 140-819, Strongid® 48. *Federal Register* 11/07/00

(Continued, next page)

ABBREVIATED NEW ANIMAL DRUG APPROVALS (Continued)

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Phoenix Scientific, Inc. (ANADA 200-286)	Ivermectin Paste (Phonectin™)	Horses. For the treatment and control of various species of harmful gastrointestinal parasites.	**ORAL**—The ANADA is a generic copy of Merial Ltd.'s NADA 134-314, Eqvalan® paste for horses. *Federal Register* 11/27/00

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPROVALS

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Ivy Laboratories, Inc. (ANADA 200-221)	Trenbolone Acetate, Estradiol, Tylosin Tartrate (Component™ TE-G)	Pasture cattle (slaughter, stocker, feeder steers and heifers). For increased rate of weight gain.	**SUBCUTANEOUS**—The ANADA provides for the addition of tylosin tartrate as a local antibacterial to an approved subcutaneous cattle ear implant containing trenbolone and estradiol. This approval qualifies for 3 years of marketing exclusivity. *Federal Register* 11/27/00

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Public Health Service
Food and Drug Administration
Rockville MD 20857

Official Business
Penalty for Private Use $300

BULK RATE
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Use of funds to print the **FDA Veterinarian** has been approved by the Office of Management and Budget.

01-2067.p65