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Center for Veterinary Medicine

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CVM Approves First Insulin Product for Animals

The Food and Drug Administration's Center for Veterinary Medicine has approved an insulin product for treatment of diabetes in dogs, making it the first diabetes drug approved for animals.

The drug's sponsor, Intervet, Inc., Millsboro, Del., earlier this year received approval to begin marketing a drug for use in dogs to treat the clinical signs of diabetes, which include excessive thirst, urination and appetite, along with weight loss despite a good appetite.

Intervet's product, called Vetsulin, is made from porcine insulin.

Previously, veterinarians would prescribe insulin approved for human use. Intervet's product is made from porcine insulin and has the same amino acid sequence as canine insulin. By contrast, human insulin differs from the canine insulin by one amino acid, and bovine insulin differs from canine insulin by two amino acids.

The product will be available only through veterinarians, but owners will administer the drug to their dogs. The veterinarian can monitor the treatment to make all the necessary dosage adjustments until the optimum dose is found. The dogs will be treated either once or twice a day, based on their individual response to the drug.

The treatment is administered by injection along the dog's back. Veterinarians will instruct owners on how to inject the dog, and the company will supply information sheets along with the drug to answer other questions.

Owners will need to be careful not to inject themselves with the product because it could cause hypoglycemia, a dangerously low level of sugar. However, the product has been used in other countries for many years with owners facing little difficulty.

According to FDA Acting Commissioner, Dr. Lester Crawford, the product "promises to improve the health and quality of life of dogs who suffer from this debilitating disease." As many as one out of 200 dogs suffers from diabetes. Female dogs are twice as likely to develop the disease, and it usually starts when a dog is seven to nine years old.

The product should be generally available later this year, the company said.

CVM Offers Advice on Raw Meat Diets for Pets, Captive Animals

Commercially prepared raw meat diets for pets, which are gaining in popularity with pet owners and professional animal caretakers, carry an increased risk of bacterial contamination for the animals and their human handlers, and some potential risk of injury to the animal from shards of bones or other hard substances in the meat, the Center for Veterinary Medicine said in a "Guidance for Industry" issued in May 18.

The guidance makes clear that the CVM or the Food and Drug Administration does not support the use of raw meat diets, saying in the guidance that raw meat diets for animals are not "consistent with the goal of protecting the public from significant health risks, particularly when such products are brought into the home and/or used to feed domestic pets."

CVM officials decided that the issue of raw meat diets needed to be addressed when they saw an increasing trend toward use of raw meat diets for companion animals, such as dogs, as well as non-companion, captive animals.

CVM presented its non-binding recommendation in Guidance for Industry #122, "Manufacture and Labeling of Raw Meat Foods for Companion and Captive Noncompanion Carnivores and

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FOOD AND DRUG ADMINISTRATION

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Omnivores." It is available on the CVM's website at *www.fda.gov/cvm/guidance/Guide122.doc*.

In the guidance document, CVM said that objective data about the risks from the use of commercially prepared raw meat diets is limited, but by reviewing data on risks to consumers from foodborne pathogens, including those from raw foods, CVM concluded that the risks are significant enough that consumers and others using commercially prepared raw meat diets for animals should take the precautions offered in the guidance document.

The guidance . . . [states] that raw meat diets for animals are not "consistent with the goal of protecting the public from significant health risks, particularly when such products are brought into the home and/or used to feed domestic pets."

Sources of meat

Depending on the source of the raw meat used in commercially prepared diets, risk of contamination by bacteria or other pathogens can vary, CVM said. The best source is a U.S. Department of Agriculture-inspected slaughter facility, and the best meat is that which has passed USDA inspection for human consumption, the guidance said.

By contrast, raw meat from animals that died from causes other than slaughter at a USDA facility is likely to have higher levels of pathogens. Even meat that is produced at an inspected slaughter plant, but was not approved for human food, and instead approved only for animal feed, is likely to have higher pathogen loads, the guidance said.

CVM also recommended that any other ingredients added to the raw meat diets should be suitable for use in pet diets.

Manufacturing

The guidance pointed out that the physical form of the ingredients is important. Bones can cause dental or gastrointestinal injury, it said. Therefore, any bone or hard material contained in the raw meat diet should be ground.

Although CVM does not have any Good Manufacturing Practice (GMP) guidelines for non-medicated feed, such as raw meat diets, the guidance suggests that manufacturers use practices to reduce contamination. For instance, the guidance recommended that manufacturers irradiate the product after it is in its final packaging. It also said that manufacturers should participate in USDA's voluntary inspection program, practice using the same GMPs as used for human food or develop and use a Hazard Analysis and Critical Control Point program, which identifies points at which hazards can be introduced in the manufacturing process, determines how the hazards can be controlled, and implements processes to monitor the controls.

The guidance recommended that, if the raw meat products are freeze-dried, then they should remain frozen until used to help reduce pathogens.

Just as USDA requires instructions about handling raw meat products destined for human consumption, CVM suggested that raw meat diets for animals also have handling instructions to help the consumer avoid contamination.

Nutritional adequacy

Although some commercial animal food manufacturers may assert that raw meat diets are better than other types, "FDA is not aware of scientific evidence to support such claims," the guidance document said. "Calcium and phosphorus are often deficient in foods based on raw meat, and should be supplemented accordingly," it said. Large pieces of bone are not readily digested, so even though the diet contains adequate amounts of calcium, the animal may not be getting all it should. Vitamin A can be excessive, causing toxicity over the long term, and other fat soluble vitamins could be excessive or deficient in a raw meat diet, the guidance said.

Neither CVM nor FDA has issued regulations that specify standards for nutritional adequacy of sole source foods, but the Association of American Feed Control Officials has proposed a rule that raw meat diets be formulated to meet AAFCO dog or cat food nutrient profiles, or that the diets pass appropriate feeding trials. For other types of animals, CVM recommended that diets intended to be the sole source of nutrients be formulated according to standards developed by "authoritative scientific review committees knowledgeable in the nutrient requirements of the specific species," if such information exists.

Also, the guidance said that claims made about raw meat diets must be appropriate and comparative claims about other products must be supported by scientific evidence. In addition, claims that the product is "USDA certified," "USDA inspected" or "human grade" must be true according criteria spelled out in regulations.

FDA VETERINARIAN

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In GAO Response, DHHS Cites Studies Showing Human Health Effects Linked to Antimicrobial Resistance

In response to a General Accounting Office (GAO) report that said some researchers see little public health risk from resistant bacteria in food-producing animals, the Department of Health and Human Services (DHHS) provided information on 11 studies to show the strong link between resistance and increased risk to human health.

In May, GAO issued its report, "Antibiotic Resistance: Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals."

The report described the efforts of Federal agencies to address the risks of resistant bacteria resulting from the use of antimicrobials in food-producing animals. The report said that Federal agencies had expanded their efforts in this area, but mentioned that, although many studies have shown the link between the use of antimicrobials in animals and resistant bacteria causing health problems for people, "other researchers contend that the clinical consequences of the transference, if it occurs, is small."

DHHS developed a response to the points made in the report, and GAO published the response as an appendix in the report.

In its response, DHHS said the report was thorough and generally accurate, but GAO did not consider several reports that establish the risk to human health from certain antimicrobial uses in animals.

The reports that DHHS described focused on the public health risks caused by resistant *Salmonella* and *Campylobacter*, which can prolong the duration of illness, and increase rates of bacteremia, hospitalization and death.

The studies also showed that the majority of *Salmonella* and *Campylobacter* infections in developed countries are due to antimicrobial use in food animals, DHHS said.

Salmonella

In one study DHHS cited, a researcher studied *Salmonella* outbreaks that had been investigated by the Centers for Disease Control and Prevention (CDC) between 1971 and 1983 "and found a higher case fatality rate for patients infected with antimicrobial-resistant *Salmonella* (4.2 percent) than for those with antimicrobial-sensitive infections (0.2 percent)," DHHS said.

The reports that DHHS described focused on the public health risks caused by resistant* Salmonella *and* Campylobacter*, which can prolong the duration of illness, and increase rates of bacteremia, hospitalization and death.

In a similar study done in 1987, "among community outbreaks in which hospitalization rates were reported, 57 percent of cases in resistant salmonellosis outbreaks were hospitalized, compared with 24.5 percent in outbreaks caused by susceptible strains," DHHS said.

"A more recent CDC study of 24 *Salmonella* outbreaks that occurred between 1984 and 2002 also found that outbreaks caused by resistant *Salmonella* resulted in higher hospitalization rates than outbreaks caused by susceptible *Salmonella*," the DHHS comments said.

"Studies of salmonellosis cases not limited to outbreaks have also demonstrated that resistance is associated with higher morbidity and mortality. In a prospective CDC study of 758 salmonellosis cases, patients with resistant infections were significantly more likely be hospitalized than were those with susceptible infections, even after accounting for underlying illness and prior antimicrobial exposure using multivariate techniques. Patients with resistant infections also tended to be ill longer (median, 10 versus 8 days) and hospitalized longer (median, 5 versus 4 days) than patients with susceptible infections," the comments said.

Recent studies that have used epidemiological or statistical methodologies to account for factors such as serotype and age that could confound the outcome "have provided further support for the association between resistance in *Salmonella* and increased morbidity and mortality," DHHS said. In one case, a researcher after studying *Salmonella* cases in the United States between 1996 and 2000 found that "antimicrobial resistance was associated with increased hospitalization and bloodstream infections. Patients with *Salmonella* isolates resistant to any antimicrobial agent or to commonly used agents (cephalosporins, quinolones, or aminoglycosides) were hospitalized more often than patients with pansusceptible isolates, even after controlling for age, race, surveillance site, serotype, and bloodstream infection in a multivariate analysis."

A large study in Denmark determined mortality rates associated with different drug resistance patterns in *S. Typhimurium*. "Patients with pansusceptible strains of *S. Typhimurium* were 2.3 times more likely to die within two years than the general Danish population, whereas patients infected with R-type ACSSuT (resistance to ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline)

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. . . DHHS Cites Studies Showing Human Health Effects Linked to Antimicrobial Resistance *(Continued)*

were 4.8 times more likely to die," DHHS reported.

Resistance to nalidixic acid, which often leads to increased resistance to fluoroquinolones, can result in higher mortality. The Danish study found that "patients infected with nalidixic-acid-resistant strains were 10.3 times more likely to die than the general population, (and) those infected with strains resistant to nalidixic acid as well as (resistant to) ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline (ACSSuT) were 13.1 times more likely to die," DHHS said.

In another recently completed Danish study of patients with culture-confirmed *S. Typhimurium* between 1995 and 2000, researchers found that "patients with nalidixic acid-resistant infections were more likely to have bloodstream infections or die in the 90 days following specimen collection than those with susceptible infections."

A Canadian study in 1999 and 2000 looked at the increased burden of illness in patients with *S. Typhimurium* and both definitive phage type 104 (DT104) and antimicrobial resistance. "In this study, after controlling for significant risk factors and confounding variables, including age, hospitalization was 2.3 times more likely to occur among patients whose infections were resistant to at least ampicillin, kanamycin and/or chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (R-type AK/CSSuT), compared with AK/CSSuT-susceptible patients (p=0.003) and 3.6 times more likely to occur among patients with non-DT104 R-type AKSSuT infections compared with patients with non-DT104 R-type AKSSuT-susceptible infections (p=0.005)," DHHS said.

Campylobacter

Studies of *Campylobacter* show similar problems with resistance. "Several *Campylobacter* case-control studies in the United States and Denmark have demonstrated a relationship between quinolone resistance and prolonged duration of illness," DHHS said. Although the GAO report mentioned a *Campylobacter* study in Minnesota, still "there are several others that GAO ignores," the comments said. In one 1996-1997 study in Denmark, the researchers found that patients infected with ciprofloxacin-resistant strains of *Campylobacter* who were treated with fluoroquinolones or other antibiotics were ill for a median duration of 14 days. Patients with susceptible strains recovered in nine days.

In a multi-State case-control study of sporadic *Campylobacter* cases in the United States in 1998 and 1999, researchers found that resistant *Campylobacter* could be more virulent than susceptible *Campylobacter*. When comparing patients who did not take an antidiarrheal medication, those with ciprofloxacin-resistant infections had a nine-day mean duration time for the symptom of diarrhea, compared with a seven-day mean for those with ciprofloxacin-susceptible infections. Patients who did not take an antidiarrheal or an antibiotic suffered the illness for a mean time duration of 12 days if infected with ciprofloxacin-resistant *Campylobacter*, compared with a mean time of six days for those patients infected with ciprofloxacin-susceptible *Campylobacter*, which suggests that resistant *Campylobacter* is more virulent.

In another Danish study DHHS mentioned, researchers evaluated the relationship between resistance in *Campylobacter* and increases in both bacteremia and mortality. Among patients with culture-confirmed campylobacteriosis from 1995 to 2000, those with fluoroquinolone-resistant or erythromycin-resistant *Campylobacter* infections "were more likely to have a bloodstream infection or die in the 90 days following specimen collection than those with susceptible infections," the report said.

The DHHS comments also mentioned the Food and Drug Administration's proposal to withdraw approval of an enrofloxacin approved for use in poultry water. In his initial ruling, the Administrative Law Judge presiding in the case concluded, "The preponderance of the evidence establishes that fluoroquinolone-resistant *Campylobacter* results in an increased severity of campylobacteriosis in humans," the DHHS comments said.

Drug use data

DHHS agreed with the GAO that drug use data are necessary for obtaining a true picture of the extent of resistance and to get a clear idea of the mitigation steps needed to control it.

Also, data from actual use when combined with surveillance of resistance can show stakeholders the extent of the problem.

While GAO recommended that DHHS work with the U.S. Department of Agriculture to develop a plan to collect information about antimicrobial use in food-producing animals, DHHS said "the most useful and reliable data are those maintained by the drug sponsors." The problem is, though, that the sponsors do not have to present that information to FDA. "Sponsors typically provide a quantity for each of the dosage forms marketed, but the information is not differentiated by animal species, label indication(s), route of administration or geographic region," DHHS said.

As a solution, the DHHS comments said, the data collection requirements could be changed so the sponsors would present usable data. DHHS added, "This would require notice and comment rulemaking to revise the current regulation."

International Activities

CVM Participates in Four-Country Food Safety Meeting

The issues of food safety and animal health are not limited to any one country, and some of the issues do not lend themselves to being addressed in a strictly formal regulatory manner. In that spirit, four countries have been meeting for the past 13 years routinely to discuss mutual food safety and animal health concerns.

The meetings involve four principal countries—the United States, Canada, Australia and New Zealand—so the meetings are formally known as the Quadrilaterals, but more commonly referred to as the "Food Safety Quads" and the "Animal Health Quads."

The most recent "Quads" meeting was held April 19-22 in Vancouver, British Columbia. It was hosted by the Canadian Food Inspection Agency and Health Canada.

The purpose of these annual meetings is to provide a forum for officials responsible for food safety, regulation and standards to discuss and collaborate on issues of mutual interest, thereby fostering understanding and agreement among the quadrilateral countries with the goal to enhance public health as it relates to food safety.

For the past several years, the participants attending the meeting to discuss animal health have devoted one full day to a joint meeting with those addressing food safety, because the issues align in many ways.

Topics discussed during the joint animal health/food safety session included national food safety and security strategies, outcome-based food safety standards, risk-based inspection, emerging microbiological and chemical issues, BSE, animal feed, antimicrobial resistance, and transgenic animals/cloning.

CVM Deputy Director Dr. Tollefson participated with other Food and Drug Administration staff from the Center for Food Safety and Applied Nutrition, the Office of Regulatory Affairs, and the Office of the Commissioner. Also attending the meeting were representatives from the U.S. Department of Agriculture's Food Safety and Inspection Service.

The meetings generate a list of action items of mutual concern to all four countries. The countries work on the action items during the year between meetings. □

CVM Hosts NRSP-7 Semi-Annual Committee Meeting

by Meg Oeller, DVM, FDA Liaison to the NRSP-7 Program

In the United States there is a critical shortage of approved animal drugs intended for the less common (minor) animal species or for major animal species with less common diseases or conditions, something which the National Research Support Project #7 (NRSP-7) is designed to address.

Veterinarians, pet owners, livestock producers, zoo and wildlife biologists have limited-to-no options for treating these animals if they become ill. The shortage of approved drugs results in animal suffering, loss of animal life, financial loss to those who raise the animals, and potential public health hazards through the transmission of disease-producing organisms from untreated animals to humans.

The U.S. Department of Agriculture with the cooperation of several universities and the Food and Drug Administration's Center for Veterinary Medicine took steps to deal with this problem. It created the NRSP-7, a program to move much-needed minor use or minor species drugs through the drug approval process.

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. Commercial sponsors are able to use these data in conjunction with their own manufacturing and labeling information to pursue a new animal drug approval. The scope of the program includes minor species of agricultural importance, but generally excludes companion animals.

The NRSP participants meet regularly to keep the process on track. The semi-annual meeting of the technical committee and administrative advisors was held on April 26 at the CVM offices in Rockville, Md.

Meeting attendees

The NRSP-7 technical committee is made up of a national coordinator, four regional coordinators, four regional administrative advisors, and liaisons from USDA and FDA.

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. . . NRSP-7 Semi-Annual Committee Meeting *(Continued)*

- 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. Ronald Griffith (Iowa State University), and Dr. Paul Bowser (Cornell University).
- The administrative advisors are Dr. Kirklyn Kerr (University of Connecticut), Dr. Garry Adams (Texas A&M), Dr. David Thawley (University of Nevada), and Dr. Don Robertson (Kansas State University).
- The USDA representative is Dr. Larry Miller (Washington, D.C.).
- I am the FDA liaison (Dr. Meg Oeller, Rockville, Md).

This meeting was also attended by Rosalie (Roz) Schnick, the national New Animal Drug Application coordinator for aquaculture, and by Dr. Mark Feldlaufer of the USDA bee lab in Beltsville, Md., as well as by stakeholders and several reviewers and managers from FDA/CVM.

Stakeholder pesentations

The NRSP-7 program recently underwent its five-year review, and one of the recommendations of the independent review committee was that the NRSP-7 committee do more outreach to stakeholders. To forward that goal, the committee invited Dr. Chris Hayhow from the American Rabbit Breeders Association, Mr. Gene Brandi representing American beekeepers, and Dr. Thomas Bell of the U.S. Fish and Wildlife Service to make presentations at the meeting.

The speakers provided a picture of the rabbit, bee and public aquaculture industries that included husbandry practices and veterinary-drug needs for management and disease treatment. The information they provided was very helpful to the committee.

Demonstration of aquaculture database

Dr. Renate Reimschuessel of the CVM's Office of Research gave a demonstration of her newly developed database of information about pharmacokinetics of drugs in fish, called FDA "Phish-Pharm." Phish-Pharm includes information from published literature covering 86 species of fish and shrimp, 117 drugs or chemicals and 12 routes of administration. This database will be available online in the near future and will serve as a reference for scientists involved with aquaculture.

Regional Coordinators' Reports

NORTHEAST REGION: *Dr. Paul Bowser*

Dr. Bowser's projects center on an investigation of the ability to group similar species to demonstrate safety and/or effectiveness of new animal drugs. If it can be shown, for example, that many fish species react in the same way to a drug, then studies could be done in a single species to represent the whole group. This would greatly simplify the approval process for aquaculture drugs. Although many of these projects are intended to support species grouping, the data will be accumulated to support individual drug approvals for the drugs under study. Current projects include oxytetracycline for finfish, sulfadimethoxine/ormetoprim (Romet-30™) for finfish, florfenicol for finfish, and sulfadimethoxine/ormetoprim (Rofenaid™) for pheasants.

SOUTHERN REGION: *Dr. Alistair Webb*

Dr. Webb reported that current projects include ivermectin for rabbits, fenbendazole for deer, lasalocid for deer and goats, fenbendazole, nitarsone and zoalene for gamebirds, and crude carp pituitary for fish. Dr. Webb also reported that they are completing the set up of their Good Laboratory Practices certified lab.

NORTH CENTRAL REGION: *Dr. Ronald Griffith*

The major current project is the controlled intravaginal drug release (CIDR-g) progesterone device for sheep for estrus synchronization. The U.S. sheep industry lists this product as its number one need. Target animal safety and human food safety studies are complete and data analysis is underway. New projects for florfenicol for necrotizing hepatopancreatitis in shrimp and lasalocid for coccidiosis in pheasants are in development. The project for florfenicol in veal calves has been discontinued pending a decision on eligibility for a waiver from the newly imposed FDA user fees.

WESTERN REGION: *Dr. Arthur Craigmill*

Dr. Craigmill reported on several projects. Several of these are cooperative projects with other regions, such as the CIDR-g for sheep and Rofenaid™ for gamebirds. The final report for the effectiveness study for the use of florfenicol for respiratory disease in sheep has been submitted and is under review at CVM. Tissues are currently being analyzed to complete the residue depletion study for that project. The Western Region is also responsible for the nearly completed projects for tylosin and lincomycin for American Foulbrood disease in honeybees and for the project for otolith marking of salmonids with strontium chloride immersion. The project for the use of erythromycin for bacterial kidney disease in salmonids is also in its final stages. A new project for pirlimycin for mastitis in goats is about to begin. Some species grouping work is underway in gamebirds.

Administrative Advisors' Report

The Administrative Advisors discussed the need for each region to give a 10-minute presentation about the program to the annual meetings of the regional meetings at regional experiment stations. They also encouraged continued outreach to stakeholders.

USDA Representative's Report

Dr. Miller related that the program's funding was cut 10 percent in the 2004 budget, but that may be restored in the 2005 budget.

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. . . NRSP-7 Semi-Annual Committee Meeting *(Continued)*

FDA'S NRSP-7 Liaison Report

The Minor Use/Minor Species Animal Health Act of 2004 (the MUMS Bill) has been passed by the Senate. It is currently under consideration by the Energy and Commerce Committee of the House of Representatives. If enacted, this legislation would make incentives available to pharmaceutical sponsors, allow for conditional approval of MUMS drugs, and allow legal marketing of some products for non-food producing animals under an indexing system.

The impact of the Animal Drug User Fee Act was explored. The NRSP-7 program was able to procure a waiver of sponsor fees for fiscal year 2004 based on the fact that all projects are for minor species. Sponsors who use NRSP-7 Public Master Files to support their New Animal Drug Applications will need to request waivers of filing fees prior to submitting their applications. The improved efficiency of drug evaluation from user fees is expected to benefit all applications, whether they are charged fees or not.

National Coordinator's Report

Dr. Babish reported on the annual report for the program and the results of the five-year review. The committee was complimentary of the program, but recommended more outreach to stakeholders, more use of electronic tracking of projects and higher visibility to solicit increased funding of the program.

Other Reports

Roz Schnick gave a presentation, "Food Fish Industry – Background and Needs." She described the achievements of the Federal-State Aquaculture Drug Approval Partnership Project. The partnership's projects include claims for Aqui-S™ (anesthetic), Chloramine-T, Copper Sulfate, Florfenicol, Formalin, hydrogen peroxide, potassium permanganate, and oxytetracycline. This group has also conducted studies to support species grouping.

The 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 and stakeholders.

This table presents the active NRSP-7 projects

Drug	*Route of Administration*	*Species*	*Indication*	*Region*
IVERMECTIN	injection	rabbits	ear mites	S
ERYTHROMYCIN	oral (feed)	salmonids	bacterial kidney disease	W
TYLOSIN	soluble powder	honey bees	American foulbrood	W
LASALOCID	oral (feed)	pheasant	coccidiosis	NC
PROGESTERONE	CIDR	sheep	estrus synchronization	NC
CARP PITUITARY	injection	various fish	spawning aid	S
SULFADIMETHOXINE/ ORMETOPRIM	oral (feed)	pheasants	bacterial infections and coccidiosis	NE
FENBENDAZOLE	oral (feed)	pheasants, partridges & quail	gapeworm, capillaria	S
OXYTETRACYCLINE	oral (feed)	finfish	bacterial infections	NE
LASALOCID	oral (feed)	deer	coccidiosis	S
STRONTIUM CHLORIDE	immersion	finfish	otolith marking	W
FLORFENICOL	oral (feed)	finfish	bacterial infections	NE
PIRLIMYCIN	intramammary	goats	mastitis	W
LINCOMYCIN	soluble powder	honey bees	American foulbrood	W
FLORFENICOL	injection	sheep	respiratory infections	W
SULFADIMETHOXINE/ ORMETOPRIM	oral (feed)	finfish	bacterial infections	NE
FLORFENICOL	oral (feed)	shrimp	necrotizing hepatopancreatitis	NC

International Workshop

The NRSP-7 program traditionally hosted a workshop on a minor species concern every two 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 toward activities other than the sponsorship of workshops. Now, NRSP-7 in partnership with the FDA/CVM will host an International Workshop for Minor Uses and Minor Species. The meeting will be held at the DoubleTree Hotel in Rockville, Md., October 7-8, 2004. Speakers from Europe, Africa, Japan, China, Australia among others will be presenting information about minor species and drug approvals in their countries. Registration will soon be possible through the CVM or the NRSP-7 websites. See: *http://www.fda.gov/cvm* or *http://www.nrsp7.org*.

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

NARMS Retail Meat Survey Finds *Campylobacter* Common, Some Resistant to Antimicrobials

by David G. White, Ph.D., a research microbiologist in the Division of Food and Animal Microbiology, Office of Research;
Robert D. Walker, Ph.D., Division Director, Division of Food and Animal Microbiology, Office of Research; and Joanne M. Kla, Assistant Editor

Federal officials earlier this year reported the results from a survey of antibiotic-resistant bacteria taken from retail cuts of meat.

In 2002, the officials expanded a surveillance program—the National Antimicrobial Resistance Monitoring System-Enteric Bacteria (NARMS), which is designed to monitor the development of resistant bacteria—to include surveillance of retail cuts of meat. The program was originally implemented to track the development of resistant bacteria in animals that produce food and relate that to resistant bacteria recovered from people suffering from foodborne illness.

NARMS was created by three branches of the Federal government—the Food and Drug Administration, the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA)—to advance the safety of food in the U.S.

NARMS retail meat surveillance is a collaborative effort among FDA, CDC and the Foodborne Diseases Active Surveillance Network (FoodNet). FoodNet is the principal foodborne disease component of CDC's Emerging Infections Program (EIP).

NARMS monitors changes in susceptibility of selected enteric bacteria to antimicrobial agents of human and veterinary importance.

The Federal managers of the NARMS program expanded it to include surveillance of retail foods of animal origin after conducting a feasibility study in Iowa. The retail food component of NARMS provides data on the prevalence of antimicrobial resistant foodborne pathogens and commensal bacteria among retail meat and poultry samples. Zoonotic foodborne bacterial pathogens currently under surveillance include *Campylobacter* and *Salmonella*, and are typically acquired through exposure to contaminated animal food products. Commensal bacteria of the intestinal tract that are under surveillance include enterococci and *E. coli*. These bacteria ordinarily colonize humans without causing disease, but on occasion, cause opportunistic infections such as wound or bloodstream infections.

NARMS retail meat surveillance is a collaborative effort among FDA, CDC and the Foodborne Diseases Active Surveillance Network (FoodNet). FoodNet is the principal foodborne disease component of CDC's Emerging Infections Program (EIP). FoodNet is a collaborative project of the CDC, 10 EIP sites (California, Colorado, Connecticut, Georgia, New York, Maryland, Minnesota, Oregon, Tennessee and New Mexico), USDA and FDA. The project consists of active surveillance for foodborne diseases and related epidemiologic studies designed to help public health officials better understand the epidemiology of foodborne diseases in the United States.

The NARMS/FoodNet retail meat surveillance program started with FoodNet laboratories in six States—Connecticut, Georgia, Maryland, Minnesota, Oregon and Tennessee. By January 2004, the number of sites had increased to 10 with the addition of FoodNet laboratories in New York, California, Colorado and New Mexico.

For the NARMS retail meat surveillance program, participating FoodNet laboratory personnel collect retail meat samples from local grocery stores. All NARMS FoodNet participants follow a similar retail meat sampling scheme. Laboratory personnel from each site purchase approximately 40 food samples per month, including 10 samples each of chicken breasts, ground turkey, ground beef and pork chops.

All 10 FoodNet laboratories culture for *Campylobacter* and *Salmonella* using standard methods described by FDA. Four sites also culture for the presence of enterococci and *E. coli*.

Once the FoodNet staff have isolated and identified bacterial isolates, they ship them to the Center for Veterinary Medicine's Office of Research to confirm species identification.

A comprehensive antibiogram (which is the antimicrobial susceptibility profile of an organism) is

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NARMS Retail Meat Survey Finds *Campylobacter* Common, Some Resistant to Antimicrobials *(Cont.)*

determined for the *Salmonella, E. coli* and enterococcal isolates using the NARMS antimicrobial panels. Both the E-test and agar dilution method are used to determine antimicrobial susceptibility patterns of *Campylobacter* species.

Antimicrobial susceptibility results are interpreted, where appropriate, according to internationally recognized standards established by the National Committee for Clinical Laboratory Standards (NCCLS). All *Salmonella* and *Campylobacter* isolates are also subjected to Pulsed-field gel electrophoresis (PFGE) to determine genetic relatedness. Resultant PFGE patterns are submitted to the CDC led PulseNet program (which is a national network for DNA fingerprinting of foodborne pathogens).

Participating FoodNet Emerging Infections Program Laboratories

- California Department of Health Services
- Colorado Department of Public Health and Environment
- Connecticut Department of Public Health
- Georgia Department of Human Resources
- Maryland Department of Health and Mental Hygiene
- Minnesota Department of Health
- New Mexico Department of Health
- New York State Department of Health
- Oregon Department of Human Services
- Tennessee Department of Health

Retail Food Study Sites; FoodNet laboratories

Preliminary data

In 2002, 2,513 retail meats were analyzed for the presence of *Campylobacter* and *Salmonella*. These samples included 616 chicken breasts, 613 pork chops, 642 ground beef and 642 ground turkey samples.

Preliminary data indicate that *Campylobacter* was recovered from 47% of the chicken breasts sampled, which means that *Campylobacter* was recovered more often from chicken breast that from the other three meat types tested.

C. jejuni was the predominant species identified, followed by *C. coli*.

Because there are presently no NCCLS-approved interpretive criteria (susceptible, intermediate or resistant breakpoints) for *Campylobacter*, "resistance" refers to those isolates exhibiting ciprofloxacin minimum inhibitory concentrations (MIC) of more than 4 µg/ml and erythromycin MICs of more than 8 µg/ml.

Fifteen percent of *C. jejuni* recovered from chicken breast exhibited MIC > 4 µg/ml to ciprofloxacin (meaning the bacteria were resistant), as compared with 9 percent of *C. coli*. Twenty percent of *C. coli* exhibited MICs more than or equal to 8 µg/ml to erythromycin (making the bacteria resistant), as compared with 0 percent *C. jejuni*.

Salmonella was recovered from ground turkey in 13 percent of the samples, which was more often than the other three meat types tested. *S. Heidelburg* was the predominant serotype recovered (found in 34 of the 153 samples) and was more often associated with ground turkey samples (62 percent).

Overall, antimicrobial resistant phenotypes differed by *Salmonella* serotype and retail food of animal origin. For example, five multi-drug resistant *S. Newport* strains of bacteria were recovered from ground beef, ground turkey and pork chops. The majority of *S.* Newport isolates exhibited resistance to at least nine antimicrobials including cefoxitin, chloramphenicol and trimethoprim/sulfamethoxazole.

Salmonella isolates also showed decreased susceptibility to ceftriaxone (16-32 µg/ml). Nalidixic acid resistant *Salmonella* were isolated only from ground turkey and were predominantly *S. Saintpaul* (found in four of the six samples).

Indistinguishable *Salmonella* genetic DNA finger prints (PFGE patterns) were also recovered from different retail meats collected at different sampling times and from different States.

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NARMS Retail Meat Survey Finds *Campylobacter* Common, Some Resistant to Antimicrobials *(Cont.)*

With regards to *Enterococcus* and *E. coli* prevalence, 1,574 meat samples were analyzed (only four of the NARMS/FoodNet sites participate in *E. coli/Enterococcus* surveillance). Sixty-eight percent of these retail meat samples were contaminated with *E. coli*. The majority of the 1,070 *E. coli* isolates recovered were susceptible to the antimicrobials tested. However, 52 percent were resistant to tetracycline, 36 percent to streptomycin, 28 percent to sulfamethoxazole, 19 percent to ampicillin and 14 percent to gentamicin.

Ninety-seven percent of the 1,574 retail meat samples were contaminated with enterococci. Among the 1,527 enterococci speciated, *Enterococcus faecalis* was the predominant species (recovered 59 percent of the time), followed by *E. faecium* (33 percent) and *E. hirae* (7 percent). Resistance to linezolid or vancomycin was not detected in any isolate, but high-level gentamicin resistance was observed in 9 percent of enterococci isolates.

Results from the NARMS retail 2002 survey demonstrate that retail meats, in particular chicken breast, are contaminated with* Campylobacter*, including antimicrobial-resistant variants.

Summary

Results from the NARMS retail 2002 survey demonstrate that retail meats, in particular chicken breast, are contaminated with *Campylobacter*, including antimicrobial-resistant variants.

Salmonella may also be found on retail meats, in particular ground turkey. On several occasions, indistinguishable *Salmonella* genetic finger prints were recovered from different retail foods of animal origin collected at different sample times and by different participating FoodNet laboratories, suggesting the dissemination of specific bacterial clones throughout the food supply.

These results demonstrate the dissemination of specific bacterial clones throughout the food supply.

Because campylobacteriosis and salmonellosis are transmitted primarily through contaminated food or water, the presence of antimicrobial-resistant variants in raw meat products has important public health implications. Further studies are needed to determine the relationships between antimicrobial use in animal husbandry with antimicrobial resistance development in these organisms as well as exploring mitigation strategies to reduce the presence of these foodborne pathogens on retail foods of animal origin.

Our observations also suggest that *Enterococcus* spp. and *E. coli* commonly contaminate retail meat products and that differences observed in antimicrobial susceptibility phenotypes may reflect the extent of use of antimicrobials in specific food animal production environments. Enterococci of foodborne origin have not been conclusively identified as direct causes of clinical infections; however, the consumption of meat carrying antibiotic-resistant bacterial populations is a possible route of transfer and could result in either colonization or transfer of resistance determinants to host-adapted strains.

Also, with the possible exception of *E. coli* O157:H7 and other shiga-toxin producing strains, the current data are insufficient to accurately assess the hazard and the potential public health risk associated with the presence of *E. coli* in foods, regardless of their antimicrobial resistance traits. Further study is also warranted to determine the significance and virulence potential of these organisms that contaminate retail food of animal origin.

Ask CVM

Q: *We are not comfortable with testing of human and animal pharmaceuticals on animals. It sounds cruel. Can't the tests be done in other ways that don't involve animals?*

A: At this time, the state of testing technology and the requirements to protect and promote public health require the use of animal testing in some cases. But do not confuse the use of animals for testing products with animal cruelty.

Animal welfare regulations are in place to provide for the humane care and use of animals in research, testing and teaching environments. FDA advocates full observance of all applicable animal welfare regulations and guidelines. Further, all FDA animal care and use programs conform to the stringent standards that the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) uses in its

(Continued, next page)

Ask CVM *(Continued)*

program evaluations. All of FDA's animal care and use programs have attained and continue to maintain full AAALAC accreditation. AAALAC is an independent peer review organization dedicated to the welfare of animals used in research, teaching and testing.

FDA's mission is to promote and protect public health by facilitating approval of safe and effective products in a timely manner. Testing pharmaceuticals is essential to protecting the health of humans and animals. It is required under the Federal Food, Drug and Cosmetic Act, which establishes the framework in which FDA fulfills its mission. The Act requires that manufacturers of certain consumer products demonstrate the safety and effectiveness of their products and that the products are properly labeled before the manufacturers can market those products.

FDA regulations describe the type and extent of pre-market safety and effectiveness testing that manufacturers must conduct. Those regulations take into account the applicable legal requirements and the technology available to determine the tests required.

FDA encourages the use of the most reliable scientific evidence in assessing the safety of FDA-regulated products, in part because many of the products are used for children or the elderly. The testing of human products can include chemical and physical studies, nonclinical studies, clinical trials involving humans and animal tests.

The use of animals, which represent intact living systems, is important in the evaluation process for determining the safety and effectiveness of a new drug, biologic or medical device. While many different test methods used in the evaluation process do not involve testing on animals, the toxicological effects of a given drug can best be evaluated in a whole-animal test system. Often a drug may have an effect, good or bad, on an organ system other than the one targeted.

Nonetheless, the use of animals in product safety determinations has been in a steady decline due to advances in science. FDA fully supports the use of alternative methodologies where appropriate, and responsible animal care and use when animal testing is necessary.

Q: *Why don't pet food companies list carbohydrates and calories on their labels? That information would help especially in developing appropriate diets for sick pets.*

A: No Federal law or regulation prohibits a company from guaranteeing carbohydrate content, but also no Federal law or regulation requires that they do so.

Some States have adopted AAFCO's Model Regulation concerning pet food, which allows for guarantees for nonessential nutrients such as carbohydrate, as well as information about calories to be on label.

Keep in mind that, in many cases with sick pets, the consistency of the diet within certain nutrient parameters is more important than just the carbohydrate and caloric content of the product. Consult your veterinarian for advice on nutrient parameters for a pet with an illness.

More information about how FDA regulates pet food may be found at: *http://www.fda.gov/cvm/index/animalfeed/petfoods.htm*

Q: *I want to buy drugs for my pets from overseas suppliers and bring the drugs into the U.S. Is it legal for me as a citizen to import drugs?*

A: Sometimes veterinarians can import animal drugs into the U.S., but only if the drugs are not available in the U.S. But, drugs that have been approved by FDA and are available in the U.S. cannot be imported. The most important reason for this is the safety of your pet. You have no assurances that the drugs manufactured overseas and sold overseas were produced in accordance with FDA requirements.

Q: *Do you have a list of discontinued veterinary drugs?*

A: No. But our "Green Book," which is accessible through CVM's website, contains a list of products voluntarily withdrawn by their sponsors. The list extends back to November 16, 1988. The products are listed in Chapter 6 of the "Greenbook" (*http://www.fda.gov/cvm/greenbook/greenbook.html*). (The Greenbook got its name when it was published on paper with green covers.)

Q: *Where can I find out about a new tick control medicine I just heard about?*

A: You can always check for drug approvals on CVM's website. Click on the button for the "Greenbook" (*http://www.fda.gov/cvm/greenbook/greenbook.html*), which is a database with all drug approvals listed. However, the tick control product you are asking about could be considered a pesticide and fall under the jurisdiction of the Environmental Protection Agency. EPA's Home Page is: *http://www.epa.gov/* . When you get to that page, click on "Pesticides." Under the "Frequent Questions" section (located at: *http://www.epa.gov/pesticides/about/faqs.htm#product*) on the "About Pesticides" page, the site gives the following information:

"If you have questions concerning a specific pesticide product, contact the National Pesticide Information Center (NPIC) either via telephone at 1-800-858-7378, or via e-mail at npic@ace.orst.edu. For more information about NPIC, visit the NPIC Web site, *http://npic.orst.edu/*."

Food Additive Petition

The Food and Drug Administration is amending the regulations for food additives permitted in feed and drinking water of animals to provide for the safe use of natamycin in broiler chicken feeds. Natamycin will be added to broiler chicken feed at a level of 11 parts per million (ppm) to retard the growth of *Aspergillus parasiticus* in the feed for up to 14 days after the addition of natamycin. This action is in response to a food additive petition (FAP 2234) filed by Arkion Life Sciences of Wilmington, Del.

Federal Register 04/13/04

Comings and Goings

NEW HIRES

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Matthew D. Anderson, Ph.D., Staff Fellow
- Bharati R. Dhruva, Ph.D., Staff Fellow
- Michelle L. Kornele, D.V.M., Staff Fellow
- Charles P. O'Brien, Ph.D., Staff Fellow
- Ruby Singh, Ph.D., Microbiologist, (permanent appointment with the Office of New Animal Drug Evaluation—previously was with the Office of Research under a fellowship)
- Faye Yingning Wei, Ph.D., Staff Fellow

OFFICE OF MANAGEMENT

- Michelle L. Mathias, Management Officer
- Ann Norris, Program Analyst

OFFICE OF SURVEILLANCE AND COMPLIANCE

- Sharon Ricciardo, Consumer Safety Officer

Departures

OFFICE OF THE DIRECTOR

- Clifford Johnson, D.V.M., Veterinary Medical Officer

OFFICE OF NEW ANIMAL DRUG EVALUATION

- Monica Brown-Reid, D.V.M., Veterinary Medical Officer

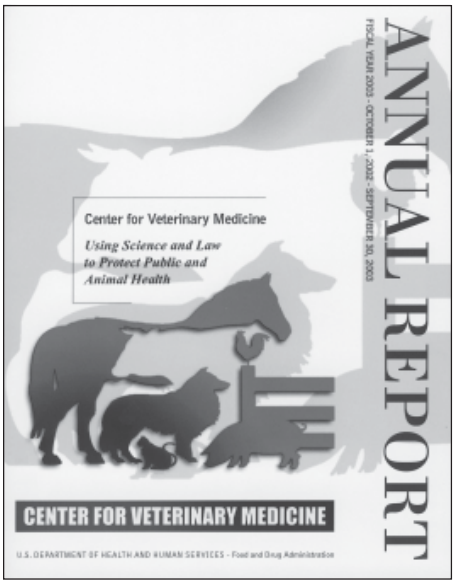
CVM Publishes Annual Report for Fiscal Year 2003

The Center for Veterinary Medicine (CVM) has published an Annual Report for fiscal year 2003.

CVM has the dual role of protecting animal and human health. It has the responsibility for regulating animal feed, pet food, and drugs for all animals, including animals that produce food as well as pets and other companion animals.

This first-ever CVM annual report discusses in detail CVM's accomplishments in reviewing veterinary drugs to increase the availability of products to treat animals (including drugs for fish and drugs for minor species). It also presents information about the Center's activity in reducing risks from antimicrobial resistance and controlling BSE in the U.S. cattle herd.

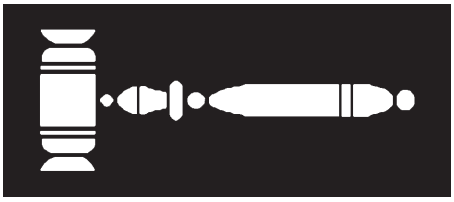
In addition, the report describes the Center's work to avoid unsafe drug residues in human food, ensure the safety of the feed supply, and protect the health of animals that are produced through biotechnology.



The report will be available on CVM's website, and hard copies are available from the CVM's Communications Staff; 7519 Standish Place, HFV-12, Rockville, MD 20855; 301-827-3800.

Regulatory Activities

by Marilyn Broderick, CVM Communications Staff



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

- Dennis Lagler, Owner, Lagler Dairy, Vancouver, Wash.
- Phil Bauer, President, Phillips Cattle Company, Beverly Hills, Calif.
- Robert A. Lofton, Co-Owner, Superior Cattle Feeders LLC, Calipatria, Calif.
- Ronald Hilarides, Manager Partner and Peter Schaafsma, Partner, S & H Dairy, Oakdale, Calif.
- John and Arend J. Bos, Co-Owners, Maple Dairy, Bakersfield, Calif.
- Kevin Finnerty, Epicenter Dairy, Alta Loma, Calif.
- Melvin J. Simoes, Owner, Melvin Simoes Dairy #3, Tulare, Calif.
- Donald Statz, Co-Owner, Statz Farms and Sons, aka Statz Brothers, Inc., Sun Prairie, Wis.
- Edward L. Hoekstra, Managing Partner, Hillcrest Dairy, LLC, Le Grand, Calif.
- Pete and John P. Dykstra, Co-Owners, John Dykstra Dairy, Tulare, Calif.
- Paul J. Wawrzyniak, Owner, Red Creek Farms, Alden, N.Y.
- Frank Kilpatrick, Lewisburg, Tenn.
- Edward M. Ciocca, Owner, Ciocca Dairy, Wendell, Idaho

(Continued, next page)

Regulatory Activities *(Continued)*

- Gary De Bruin, Owner, De Bruin Farm, Lynden, Wash.
- John M. Vosters, President, Tidy View Dairy, Inc., Kaukauna, Wis.
- Mike A. Schoneveld, Owner, Country Side Dairy, Ferndale, Wash.
- Lyn F. Main, Owner, Berkshire Valley Holsteins, Copake, N.Y.
- William M. Brinsfield, Jr., Owner, Udder Delight Dairy, Cordova, Md.

The above violations involved penicillin in dairy cows, tilmicosin in a culled beef cow, sulfadimethoxine in culled beef and dairy cows and dairy cows, neomycin in a cow and bob veal calves, flunixin in cows, tetracycline in a cow, and gentamicin in dairy cows.

Warning letters were issued to the following because investigations into illegal tissue residues in animals sold for slaughter as human food revealed serious deviations from the regulations for Extralabel Drug Use in Animals. These deviations caused an animal drug to be used in a manner that was unsafe and adulterated under the Federal Food, Drug and Cosmetic Act.

- Ralph L. Buckel, DVM and Gary R. Hash, DVM, Co-Owners, Chestertown Animal Hospital, Chestertown, Md.
- Richard Wedig, DVM, Co-Owner, Prairie Veterinary Associates, Sun Prairie, Wis.
- Howard S. Warner, DVM, Meredith-Warner Animal Clinic, Lewisburg, Tenn.

Warning letters were sent to the following individuals and firms for significant deviations form the Current Good Manufacturing Practice (cGMP) regulations for Medicated Feeds.

- Donald E. Orr, Jr., President & General Manager, United Feeds, Inc., Sheridan, Ind.
- Joseph F. Sanderson, Jr., President/CEO, Sanderson Farms, Inc., Laurel, Miss.

Warning letters were received by Thomas S. Hurst, Jr., Owner, Bardstown Mill, Inc., Bardstown, Ky., and Ralph K. Halter, President, Halter Feed & Grain, Inc., Robertsville, Ohio, for significant deviations from the requirements set forth in Title 21 Code of Federal Regulations (CFR), Part 589.2000 – Animal Proteins Prohibited in Ruminant Feed. This regulation is intended to prevent the establishment and amplification of Bovine Spongiform Encephalopathy (BSE). The inspection at Bardstown Mill, Inc. revealed that the firm failed to label feeds or mark the invoice of feeds that contain or may contain prohibited materials with the required cautionary statement "Do Not Feed to Cattle or Other Ruminants." The inspection at Halter Feed & Grain, Inc., found failure to label products that contain, or may contain prohibited materials with the caution statement; failure to establish and maintain written procedures, including clean-out and flushing procedures to avoid commingling and cross-contamination of common equipment; and failure to maintain records sufficient to track prohibited materials throughout their distribution.

A warning letter was issued to David R. Morris, President, Premium Nutritional Products, Inc., Shawnee, Kan., because an inspection of the own-label animal food distributor operations found a failure to label canned cat food with the cautionary statement "Do Not Feed to Cattle or Other Ruminants" in violation of Title 21 CFR Part 589.2000.

APPROVALS FOR MARCH AND APRIL 2004

New Animal Drug Approvals

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Alpharma, Inc. (NADA 141-223)	Diclazuril plus Roxarsone (Clinacox plus 3-Nitro)	Broiler chickens. For the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. brunette, E. mitis (mivati),* and *E. maxima.* Because diclazuril is effective against *E. maxima* later in its life cycle, subclinical intestinal lesions may be present for a short time after infection. Diclazuril was shown in studies to reduce lesion scores and improve performance and health of birds challenged with *E. maxima*. For increased rate of weight gain, improved feed efficiency, and improved pigmentation in broiler chickens.	**ORAL**—The NADA provides for the use of approved, single-ingredient Type A medicated articles containing diclazuril and roxarsone to formulate two-way combination drug Type C medicated feeds for broiler chickens. *Federal Register* 03/03/04

(Continued, next page)

New Animal Drug Approvals *(Continued)*

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Elanco Animal Health (NADA 141-224)	Ractopamine Hydrochloride plus Monensin Sodium plus Tylosin Phosphate (Optaflexx plus Rumensin plus Tylan)	Cattle. Increased rate of weight gain, improved feed efficiency, and increased carcass leanness; for prevention and control of coccidiosis due to *E. bovis* and *E. zuernii*; and for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces (Corynebacterium)* pyogenes in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.	**ORAL**—The NADA provides for use of ractopamine, monensin and tylosin phosphate Type A medicated articles to make dry and liquid three-way combination Type B and Type C medicated feeds for cattle fed in confinement for slaughter. *Federal Register* 03/15/04
Elanco Animal Health (NADA 141-225)	Ractopamine Hydrochloride plus Monensin Sodium (Optaflexx plus Rumensin)	Cattle. For increased rate of weight gain, improved feed efficiency and increased carcass leanness; and for prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.	**ORAL**—NADA provides for use of ractopamine and monensin Type A medicated articles to make dry and liquid two-way combination Type B and Type C medicated feeds for cattle fed in confinement for slaughter. *Federal Register* 03/15/04
Merial Ltd. (NADA 141-227)	Omeprazole Paste (Ulcergard)	Horses. For the prevention of gastric ulcers.	**ORAL**—The NADA provides for oral administration of omeprazole paste to horses for the prevention of gastric ulcers. *Federal Register* 03/22/04
Phibro Animal Health (NADA 141-226)	Semduramicin Sodium plus Virginiamycin plus Roxarsone (Aviax plus Stafac plus 3-Nitro)	Broiler chickens. Used for the prevention of coccidiosis caused by *Eimeria acervulina, E. brunetti, E. maxima, E. mivati/E. mitis, E. necatrix* and *E. tenella*; for prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to virginiamycin; and for increased rate of weight gain, improved feed efficiency and improved pigmentation in broiler chickens.	**ORAL**—The NADA provides for the use of approved, single-ingredient Type A medicated articles containing semduramicin, virginiamycin and roxarsone to formulate three-way combination drug Type C medicated feeds for broiler chickens. *Federal Register* 03/22/04

Supplemental New Animal Drug Approvals

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Fort Dodge Animal Health, Division of Wyeth (NADA 141-216)	Moxidectin plus Praziquantel Gel (Quest Plus)	Horses and ponies. For the treatment and control of various species of internal parasites in horses and ponies.	**ORAL**—The supplemental NADA provides for the speciation of adult small strongyles in product labeling. *Federal Register* 04/23/04

(Continued, next page)

Supplemental New Animal Drug Approvals *(Continued)*

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Pharmacia & Upjohn Co. (NADA 140-338)	Ceftiofur Sodium Sterile Powder for Injection (Naxcel)	Horses. For treatment of respiratory infections in horses associated with *Streptococcus zooepidemicus.*	**INTRAMUSCULAR OR SUBCUTANEOUS**—The supplemental NADA provides updated susceptibility data for equine respiratory pathogens listed in the clinical microbiology section of labeling and added the National Committee for Clinical Laboratory Standards' interpretive criteria for equine isolates. *Federal Register* 04/15/04
Schering-Plough Animal Health Corp. (NADA 112-051)	Levamisole hydrochloride (Levasole Soluble Drench Powder)	Cattle and sheep. A broad spectrum anthelmintic and is effective against various adult nematode infections.	**ORAL**—The supplemental NADA revises the description of various internal parasites in labeling for levamisole powder used to make a drench solution for oral administration. *Federal Register* 03/02/04

Abbreviated New Animal Drug Approvals

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Vetoquinol N.-A., Inc. (ANADA 200-307)	Penicillin G Potassium	Turkeys. The treatment of erysipelas caused by *Erysipelothrix rhusiopathiae.*	**ORAL**—The ANADA provides for the use of penicillin G in the drinking water of turkeys for the treatment of erysipelas caused by *Erysipelothrix rhusiopathiae.* Vetoquinol N.-A., Inc.'s Penicillin G Potassium, USP, is approved as a generic copy of Fort Dodge Animal Health's Penicillin G Potassium, USP, approved under NADA 055-060. *Federal Register* 03/03/04
Phoenix Scientific, Inc. (ANADA 200-345)	Lincomycin hydrochloride monohydrate/Spectinomycin dihydrochloride pentahydrate (Lincomycin and Spectinomycin Soluble Powder)	Chickens. For administration to chickens up to seven days of age as an aid in the control of airsacculitis caused by either *Mycoplasma synoviae* or *Mycoplasma gallisepticum* susceptible to lincomycin-spectinomycin and complicated chronic respiratory disease (air sac infection) caused by *Escherichia coli* and *M. gallisepticum* susceptible to lincomycin-spectinomycin.	**ORAL**—The ANADA provides for oral use of lincomycin and spectinomycin soluble powder to make medicated drinking water for administration to chickens up to seven days of age as an aid in the control of several bacterial respiratory diseases. Phoenix Scientific's Lincomycin-Spectinomycin Water Soluble Powder is approved as a generic copy of Pharmacia & Upjohn's L-S 50 (lincomycin hydrochloride monohydrate/spectinomycin sulfate tetrahydrate) Water Soluble Powder, approved under NADA 046-109. *Federal Register* 03/22/04

Supplemental Abbreviated New Animal Drug Approvals

Company	*Generic and (Brand) Names*	*Indications*	*Routes/Remarks*
Ivy Laboratories, Division of Ivy Animal Health, Inc. (ANADA 200-221)	Trenbolone acetate plus Estradiol plus Tylosin tartrate (Component TE-IS plus Tylan)	Feedlot steers. Used for increased rate of weight gain and improved feed efficiency in steers fed in confinement for slaughter.	**SUBCUTANEOUS IMPLANT**—The supplemental ANADA provides for the addition of a pellet containing tylosin tartrate to an approved subcutaneous implant containing trenbolone and estradiol. *Federal Register* 03/16/04
Ivy Laboratories, Division of Ivy Animal Health, Inc. (ANADA 200-346)	Trenbolone acetate plus Estradiol plus Tylosin tartrate (Component TE-IH plus Tylan)	Feedlot heifers. Used for increased rate of weight gain in heifers fed in confinement for slaughter.	**SUBCUTANEOUS IMPLANT**—The supplemental ANADA provides for the addition of a pellet containing tylosin tartrate to the approved implant containing trenbolone and estradiol. *Federal Register* 03/24/04

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