

## **Regulation of Antimicrobials in Livestock and the Effects on Animal Agriculture 2010 Kansas Farm Bureau Commodity Conference**

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### **I. Critical Legislation in the U.S. House and Senate**

The most critical bill related to the practice of veterinary medicine on the date these proceedings were prepared is HR 1549 - The Preservation of Antibiotics for Medical Treatment Act of 2009. The companion bill in the Senate is S 619

Thomas.gov is a government site for reading and tracking bills introduced in the U.S. Senate and House. By searching on the Bill Number you can find the available information on the text of the bill, related bills, all congressional actions and other information.

#### **H.R. 1549 SUMMARY AS OF: 3/17/2009--Introduced.**

Preservation of Antibiotics for Medical Treatment Act of 2009 - Amends the Federal Food, Drug, and Cosmetic Act to require the Secretary of Health and Human Services to deny an application for a new animal drug that is a critical antimicrobial animal drug unless the applicant demonstrates that there is a reasonable certainty of no harm to human health due to the development of antimicrobial resistance attributable to the nontherapeutic use of the drug. Defines "critical antimicrobial animal drug" as a drug intended for use in food-producing animals that contains specified antibiotics or other drugs used in humans to treat or prevent disease or infection caused by microorganisms.

Requires the Secretary to withdraw approval of a nontherapeutic use of such drugs in food-producing animals two years after the date of enactment of this Act unless certain safety requirements are met. Directs specified congressional committees to hold hearings on the implementation of such a withdrawal of approval.

From the text of the bill:

Critical Antimicrobial Animal Drug- The term `critical antimicrobial animal drug' means a drug that--

- `(1) is intended for use in food-producing animals; and
- `(2) is composed wholly or partly of--
  - `(A) any kind of penicillin, tetracycline, macrolide, lincosamide, streptogramin, aminoglycoside, or sulfonamide; or
  - `(B) any other drug or derivative of a drug that is used in humans or intended for use in humans to treat or prevent disease or infection caused by microorganisms.

`(ss) Nontherapeutic Use- The term `nontherapeutic use', with respect to a critical antimicrobial animal drug, means any use of the drug as a feed or water additive for an animal in the absence of

any clinical sign of disease in the animal for growth promotion, feed efficiency, weight gain, routine disease prevention, or other routine purpose.!

## **Representative slaughter has recently promoted this bill further through a house briefing.**

Antibiotic Resistance: A Multi-Billion Dollar Health Care Crisis Wednesday, December 2 at 9:30am Rayburn House Office Building Room 2168

Featuring:

- Rep. Louise Slaughter (D-NY)
- Michael Blackwell, DVM, MPH-former Vice Chair, Pew Commission on Industrial Farm Animal Production; Assistant Surgeon General, USPHS (ret.); Former Dean, College of Veterinary Medicine, University of Tennessee, Knoxville, TN.
- Robert Lawrence, MD-Director, The Johns Hopkins Center for a Livable Future, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
- Ramanan Laxminarayan, PhD, MPH-Senior Fellow, Center for Disease Dynamics, Economics, and Policy, Resources for the Future, Washington, DC
- Robert Martin-Senior officer, Pew Environmental Group; former Executive Director, Pew Commission on Industrial Farm Animal Production, Washington, DC
- Lance Price, PhD- Director, Center for Metagenomics and Human Health, Translational Genomics Research Institute, Flagstaff, AZ

## **II. And speaking of PEW, their full report on industrial farm animal production and executive summary may be accessed at <http://www.ncifap.org/>**

**(News release from the PEW website) Antibiotic Resistance and the Need to Ban Antibiotics in Food Animals Described to House Energy and Commerce Subcommittee by Executive Director of Bipartisan Pew Commission**

Hill Appearance Comes Just Weeks After Commission Released Final Recommendations

(Washington, DC - June 5, 2008) -- Robert P. Martin, executive director of the Pew Commission on Industrial Farm Animal Production, today reiterated the Commission's call for a phase out and ban on antimicrobials for non-therapeutic use in food animals. Mr. Martin testified at a hearing of the House Energy and Commerce Subcommittee on Health on the reauthorization of the Animal Drug User Fee Act. Mr. Martin's testimony comes just one month after the Commission released the findings and recommendation from its two-year examination of the impact of intensive confinement practices in industrial farm animal production. "Capitol Hill has been quick to recognize that through the diligence of our Commissioners there are tangible steps that can be taken right away to curb the overuse of antimicrobials," said Martin. "Eliminating the non-therapeutic use of these drugs will begin to lessen the problem of antibiotic resistance."

## **III. American Veterinary Medical Association response to the PEW report.**

The AVMA has responded to the PEW report. This may be accessed by the public at <http://www.avma.org/advocacy/PEWresponse/> (Accessed 12-14-09)

#### **IV. At the time of writing these proceedings, we await the final rule on the extralabel use of cephalosporins in food animals.**

The original order of prohibition put out for comment was issued on July 2, 2008. It was revoked November 25, 2008 due to over 200 substantive comments. The FDA Center for Veterinary Medicine had another call for input and numerous discussions with stakeholders in the Spring of 2009. The final rule is under review within the agency at the time of this writing.

#### **V. For several years, the FDA Center for Veterinary Medicine had withdrawn their compliance policy guideline for compounding (see regulations section below) after legal challenges to the authority of the FDA to regulate compounded products.**

A decision by the Fifth Circuit Court of Appeals, filed July 18, 2008, held that the FDA Center for Veterinary Medicine has the authority to regulate compounded drugs as “New Animal Drugs”. An excerpt from the court ruling follows (the FDCA is the Federal Food Drug and Cosmetic Act).

“We therefore conclude, in agreement with the two other circuits that have considered the issue,<sup>50</sup> that compounded drugs are “new animal drugs” within the meaning of § 321(v)(1) of the FDCA. And unless the compounded drugs are exempt under the FDCA’s AMDUCA provisions, § 360b(a)(4) and (5), compounded animal drugs are subject to the FDCA’s unsafe, adulteration, and misbranding requirements. As with human drugs, the FDCA contains no blanket “implicit exemption” for animal drugs produced by compounding.”

#### **VI. Current drug use regulations for extra-label use.**

There are two primary documents that serve as guides when evaluating extralabel drug use (ELDU) in food animals. The Animal Medicinal Drug Use Clarification Act (AMDUCA) Regulations were published in the Federal Register on November 7, 1996 (21 CFR part 530).

In addition, the revised compliance policy guideline (CPG) 608.400, entitled Compounding of Drugs for Use in Animals, was printed in the Federal Register on July 14, 2003. Both of these documents may be downloaded from the Food and Drug Administration Center for Veterinary Medicine (FDA/CVM) website at [www.fda.gov/cvm](http://www.fda.gov/cvm).

A handy guide that summarizes these documents in flow-chart format is available as a brochure from the AVMA. Copies of this brochure may be obtained by calling the AVMA Scientific Activities Division at 847-925-8070 and asking for the Extralabel Drug Use or AMDUCA brochure.

The AMDUCA regulations establish a hierarchy of drug use based on label characteristics of the drugs being considered for use.

**1. If a drug is labeled and effective for an application in food animals, then this drug must be used for that application according to label directions.**

**2. If the labeled drug is ineffective for the application, then is there a drug approved for food animals that would be effective when used in an extralabel manner?**

**Notes:** Although not required in the regulations, in my opinion it makes sense to first evaluate extralabel use of a compound labeled for this application (that was found to be ineffective when used according to label directions) before evaluating other food animal drugs.

Check to make sure that the drug being considered for ELDU is not banned for ELDU in food animals. An updated list was published in a 9-19-2002 CVM Update.

“The following drugs (both animal and human), families of drugs, and substances are prohibited for extra-label uses in all food-producing animals:

- Chloramphenicol;
- Clenbuterol;
- Diethylstilbestrol (DES);
- Dimetridazole;
- Ipronidazole;
- Other nitroimidazoles;
- Furazolidone, Nitrofurazone, other nitrofurans;
- Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine);
- Fluoroquinolones; and
- Glycopeptides.”

In addition, a more recent CVM update (2-28-2003) added ELDU of phenylbutazone in female dairy cattle 20 months of age or older to this list.

The AMDUCA regulations provide only for ELDU related to therapeutic purposes, and not production purposes

ELDU is legal only when carried out by or under the supervision of a licensed veterinarian within the scope of a valid veterinary-client-patient relationship (VCPR).

(i) A valid veterinarian-client-patient relationship is one in which:

(1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of

the veterinarian;

(2) There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and

(3) The practicing veterinarian is readily available for followup in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.

ELDU is not legal for drugs administered in the feed. Water and milk replacer are not considered feeds in this context.

The AMDUCA regulations apply only to drugs with a veterinary or human drug approval. Drugs without one of these approvals are considered adulterated when introduced into a food animal.

ELDU in food animals is allowed only if there is sufficient information to establish an extended withdrawal time. If there is not sufficient information available, then treated animals may not be entered into the food chain. Treated animals must be identified, either individually or as groups, to enable observation of the extended withdrawal time.

Cost of therapy is not established as a valid reason for ELDU in the AMDUCA regulations.

There are specific labeling and record requirements for ELDU. Refer to the Federal Register AMDUCA regulation notice for these requirements.

**3. If no food animal labeled drug is effective when used in an extralabel manner, then is there a human drug or a veterinary drug labeled for non-food animals that would effectively treat the condition when used in an extralabel manner?**

**Notes:** All of the restrictions under #2 also apply here. There should be even more emphasis on establishing a withdrawal time because, for many of these compounds, there may not be sufficient pharmacokinetic information to establish a slaughter withdrawal time.

**4. If there is no veterinary or human labeled drug that will effectively treat the condition when used in an extralabel manner, is it possible to compound from approved drugs to create a drug formulation that will effectively treat the condition?**

**Notes:** The AMDUCA regulations and CPG 608.400 directly address the issue of compounding. The CPG is especially valuable in evaluating compounding practices as there are examples of practices where the FDA would take regulatory action.

The veterinarian or pharmacist is required to adhere to good compounding practices.

Compounding is only allowed from drugs with a veterinary or human approval. You are expected to compound from a veterinary drug, if this is possible, before resorting to utilizing a human drug. A list of “bulk” (no veterinary or human approval) drugs from which compounding will be allowed by the FDA is included in Compliance Policy Guide (CPG) 7125.40 (CPG Section 608.400). These are primarily antidotes. Other than these few, specific drugs, compounding from bulk substances is illegal.

As stated above, cost is not a valid reason for ELDU, including compounding.

Although this summary may be helpful in understanding the basics of the AMDUCA regulations, it is no substitute for reading and becoming familiar with these regulations ([http://www.access.gpo.gov/nara/cfr/waisidx\\_08/21cfr530\\_08.html](http://www.access.gpo.gov/nara/cfr/waisidx_08/21cfr530_08.html) as published in the Federal Register) and CPG 7125.40 (CPG section 608.400). Veterinarians who have questions about AMDUCA or the extra-label use of drugs may contact the FDA/CVM Division of Compliance, 7519 Standish Place, HFV-230, Rockville, MD 20855, 301-827-1168.

Also, know the Pasteurized Milk Ordinance regulations for the state you are in. The PMO consists of “model” federal regulations that may be adopted as they are by states or may be modified with additional regulations. An example of something to be aware of is the substantial penalty in the inspection report for finding DMSO on the dairy. The PMO includes regulations on many areas, including proper drug storage.