The Veterinary Feed Directive Final Rule: What Veterinarians Need To Know

Antibiotic-resistant "superbugs" are becoming more and more of a concern around the world. According to the Centers for Disease Control and Prevention (CDC), each year in the United States, approximately two million people become infected with bacteria that are resistant to antibiotics. People with these drug-resistant infections require longer, more complicated hospital stays with higher medical expenses. Unfortunately, around 23,000 of these individuals die from infections. The Food and Drug Administration (FDA) and its counterparts around the world consider antibiotic-resistant bacteria a major public health risk. In the United States, the FDA is working to identify and contain antimicrobial resistance with efforts to reduce drug-resistant bacteria in foods and in animals that enter the food supply. In addition, FDA seeks to facilitate the development of new antibiotics to treat patients while preserving the effectiveness of existing antibiotics.

Veterinarians working alongside farmers and feed manufacturers will play a vital role in this effort. In fact, veterinarians will assume a greater role and increased responsibility for the use of some categories of drugs under the recently adopted Veterinary Feed Directive (VFD) Final Rule effective October 1, 2015. This course provides an overview of veterinarian's changing roles, focusing on new aspects related to the VFD Final Rule.

Additionally, two FDA guidance documents (#209, #213), summarized below, provide direction and background information to veterinarians and biologics companies related to the new VFD rule. They speak to the judicious use of medically important antibiotics in livestock production and implementation of new practices for labeling and changing of drug claims by drug companies. These documents represent FDA's current thinking on these topics and, unlike the VFD Final Rule, do not establish legally enforceable responsibilities and are not lawfully binding.

Guidance for Industry #209: This is a guidance document in which the FDA summarizes key reports and scientific literature related to the use of antimicrobial drugs in animal agriculture and outlines proposed strategies for assuring that medically important antimicrobial drugs are used judiciously to help minimize development of antimicrobial resistance. The FDA recommends phasing-out growth promotion claims on medically important antibiotics and phasing-in veterinary oversight of medically important antibiotics. (The term "medically important antibiotics" generally refers to antibiotics that are important for therapeutic use in humans. Some examples of medically important antibiotics to humans are: penicillins, tetracyclines, macrolides and streptogramins. A list can be found in Guidance 152, Appendix A.) The VFD rule covers only in-feed and water uses of these medically important compounds. Compounds like ionophores, which are not used in human medicine, or bacitracin, which is used for minor human uses, are not covered by this rule.

Guidance for Industry #209 is available online at: www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm216936.pdf.

Guidance for Industry #152 is available at: www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf.

Guidance for Industry #213: This document outlines the process by which a company can withdraw any growth promotion claims from the label of products that contain medically important antibiotics. The guidance establishes implementation processes for moving medically important antibiotics used in feed from over-the-counter status to VFD status and for moving medically important antibiotics used in drinking water from over-the-counter status to prescription or Rx status. The document also provides guidance on how companies can apply for a prevention and/or therapeutic claim on a product previously labeled for growth promotion only. As always, extra label use of antibiotics in feed continues to be prohibited. Guidance for Industry #213 is available online at: www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm299624.pdf.

Veterinary Feed Directive Final Rule: The VFD Final Rule was published in April 2015 and took effect on October 1, 2015. VFDs are the mechanism the FDA is using to apply veterinary oversight to medically important antibiotics in animal feed. VFDs were first used in the late 1990's. The FDA is moving all medically important antibiotics from over-the-counter (OTC) status to VFD status. The FDA will require livestock producers to obtain approval from a veterinarian to place antibiotics in animal feed. This ensures that medically important antibiotics are only used judiciously for therapeutic reasons. Growth promotion is no longer an acceptable use.

The VFD Final Rule does not cover water-soluble antibiotics. In accordance with Guidance for the Industry #209, manufacturers of antibiotics for use in drinking water will transition these products from over-the-counter status to Rx status. A producer will need to acquire water-soluble antibiotics from a veterinarian or get a written prescription from a veterinarian. The goal of the FDA is to have this transition fully implemented by December 12, 2016.

Issuing VFDs

Veterinarians who issue VFDs will have to do so within the context of a veterinarian-client-patient-relationship (VCPR). The VFD rule specifies that the veterinarian must work with the client and assumes responsibility for making clinical judgments about animal health, has sufficient knowledge of the animal(s) by virtue of examinations and/or visits to the farm where the animals are located, and provides for any necessary follow-up evaluation or care. The final rule also requires veterinarians to follow state-defined VCPR requirements. If the FDA determines that no applicable or appropriate state

VCPR requirements exist, the veterinarian will have to follow federally defined VCPR requirements. Veterinarians will need to adhere to the VCPR included in the final rule.

In Indiana, the VCPR is defined as the following:
IC 25-38.1-1-14.5 "Veterinarian-client-patient relationship"
Sec. 14.5. "Veterinarian-client-patient relationship" means a relationship between a veterinarian and client that meets the following conditions:

1. The veterinarian has assumed the responsibility for making clinical judgments regarding the health of the animal and the need for medical treatment, and the client has agreed to follow the veterinarian's instructions.

2. The veterinarian has sufficient knowledge of the animal to initiate a diagnosis of the medical condition of the animal. The veterinarian has recently seen and is personally acquainted with the keeping and care of the animal by either of the following:

    a. An examination of the animal.

    b. By recently seeing and being personally acquainted with the keeping and care of representative animals and associated husbandry practices by making medically appropriate and timely visits to the premises where the animal is kept.

3. The veterinarian is readily available or has arranged for emergency coverage for follow-up evaluation if there is an adverse reaction or failure of the treatment regimen.

4. When appropriate, the veterinarian has arranged for continuing care with another licensed veterinarian who has access to the animal's medical record.
   As added by P.L.58-2008, SEC.14.

Indiana's VCPR is available online at: www.invma.org/?page=382.

A VCPR must be in place for a veterinarian to provide treatment, prescribe medications, or administer vaccines to an animal legally.

Note: Veterinarians should check with licensing authorities in each state individually to confirm standards where he/she practices. Requirements can vary.

VFD orders may be obtained from the drug sponsor or a veterinarian may write a VFD order themselves for VFD drugs.

VFD orders may only be written for VFD drugs.

VFD Distribution and Retention

VFD orders may be issued on paper (hardcopy) or electronically. The veterinarian must retain the original VFD order. For paper VFD orders, veterinarians may make copies of the original VFD order for the distributor and client or the veterinarian may fax or scan and email the VFD order to the distributor

and client. Paper VFDs that are emailed or faxed are not considered true electronic VFDs due to their lack of authenticated electronic signatures. Electronic VFDs (eVFD) are issued using the internet. To issue eVFDs the veterinarian must use a computer that is compliant with Title 21, part 11 of the Code of Federal Regulations (21 CFR 11). Because the eVFD order is considered the original, signed VFD, no follow-up paper copy is needed.

VFD orders cannot be issued via the telephone.

Veterinarians must retain the original VFD in its original format for 2 years. All other involved parties (client and distributer) must retain a copy of the VFD for2 years.

Veterinarian's Responsibilities

- No extra-label use. Extra-label use (i.e., use of VFD feed for unapproved indications or at unapproved doses) is strictly prohibited.
- Be appropriately licensed (i.e., practitioner has a valid veterinary license in the state where the animals are located and to be treated).
- Have a valid VCPR (as defined by the state, or FDA if undefined).
- Accurately complete and sign VFD orders. Preprinted, multipart forms (preapproved by the FDA's Center for Veterinary Medicine) are often supplied by the drug manufacturer. For example, a VFD for Pulmotil® (tilmicosin) is provided by Elanco. These forms will be available for download at the drug manufacturer's website. The producer may present the VFD order to the feed supplier, who will manufacture and distribute the feed in accordance with the VFD.

  For a valid VFD, the following information is required:

  1. Veterinarian's name, address, telephone number and fax number
  2. Veterinarian's license number and state where it is issued
  3. Producer's name, address, and telephone number
  4. Species of animals being treated
  5. Animals' identification numbers/descriptions and number of animals being treated
  6. Animals' location, as a postal address, legal description, or premise ID
  7. Date of treatment and the date the VFD order is issued
  8. Name of the drug and drug's approved or indexed listed indications for use

9. If approved combinations of drugs are used, both drugs must be listed
    - In addition to the drug names, the indication(s) of use, the levels of the drugs in the VFD feed and duration of use, the withdrawal time, special instructions, and cautionary statements necessary for use of the combination VFD drug must also be included in the VFD.
10. Level of drug in the feed and amount of feed required to treat animals
    - In cases where a VFD drug is approved for use at multiple drug levels, or for use in a range of drug levels, the veterinarian may specify a particular drug level within that range, or authorize the use of any level within the range by putting the entire authorized range on the VFD.
11. Feeding instructions with the withdrawal time (even if withdrawal is zero)
12. Any special instructions and caution statements necessary for use of the drug in conformance with the approval
13. VFD order's expiration date; the expiration date cannot exceed 6 months or is limited by the expiration date of the product
14. Number of refills, if necessary and if permitted by the approval
15. The statement: "Extra-label use, (i.e., use of the VFD feed in a manner other than as provided for in the VFD drug approval) is strictly prohibited", must be on the VFD
16. Any other information required by the VFD drug approval regulation

- Electronically sign eVFD orders (when applicable).
- Provide the feed distributor with the original VFD order.
- Give a copy of the VFD or eVFD order to the producer.
- Maintain copies of VFD orders in the original format (paper or electronic) for a minimum of 2 years.
- Have VFD orders available for inspection by the FDA.
- The VFD requirements apply to all VFD drugs for use in all species. One VFD drug is already approved for use in minor species (i.e., florfenicol in aquaculture). Other medicated feed drugs for minor species are expected to convert from their present over-the-counter (OTC) status to VFD status (e.g., oxytetracycline in honey bees) and at that time, a VFD will be required for their use.

Remember: Under 21 CFR 558.6 a veterinarian must complete the VFD in writing and sign it. VFD orders that are incomplete or unsigned are considered invalid. Feed mill operators and distributors may not fill incomplete or unsigned VFD orders. The veterinarian is responsible for the accuracy and completeness of the information in the VFD order. If a copy of the VFD is used to fill the order, the veterinarian must verify the feed mill or distributor is given the original paper order within 5 business days.

The VFD Final Rule is available online at: www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm071807.htm.

Questions and answers about the VFD are available online at: www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052660.pdf.

More information on VFD Requirements for veterinarians is available online at: www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm455416.htm.

The new VFD rules will require some producers to change the way they work with their veterinarians. The livestock industry continues to make strides in improving the use of antibiotics in food-producing animals. Residue prevention protocols are working at least in the dairy section. A drug residue study of milk conducted by the Food and Drug Administration in 2012 and released March 2015 found that less than 1% of the milk samples had drug residues. The study results are available online at: http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/ucm264049.htm.