New Rules

A quick, updated glance at the veterinary feed directive as it takes effect Jan. 1.

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On Jan. 1, 2017, the impact of FDA's veterinary feed directive (VFD) rule on some antibiotic drugs used in feed officially took effect. While it's been in the process for a decade, and the rule became effective Oct. 1, 2015, the VFD labeling transition of feed-grade antimicrobials used to treat animals and considered "medically important" to human medicine was targeted to become complete on the first of the year.

It's an issue of antimicrobial resistance. It's a complex, multifactorial issue, said Mike Murphy, veterinary medical officer at the FDA Center for Veterinary Medicine (CVM), during a webinar hosted by the National Cattlemen's Beef Association (NCBA) in October.

"One of the issues that drives antimicrobial resistance is use — use in animal medicine, human medicine, horticultural uses and other uses. And although this has been the subject of significant scientific and policy debate for decades, and things continue to evolve, the intent on the part of the agency is to implement measures that would address the public health concern while assuring that animal health needs are met," Murphy said. "I always repeat the 'while assuring that animal health needs are met,' part of it."

According to the FDA, the VFD changes are intended to make the process more efficient while continuing to provide public health protections.

Relevant guidance documents

Murphy outlined the three guidance documents that are of greatest concern to cattle producers: Guidance for Industry (GFI) #209, #213 and #152.

GFI #209 aims to limit the use of medically important antimicrobial drugs in food-producing animals to those uses (1) considered necessary for assuring animal health (therapeutic uses) and (2) that include veterinary oversight/consultation.

December 2016 was the target for drug sponsors to implement changes to use conditions of medically important antibiotics in or on food and in drinking water to withdraw approved production uses such as increased rate of weight gain or improved feed efficiency — the principle of GFI #213. After the label changes take effect, those production uses will no longer be legal; however, it is intended that the therapeutic uses are to be retained (treatment, control and prevention indications).

"We're having a transition to veterinary oversight in the use of these products," Murphy explained.

A key principle for the VFD is to include the veterinarian in the producer's decision-making process. Murphy pointed out that this does not require direct involvement from the veterinarian during drug administration, but it does require use of the drug to be authorized by a licensed veterinarian in the context of a veterinarian-client-patient relationship (VCPR).

This means the marketing status for those drugs will change from over-the-counter (OTC) to prescription or VFD. Water soluble products (medicated drinking water) will transition to prescription, while products used in or on feed (medicated feed) will transition to VFD.

What's affected?

Only antibiotics that are medically important (important or significant in human medicine) and administered in or on feed or in drinking water are affected by the GFI #213 change. Other dosage forms of administration, including injectable or bolus, etc., are not affected in this transition.

Medically important antibiotics are antimicrobial drugs that are considered important for therapeutic use in humans. These include all antimicrobial drugs or drug classes that are listed in Appendix A of the FDA's GFI #152, which can be viewed at *www.fda.gov/OHRMS/DOCKETS/98fr/98d-1146-gdl0001.pdf.*

In addition, a list of each specific application that is affected can be found at *http://bit.ly/antimicrobial-use.*

Drugs commonly used in the treatment of cattle that are expected to change from OTC status to VFD status in 2017 include neomycin, tylosin, virginiamycin, chlortetracycline and oxytetracycline.

There are a total of about 292 applications affected by the GFI #213 transition process. A complete list of affected applications is available at *www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/ucm390429.htm.*

New legal category

Murphy noted that Congress, in the *Animal Drug Availability Act*, instructed the CVM that neither the VFD drug nor the medicated feed containing the VFD drug shall be deemed a prescription article by state or federal law.

"Our understanding of Congress's intent on that was to create this legal category of drugs called 'veterinary feed directive drugs' so as not to fall under the State Board of Pharmacy authority like the prescription drugs do."

That means there are now three legal classes or categories of drugs available to producers: OTC, prescription and VFD.

Learning the language

Approximate number of animals. Rather than specifying the amount of feed to be fed, the VFD requires an approximate number of animals anticipated to be consuming the medicated feed within the expiration date of the VFD order. Clients will be required to give an approximate number of animals of the species and production class identified on the VFD that will be fed the VFD or combination VFD feed.

Murphy said the expectation is that feedmills will work with clients and veterinarians to determine an appropriate amount of feed to manufacture and distribute under the VFD.

"We're asking veterinarians to work with their producers on the approximate number of animals that are going to get fed, not the approximate number of tons of feed," he said. "We appreciate that this is fostering communication between veterinarians and the folks in the mills to figure out the amount of feed those animals are going to be consuming."

Categories. Feed-use drugs are assigned to one of two categories: Category I or Category II. Category I drugs are classified as having the lowest potential for residues. Category II drugs are classified as having the highest potential for residues. The category determines whether a facility needs to be licensed to handle the drug in Type A form.

Murphy noted that the definition of Category II was revised to eliminate the automatic classification of VFD drugs into Category II. The change applies to existing approved VFD drug products, and products that will become VFD drugs under GFI #213.

Combination VFD drugs. Combination VFD drugs are, rather simply, "a VFD drug plus another drug," Murphy explained. The combination could be two VFD drugs, for example, he noted, neomycin and oxytetracycline; or the other drug could be an OTC drug, like tilmicosin and monensin.

Distributors. A "distributor" is any person who distributes a medicated feed containing a VFD drug to another person. A distributor can be someone who only distributes VFD feed, or who manufactures and distributes VFD feed. The rule requires a one-time notification to FDA of intent to distribute VFD feed.

Duration of use. The duration of use describes the length of time the animal is ingesting the medicated feed for its therapeutic benefits, Murphy said.

"If we get into a situation where the animals are ingesting the medicated feed and the VFD order expires, we've asked the client to contact his or her veterinarian

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and to request a new VFD order so they can continue feeding those animals so they get the therapeutic benefit of the feed," he said.

Expiration date. The expiration date on any VFD drugs specifies the period of time for which the VFD authorization is valid.

"This is the expiration date of the veterinary feed directive order authorizing the client to obtain and use a medicated feed," Murphy explained. "This is not the expiration date on the Type A medicated article from which that medicated feed is made." These are two separate and distinct concepts that unfortunately share the same terminology, he said.

A VFD-issued feed should not be fed after the printed expiration date, or the date at which the VFD authorization expires.

If a VFD expiration date is not specified on the drug's label, the veterinarian may authorize the VFD for up to six months following the date of issuance. A veterinarian may use his or her judgment to make the unspecified VFD expiration date shorter than six months, but not longer.

Refills. Refills, or reorders, are only permitted to be issued by veterinarians if the drug approval, conditional approval or index listing expressly allows it. If a label doesn't specify, a refill is not authorized. Murphy pointed out that there are currently no approved VFD drugs that allow refills or reorders as a condition of their approval, conditional approval or index listing.

Substitution. In some cases, a generic VFD drug may be used as a substitute for an approved pioneer VFD drug, in cases where the pioneer is identified on the VFD. According to the VFD, if the veterinarian does not specify that a substitution is not allowed, the feed manufacturer may use either the approved pioneer drug or an approved generic VFD drug to manufacture the VFD feed. However, the feed manufacturer may not substitute a generic VFD drug in a combination VFD feed if the generic VFD drug is not part of an approved combination VFD drug.

So, what's the take-away?

"For the current VFD drugs, there is no generic option available except for tilmicosin for the use in control of swine respiratory disease (SRD), but not in cattle," Murphy said.

Veterinarian-client-patient relationship (VCPR). The VCPR describes the relationship and interactions between the veterinarian, client (producer) and patient (animal) as it pertains to the VFD rule. Veterinarians issuing a VFD are required to be licensed to practice veterinary medicine and operate in compliance with either a state-defined or federally defined VCPR. The state-defined VCPR is defined by state and includes the key elements of a valid VCPR defined by the FDA. If a state VCPR fails to meet the key elements defined by the FDA, a federally defined VCPR takes over.

Tom Portillo, manager of animal health with Friona Industries, said his understanding of the rule is that individual states can make their requirements more strict, but not more lax than the federal requirements.

Implementation timeline

The VFD rule went into effect in October 2015 and applies to all current VFD drugs. December 2016 was the target for drug sponsors to implement changes to use conditions of products affected by GFI #213, and Jan. 1, 2017, is the target for all medically important antimicrobials used in or on feed to require a VFD.

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