Antimicrobial Resistance and the Veterinary Feed Directive

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Implementation Timeline Summary

- October 1, 2015 – VFD Final Rule goes into effect
  - Applies to current VFD drugs
- June 30, 2016 – Sponsors meet with ONADE and agree upon label changes
- January 1, 2017 – Target for all medically important antimicrobials for use in or on feed to require a VFD
  - December 2016 – Target for drug sponsors to implement changes to use conditions of products affected by GFI #213

Updates to VFD Regulation

- Changes intended to make process more efficient while continuing to provide public health protections
  - Caution statement revised
  - Affirmation of intend statement regarding whether it can be used with approved combinations
  - Number on animals fed instead of amount of feed
  - Original order not required to be mailed to feed mill
  - Cat II definition revised to eliminate automatic Cat II classification
  - VCPR definition revised to recognized state licensing
  - October 1, 2015 – VFD final rule becomes effective

Information Required on VFD Form

- Regulation lists all information that must be included on VFD in order for it to be lawful
- Veterinarian is responsible for making sure the form is complete and accurate
- See brochures for listing of required information

Current VFD Drugs

Currently Approved VFD Drugs	Approved for Use in the Following Species
Avilamycin	Swine – reduction of diarrhea – E. coli.
Florfenicol	Fish – control of mortality (various diseases by fish type) Swine – control of SRD
Tilmicosin	Cattle – control of BRD Swine – control of SRD

Note: Only the drugs that are currently approved as VFD drugs (above) will be affected by the VFD final regulation when it goes into effect on October 1, 2015.

Drugs Not Affected by Guidance #213

- Antibiotics
  - Already VFD – avilamycin, florfenicol, tilmicosin; or Rx - Tylosin.
  - Not medically important for example:
    - Ionophores (monensin, lasalocid, etc.)
    - Bacitracin (BMD, bacitracin zinc)
    - Bambermycins
- Other drugs (that are not antibiotics), including:
  - Anthelmentics: Coumaphos, Fenbendazole, Ivermectin
  - Beta agonists: Ractopamine, Zilpaterol
  - Coccidiostats: Clopidol, Decoquinate, Diclazuril

What drugs are affected, which ones are not on January 1, 2017?

“Medically Important” Antibiotics

- Includes antimicrobial drugs that are considered important for therapeutic use in humans
- Guidance #213 defines “medically important” to include:
  - All antimicrobial drugs/drug classes that are listed in Appendix A of FDA’s Guidance #152

Affected Feed-use Antibiotics

Antimicrobial Class	Specific drugs approved for use in feed
Aminoglycosides	Apramycin, Hygromycin B, Neomycin, Streptomycin
Diaminopyrimidines	Ormetoprim
Lincosamides	Lincomycin
Macrolides	Erythromycin, Oleandomycin, Tylosin
Penicillins	Penicillin
Streptogramins	Virginiamycin
Sulfas	Sulfadimethoxine, Sulfamerazine, Sulfamethazine, Sulfaquinoxaline
Tetracycline	Chlortetracycline, Oxytetracycline

Affected Water-use Antibiotics

Antimicrobial Class	Specific drugs approved for use in water
Aminoglycosides	Apramycin, Gentamicin, Neomycin, Spectinomycin, Streptomycin
Lincosamides	Lincomycin
Macrolides	Carbomycin, Erythromycin, Tylosin
Penicillins	Penicillin
Sulfas	Sulfachloropyrazine, Sulfachlorpyridazine, Sulfadimethoxine, Sulfamerazine, Sulfamethazine, Sulfaquinoxaline
Tetracycline	Chlortetracycline, Oxytetracycline, Tetracycline

VFD Final Rule: Distributors

- A ‘‘distributor’’ means any person who distributes a medicated feed containing a VFD drug to another person.
  - Such other person may be another distributor or the client-recipient of the VFD medicated feed.

  There are two kinds of distributors:

  1. Only distributes VFD feed
  2. Manufactures and distributes VFD Feed
- Distributors must notify FDA:
  - Prior to the first time they distribute animal feed containing a VFD drug
  - Within 30 days of any change of ownership, business name, or business address

Expiration Date and Duration of Use

- Expiration Date –
  - Specifies the period of time for which the VFD authorization is valid
  - A VFD feed should not be fed after the expiration date (i.e., after VFD authorization expires)
  - May be specified on the product label; if not – it cannot exceed 6 months after the date of issuance.
  - The veterinarian can use his or her medical judgment to determine whether a more limited period is warranted

Expiration Date and Duration of Use

- The Duration of Use –
  - A separate concept from the expiration date
  - The length of time that the animal feed containing the VFD drug is allowed to be fed to the animals
  - Established as part of the approval, conditional approval, or index listing process
  - If the VFD order will expire before completing the duration of use on the order, the client should contact his/her veterinarian to request a new VFD order

Refills

- Refills (reorders) – Are only permitted to be issued by veterinarians if the drug approval, conditional approval, or index listing expressly allows a refill (or reorder)
  - If a label is silent on refills, a refill may not be authorized
  - Currently, there are no approved VFD drugs that allow refills or reorders as a condition of their approval, conditional approval, or index listing

Approximate Number of Animals

- VFD must include an **approximate** number of animals:
  - The potential number of animals of the species and production class identified on the VFD that will be fed the VFD feed or combination VFD feed manufactured according to the VFD at the specified premises by the expiration date of the VFD

Affirmation of Intent Statements

- The VFD only authorizes the use of the VFD drug(s) cited in this order and is not intended to authorize the use of such drug(s) in combination with any other animal drugs
- This VFD authorizes the use of the VFD drug(s) cited in this order in the following FDA-approved, conditionally approved, or indexed combination(s) in medicate feed that contains VFD drug(s) as a component
- This VFD authorizes the use of the VDS drug(s0 cited in this order in the following FDA-approved, conditionally approved, or indexed combinations(s) in medicated feed that contains the VFD drug(s) as a component.

Substitution of VFD drugs

Use of an approved generic VFD drug as a substitute for an approved pioneer VFD drug in cases where the pioneer VFD drug is identified on the VFD.

- If the veterinarian does not specify that a substitution is not allowed, the feed manufacturer may use either the approved pioneer or an approved generic VFD drug to manufacture the VFD feed.
- However, the feed manufacturer may not substitute a generic VFD drug for a pioneer VFD drug in a combination VFD feed if the generic VFD drug is not part of an approved combination VFD drug.

Veterinary Client Patient Relationship (VCPR)

- Veterinarian issuing a VFD is required to be licensed to practice veterinary medicine and operate in compliance with either:
  - **State-defined VCPR** – if VCPR defined by such State includes the key elements of a valid VCPR defined in § 530.3(i); or
  - **Federally-defined VCPR** - where no applicable or appropriate State VCPR requirements exist

Veterinary Client Patient Relationship (VCPR)

- FDA is working with State regulatory authorities to verify whether that state has VCPR requirements in place that:
  - apply to the issuance of a VFD, and
  - include the key elements of the federally-defined VCPR

Ongoing activities/Next steps

- GFI # 120:
  - Review comments received on GFI #120
  - Publish final version of GFI #120

    Publish VCPR list, by 1 October 2015

- Develop guidance on format of VFD form

Thank You

Combination VFD drugs

Combination VFD drug

- Limited to use under the supervision of a licensed veterinarian, and at least one of the new animal drugs in the combination is a VFD drug.
  - New VFD rule requires the veterinarian to include one of three "**affirmation of intent**" statements to affirm his or her intent as to whether the VFD drug being authorized can or cannot be used in approved combinations
  - Expect that this will be addressed through inclusion of a check box on the VFD form

Veterinary Client Patient Relationship (VCPR)

- FDA will provide an online list of such states at the time the final GFI #120 publishes
  - CVM intends to publish this list on its VFD website by October 1, 2015
  - This list will be updated periodically as FDA receives and verifies information from states if they change their VCPR definition or its applicability

FDA's Judicious Use Strategy

Two key principles outlined in Guidance #209:

1. Limit medically important antimicrobial drugs to therapeutic purposes (i.e., those uses considered necessary for ensuring animal health)
2. Require veterinary oversight or consultation for such therapeutic uses in food-producing animals

Guidance #213: Overview

- December 2016 - Target for drug sponsors to implement changes to use conditions of medically important antibiotics in food and water to:
  - Withdraw approved production uses
    - such as “increased rate of weight gain” or “improved feed efficiency”
  - Such production uses will no longer be legal

Guidance #213: Removing Production Uses

- However, therapeutic uses are to be retained
- treatment, control, and prevention indications
- Require veterinary oversight