National Grain and Feed Association

FDA's Antimicrobial Resistance Policies and the Veterinary Feed Directive

Impacts on Medicated Feed

July 2016

Presentation Outline

1. Regulatory Terminology for Animal Drugs/Feed
2. History of the Veterinary Feed Directive
3. FDA's Antimicrobial Resistance Policies
4. Revisions to the Veterinary Feed Directive
5. Implementation Issues
6. Frequently Asked Questions

Regulatory Terminology

- **New Animal Drugs - Categories**
  - **Category I** new animal drugs are drugs that require no withdrawal period at the lowest use level in each species for which they are approved.
  - **Category II** new animal drugs are drugs that: (1) require a withdrawal period at the lowest use level for at least one species for which they are approved; or (2) are regulated on a "no-residue" basis or with a zero tolerance because of a carcinogenic concern regardless of whether a withdrawal period is required, ~~or (3) are veterinary feed directive drugs~~.*
  - 21 Code of Federal Regulations (CFR) 558.4(d) identifies each drug by Category I or Category II

*** Red text indicates changes made when revised VFD regulation was issued in June 2015**

Regulatory Terminology

- **Type A medicated articles** are intended solely for use in the manufacture of other Type A medicated articles and/or a Type B or Type C medicated feeds and consist of an approved new animal drug(s), with or without carrier (e.g., calcium carbonate, rice hulls, corn gluten) and with or without inactive ingredients
- **Type A medicated articles** contain a drug(s) at an approved potency higher than what is permitted in Type B feed levels (see 21 CFR 558.4(d))
- **FDA-approved Medicated Feed Mill License (MFML)** required to produce medicated feed from Category II, Type A medicated articles and in some other situations related to medicated free-choice and liquid feeds

Regulatory Terminology

- **Type B medicated feeds** are intended solely for the manufacture of other Type B and/or Type C medicated feeds and contain a substantial quantity of nutrients including vitamins and/or minerals and/or other nutritional ingredients in an amount not less than 25% of the weight. Type B medicated feeds are manufactured by diluting a Type A medicated article or another Type B medicated feed.
- **Type C medicated feeds** are intended for feeding as a complete feed or manufacture of other Type C feeds and may be fed free-choice or as a top dress if approved for such use. Type C medicated feeds are manufactured by diluting a Type A medicated article, or a Type B or Type C medicated feed.

Veterinary Feed Directive

- VFD law enacted in 1996 as part of the Animal Drug Availability Act
  - Serves as an alternative to prescription (Rx) feed
  - Directs that feed containing VFD drug(s) may only be distributed to animal producers under a veterinarian's supervision and written order
  - FDA VFD initial regulation directed that all Type A VFD drugs be designated as Category II (MFML required to handle Type A products), this is no longer the case
- Currently only three VFD drugs
  - Tilmicosin (Pulmitol – swine, beef)
  - Florfenicol (Aquaflor and Nuflor – fish, swine)
  - Avilamycin (Kavault *(new)* – swine)

VFD Process - Overview

1. FDA approval of drug designates VFD marketing status
2. Feed mill provides **"one-time distributor notification"** to FDA of intent to distribute VFD feed (medicated feed containing VFD drug(s)), in accordance with requirements; feed mill obtains VFD drug
   - "One-time distributor notification", but a distributor must notify FDA within 30 days of any change in ownership, business name or business address

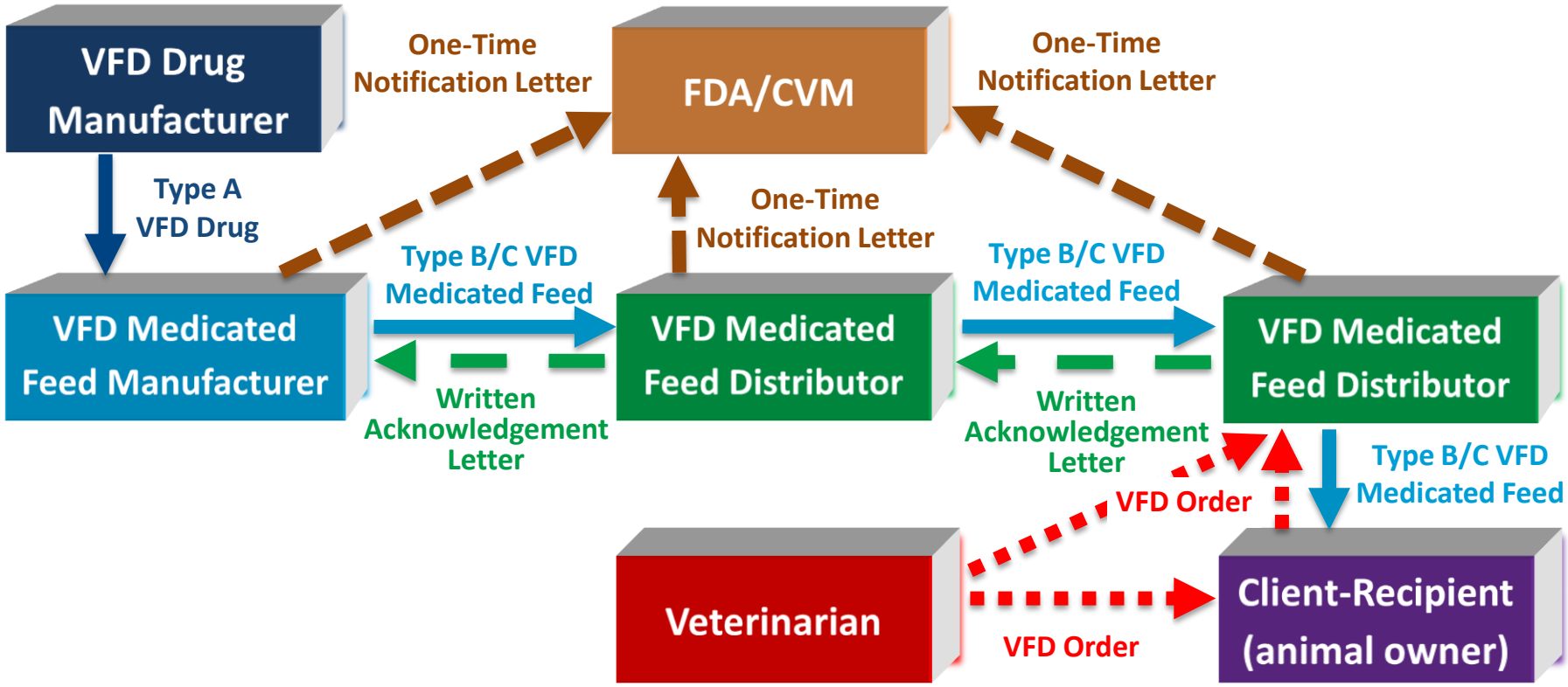
VFD Process - Overview

3. If intermediate distributors (i.e., dealers) are involved in delivering VFD feed then distributors are to, prior to distributing VFD feed:
   - Send **"one-time distributor notifications"** to FDA
   - Provide shipping distributor (consignor) a written **"acknowledgement letter"** affirming that receiving distributor (consignee) will not distribute VFD feed to an animal producer that does not have a lawful VFD order, and will not distribute VFD feed to another distributor without receiving a similar "acknowledgement letter" from that distributor.
     - Consignor and consignee must retain the acknowledgement letter for two years

VFD Process - Overview

4. VFD feed may be floor stocked within the distribution chain so long as required “one-time notification letters” and “acknowledgement letters” are completed
5. Veterinarian writes lawful VFD order for animal producer to use VFD feed for specified animals **before** VFD feed can be delivered to animal producer
6. Lawful VFD order is provided to distributor who may then provide VFD feed to animal producer in accordance with the VFD order

Example VFD Feed Distribution Schematic



Resistance to Antimicrobial Drugs

- **FDA Policy Position (Guidance #209) on Judicious Use of Drugs in Animal Feed – April 13, 2012**
  - Antimicrobial drugs important in human medicine are only to be used for therapeutic uses in food-producing animals
    - Eliminates feed efficiency/production claims
  - Antimicrobial drugs important in human medicine are only to be used with veterinary oversight
    - Dramatically expands use of VFD process in feed industry

Antimicrobial Drugs Impacted

Drugs Transitioning From OTC to VFD Status

Established drug name	Examples of proprietary drug name(s)[$]
chlortetracycline (CTC)	Aureomycin, CLTC, CTC, Chloratet, Chlorachel, ChlorMax, Chlortetracycline, Deracin, Inchlor, Pennchlor, Pfichlor
chlortetracycline/sulfamethazine*	Aureo S, Aureomix S, Pennchlor S
chlortetracycline/sulfamethazine/penicillin*	Aureomix 500, Chlorachel/Pficlor SP, Pennchlor SP, ChlorMax SP
hygromycin B	Hygromix
lincomycin	Lincomix
oxytetracycline (OTC)	Aureomycin, TM, OXTC, Oxytetracycline, Pennox, Terramycin
oxytetracycline/neomycin*	Neo-Oxy, Neo-Terramycin
penicillin[+]	Penicillin, Penicillin G Procaine
sulfadimethoxine/ormetoprim*	Rofenaid, Romet
tylosin	Tylan, Tylosin, Tylovet
tylosin/sulfamethazine*	Tylan Sulfa G, Tylan Plus Sulfa G, Tylosin Plus Sulfamethazine
virginiamycin	Stafac, Virginiamycin, V-Max

Antimicrobial Drugs Impacted

- Among drugs not subject are:
  - Wormers, ionophores, bacitracin methylene disalicylate (BMD) and bambermycin, carbadox, tiamulin

Antimicrobial Drugs Impacted

- **FDA policy implementation timelines -**
  - Drug sponsors currently are changing the marketing status of their products to align with FDA policies
    - 26 drug sponsors, 293 NADA's affected
    - Two week period in Dec. 2016 in which all affected NADA's will be transitioned to VFD marketing status effective Jan. 1, 2017 – ***no more over-the-counter (OTC) use***
  - FDA issued revised VFD regulation on June 3, 2015 intended to streamline and facilitate expanded use of process; revised VFD regulation effective Oct. 1

Resistance to Antimicrobial Drugs

- FDA wants metrics to evaluate success of judicious use policies
  - Drug sponsors already required to report sales data to FDA for various drug classes
  - FDA/USDA/CDC conducted Sept. 30, 2015 public meeting to discuss possible collection of on-farm use data

Revised VFD Regulation – Provisions

- VFD feed may only be fed to animals in accordance with a lawful VFD order
- VFD feed is not to be fed after the expiration date of the VFD order ***(change)***
- VFD feed is to be used in accordance with approved use - no extra label use allowed
- VFD drug **not** automatically classified as Category II, each drug evaluated based upon FDA criteria ***(new)***
  - Medicated feed mill license may or may not be required
- All parties involved with VFD order are to maintain copy of order for 2 years; veterinarian is to keep original
- All required VFD records are to be made available to FDA upon request

*** Red text indicates changes made when revised VFD regulation was issued in June 2015**

Revised VFD Regulation - Provisions

- All labeling and advertising for VFD drugs, combination VFD drugs, and feeds containing VFD drugs or combination VFD drugs are to prominently display cautionary statement: ‘‘***Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.’’ (revised)***
- Veterinarian issuing VFD order is to be licensed to practice veterinary medicine and have a valid veterinarian-client-patient relationship (VCPR) as defined by the State, or, if none, as defined by FDA ***(revised)***
- Veterinarian must issue a written VFD order – no phone orders allowed

VFD Orders – Mandatory Content

- Veterinarian's name, address, telephone number
- ~~Veterinarian license number and state~~
- Client's (animal producer) name, business or home address, telephone number
- Premises at which animals are located
- Date of VFD issuance
- Expiration date of VFD, not to exceed date specified in drug approval, or, if no date specified, no longer than 6 months
- Name of VFD drug(s)
- Species and production class of animals to be fed
- ~~Amount of feed required to treat the animals~~ (However, FDA expects feed distributor to know approximate feed volume associated with VFD order
- Approximate number of animals to be fed prior to expiration of VFD

VFD Orders – Mandatory Content

- Indication for use of VFD feed
- Level of VFD drug in feed and duration of use
- Withdrawal time, specials instructions, etc. in conformance with drug approval
- Number of reorders (refills) authorized
- Statement: ***"Use of feed containing this veterinary feed directive (VFD) drug in a manner other than as directed on the labeling (extra label use) is not permitted." (revised)***
- Affirmation of intent ***(new)*** - VFD drug may:
  - Not be used in combination with any other animal drug, **or**
  - Be used in an approved combination with other specified animal drug(s), **or**
  - Be used in an approved combination with any other animal drug(s)
- Veterinarian's electronic or written signature

VFD Orders – Optional Content

- Veterinarian may include on VFD order:
  - More specific description of location of animals to be fed, i.e., site, pen, barn, tanks, etc.
  - Approximate age range of animals
  - Approximate weight range of animals
  - Other information deemed to be appropriate to identify animals specified in VFD

VFD Orders – Other Details

- Veterinarian to:
  - Send copy of VFD order to feed distributor either directly or through client by hardcopy, facsimile (fax), or by electronic means, i.e., scanned attachment in email
  - Provide copy of VFD order to client
  - **Not** required to send the "original" copy to the distributor ***(new)*** – requirement to receive "original" VFD within 5 days eliminated
- VFD orders created and issued electronically by veterinarians must be done so with electronic systems compliant with 21 CFR part 11, and electronic VFD orders received and electronically stored by distributors and clients must also be compliant with 21 CFR part 11. 21 CFR part 11 does not apply to paper records that are, or have been, transmitted by electronic means (such as facsimile, email attachments, etc.)

VFD Orders – Other Details

- Feed mills or other distributors cannot lawfully distribute VFD feed to animal producer without VFD order
- If VFD order is **not** complete, order is unlawful and VFD feed is **not** to be distributed to animal producer
- Manufacturing distributors of VFD feed are to keep manufacturing records for 1 year in accordance with 21 CFR Part 225

Feed Industry Implementation Issues

- Industry interacting with FDA on time periods to facilitate orderly transition of products to VFD status
- Labeling of medicated feeds that will become VFD feeds prior to Jan. 1, 2017:
  - **"Transitional labeling" on VFD feeds**: "Beginning January 1, 2017, this product will require a veterinary feed directive issued by a licensed veterinarian and will be subject to the following restriction:

    'Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.'"
  - **"Transitional labeling" on products with production indications:** "Effective January 1, 2017, this product will no longer be approved for [insert all production indications as they appear on labeling] which means the use of this product for that [/these] purpose[s] will no longer be legal."

Feed Industry Implementation Issues

- Labels for VFD feeds after Jan. 1, 2017:
  - Product in distribution channels (i.e., no longer under manufacturer's control) either is 1) labeled with "new" final printed label, 2) has a sticker affixed to the product that includes the "new" final label language, or 3) is labeled with "transitional label" statement(s).

Frequently Asked Questions

- ***Question:*** How is the expiration date of a VFD determined and what does it mean to the animal producer and VFD feed distributor?
- ***Answer:*** The expiration date on the VFD specifies the last day the VFD feed can be fed. In other words, a VFD feed or combination VFD feed must not be fed to animals after the expiration date on the VFD.

  In certain cases, FDA determines the expiration date of a VFD as part of the drug approval. In cases where the expiration date is not specified in the drug approval, the expiration date of the VFD must not exceed 6 months after the date of issuance. This provision allows veterinarians, based on their medical judgment and knowledge of the animal production operation, to determine on a case-by-case basis whether the maximum 6-month period is an appropriate expiration date for the VFD, or whether a more limited period is warranted.

  The date of expiration should be calculated by the calendar date, not the number of days. For example, using a 6-month expiration date for a VFD, if the VFD is written on July 10, then the expiration date would be January 10 of the following year.

  During an inspection at a VFD feed manufacturer, FDA will review VFD orders and compare them to manufacturing records. FDA expects that the amount of medicated feed produced and distributed to fill that VFD, whether in one or several batches would be commensurate with the amount of feed necessary for the approximate number of animals the VFD authorizes to be fed. In addition, FDA expects that the feed would be distributed in such a manner that it would be consumed by the specified animals by the expiration date of the VFD.

Frequently Asked Questions

- ***Question:*** If a veterinarian writes a lawful VFD, scans it and sends it to the feed distributor or producer, does the veterinarian have to use a FDA Part 11 (electronic) compliant system?
- ***Answer:*** If the VFD order is created electronically by the veterinarian, then the electronic system used must be Part 11 compliant. A veterinarian may handwrite a VFD order, scan the order, and send via an electronic system that is not Part 11 compliant. Electronic VFD orders received by the feed distributor (i.e., from a Part 11 compliant system or scan of paper VFD order sent as email attachment) may be stored electronically by the feed distributor only if the electronic storage system is Part 11 compliant. Otherwise, the electronic VFD order received by the feed distributor must be printed as a paper copy and stored.

Frequently Asked Questions

- ***Question:*** Can Type B VFD feeds be shipped to an animal producer without a valid VFD? Many producers have grind and mix and need Type B products on hand to use when there's an outbreak after receiving a valid VFD.
- ***Answer:*** When a Type B VFD feed is distributed to a client-recipient (animal producer), the animal producer may manufacture a Type C VFD feed to either feed the VFD feed to his or her own animals and/or further distribute the Type C VFD feed to another distributor or client-recipient. If the Type B VFD feed is being shipped to an animal producer who is not a distributor, the animal producer must provide a VFD for the receipt of the Type B VFD feed from the distributor. If the Type B VFD feed is being shipped to an animal producer who is a distributor that has sent a one-time notification to FDA, the animal producer must supply either an acknowledgment letter or a VFD for the receipt of the Type B VFD feed from the distributor. In all cases the animal producer must have a valid VFD on hand prior to feeding the Type C VFD feed to his or her own animals.

Frequently Asked Questions

- ***Question:*** May a generic drug be used in a VFD feed when the VFD order specifies a pioneer drug (i.e., Tylovet versus Tylan)?
- ***Answer:*** The veterinarian is required to write the name of the VFD drug on the VFD. The veterinarian may choose to write the name of the pioneer or a generic (if available) VFD drug to complete this requirement. The veterinarian may choose to specify that a substitution by the feed manufacturer of either the pioneer or generic VFD drug identified on the form is not allowed. 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.

Frequently Asked Questions

- ***Question:*** Can feed distributed in accordance with one VFD order to multiple premises come from multiple distributors?
- ***Answer:*** FDA's position is that a given VFD order should be associated with only three parties – producer, veterinarian, and a single VFD feed distributor. If the animals that are to receive VFD feed are located in such a manner that the VFD feed will be provided by multiple VFD feed distributors, then FDA states separate VFD orders should be written for each VFD feed distributor.

  However, FDA acknowledges that in special circumstances (e.g., if the VFD feed manufacturer runs out of a VFD drug and the client needs the VFD feed immediately to adhere to a treatment regiment, or the VFD feed distributer experiences mechanical problems that prevent the distribution of the VFD feed), there may be a need for two VFD feed distributors to fill the entire order. If that is the case, the client and the multiple distributors should keep all records documenting the situation so that it is clear that the animals received only the treatment authorized by the VFD.

Frequently Asked Questions

- ***Question:*** What is FDA's definition of a single feed distributor?
- ***Answer:*** Multiple locations are considered to be one distributor if owned by the same corporation. Therefore, one distributor may have multiple locations and it is acceptable for that distributor to fill a VFD from any of its locations.

  However, it is the distributor's responsibility to comply with the applicable requirements including the requirement to distribute a VFD only if it complies with the terms of the VFD and the requirement to keep records of receipt and distribution of all VFD feed for 2 years. Therefore, FDA expects a distributor filling a VFD from multiple locations would have required manufacturing records and VFD distribution records that support that these requirements have been met.

Frequently Asked Questions

- ***Question:*** Are written acknowledgement letters required for intracompany transfers of VFD feeds?
- ***Answer:*** An acknowledgement letter is a letter that a distributor obtains from a consignee-distributor (the distributor receiving the VFD feed) when the distributor ships an animal feed containing a VFD drug in the absence of a valid VFD. The written acknowledgement letter must be provided to the distributor from the consignee-distributor and must affirm: 1) that the consignee-distributor will not ship such VFD feed to an animal production facility that does not have a VFD; 2) that the consignee-distributor will not ship such VFD feed to another distributor without receiving a similar written acknowledgment letter; and 3) that the consignee-distributor has complied with the distributor notification requirements.

  In the case of transfers of VFD feeds between facilities owned by same corporate entity, FDA does not consider the corporate entity to be distributing to another person. Therefore, an acknowledgment letter would not be required for transfers within the same corporate entity.

Frequently Asked Questions

- ***Question:*** Do animal producers that manufacture VFD feed need a valid VFD order to receive a Type A VFD medicated article or Type B or C medicated feed?
- ***Answer:*** If the animal producer is not a distributor, they must have a VFD to receive a Type B or C VFD medicated feed. If the producer is also a distributor (because they will ship feed to another person as defined by the regulation) they can provide either an acknowledgment letter or VFD to their distributor to receive a Type B or C VFD medicated feed.

  If the producer is obtaining a Type A medicated article that is not a VFD feed, the producer does not need to provide an acknowledgment letter or VFD to receive the Type A medicated article. The producer will need a VFD prior to feeding any resulting Type C medicated feed that they mix from the Type A medicated article.

More VFD Information

- **FDA VFD Brochures**
  - Veterinary Feed Directive Producer Requirements
  - Veterinary Feed Directive Requirements for Distributors (Who Manufacture VFD Feed)
  - Veterinary Feed Directive Requirements for Distributors (Who Do Not Manufacture VFD Feed)
  - Veterinary Feed Directive Requirements for Veterinarians
  - Veterinary Feed Directive Requirements for Veterinarians - For Veterinary Students
- FDA Guidance for Industry: Veterinary Feed Directive Regulation Questions and Answers
- FDA FACT SHEET: Veterinary Feed Directive Final Rule and Next Steps