Antibiotic Use in Animal Health

Understanding FDA final VFD ruling
Overview

• Consumer attitudes
• Access to antibiotics
• VFD implementation timeline
• Final VFD rules
• Implementing a VFD
• Electronic VFDs
• Impact on Elanco
Consumer Attitudes
Consumer Attitudes

• Antibiotic use is a public health issue

• Important for animal agriculture to:
  – Be proactive & take a leading role
  – Maintain confidence in food supply
  – Build consumer trust

<table>
<thead>
<tr>
<th>Consumer attitudes*</th>
<th>48%</th>
<th>71%</th>
<th>53%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feel <strong>uncomfortable</strong> about antibiotic use in animal production</td>
<td></td>
<td>Have “<strong>serious or some concerns</strong>” about conventional methods</td>
<td>Frequently wonder if the food they buy is safe</td>
</tr>
</tbody>
</table>

* Source: ml&p research for USFRA, 10/11, n=1,400.
### Consumer Attitudes

<table>
<thead>
<tr>
<th><strong>You say</strong></th>
<th><strong>They hear</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>We use antibiotics to be more efficient</td>
<td>Because you only care about making money</td>
</tr>
<tr>
<td>We use antibiotics to keep animals healthy</td>
<td>You HAVE to use antibiotics because animals are kept in poor conditions</td>
</tr>
<tr>
<td>Regulatory agency reviews have approved antibiotics as safe after rigorous review process</td>
<td>We don’t know if it’s safe for the long term. They’ve been wrong before.</td>
</tr>
<tr>
<td>There are rules that dictate maximum residue limits allowed in animals</td>
<td>How can we be sure ANY residue is safe?</td>
</tr>
<tr>
<td>There is no evidence that use of antibiotics in animals causes resistance in humans</td>
<td>Yeah, right. We’re using so many, that has to be part of the reason.</td>
</tr>
</tbody>
</table>
Access to Antibiotics
Access to Antibiotics

• A public health issue

• Access to effective antibiotics:

  Critical for public health

  Vital for livestock & poultry production

  Essential for animal well-being
Access to Antibiotics

- U.S. Food and Drug Administration:
  - Concerned overuse in animals may reduce effectiveness in humans
  - Is making important changes to antibiotic use in animals
  - Goal is to promote judicious use of antibiotics, protect public health, and help curb the development of antimicrobial resistance
Access to Antibiotics

• FDA issues 3 documents proposing to modify use of medically important antibiotics in food-producing animals
Guidance for Industry #209

• The “what” component

• Establishes “judicious use” principle
  – Limits shared-class antibiotics to therapeutic purposes

• Key: Use of *medically important* antimicrobial drugs in food-producing animals should be limited to:

1. Uses necessary to assure animal health
   - Prevention
   - Control
   - Treatment

2. Uses that include veterinary oversight
   - **Feed:** OTC to VFD
   - **Water:** Rx (*specified in GFI #213*)
Performance Indications (GFI #209)

- Phases out performance indications for certain antibiotics

**Therapeutic uses (still allowed)**

**Disease treatment**
Administration of an antimicrobial to an animal or group of animals that exhibit clinical disease

**Disease control**
Administration of an antimicrobial to an animal or group of animals in which morbidity or mortality has exceeded baselines

**Disease prevention**
Administration of an antimicrobial to an animal or group of animals that are considered to be at risk, but prior to onset of clinical disease

**Performance uses (prohibited)**

**Growth, nutrition, health maintenance**
Administration of an antimicrobial to an animal or group of animals that results in improved performance, e.g., weight gain or feed conversion
# Products Affected vs. Unaffected as Defined by FDA Guidance 152

<table>
<thead>
<tr>
<th>Unaffected</th>
<th>Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Medically Important</strong>&lt;br&gt;Products used exclusively in animals:&lt;br&gt;- Ionophores (Rumensin®)&lt;br&gt;- Polypeptides&lt;br&gt;- Carbadox&lt;br&gt;- Bambermycin&lt;br&gt;- Pleuromutilin</td>
<td><strong>Medically Important</strong>&lt;br&gt;Products deemed “important for human medicine” &amp; used by both animals &amp; humans, such as:&lt;br&gt;- Penicillins&lt;br&gt;- Cephalosporins&lt;br&gt;- Quinolones&lt;br&gt;- Fluoroquinolones&lt;br&gt;- Tetracyclines&lt;br&gt;- Macrolides&lt;br&gt;- Sulfas&lt;br&gt;- Glycopeptides&lt;br&gt;- Others</td>
</tr>
</tbody>
</table>

**Therapeutic uses** — still allowed under veterinary supervision
- Treat animals diagnosed with an illness
- Control the spread of illness in a herd
- Prevent illness in healthy animals when exposure is likely

**Production uses** — Still allowed
- Enhance growth or improve feed efficiency

**Production uses** — No longer allowed
- Enhance growth or improve feed efficiency
**Antibiotics Affected (from GFI #152)**

- “Medically important” for human use

<table>
<thead>
<tr>
<th>Affected</th>
<th>Clindamycin (Lincosamide class)</th>
</tr>
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<tbody>
<tr>
<td>Penicillins</td>
<td></td>
</tr>
<tr>
<td>- Penicillin G</td>
<td></td>
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<tr>
<td>- Penicillin V</td>
<td></td>
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<tr>
<td>Cephalosporins</td>
<td></td>
</tr>
<tr>
<td>Tetracyclines</td>
<td></td>
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<tr>
<td>- Oxytetracyclines</td>
<td></td>
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<tr>
<td>- Chlortetracycline (CTC)</td>
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<tr>
<td>- Aureomycin®</td>
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<tr>
<td>Penicillins</td>
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<tr>
<td>Carbapenems</td>
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<td>Sulfas</td>
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<tr>
<td>- Sulmet</td>
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<td>- ASP, CSP 250</td>
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<tr>
<td>Monobactams</td>
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<tr>
<td>Pyrazinamide</td>
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<tr>
<td>Quinolones</td>
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<tr>
<td>Glycopeptides</td>
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<tr>
<td>Fluoroquinolones</td>
<td></td>
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<tr>
<td>Oxazolidinones</td>
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<tr>
<td>Aminoglycosides - Neomix®</td>
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<tr>
<td>Streptogramins - Stafac®</td>
<td></td>
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<tr>
<td>Macrolides</td>
<td></td>
</tr>
<tr>
<td>- Tylan® (tylosin)</td>
<td></td>
</tr>
<tr>
<td>- Pulmotil® (tilmicosin)</td>
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</table>

**Blue** = shared feed and/or water
Implications

• Food producers aren’t losing all feed-grade antibiotics
• The way they’re used will change
• Key phrase is “medically important”
  – Refers to drugs important for therapeutic use in humans
Guidance for Industry #213

• The “how” component

• Recommendations for voluntarily aligning products with GFI #209

• Advises companies on how to revise:
  – Labeling
  – Promotion

• 2 options to change product labels
  – Voluntarily remove production indications
  – Seek new therapeutic indications at current doses

• Provides 3 years to comply (Dec. 2016)
21 CFR 558

• Proposes changes to VFD process
  – Strives toward less burdensome process
  – Provides greater flexibility for veterinarians to exercise professional training
  – Streamlines FDA administrative procedures
Veterinary Feed Directive (VFD)

• Existing regulatory framework for veterinary oversight of feed-use drugs (21 CFR 558)
• Designates VFDs as medicated feeds needing veterinary oversight
• Limits use of such products to veterinary oversight
• Requires a written statement (form) issued by a veterinarian
  – Authorizes manufacture & use of feed containing a drug
VFD Modernization

• Over a decade since introduction of VFDs
• Significant expansion of feed grade antibiotics requiring VFDs
• Streamlining current process is critical to facilitate transition of marketing status from OTC to VFD
• Goal: clarify requirements associated with veterinary authority & the use of VFD drugs
VFD Modernization

• GFI #209 assigns VFD status to more feed grade antibiotics

• This shift raised concerns around:
  – Limited experience with VFD process
  – Logistical & administrative burden
  – Access to veterinarians
  – Increased cost (producer, vet, feed mills)

• Draft for comment Dec. 2013

• Final rule June 3, 2015
  – Effective Oct. 1, 2015
VFD Modernization

• Because of those concerns, FDA modified VFD process

• Goals of modification
  – Improve the efficiency of the VFD program while continuing to protect public health (human & animal health)
  – Striving toward less burdensome process for all
  – Providing greater flexibility to veterinarians
  – Streamlining FDA administrative procedures
VFD Implementation Timing
Compliance Timeline

• FDA pursuing voluntary compliance
• FDA to evaluate progress 3 years after final publication
  – FDA will consider “further actions” as warranted
Compliance Timeline

• Voluntary approach:
  – Enables companies to efficiently make transitions
  – Provides time to understand policies
  – Enables companies to vary their own timelines
  – Acknowledges a significant undertaking by affected parties

• Approach **not voluntary** for producers or feed manufacturing once labels have been transitioned
Compliance Timeline

• 26 affected companies

• 100% have confirmed intent to engage with written response to FDA
Implementing Changing Antibiotic Regulations (VFD/209/213):

Impact to the industry
Four steps to prepare for on-farm VFD implementation: Producers can get a start making sure their health and feeding programs reflect the new VFD rules with four key steps:

1. Strengthen relationships with your veterinarian and feed supplier, enlisting their help as you review your operation’s current health protocols.

2. Evaluate the various rations and feeds in your operation, and identify the ones that include shared-class antibiotics affected by VFD rules.

3. Work with your veterinarian and feed supplier to update standard operating procedures (SOPs) for antibiotic use, and begin training employees on the revised SOPs.

4. Mark your calendar to review SOPs at regular intervals, perhaps annually, to ensure your health protocols remain up-to-date and effective.
Current Questions

• Valid Client Patient Relationship
  – What is required to establish a valid VCPR?
  – What diagnostics and farm/animal visits are required?

• Electronic Forms
  – Who currently has these forms and who needs them?
  – How easy is it for feed mills to utilize these forms and systems?
What is a Veterinary Feed Directive?

• A VFD is:
  – A written (non-verbal) statement issued by a licensed veterinarian in the course of the veterinarian’s professional practice
    • Orders the use of a VFD drug or combination in/on animal feed
    • Authorizes the client to obtain and use the feed with the VFD drug
    • Allows for treatment of that client’s animals only
Important Definitions

• Client: Refers to the person responsible for the care and feeding of the animals receiving the VFD feed; may be the owner of the animals or a caretaker

• Premises: Physical location of the animals to sufficiently allow for someone to locate the animals
  – Physical address or GPS; may include barn # or pen #
  – A veterinarian may write a VFD that covers animals in multiple locations—provided they can still follow the licensing requirements and practice act
What is required for the VFD to be lawful?

• Issued in compliance with 21 CFR 558.6
  – VFD issued by a veterinarian
  – Licensed to practice veterinary medicine
    • In compliance with all licensing and practice requirements
  – Within the context of a Valid Client Patient Relationship (VCPR)
What is a Valid Client Patient Relationship?

- Federal Definition: 21 CFR 530.3(i)
  - Engage with the client to assume responsibility for making clinical judgments about patient health
  - Have sufficient knowledge of the patient by virtue of examination and/or visits to the facility where they are managed
  - Provide for necessary follow up evaluation or care
### Valid Client Patient Relationship

<table>
<thead>
<tr>
<th>States following Federal VCPR²</th>
<th>States following State VCPR²</th>
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<tbody>
<tr>
<td>• Alabama</td>
<td>• Arizona</td>
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<td>• Alaska</td>
<td>• California</td>
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<td>• Arkansas</td>
<td>• Colorado</td>
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<td>• Connecticut</td>
<td>• Idaho</td>
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<td>• Delaware</td>
<td>• Illinois</td>
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<td>• DC</td>
<td>• Indiana</td>
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<td>• Florida</td>
<td>• Iowa</td>
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<td>• Georgia</td>
<td>• Kentucky</td>
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<td>• Hawaii</td>
<td>• Louisiana</td>
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<td>• Kansas</td>
<td>• Maine</td>
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<td>• Missouri</td>
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<td>• Nevada</td>
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<td>• New Hampshire</td>
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<td>• North Carolina</td>
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<td>• South Carolina</td>
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<tr>
<td></td>
<td>• Utah</td>
</tr>
<tr>
<td></td>
<td>• Wyoming</td>
</tr>
</tbody>
</table>
What documentation is required by the veterinarian?

• The Model practice Act, Federal definition of VCPR (21 CFR 530.3(i)) and most state definitions do not define documentation requirements
  – There are no specific legal requirements for the following:
    • Diagnostic work up
Requirements for a Valid VFD

- Veterinarian’s name, address, telephone #
- Client’s name, address, telephone #
- Premise identification
- Date of VFD issuance
- Expiration Date of VFD
- Name of VFD drug(s)
- Species and Production class of animals
- Approximate # of animals to be treated
- Indication of use
- Dosage and Duration
- Withdrawal time
- Special Instructions and Caution statements
- # of Reorders (if permitted)
- Affirmation of intent for combination VFD drugs as described in 21 CFR 558.6(b)(6)
- Veterinarian’s electronic signature

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.”
Electronic Record Keeping Requirements

• 3 Forms are required to be maintained in records for 2 years
  – Veterinarian—maintains original VFD order (in original format)
  – Distributor of the feed—keeps copy
    • Manufacturing records of VFD feeds need to only be maintained for 1 year
  – Client—keeps copy

• Veterinarian holds the responsibility for ensuring that all parties have received copies of the VFD order
Electronic VFD

• Resources:
  – Global Vet Link: Currently has VFD capabilities with several products
  – Other companies are developing software
    • RxExpress
    • AgData
Hard Copy VFD Form

• VFD form for Elanco products, contact your Elanco representative

• VFD forms for other animal health products, contact the respective company

• Veterinarian can write their own version
  – DO NOT miss any important points
Key Responsibilities of Veterinarians

• License to practice veterinary medicine and in compliance with all laws
• Valid Client Patient Relationship
• Only use VFD in compliance with laws
• Prepare written VFD, with all required information including signature
  – Can include discretionary information if desired
• Must provide distributor and client a copy
• Retain records for 2 years
• Provide VFD orders for inspection if requested by FDA
Key Responsibilities of Distributor

- File one-time notice with FDA of intent to distribute VFD drugs
- Notify FDA within 30 day if change of ownership, business name or address
- Fill a VFD order only if it contains all required information
- Ensure all label and advertising prominently displays the cautionary statement
- Retain VFD orders for 2 years
- Retain records of receipt and distribution of all medicated feed containing a VFD drug for 2 years
- Retain records of VFD manufacturing for 1 year
- If you are an originating distributor, you must obtain an acknowledgement letter from receiving distributor prior to shipping feed—and retain this for 2 years
- Provide VFD orders for inspection if requested by FDA
Two Distribution Forms

1. One Time Notice of distribution:
   – One time notice to FDA on intent to distribute VFD drugs.
   – If the distributor is fulfilling VFD’s they need to submit this form.
   – All distributors of VFD feed must notify FDA before they distribute for the first time. A distributor must also notify FDA within 30 days of a change in ownership, business name, or business address.

2. Acknowledge of distribution: or Acknowledgement letter
   – This is a letter provided from one distributor to another that confirms that they will follow the rules. An “acknowledgement letter” is a written (nonverbal) communication provided to you (consignor) from another distributor (consignee) for distribution of Type A & B feeds.
   – Such letter, provided either in hardcopy or through electronic media, must affirm:
     • that the distributor will not ship such VFD feed to an animal production facility that does not have a VFD;
     • that the distributor will not ship such VFD feed to another distributor without receiving a similar written acknowledgement letter; and
     • that the distributor has complied with the distributor notification requirements. If you issue VFD feed only to a client under a VFD order, you will not need to have an acknowledgement letter.
# Record keeping summary

What record(s) am I required to keep and for how long?

Depending on whom you distribute VFD feed to, the following applies:

<table>
<thead>
<tr>
<th>If you ship VFD feed to</th>
<th>Record</th>
<th>Retained for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clients only</td>
<td>VFD (order)</td>
<td>2 years</td>
</tr>
<tr>
<td>Other distributors only</td>
<td>Acknowledgement letter(s)</td>
<td>2 years</td>
</tr>
<tr>
<td>Both clients and other distributors</td>
<td>VFD (order) and acknowledgement letter(s)</td>
<td>2 years</td>
</tr>
</tbody>
</table>

For the VFD feed you manufacture you also need:

<table>
<thead>
<tr>
<th>Manufacturing Record</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Required per</td>
<td>Retained for</td>
</tr>
<tr>
<td>21 CFR 225 (cGMP)</td>
<td>1 year</td>
</tr>
</tbody>
</table>

Requirements for Distributors (Who Manufacture VFD Feed) 2015
Key Responsibilities of Client

- Ensure only those intended animals covered under the VFD receive the VFD feed
- Feed to those animals prior to the expiration date on the VFD medicated feed
- Provide copy of the VFD order to the feed distributor (if VFD only provided to client)
- Maintain copy of VFD order for 2 years
- Provide VFD orders for inspection if requested by FDA
VFD/209/213 References

2. Requirements for distributors (www.fda.gov/safefeed)
3. Swine Antibiotic Product Classification
4. Veterinary Feed Directive Regulation Update
Four steps to prepare for on-farm VFD implementation: Producers can get a start making sure their health and feeding programs reflect the new VFD rules with four key steps:

1. Strengthen relationships with your veterinarian and feed supplier, enlisting their help as you review your operation’s current health protocols.

2. Evaluate the various rations and feeds in your operation, and identify the ones that include shared-class antibiotics affected by VFD rules.

3. Work with your veterinarian and feed supplier to update standard operating procedures (SOPs) for antibiotic use, and begin training employees on the revised SOPs.

4. Mark your calendar to review SOPs at regular intervals, perhaps annually, to ensure your health protocols remain up-to-date and effective.
Final VFD Rules

June 2015
VFD form requirements

- The veterinarian’s name, address and telephone number
- The client’s name, business or home address and telephone number
- The premises at which the animals specified in the VFD are located
- The date of VFD issuance
- The expiration date of the VFD
- The name of the VFD drug(s)
- The species and production class of animals to be fed the VFD feed
- The approximate number of animals to be fed the VFD feed by the expiration date of the VFD (no longer need to include total pounds of feed)
- The indication for which the VFD is issued
- The level of VFD drug in the feed and duration of use
- The withdrawal time, special instructions and cautionary statements necessary for use of the drug in conformance with the approval
- The number of reorders (refills) authorized, if permitted by the drug approval, conditional approval or index listing
- **The statement**: “Use of feed containing this veterinary feed directive (VFD) drug in a manner other than as directed on the labeling (extralabel use) is not permitted”
- An affirmation of intent for combination VFD drugs as described in 21 CFR 558.6(b)(6)
- The veterinarian’s electronic or written signature
VFD Recordkeeping Requirements

• Maintains record keeping requirement for VFDs for 2 years for veterinarian, client & distributor
  – Vet now maintains original VFD & sends copy to client & distributor

• Permits electronic storage of VFD records
  – If VFD is transmitted electronically, veterinarian no longer required to send hard copy to distributor

• All creation & storage of electronic forms needs to be 21 CFR 11 compliant

• Prohibits verbal issuance of VFD (e.g., by telephone)
VCPR Requirements

• Any veterinarian issuing a VFD be licensed to practice veterinary medicine and operate in compliance with appropriate State-defined veterinarian-client-patient relationship requirements

  - In States where the practice requirements do not require that a VFD be issued within the context of a State-defined VCPR, FDA is requiring that the VFD be issued within the context of a Federally-defined valid VCPR, as outlined in 21 CFR 530.3(i)

• VCPR requires that the veterinarian:

  1. Engage with the client to assume responsibility for making medical judgments about animal health and the need for medical treatment
  2. Have sufficient knowledge of the animal by virtue of examination and/or visits to the facility where animal is managed to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s), and
  3. Provide for any necessary follow-up evaluation or care
VFD Product Classification

• Eliminates current automatic classification of VFD products to Category II
  – Access to Type A Concentration Category II products is restricted to licensed feed mills only
  – Change allows VFD products to be Category 1
    • Allows unlicensed feed manufacturers continued access to Type A medicated articles at concentrations currently used
  – As before, distributor must notify FDA before distributing VFD products for the first time

• Veterinarian is required to write the name of the VFD products on the VFD
  – The vet may choose to write the name of a pioneer or generic product name
  – The vet may choose to specify that a substitution of a product is not allowed; if the vet does not specify, the feed manufacturer may choose to use either
Combination Drugs

• Veterinarian must specify whether the VFD drug:
  – May be used in any approved combination in VFD feed
  – May be used in only specific approved combinations in VFD feeds
  – May not be used in any approved combination in VFD feed

• 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 VFD drug
Extra Label Use is Not Permitted

• “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”
Expiration vs. Duration

- The **expiration** date defines the period of time for which the authorization to feed an animal feed containing a VFD drug is lawful
  - The expiration date on the VFD specifies the last day the VFD feed can be fed to the group of animals
  - The vet should use the expiration date that is specified in the label approval (e.g., 45 days for tilmicosin in beef cattle); where such date is not specified, the vet can write a date up to 6 months

- The **duration** determines the length of time the VFD feed is allowed to be fed to the animals, as specified on the product label (e.g., 14 days for tilmicosin in beef cattle)
Specifying Animals & Location

• The veterinarian should enter information about the location of the animals that would allow someone to locate the animals (e.g., address, GPS)
  – The vet may use his/her discretion to enter additional information (e.g., lot, site, pen) & should work with client to determine whether animals remain at the more specific location until the expiration date of the VFD
  – If a VFD is intended to authorize the use of a VFD feed in a group of animals that are located at more than one physical location, it is acceptable to include multiple specified locations for that group to be fed on the VFD feed by the expiration date on the VFD, provided 1) they can do so in compliance with professional licensing and 2) the feed is supplied by a single feed manufacturer/distributor
Defining Feed Distributors

• On-farm mixers that only manufacture medicated feeds for use in their own animals are not distributors

• On-farm mixers must only be manufacturing VFD feed for their use in their own animals on their own farm, meaning that the ownership of the feed mill, the animals and the animal production facility must be the same and the on-farm mixer must be the person using the VFD feed
  – If an on-farm mixer distributes to another producer, that mixer will be considered a distributor
Distribution Regulation

• Must only fill a VFD if the VFD contains all required information

• One-time notifications
  – *Notice To FDA of Distribution of VFD Feeds* to FDA that you intend to handle/distribute VFD drug-containing medicated feeds
  – *Acknowledgement of Distribution Limitations for VFD Feeds* document stating that the purchasers will sell the VFD feeds only to producers with valid VFD orders or to other distributors for whom they have acknowledgement notices
FDA Enforcement Strategy

- FDA first intends to provide education and training for stakeholders subject to this final rule such as veterinarians, clients (animal producers), feed mill distributors and other distributors

- FDA will then engage in risk-based general surveillance, as well as for-cause inspection assignments
  - FDA intends to use information such as history of VFD use and the volume of VFD feed being produced to focus inspectional resources within the industry based on risk
  - FDA anticipates that it will utilize various sources for obtaining such information including FDA food and drug registration information, feed mill licensing information, the VFD distributor notifications FDA receives, and VFD distribution records maintained by drug sponsors
Notice To FDA of Distribution of VFD Feeds

I/we hereby notify the Food and Drug Administration that I/we have begun distributing VFD feeds.

______________________________
Signature

______________________________
Name of firm or individual

______________________________
Business Address

______________________________
Date

This notice should be sent to: Center for Veterinary Medicine (HFV-226)
7500 Standish Place
Rockville, MD 20855

Acknowledgment of Distribution for VFD Feeds

I/we hereby acknowledge that, as required by federal law, I/we shall distribute VFD feeds received by me/us from;

______________________________
(Name and address of shipper)

As follows:

1. To an animal production facility, if the owner or operator of that facility provides me/us with a copy of a veterinary feed directive covering the quantity of feed involved and the animal production facility to which the feed is being distributed; or

2. To another person for further distribution, if that person provides me/us with a written acknowledgment similar to this acknowledgment.

______________________________
Signature

______________________________
Name of firm or individual

______________________________
Street Address

______________________________
Date

______________________________
By signing this Acknowledgment of Distribution I/we affirm that I/we have notified FDA of our intent to distribute VFD medications.
Pulmotil® (tilmicosin) Swine Veterinary Feed Directive

Also to be included:
- Name of VFD drug
- Indication
- Level of VFD drug in feed & duration
- Withdrawal time, special instructions & cautionary statements
- Affirmation of intent for combination drugs

No longer requires license # & state
Expiration date length dependent on product label
Implementing a VFD (Swine)
Current Pulmotil Swine VFD Form

Pulmotil® (timolol) Swine Veterinary Feed Directive

USBBUMUL01265

Client: 
Address: 

Veterinarian: 
Address: 

Phone #: 
Fax #: 

Special instructions: 

Swine to be treated (number and location): 

Mix into Type C medicated feed to provide: 

Type C feed at 0.5% of diet: 

Type C feed at 1% of diet: 

Type C feed at 1.5% of diet: 

Amount of feed (Type C feed): 

VFD expiration date: 

Month/Day/Year (not to exceed 90 days): 

License # or registration #: 

Date of issuance: 

July 1, 2015

FDA:

Drug name: Pulmotil

Veterinarian:

Signature:

*tVFD form expected to change in late 2015.*
Caution Statement

- Each product approved under the VFD regulations includes the following caution:

Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.
Distribution of VFD form

- Original form must be stored by veterinarian

White Copy — Veterinarian

Canary Copy — Client

Pink Copy — Supplier

Note: color-coded forms are Elanco-only forms.
Electronic VFDs
FeedLINK Features – eVFD

• Ease the burden of paperwork
  – Spend less time creating VFDs and reduce manual inaccuracies by creating electronic VFD prescriptions

• Provide a reliable source of documentation
  – Maintain VFD compliancy easily with a secure, web-based software solution
  – FeedLINK retains veterinarians’ eVFDs for the required two-year period

• Enhance communication with stakeholders
  – Automatically send VFDs to feed suppliers and producers upon creation
  – Renew VFD orders in seconds with an email notification linking to the pre-populated VFD

• 21 CFR Part 11 Compliant
Visit globalvetlink.com to get started
Click “Login/Sign Up” in the top-right corner to create a new account or to sign in
Click “eVFD”, and then provide your business name and other pertinent business information.
To create an eVFD, first either ‘find by name’ a previous producer who you intend to create an eVFD for or click the “+” to create a new contact.

Always use the TAB button on your keyboard to navigate the site; pressing ENTER will attempt to submit an incomplete eVFD.
Contact GlobalVetLINK

• Sales team: (515) 817-5703
  – For training and sales support with new clients

• Technical support: (515) 817-5704
  – To set up accounts, add feed suppliers, or other technical system support

• Monday-Friday, 8 a.m.-5 p.m. (CST)

www.globalvetlink.com
Elanco’s Position

• For medically important antimicrobials, Elanco supports:
  – The responsible use for therapeutic purposes with veterinarian oversight
  – Voluntarily narrowing use to therapeutic uses only
  – No longer promoting use for performance purposes
  – Transitioning label indications to therapeutic uses only
Elanco’s Position

• Invest in innovation

Pursue advances & treatments that lessen reliance on antibiotics

Seek new therapeutic indications for treatment, control & prevention of diseases

Support use of antimicrobials used only in animals for growth & performance (where permitted)

Provide services that help verify & validate responsible product use
How to use Tylan® premix for swine

<table>
<thead>
<tr>
<th>For ileitis control:</th>
<th>Recommendation:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feed Tylan at 100 g/ton for at least 3 weeks, followed by 40 g/ton to market weight.</td>
<td>Begin feeding Tylan at 12-15 weeks of age or 3 weeks prior to seroconversion,¹ ² because gross or microscopic lesions appear well in advance of seroconversion/disease.</td>
</tr>
</tbody>
</table>

* No withdrawal required when fed according to label directions.

How to use Tylan® premix for poultry

- For increased rate of weight gain and improved feed efficiency in broilers (indication to be withdrawn), feed Tylan at
  - Tylan 40 per ton of Type C Feed: 0.1 to 1.25 lbs.
  - Tylosin per ton of Type C Feed: 4 to 50 g
- Feed continuously as the sole ration
- To aid in the control of chronic respiratory disease associated with Mycoplasma gallisepticum in broilers
  - Tylan 40 per ton of Type C Feed: 20 to 25 lbs.
  - Tylosin per ton of Type C Feed: 800 to 1,000 g* ¹
- To aid in the control of chronic respiratory disease associated with Mycoplasma gallisepticum in replacement chickens
  - 1,000 g/ton
- Tylan requires a 5-day withdrawal period before slaughter when fed at 800 to 1,000 g/ton.

* No withdrawal required when fed according to label directions.

How to use Tylan® Premix for beef cattle

- For reduction of incidence of liver abscesses associated with Fusobacterium necrophorum and Arcanobacterium pyogenes:
  - Feed tylosin continuously at 8-10 g/ton (90% DM) to deliver 60-90 mg/hd/d.

Hygromix® directions for use

- For use as an aid in the control of parasite infections in chickens associated with Ascaris galli, Heterakis gallinae and Capillaria obsignata.
- Mix 1.0-1.5 lbs. Hygromix 8 per ton of Type C medicated feed for 8-12 g of hygromycin B per ton.
- Feeds containing Hygromix must be withdrawn 3 days prior to slaughter.

The labels contain complete use information, including cautions and warnings.
Always read, understand and follow the label and use directions.
Pulmotil® directions for use for cattle

- Feeds containing tilmicosin must be withdrawn 28 days prior to slaughter.
- **CAUTION**: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian’s professional practice.
- **For the control of Bovine Respiratory Disease (BRD) in groups of beef and non-lactating dairy cattle, where active BRD has been diagnosed in at least 10% of the animals in the group**: Feed continuously for a single, 14-day period at 568 to 757 g/ton of tilmicosin (100% DM basis) in a Type C medicated feed as the sole ration to provide 12.5 mg/kg of body weight/hd/d.

Pulmotil® directions for use for swine

- Feeds containing tilmicosin must be withdrawn 7 days prior to slaughter.
- **CAUTION**: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice.
- **For the control of swine respiratory disease associated with Actinobacillus pleuropneumoniae and Pasteurella multocida**, feed continuously at 181–363 g/ton for a 21-day period, beginning approximately 7 days before an anticipated outbreak.

The labels contain complete use information, including cautions and warnings. Always read, understand and follow the label and use directions.
Tylosin Tartrate

Equivalent to 100 g (3.53 oz) tylosin base

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. For oral use in chickens, turkeys, swine, and honey bees. Macrolide Antibiotic, NADA 13-076, approved by FDA.

Indications:

- **Chickens:** For the control of mortality caused by necrotic enteritis (NE) associated with *Campylobacter jejuni* in broiler chickens. As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* in breeder and replacement chickens. For the control of CRD associated with *Mycoplasma gallisepticum* at the time of vaccination or other stress in chickens. For the control of CRD associated with *Mycoplasma synoviae* in broiler chickens.
- **Turkeys:** For the reduction in severity of effects of infectious enteritis associated with *Mycoplasma gallisepticum*.
- **Swine:** For the treatment and control of swine dysentery (SD) associated with *Brachyspira hyodysenteriae*. For the treatment and control of SD associated with *Brachyspira hyodysenteriae* when followed immediately by Tylosin A medicated article in feed.
- **Honey Bees:** For the control of *American Foulbrood* (Paenibacillus larvae).

Ingredients:

Tylosin (is tylosin base).......................................................... 100 g

Dosages:

- **Chickens:**
  - NE Indications: 851 to 1,419 mg/gallon (225 to 375 ppm) in drinking water.
  - CRD Indications: 2,020 mg/gallon (525 ppm) in drinking water.
- **Turkeys:** 2,020 mg/gallon (525 ppm) in drinking water.
- **Swine:** 250 mg/gallon (64 ppm) in drinking water.
- **Honey Bees:** 200 mg/gallon in feeders/powdered sugar.

Mixing Directions for Medicating Drinking Water:

Always add the water to the powder. Do not pour the powder into the water. Prepare a fresh Tylosin Soluble solution every three days. When mixing and handling tylosin, use protective clothing and impervious gloves. If using a water medicating pump, see table below, otherwise mix as follows:

- To assure thorough dissolution, first place the contents of one jar in a mixing container and add one gallon of water (3765 mL) to the powder to make a concentrated solution. To make medicated drinking water containing 250 mg/gallon (64 ppm), mix this concentrated solution with water to make 400 gallons (1514 liters) of medicated drinking water. To make medicated drinking water containing 851 to 1,419 mg/gallon (225 to 375 ppm), mix this concentrated solution with water to make from 117 gallons + 51 ounces (444 liters to 70 gallons + 64 ounces) of medicated drinking water. To make medicated drinking water containing 2,020 mg/gallon (525 ppm), mix this concentrated solution with water to make 50 gallons (189 liters) of medicated drinking water.

Mixing Directions for Water Medicating Pump (1:120 inclusion):

<table>
<thead>
<tr>
<th>Desired Concentration</th>
<th>Jars of Tylosin Soluble</th>
<th>Volume of Water to Make Stock Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg/gallon (60 ppm)</td>
<td>1</td>
<td>3 gallons + 13 ounces</td>
</tr>
<tr>
<td>655 mg/gallon (225 ppm)</td>
<td>5</td>
<td>4 gallons + 71 ounces</td>
</tr>
<tr>
<td>1,419 mg/gallon (525 ppm)</td>
<td>10</td>
<td>5 gallons + 6 ounces</td>
</tr>
<tr>
<td>2,020 mg/gallon (525 ppm)</td>
<td>10</td>
<td>3 gallons + 115 ounces</td>
</tr>
</tbody>
</table>

*This table applies only if the water medicating pump is set to deliver 1 ounce of stock solution per gallon of drinking water.

Mixing Directions for use in Honey Bees: Mix 200 mg tylosin in 20 g confections/powdered sugar. Use immediately.

Directions for Use:

- **Chickens:** NE Indication: Administer medicated drinking water for a single five-day period in broiler chickens. To assure both food safety and responsible antimicrobial drug use in chickens: 1) Use in flocks exhibiting signs or a necrotic enteritis outbreak, for example, increased mortality and lesions characteristic of necrotic enteritis upon necropsy. 2) Administer the full dose and dosing regimen once medication is initiated. 3) Use of Tylosin Soluble or another macrolide is not advised if additional therapy is needed beyond the original course of medication. CRD Indications: Administer medicated drinking water for three days; however, medicated water may be administered for one to five days depending upon severity of infection. Treated chickens must consume enough medicated water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.
- **Turkeys:** Administer medicated drinking water for three days; however, medicated water may be administered for one to five days depending upon severity of infection. Treated turkeys must consume enough medicated water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.
- **Swine:** SD Indication: Administer medicated drinking water for 3 to 10 days, depending upon severity of infection. Alternatively, administer medicated drinking water for 3 to 10 days, followed by 40 to 100 g tylosin per ton of complete feed (Type C medicated feed manufactured from Tylosin Type A medicated article) for 2 to 6 weeks. Only medicated water should be available to swine while medicating with Tylosin Soluble. PPE Indication: Administer medicated drinking water for 3 to 10 days, followed by 40 to 100 g tylosin per ton of complete feed (Type C medicated feed manufactured from Tylosin Type A medicated article) for 2 to 6 weeks. Only medicated water should be available to swine while medicating with Tylosin Soluble.
- **Honey Bees:** Colonies: Administer three treatments of medicated confections/powdered sugar once weekly for 3 weeks. The 200 mg dose is applied dusted over the top bars of the brood chamber.

Warnings:

- **User Safety Warnings:** Not for human use. Keep out of reach of children. Avoid contact with human skin. Exposure to tylosin may cause a rash.
- **Residue Warnings:** Chickens must not be slaughtered for food within 24 hours after treatment. Do not use in layers producing eggs for human consumption. Turkeys must not be slaughtered for food within five days after treatment. Swine must not be slaughtered for food within 48 hours after treatment. Honey bees: The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins. To avoid contamination of production honey, complete treatments at least 4 weeks prior to main honey flow.

Manufactured:

- **Elanco Animal Health**
- **A Division of Eli Lilly and Company**
- **Indianapolis, IN 46205, USA**
- **Product of the United Kingdom**
- **Avoid Moisture**

Restricted Drug (California) – Use Only as Directed.

To report suspected adverse events, for technical assistance, or to obtain a Material Safety Data Sheet (MSDS), call 1-800-428-4441. Elanco, Tylosin and the diagonal bars are trademarks owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

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