Antibiotic Use in Animal Health

Understanding FDA’s final VFD ruling

Montana Nutrition Conference 2016
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Beef Technical Consultant
Overview

• Consumer Attitudes
• Access to Antibiotics
• Veterinary Feed Directive (VFD) Implementation Timeline
• Final VFD Rules
• Implementing a VFD
• Electronic VFDs
• Impact on Elanco
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

## Consumer Attitudes

<table>
<thead>
<tr>
<th>You say</th>
<th>They hear</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 that 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 issued three 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 production 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, including 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></td>
<td><strong>Medically Important</strong></td>
</tr>
<tr>
<td>Products used exclusively in animals or deemed “non-medically important” if used by both humans &amp; animals:</td>
<td>Products deemed “important for human medicine” &amp; used by both animals &amp; humans, such as:</td>
</tr>
<tr>
<td>- Ionophores (Rumensin®)</td>
<td>- Penicillins</td>
</tr>
<tr>
<td>- Polypeptides</td>
<td>- Cephalosporins</td>
</tr>
<tr>
<td>- Carbadox</td>
<td>- Quinolones</td>
</tr>
<tr>
<td>- Bambermycin</td>
<td>- Fluoroquinolones</td>
</tr>
<tr>
<td>- Pleuromutilin</td>
<td>- Tetracyclines</td>
</tr>
<tr>
<td><strong>Production uses</strong> — Still allowed</td>
<td><strong>Production uses</strong> — No longer allowed</td>
</tr>
<tr>
<td>Enhance growth or improve feed efficiency</td>
<td>Enhance growth or improve feed efficiency</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
Antibiotics Affected (from GFI #152)

- “Medically important” for human use

<table>
<thead>
<tr>
<th>Affected</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins</td>
<td>Tetracyclines</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>- Penicillin G</td>
<td>- Oxytetracyclines</td>
<td>(Lincosamide class)</td>
</tr>
<tr>
<td>- Penicillin V</td>
<td>- Chlortetracycline (CTC)</td>
<td>- Lincomix®</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Tetracyclines</td>
<td>Polymyxin B</td>
</tr>
<tr>
<td></td>
<td>- Oxytetracyclines</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Chlortetracycline (CTC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Aureomycin®</td>
<td></td>
</tr>
<tr>
<td>Carbapenems</td>
<td>Trimethoprim/sulfamethoxazole</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monobactams</td>
<td>Sulfas</td>
<td>Metronidazole</td>
</tr>
<tr>
<td></td>
<td>- Sulmet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ASP, CSP 250</td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td>Pyrazinamide</td>
<td>Rifamycins</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Glycopeptides</td>
<td>Isoniazid</td>
</tr>
<tr>
<td></td>
<td>Oxazolidinones</td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Streptogramins</td>
<td>Macrolides</td>
</tr>
<tr>
<td>- Neomix®</td>
<td>- Stafac®</td>
<td>- Tylan® (tylosin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pulmotil® (tilmicosin)</td>
</tr>
</tbody>
</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
- Two options to change product labels
  - Voluntarily remove production indications
  - Seek new therapeutic indications at current doses
- Provides three years to comply (Dec. 2016)
21 CFR 558 & 21 CFR 514

- VFD process changes:
  - Strive toward less burdensome process
  - Provide greater flexibility for veterinarians to exercise professional training
  - Streamline FDA administrative procedures
Veterinary Feed Directive

- 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 three years after final publication
  - Guidance for Industry #213 finalized Dec. 2013
  - FDA will consider further actions as warranted

**Q2, 2012:**
209/213/VFD published

**Q3, 2012:**
Docket comments due

**Q2, 2013:**
Public hearings

**Dec. 11, 2013:**
Release of final 213 & draft VFD rule

**Q1, 2014:**
Sponsors must notify CVM of intent to engage

**June 3, 2015:**
Release of final VFD rule

**Oct. 1, 2015:**
Final VFD rule went into effect

**Jan. 1, 2017:**
Implementation complete
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 manufacturers once labels have been transitioned
Compliance Timeline

• 26 affected companies
• 100% have confirmed intent to engage with written response to FDA
Final VFD Rules

October 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 (extra-label 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 Record Keeping Requirements

• Maintains record keeping requirement for VFDs for two 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 must be licensed to practice veterinary medicine and operate in compliance with appropriate State-defined veterinarian-client-patient relationship (VCPR) 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 after date of issuance.

- 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 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 manufacture medicated feeds only for use in their own animals are not distributors.

• On-farm mixers must be manufacturing VFD feed only 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 there is a chance an on-farm mixer might distribute to another producer, he/she should be aware they would then be considered a distributor bearing the same notification requirements.
Distribution Regulation: Authorized Shipments
(All VFD and/or shipping records must be maintained for two years)

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

Utilizing an AOD (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
• Maintain documentation
Notice to FDA of Distribution of VFD Feeds

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

Signature

Name of responsible party (please print or type)

Name of Firm or Individual

Business Address

Site address if different from above

City/State/Zip

Date

Send this form to:

Division of Animal Feeds (HFV-226)
Center for Veterinary Medicine
Food & Drug Administration
7500 Standish Place
Rockville, MD 20855
FAX 301/594-1812

Send this form to each of your firm's suppliers of VFD products.
Acknowledgement Of Distribution Limitations 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 feed supplier] only 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 (VFD) 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 acknowledgement similar to this acknowledgement.

__________________________
Signature

__________________________
Name of Firm or Individual

__________________________
Business Address

__________________________
City/State/Zip

__________________________
Date

Send this form to each of your firm's suppliers of VFD products.
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
VFD: Our Cooperation Will Be Crucial For Our Mutual Customers
Implementing a VFD (Cattle)
## Pulmotil Cattle VFD Form (Oct. 2015)

### Pulmotil® (tilmicosin) Veterinary Feed Directive for use in Cattle

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Client</td>
<td></td>
</tr>
<tr>
<td>Business or Home</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Phone</td>
<td></td>
</tr>
<tr>
<td>Approximate number of cattle</td>
<td></td>
</tr>
<tr>
<td>Special instructions</td>
<td></td>
</tr>
<tr>
<td>Location of animals</td>
<td></td>
</tr>
</tbody>
</table>

**Indications:** For the control of bovine respiratory disease (BRD) associated with *Mycobacterium haemolytica*, *Pasteurella multocida*, and *Hemophilus somni* 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.

**Dosage:** __________ g/ton (648 to 757 g/ton)  
**Duration:** 14 Days

**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.**

**Caution:** Do not allow horses or other equines access to foods containing tilmicosin. The safety of tilmicosin has not been established in cattle intended for breeding purposes.

To assure both food safety and responsible use in cattle, the treatment of cattle with this medicated feed is required to be initiated within the first 15 days of the production period. The treatment should not occur coincidentally with or following administration of an injectable macrolide, or within 60 days following administration of a non-macrolide injectable BVD therapy.

Use only in cattle in confinement for slaughter. Tilmicosin medicated feed has not been evaluated in cattle with severe clinical disease. Cattle with severe clinical illness should be evaluated for individual treatment with an alternative non-macrolide therapy.

The expiration date for a tilmicosin Veterinary Feed Directive (VFD) for cattle must not exceed 45 days from the time of issuance. VFDs for tilmicosin prophylaxis shall not be refilled.

**Complete Type C medicated feeds containing tilmicosin should not be palatable. Do not use in any feeds containing pentolite, eustomin, rea, or conformation hols. Derivatives, conformational, or conformational in feeds may affect the efficacy of tilmicosin.**

**Residue Warning:** Cattle intended for human consumption must not be slaughtered within 96 hours of the last treatment with this drug product. This drug product is not approved for use in female dairy cattle 20 months of age or older. Use in these cattle may cause drug residues in milk. This drug product is not approved for use in calves intended to be processed for veal. A withdrawal period has not been established in pre-nursing calves.

**Combination Feeding with Other Drugs (select one):**
- This 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 judged combinable non-macrolide medicated feeds that contain the VFD drug(s) as a component of the approved combination.
- This VFD authorizes the use of the VFD drug(s) cited in this order in any FDA-approved, conditionally approved, or judged combinable non-macrolide medicated feeds that contain the VFD drug(s) as a component.

**VFD Issuance Date:** __________  
**VFD Expiration Date:** __________  
**Veterinarian’s signature:**

For technical service call: 1-800-425-4441  
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USBBUMUL01265(2)
Filling Out a VFD Form (Cattle)

Requires approx. # of animals & dosage; does NOT require calculation of lbs of feed
Filling Out a VFD Form (Cattle)

- **Combination Feeding with Other Drugs (select one):**
  - This 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 medicated feed that contains the VFD drug(s) as a component.
    
    ___________________________ (list approved combination)

  - This VFD authorizes the use of the VFD drug(s) cited in this order in **any** FDA-approved, conditionally approved, or indexed combination(s) in medicated feed that contains the VFD drug(s) as a component.

- **VFD Issuance Date:** ________________
- **VFD Expiration Date:** ________________
  
  (Month/Day/Year)
  
  (Not to exceed 45 days from issuance date)

- **Veterinarian’s signature:** __________________________

---

**For technical service call:** 1-800-428-4441

NADA 141 - 064, Approved by the FDA.

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**White Copy (Original) – Veterinarian**

**Canary Copy – Client**

**Pink Copy – Distributor**

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**Must provide approval for any combination drugs**

**No longer requires vet license number**
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

Note: color-coded forms are Elanco-only forms.
Implementing a VFD (Swine)
Pulmotil Swine VFD Form (Oct. 2015)
Filling Out a VFD Form (Swine)

Requires approx. # of animals & dosage; does NOT require calculation of lbs of feed.
Filling Out a VFD Form (Swine)

Must provide approval for any combination drugs

No longer requires vet license number
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 (Original) – Veterinarian | Canary Copy – Client | Pink Copy – Distributor |

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
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.

Select the dropdown to update your account profile.

Add license numbers, phone numbers, etc.
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
Additional eVFD Resources

• RxExpress
  – Customer Service: 888-633-4030 or 720-837-4278
  – www.newplanettek.com

• AGDATA
  – Phil Lawler, 502-857-0103, Phil.Lawler@agdata.net
Impact on Elanco
Impact on Elanco

• Elanco publicly supports FDA initiatives:
  – Aligns with Elanco global antibiotic policy
  – Expedites VFD modernization
  – Protects long-term access
  – Helps support public health

• Elanco will support initiatives via:
  – Resources
  – Leadership
  – Commitment
Impact on Elanco

• In USA, Tylan® premix & Hygromix® use:
  – Will be under the VFD process/require veterinarian oversight
  – Transition labels for Tylan will be placed on bags beginning in May 2016 & will be effective beyond Jan. 1, 2017

• Hygromix:
  – Moves to VFD status but claims would remain

• Tylan Soluble (tylosin tartrate):
  – Moved to a prescription status
Impact on Elanco

• Tylan premix for swine
  – Claims for weight gain & feed efficiency withdrawn
  – Claims for swine dysentery & ileitis remain (requires VFD)

• Tylan premix for cattle*
  – Claim for reduction of liver abscesses remains (requires VFD)

• Tylan premix for poultry
  – High-dose use for CRD remains
  – Lower-dose use (most common) for weight gain & feed efficiency withdrawn (effectively eliminates Tylan use in poultry)

*See slide 68 for complete indications.
Impact on Elanco

• Pulmotil (tilmicosin)
  – Continues to be a VFD product
Impact on Elanco

- Ionophores remain unaffected
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
# Elanco’s “Rules of Engagement”

<table>
<thead>
<tr>
<th>Subject</th>
<th>Policy highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal governance</td>
<td>Provide oversight by global antimicrobials team</td>
</tr>
<tr>
<td>Product registrations</td>
<td>Seek therapeutic indications for all antimicrobial classes</td>
</tr>
<tr>
<td></td>
<td>Support use of animal-only products for growth/performance</td>
</tr>
<tr>
<td>New product development</td>
<td>Support existing products</td>
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<tr>
<td></td>
<td>Pursue appropriate extended uses</td>
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<tr>
<td></td>
<td>Seek new platforms for animal care</td>
</tr>
<tr>
<td>Professional oversight</td>
<td>Support oversight of antibiotic use by veterinarians</td>
</tr>
<tr>
<td>Risk-based assessment</td>
<td>Review products, resistance monitoring, data, research, etc., to protect human &amp; animal health</td>
</tr>
<tr>
<td>Partnerships</td>
<td>Collaborate with industry groups &amp; leaders</td>
</tr>
</tbody>
</table>
The labels contain complete use information, including cautions and warnings. Always read, understand and follow the label and use directions.

### How to use Tylan® premix for swine

<table>
<thead>
<tr>
<th>For control of porcine proliferative enteropathies (PPE, ileitis) associated with <em>Lawsonia intracellularis</em></th>
<th>Recommendation:</th>
</tr>
</thead>
</table>
| Feed Tylan at 100 g/ton for at least 3 weeks, followed by 40 g/ton to market weight.  
* No withdrawal required when fed according to label directions | 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. |

### How to use Tylan® premix for poultry

- 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*  
- To aid in the control of chronic respiratory disease associated with *Mycoplasma gallisepticum* in replacement chickens
  - 1,000 g/ton  
- Feed continuously as the sole ration  
- **Tylan requires a 5-day withdrawal period before slaughter when fed at 800 to 1,000 g/ton.**

### 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.  
- * No withdrawal required when fed according to label directions.
**Pulmotil® directions for use for cattle**

- For the control of Bovine Respiratory Disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* 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/day.

**Pulmotil® directions for use for swine**

- 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.

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**Cattle — Important Safety Information**

- **CAUTION:** Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.
- Cattle intended for human consumption must not be slaughtered within 28 days of the last treatment.
- To assure both food safety and responsible use, treatment must be initiated within the first 45 days of the production period. The treatment should not occur concurrent with or following administration of an injectable macrolide, or within 3 days following administration of a non-macrolide injectable BRD therapy.
- VFD expiration date must not exceed 45 days from the time of issuance. VFDs shall not be refilled.
- Use only in cattle fed in confinement for slaughter.
- Cattle with severe clinical illness should be evaluated for individual treatment with an alternative non-macrolide therapy.
- Do not use in female dairy cattle 20 months of age or older or in veal calves.
- Safety has not been established for cattle intended for breeding.
- Do not allow horses or other equines access to feeds containing tilmicosin.

**Swine — Important Safety Information**

- **CAUTION:** Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.
- Swine intended for human consumption must not be slaughtered within 7 days of the last treatment.
- Do not feed more than 21 days during each phase of production without ceasing administration for reevaluation of antimicrobial use by a licensed veterinarian before re-initiating a further course of therapy with an appropriate antimicrobial.
- VFD expiration date must not exceed 90 days from the time of issuance. VFDs shall not be refilled.
- Safety has not been established in male swine intended for breeding.
- Do not allow horses or other equines access to feeds containing tilmicosin.

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 13-078, approved by FDA

Indications

Chickens: For the control of mortality caused by mycoplasma enteritidis (ME) associated with Chlamydophila psittaci in broiler chickens. As an aid in the treatment of chlamydial respiratory disease (CRD) associated with Mycoplasma gallisepticum in broiler 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 anaplasmosis associated with Acholeplasma laidlawii.

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 Type A medicated article in feed. For the control of porcine proliferative enteropathy (PPE, Porc). For the treatment of respiratory disease (RD) associated with Mycoplasma haemolytica when followed immediately by Tylosin Type A medicated article in feed.

Honey Bees: For the control of American Foulbrood (Paenibacillus larvae).

Ingredients

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

Dosage and Administration

Dosage:

Chickens:

NE indication: 851 to 1,419 mg/gallon (225 to 375 ppm) in drinking water.

CRD indications: 2,000 mg/gallon (500 ppm) in drinking water.

Turkeys: 2,000 mg/gallon (500 ppm) in drinking water.

Swine: 250 mg/gallon (60 ppm) in drinking water.

Honey Bees: 200 mg colonyst in contaminated powdered sugar.

Mixing Directions for Medicating Drinking Water:

Always add the drug to the water. 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 (3.78 L) to the powder to make a concentrated solution. To make medicated drinking water containing 250 mg/gallon (60 ppm), mix this concentrated solution with water to make 400 gallons (1,514 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 117 gallons + 51 gallons (444 liters + 212 liters) of medicated drinking water. To make medicated drinking water containing 2,000 mg/gallon (500 ppm), mix this concentrated solution with water to make 50 gallons (189 liters) of medicated drinking water.

Mixing Directions for Water Medicating Pump (1:128 inclusion):*:

<table>
<thead>
<tr>
<th>Desired Concentration in Drinking Water</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>851 mg/gallon (225 ppm)</td>
<td>5</td>
<td>4 gallons + 77 ounces</td>
</tr>
<tr>
<td>1,419 mg/gallon (375 ppm)</td>
<td>9</td>
<td>5 gallons + 0 ounces</td>
</tr>
<tr>
<td>2,000 mg/gallon (500 ppm)</td>
<td>10</td>
<td>3 gallons + 115 ounces</td>
</tr>
</tbody>
</table>

*This table supplies 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 confectons/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 all birds receive the intended medication, only medicated water should be available. These practices should be followed to assure both food safety and responsible antimicrobial drug use in chickens: 1) Use in flock exhibiting signs of a necrobiotic enteritis outbreak, for example, increased mortality and lesions characteristic of necrobiotic enteritis upon necropsy; 2) Administer the full dose and dosing regimen since medicated water is continued; 3) Use of Tylosol or another macrolide is not advised. If additional therapy is needed beyond the original course of medication. CRD indication: 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 two to five days depending upon severity of infection. Treated turkeys must consume enough medicated water to provide 60 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 Tylosol. 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 be medicated for swine while medicating with Tylosol. Honey Bee Colonies: Administer these treatments of medicated confectons/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 honey. Complete treatments at least 4 weeks prior to main honey flow.

Manufactured For:

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 1-800-428-6441. Elanco, Tylosol and the diamond bar are trademarks owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

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Antibiotic Use in Animal Health

Understanding FDA’s final VFD ruling

QUESTIONS?