Preparing for Upcoming Changes to the Veterinary Feed Directive (VFD)

Why does FDA care about these drugs?

- Appropriate therapeutic use
- Toxicity
- Drug residues
- Antimicrobial resistance to drugs used in human medicine
  - 2014 U. S. usage (sales) data: 62% of livestock antibiotic usage (sales) was "medically important antimicrobials"
  - 70% of this 62% was tetracyclines

History of VFD

Guidance #213: December 2013
- Builds on GFI #209: intended to improve the efficiency & user-friendliness of the VFD rule
- Outlines an implementation timeline for the OTC to VFD conversion (per GFI #209)

Second Rule (The "Final" Rule): June 2015
- Further revisions to recommendations in Guidance #209 and #211
- October 2015
  - Requires (NOW) VFD from vet for drugs previously on the list
  - January 2017
  - OTC to VFD conversion complete
  - VFD will be required for all drugs on expanded list

History of VFD

What is the Veterinary Feed Directive?

Law
- Enforced by FDA to increase veterinary oversight of certain food animal medications ("VFD drugs") and eliminate the use of these drugs for purposes other than treatment, control, or prevention of disease

Written document
- Provided by veterinarians to legally purchase and use VFD drugs
- Drug ("VFD drug")
  - Administered in or on feed
  - Medically important for humans

History of VFD

Animal Drug Availability Act (ADAA amendment): 1996
- Established a new category of animal drugs for use in feed as "VFD" drugs to be used under the supervision of a veterinarian

First Rule: December 2000
- Initial implementation of the VFD provisions of the ADAA
- Required written orders & cautionary labeling for VFD drugs
- First VFD drug was tilmicosin (Pulmotil®) for use in swine

Guidance #209 (the Judicious Use Guidance) - April 2012
- Outlines a plan for phasing out growth promotion uses and limiting medically important antimicrobials to therapeutic use
- Will require veterinary oversight for such use
- Only addresses antimicrobial use via feed and water

History of VFD

Animal Drug Availability Act (ADAA amendment): 1996
- Established a new category of animal drugs for use in feed as "VFD" drugs to be used under the supervision of a veterinarian

First Rule: December 2000
- Required written orders for a small number of animal drugs

Second Rule (The "New" Rule): June 2015
- October 2015
  - Requires (NOW) VFD from vet for drugs previously on the list
  - January 2017
  - VFD will be required for all drugs on expanded list
What drugs presently require a VFD?

1) Florfenicol (Aquaflor®, Nuflor®)
2) Avilamycin (Kavault™, Intepriity™)
3) Tilmicosin (Pulmotil®, Tilmovet®—swine approval only)
   - This is the only feed grade antibiotic of the three labeled for use in cattle.

What other cattle drugs will require a VFD as of January 1, 2017?

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlortetracycline</td>
<td>(C)</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>(O)</td>
</tr>
<tr>
<td>Neomycin</td>
<td>(N)</td>
</tr>
<tr>
<td>Sulfamethazine</td>
<td>(S)</td>
</tr>
<tr>
<td>Tylosin</td>
<td>(T)</td>
</tr>
<tr>
<td>Virginiamycin</td>
<td>(V)</td>
</tr>
</tbody>
</table>

“medically important antibiotics used in feed for the prevention, control, and/or treatment of disease”

The list of “new” VFD antibiotics as of Jan. 1, 2017

Antimicrobial Class | Specific drugs that will require a VFD
Aminoglycosides | apramycin, hygromycin B, neomycin, streptomycin
Diaminopyrimides | ormetoprim
Lincosamides | lincomycin
Macrolides | erythromycin, oleandomycin, tylosin
Penicillins | penicillin
Streptogramins | virginiamycin
Sulfas | sulfadimethoxine, sulfamerazine, sulfamethazine, sulfquininaxine
Tetracyclines | chlortetracycline, oxytetracycline

Affected brand name products labeled for cattle include:

- **Aureomycin®, Chloratet™, ChlorMax®, Pennchlor® (C)**
- **Tylan®, Tylovet® (T)**
- **Pennchlor S®, Aureo S 700® (S)**
- **Neo-Oxy®, Neo-Terramycin® (N)**
- **V-Max™ (V)**

Which VFD medications does Renaissance sell?

1. Neomycin-Oxytetracycline ("Neo-Terra")
   - 22/20 AM/NT 1600/1600 BioMOS Milk Replacer (Q2576): calf label
   - Scours & Pneumonia Treatment Concentrate & Milk Replacer (Q2527, Q2525): calf label
   - Neo-Terra 10/10 (Q3240): swine, poultry labels
   - Calf Enhancer Mix (Q25255)
2. Chlortetracycline (**Aureomycin®**)
   - Aureo 4G Cattles (Q0981) and Aureo 50G (Q0982): cattle, swine, poultry, and sheep labels
3. Chlortetracycline-sulfamethazine
   - Aureo 5 700® (Q9332): beef cattle label
   - Aureomic S 10/10 (Q9291): swine label
4. Tylosin (Tylan®)
   - Tylan 10 (Q9310), Tylan 40 (Q9321): beef, swine, and chicken labels
   - Tylan 10 Sulf (Q9320): swine label

Which drugs have label approval(s) for use in dairy cattle?

- **Neomycin-Oxytetracycline**
  - In calves and non-lactating dairy cattle (replacement heifers and replacement bulls)
- **Chlortetracycline**
  - In calves and non-lactating dairy cattle (replacement heifers and replacement bulls)
- **Oxytetracycline**
  - In calves and non-lactating dairy cattle (replacement heifers and replacement bulls)
What about Aureo S 700 (#9032)?

Animal | Use Level | Indication(s) for Use
--- | --- | ---
Beef cattle | 350 mg/head/day chlortetracycline –AND– 350 mg/head/day sulfamethazine | As an aid in the maintenance of weight gains in the presence of respiratory disease such as shipping fever.

WARNING: Discontinue use 7 days prior to slaughter. Do not use in calves to be processed for veal.

LIMITATIONS FOR USE: Feed for 28 days.

Source: 2016 Feed Additive Compendium, p. 179

What is FDA’s definition of non-lactating dairy cattle?

- replacement dairy heifers, replacement dairy bulls, and dairy calves (those not to be processed for veal)

**DRY # NON-LACTATING!!**

- Once a lactating cow, always a “lactating” cow.

Where can you find product label approvals?

1. Product labels (read the tag and/or the bag!!)
2. Drug manufacturers’ web sites
3. Feed Additive Compendium
   - From the drop-down menu, choose:
     1. Title 21 - Food and Drugs,
     2. Volume 6, Browse Parts 500-599,
     3. Part 558 (New Animal Drugs for Use in Animal Feeds),
     4. Under Subpart B of the Contents, select the drug of interest by its generic name to find the label approvals

To purchase a Feed Additive Compendium:

Publisher: The Miller Publishing Company
5810 W. 78th St.
Suite 200
Bloomington, MN 55439

Phone: 800-441-1410

http://feedcompendium.com
[www.feedadditivecompendium.com](http://www.feedadditivecompendium.com)

- published in association with Feedstuffs magazine
[www.feedstuffs.com](http://www.feedstuffs.com)

Cost of the 2016 edition: **$260**
(now $234)

What are some products that will **not** require a VFD**?

- Ionomophores: Rumensin®, Bovatec®, Cattlyst®
- Other antimicrobials: Gainpro®, BMD® 60
- Dewormers: Safe-Guard®
- Coccidiostats: Deccox®, Corid.
- Others: Heifermax®, MGA®, Optaflexx®

**UNLESS** used in a label-approved combination with one of the VFD antibiotics.

Rules and Regs of Feed-Grade Antibiotic Use

**NO** Extralabel use is permitted
- Drug dose/concentration must be approved
- Must be used for a labeled indication
- Must be fed for the prescribed time period
- Must be approved for use in the species in question, and for the age/size animal(s) in question
- CANNOT be fed concurrently with another feed-grade antibiotic, unless there is an approval for the combination

These rules for disease treatment will be maintained as medications shift to VFD status. All feed efficiency and growth promotion claims will be eliminated.
VFD drug labels will change . . .

**READ THE LABEL!!**

“CAUTION: Federal Law restricts medicated feed containing this veterinary feed directive drug to use by or on the order of a licensed veterinarian.”

**Note:** Product labels do NOT typically include combination approvals, so other resources (e.g., Feed Additive Compendium, FDA Blue Bird label web site: [http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/BlueBirdLabels/default.htm](http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/BlueBirdLabels/default.htm)) may need to be reviewed if info on combination approvals is needed.

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What are the requirements for obtaining a VFD?

**Veterinarian**
- Licensed
- Veterinary Client Patient Relationship (VCPR)

**Written or electronic VFD document**
- Delivered to the distributor of the VFD drug (feed mill, etc.)

**Licensed distributor**
- Fills the order **IF** the VFD is correct and complete

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Information required on a VFD

1. Veterinarian’s name, address, and telephone number;
2. Client’s name, business or home address, and telephone number;
3. Premise(s) at which the animals specified in the VFD are located;
4. Date of VFD issuance (effective date);
5. Expiration date of the VFD;
6. Name of the VFD drug(s);
7. Species and production class of animals to be fed the VFD feed;
8. Approximate number of animals to be fed the VFD feed by the expiration date of the VFD;
9. Indication for which the VFD is issued;
10. Concentration of VFD drug in the feed and duration of use;
11. Withdrawal time, special instructions, and cautionary statements necessary for use of the drug in conformance with the approval;
12. Number of refills (if refill permitted by the drug approval)
13. 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;”
14. Affirmation of intent for combination VFD drugs as described in 21 CFR 558.8(b)(6); and
15. Veterinarian’s electronic or written signature

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Will pre-made VFD forms be available for use by veterinarians?

Yes
- GlobalVetLINK ( [www.globalvetlink.com](http://www.globalvetlink.com) )
- RxExpress™ (by New Planet Technologies)
- Manufacturers (sponsors) of the VFD medications
- AABP, AVMA and other veterinary groups
- Possibly some feed mills
- FDA? (unlikely)
Q & A

If a producer buys a bag of Aureomycin® crumbles in September of 2016, can they legally feed it to their cattle in January of 2017 without a VFD?

NOPE.

Can a veterinarian write a VFD to add Aureomycin® to a producer’s free-choice mineral mix in the summer to help control pinkeye?

NOPE.

Q & A

A producer has some pet goats that occasionally get treated for pneumonia with AS-700 crumbles. Can they continue to do that with a VFD?

NOPE.

A producer owns cattle both in PA and in MD. Can they treat both herds with the same VFD?

MAYBE...

Q & A

What happens if a veterinarian submits an incomplete or inaccurate VFD?

The VFD cannot be legally filled unless it is complete & correct.

How long is a VFD good for?

A maximum of 6 months, but potentially less, depending on product and indication.

Will a staff veterinarian for a feed company be able to write VFDs?

MAYBE...

Q & A

Does a veterinarian need to write a VFD if you treat animals with a medically important antibiotic in the water supply?

NOPE, a prescription.

A producer feeding a milk replacer medicated with Bovatec wants to treat some scouring calves by adding Neomycin-Oxytetracycline to it. Can their veterinarian write a VFD to facilitate that?

NOPE.

What do you need to do prepare?

1. Fill out your Notice to FDA of Distribution of VFD Feeds, sign and date it, and submit it to the FDA
   - one-time deal, unless business ownership and/or address changes

2. Fill out your Distributor Acknowledgement Letter, sign and date it, and submit it to Renaissance
   - five considerations for compliance...

3. Ask questions if/when you have them!
   - this will be a learning process for all involved

Distribution Limitations for VFD Feeds
(from the Ren Distributor Acknowledgement Letter)

(1) The distributor will not ship a VFD medication or feed to an animal production facility that does not have and has not provided said distributor with the required copy of a properly formulated, non-expired VFD order;

(2) The distributor will not ship a VFD medication or feed to another distributor without first receiving a written acknowledgement letter similar to this one;

(3) The distributor will comply with all necessary VFD-related record keeping;

(4) The distributor has complied with the FDA’s distributor notification requirements and forwarded a copy of their notification to Renaissance Nutrition (attn.: Caitlyn Massie);

(5) The distributor has listened to one of the Pre-Start sessions on VFD training on either 07/15/16 or 11/18/16.
Comments on Distributor #12 Procedure (mailed out w/july price & product update)

1. affected products list (already covered)
2. “V coding” - Will help with record keeping at Ren office
   - Will be added to special mixes containing a VFD drug
   - Will probably also be added at the end of the product codes for the VFD medications. Example: #9081 Aureo 4G Crumbles will become #9081LV
3. Statement will be revised (no requirement to provide Renaissance w/a copy of a VFD prior to receiving VFD products). You can have VFD products in your inventory, but cannot sell and deliver them without receiving a copy of a valid VFD.
4. You MUST send a copy of the VFD(s) in to Renaissance with your applicable sales tickets.

The bottom line . . .

1. READ THE LABEL and FOLLOW THE DIRECTIONS
2. EDUCATE YOURSELF AND YOUR CLIENTS
3. THIS MAY EVOLVE (SLIGHTLY) OVER TIME

Extra-label bull usage?

Questions???

Product label approvals: Chlortetracycline

<table>
<thead>
<tr>
<th>Animal</th>
<th>Use Level</th>
<th>Indication(s) for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef Cattle</td>
<td>350 mg/head/day</td>
<td>Control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp. susceptible to chlortetracycline.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WARNING: Withdrawal times vary by manufacturer. Read label for specific withdrawal times.</td>
</tr>
<tr>
<td>Beef Cattle (under 700 lb.)</td>
<td>350 mg/head/day</td>
<td>Control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WARNING: Withdrawal times vary by manufacturer. Read label for specific withdrawal times.</td>
</tr>
<tr>
<td>Beef Cattle (over 700 lb.)</td>
<td>0.5-2.0 mg/lb. of body weight/day</td>
<td>Control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.</td>
</tr>
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<td></td>
<td>WARNING: Withdrawal times vary by manufacturer. Read label for specific withdrawal times.</td>
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Source: 2014 Feed Additive Compendium, p. 208

Product label approvals: Chlortetracycline

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<tbody>
<tr>
<td>Calves, beef, and non-lactating dairy cattle</td>
<td>10 mg/lb. of body weight/day</td>
<td>Treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida organisms susceptible to chlortetracycline.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WARNING: Withdrawal times vary by manufacturer. Read label for specific withdrawal times.</td>
</tr>
<tr>
<td>Beef and non-lactating dairy cattle</td>
<td>0.5-2.0 mg/lb. of body weight/day</td>
<td>As an aid in the control of active infection of anaplasmosis caused by Anaplasma marginale susceptible to chlortetracycline.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LIMITATIONS: In free-choice cattle feeds such as feed blocks or salt-mineral mixes; free-choice feed must be manufactured from Aureomycin Type A medicated articles using an FDA-approved formulation. Feed mill license not required if following free-choice loose mineral formulation published in 21 CFR 556.128.</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, p. 208

Record Keeping

<table>
<thead>
<tr>
<th>VETERINARIAN</th>
<th>DISTRIBUTOR</th>
<th>PRODUCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper or electronic copy of the VFD kept for 2 years</td>
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<td>Paper or electronic copy of the VFD kept for 2 years</td>
</tr>
</tbody>
</table>

FDA can inspect or request VFD documentation from the veterinarian, distributor or producer at any time to verify compliance with VFD rules. You are legally obligated to produce records on demand.
Product label approvals: Chlortetracycline

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</tr>
</thead>
<tbody>
<tr>
<td>Calves, beef, and non-lactating dairy cattle</td>
<td>500-4,000 g/ton</td>
<td>Treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida organisms susceptible to chlortetracycline. LIMITATIONS: Hand feed continuously for not more than 5 days to provide 10 mg/lb. body weight per day; must be manufactured from Auresomycin Type A medicated articles manufactured by NADA sponsor No. 054771 (Zoetis).</td>
</tr>
<tr>
<td>Calves, beef and non-lactating dairy cattle</td>
<td>4,000-20,000 g/ton</td>
<td>Treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida organisms susceptible to chlortetracycline. LIMITATIONS: As a top-dress, varying with bodyweight and feed consumption, to provide 10 mg/lb. bodyweight per day. Treat for not more than 5 days; must be manufactured from Auresomycin Type A medicated articles manufactured by NADA sponsor No. 054771 (Zoetis).</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, pp. 208-209

Other Chlortetracycline combination label approvals

1. Chlortetracycline and decoquinate (Decoxx®) - approvals for calves, beef, and non-lactating dairy cattle
2. Chlortetracycline and laidomycin (Cattlyst®) - approvals for beef cattle in confinement
3. Chlortetracycline and lasalocid (Bovatec®) - approvals for multiple cattle production classes

Source: 2014 Feed Additive Compendium, pp. 209-212

Product label approval: Chlortetracycline plus Sulfamethazine

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<tr>
<th>Animal</th>
<th>Use Level</th>
<th>Indication(s) for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef cattle</td>
<td>350 mg/head/day chlortetracycline AND 350 mg/head/day sulfamethazine</td>
<td>As an aid in the maintenance of weight gains in the presence of respiratory disease such as shipping fever. LIMITATIONS: Discontinue use 7 days prior to slaughter.</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, p. 209

Product label approvals: Neomycin/Oxytetracycline

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<tr>
<th>Animal</th>
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<th>Indication(s) for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calves, beef, and non-lactating dairy cattle</td>
<td>To provide 10 mg/lb. of body weight/day (of each drug)</td>
<td>For treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia (shipping fever complex) caused by Pasteurella multocida susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by Escherichia coli susceptible to neomycin. LIMITATIONS FOR USE: Feed continuously for 7-14 days in feed or milk replacers. If symptoms persist after using for 2-3 days, consult a veterinarian. Treatment should continue 24-48 hours beyond remission of disease symptoms. A withdrawal period has not been established for use in pregnancy calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older.</td>
</tr>
<tr>
<td>Calves (up to 250 lb)</td>
<td>To provide 10 mg/lb. of body weight/day (of each drug)</td>
<td>For treatment of bacterial enteritis caused by Escherichia coli susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by Escherichia coli susceptible to neomycin. LIMITATIONS FOR USE: Feed continuously for 7-14 days in feed or milk replacers. If symptoms persist after using for 2-3 days, consult a veterinarian. Treatment should continue 24-48 hours beyond remission of disease symptoms. A withdrawal period has not been established for use in pregnancy calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older.</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, p. 217

Product label approval: Neomycin/Oxytetracycline

<table>
<thead>
<tr>
<th>Animal</th>
<th>Use Level</th>
<th>Indication(s) for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>To provide 0.5-2.0 g/head/day (of each drug)</td>
<td>For prevention and treatment of the early stages of shipping fever complex. LIMITATIONS FOR USE: Feed 3-5 days before and after arrival in feedlots. A withdrawal period has not been established for use in preruminating calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older.</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, p. 327

Product label approval: Tylosin

<table>
<thead>
<tr>
<th>Animal</th>
<th>Use Level</th>
<th>Indication(s) for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle (beef)</td>
<td>8-10 g/ton* to provide 60-90 mg/head/day. (Feed continuously.) *90% dry matter basis.</td>
<td>For reduction of incidence of liver abscesses in beef cattle caused by Fusobacterium necrophorum and Trupearle (Ancarcobacterium) pyogenes. LIMITATIONS FOR LIQUID FEEDS: Liquid Type B feeds must be maintained at pH 4.5-6.0. Recirculate or agitate immediately prior to use for not less than 10 minutes, ensuring not less than 1% of the tank contents per minute from the bottom of the tank to the top or creating a turbulence at the bottom of the tank that is visible at the top. Recirculate or agitate daily, even when not in use. Liquid Type B feeds shall bear an expiration date of 31 days after its date of manufacture.</td>
</tr>
</tbody>
</table>

Source: 2014 Feed Additive Compendium, p. 425
Other Tylosin combination label approvals

1. Tylosin and decoquinate (Deccox®) and monensin (Rumensin®)
   approval for cattle fed in confinement for slaughter
2. Tylosin and lasalocid (Bovatec®) and melengestrol acetate (MGA®
or Heifermax®)
   approvals for heifers fed in confinement for slaughter
3. Tylosin and melengestrol acetate
   approval for heifers fed in confinement for slaughter
4. Tylosin and melengestrol acetate and monensin
   approval for heifers fed in confinement for slaughter
5. #4 above and ractopamine hydrochloride
   approval for heifers fed in confinement for slaughter

Source: 2014 Feed Additive Compendium, pp. 425-429