Use of antibiotics in livestock production in light of new FDA guidelines

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Agenda

• Definitions
• FDA Guidance 209/213 regulations
• VFD Regulations
• Summary
Definitions

• **VFD**
  o *Veterinary Feed Directive*: A veterinary order for feeding medically important antibiotics in animal feeds.

• **VCPR**
  o *Veterinary Client Patient Relationship*: The established relationship between a livestock producer and their veterinarian who oversees the animal health for that operation.

• **FDA/CVM**
  o *Food and Drug Administration and Center for Veterinary Medicine*: Regulates all approvals of antibiotic usage.

• **OTC**
  o *Over the Counter*: Purchasing antibiotics without a prescription.

• **Rx**
  o *Prescription*: For the purchase and use of an antibiotic from a veterinarian.
So how did we get here??

Concerns about:

- Role of antibiotic use in animal medicine in creating resistance!!
- No definitive link has been established!!
Antibiotic Usage Reporting – FDA 2012

• Annually, each drug manufacturer must report the sales and distribution of antibiotics that are approved for use in food animals.
• Is reported by pounds of active ingredient.
• **Limitations:**
  • Not actual usage data.
  • Some drugs approved for food animals AND companion animals.
  • Veterinarians are authorized to change dose in non-feed related antimicrobials.
  • Not species specific.

95% of all livestock antibiotic usage is in feed and water.
Most of the antibiotic usage does NOT require a prescription from a veterinarian.

- **Rx/VFD = Veterinary Oversight**
- **OTC = “Over the Counter”**
- No veterinary oversight necessary
Summary of FDA Guidance 209/213

1. Limits “medically important” antibiotics to therapeutic purposes (to protect animal health and well-being).
   – Therapeutic Purposes
     • Treatment
     • Control
     • Prevention

2. Non-therapeutic uses of “medically important” antibiotics are NO longer permitted.
   – Growth Promotion = Improved growth and feed conversion.
Antibiotic Label Indications for Use

• **Treatment**
  o Defined as the use of an antibiotic for the treatment of animals showing clinical signs of disease.

• **Control**
  o Defined as the use of an antibiotic for the treatment of a group of animals where a percentage (usually >10% are sick) and the remainder of the group are not showing clinical signs (yet).

• **Prevention**
  o Defined as the use of an antibiotic in a group of healthy animals that are known to be at risk for, or exposed to, disease agents (before clinical signs).

• **Growth Promotion**
  o Improves growth or feed efficiency.
Summary of FDA Guidance 209/213

3. Also states the importance of *veterinary oversight* into all on-farm antibiotic decisions.

   - **Veterinary oversight** will now guide all antibiotic decisions on the farm.
     
     • All “medically important” antibiotics used in mass medication (feed or water) will have to be directed by a veterinarian.

   - Eliminates “Over the Counter” usage of medically important antibiotics used in mass medication (Feed or Water).
     
     • No longer be able to purchase “medically important” antibiotics (feed/water) without a VFD or prescription from a licensed veterinarian.
Summary of FDA Guidance 209/213

• This means changing marketing status from OTC to Rx (Scripted) or VFD (Veterinary Feed Directive)
  – Water soluble products to Rx – “medicated water”
  – Products used in or on feed to VFD – “medicated feed”

• DOES NOT APPLY to injectable antibiotics, for now.
How do you determine if an antibiotic is “medically” important?

- **FDA Guidance #152 (2003)**
- Risk assessment for veterinary drugs creating “potential” resistance issues for human medicine.
  - All scientific assessments done to date have demonstrated that the risk is negligible.
- **Classified all antibiotics into 2 classes:**
  - Medically Important for Human Use
  - Non-medically Important for Human Use
Injectable and Oral Antibiotics For Use In Swine

Antibiotics - Oral/Water Med

* Aureomycin Sulmet
* Denegard
* Gentamicin Sulfate
* Gen-Gard Soluble Powder
* Lincomycin Hydrochloride

* Neo 325, Neo-Med
* Nuflor 2.3% Concentrate
* Oxytetracycline HCl SP-343, Tetraoxy-HCA 280
* Penicillin G Potassium
* Pennchlor 64, Aureomycin
* SpectoGard
* Sulmet
* Tet-Sol 324, Duramycin 324

* Tylan

Antibiotics - Injectable

* Draxxin
* Duo-Pen, BP-48, Combi-Pen
* Excede for Swine
* Excenel
* Gentamicin Piglet Injection
* Lincomix 25, 100, 300
* Naxcel
* Nuflor
* Penicillin G Procaine
* LA-200, Duramycin 72-200, Pennox, Maxium 200
* Polyflex
* Tylan 50, 200

Yellow = Medically Important
Green = Non-medically Important

* Medically important for human use GFI #152
### Swine Feed Grade Antibiotics

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Medical Importance</th>
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</thead>
<tbody>
<tr>
<td>Bacitracin Methylene Disalicylate</td>
<td>Yellow</td>
</tr>
<tr>
<td>Bacitracin Zinc</td>
<td>Green</td>
</tr>
<tr>
<td>Bambermycins (Flavomycin)</td>
<td>Green</td>
</tr>
<tr>
<td>Carbadox (Mecadox)</td>
<td>Yellow</td>
</tr>
<tr>
<td>*Chlortetracycline (CTC – Aureomycin/Pennchlor 64)</td>
<td>Green</td>
</tr>
<tr>
<td>*Chlortetracycline/Sulfamethazine/Penicillin</td>
<td>Yellow</td>
</tr>
<tr>
<td>*Chlortetracycline/Sulfathiazole/Penicillin</td>
<td>Yellow</td>
</tr>
<tr>
<td>*Neomycin/Oxytetracycline</td>
<td>Green</td>
</tr>
<tr>
<td>*Oxtetracycline (OTC – Terramycin/LA 200/Pennox)</td>
<td>Green</td>
</tr>
<tr>
<td>*Penicillin</td>
<td>Green</td>
</tr>
<tr>
<td>Tiamulin (Denagard)</td>
<td>Yellow</td>
</tr>
<tr>
<td>*Tylosin</td>
<td>Green</td>
</tr>
<tr>
<td>*Tylosin/Sulfamethazine</td>
<td>Green</td>
</tr>
<tr>
<td>*Virginiamycin (Stafac)</td>
<td>Green</td>
</tr>
<tr>
<td>Narasin (Skycis)</td>
<td>Green</td>
</tr>
</tbody>
</table>
Antibiotics **NOT** affected by Guidance 209/213

- **Antibiotics that are already VFD or Rx based:**
  - avilamycin, florfenicol, tilmicosin; or Rx – Tylosin (beef).

- **Antibiotics that are **NOT** medically important:**
  - Ionophores (monensin, lasalocid, narasin (Skycis, etc.))
  - Bacitracin (BMD, bacitracin zinc)
  - Bambermycins (Flavomycin)
  - Carbadox (Mecadox)
  - Tiamulin (Denagard)

- **Other drugs (that are **not antibiotics**):**
  - Anthelmintics: Coumaphos, Fenbendazole, Ivermectin
  - Beta agonists: Ractopamine, Zilpaterol
  - Coccidiostats: Clopidol, Decoquinate, Diclazuril
Veterinary Feed Directive (VFD)

- Basically, it is a prescription for utilizing “medically important” antibiotics in animal feed.
  - Not technically a script, but functionally works the same.
- It requires a VFD from a veterinarian who the producer has a valid VCPR with for their operation.
- Veterinarian is responsible for filling it our correctly and then sending a copy to the producer and the distributor (feed mill)
  - All parties must retain copies for 2 years and reproduce them upon inspection.
Veterinary Feed Directive (VFD)

• Requirements:
  - Vet name, address, phone
  - Client name, address, phone
  - Premises Information (address/GPS/Prem ID)
  - Date of issuance
  - Expiration date - no longer than 6 months
    - Default to label, maybe shorter than 6 months.
  - Drug – indication, dose and duration
  - Species and production class to be fed
  - Approximate number of animals to be treated
Veterinary Feed Directive (VFD)

• New Requirements:
  o VCPR established
    o At discretion of State Pharmacy or Veterinary Practice Acts
  o Electronic signature and transmittal acceptable
    o Telephone VFDs will still not be allowed
  o Estimate of tons of feed no longer require
    o Replaced by number of days on feed and approximate number of animals to be treated during VFD period.
What is a Veterinary- Client Patient Relationship (VCPR) ?

• It is an agreement between a veterinarian and producer for the veterinarian to assume the responsibility for making medical judgements for the producers animals.
  – States can have their own VCPR definitions, but they must contain the following language, or it defaults to the federal guidelines (21 CFR 530).
Federal Veterinary- Client Patient Relationship (VCPR)

• (1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;

• (2) There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and

• (3) The practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.
What about Extra Label Use of Antibiotics?

- Federal Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994
  - Permits extra-label drug use by veterinarian with a VCPR
    - Changing dose, duration, indication, frequency, route.
    - Only applies to injectable and water soluble medication.
- Does NOT include medicated feeds, including VFD feeds
  - All medicated feed will have to be used according to label
<table>
<thead>
<tr>
<th>Previous Rule</th>
<th>Revised Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 2 year record retention</td>
<td>• 2 year record retention</td>
</tr>
<tr>
<td>• Original document to mill</td>
<td>• May email or fax document</td>
</tr>
<tr>
<td>• No extra-label use</td>
<td>• No extra-label use</td>
</tr>
<tr>
<td>• <strong>Order for tons of feed</strong></td>
<td>• <strong>Order for number of days and approximate number of animals</strong></td>
</tr>
<tr>
<td>• No refills, unless on label</td>
<td>• No refills, unless on label</td>
</tr>
<tr>
<td>• <strong>Written for one group of animals on a premise</strong></td>
<td>• <strong>Attached list of premises</strong></td>
</tr>
<tr>
<td></td>
<td>– For each mill</td>
</tr>
<tr>
<td>• VCPR required</td>
<td>• State/Federal VCPR required</td>
</tr>
<tr>
<td></td>
<td>• <strong>Max of 6 mo. expiration</strong></td>
</tr>
</tbody>
</table>
What is a Distributor?

- A “distributor” means any person who distributes a medicated feed containing a VFD drug to another person.
  - Such other person may be another distributor or the client-recipient of the VFD medicated feed.
  - There are two kinds of distributors:
    - Only distributes VFD feed
    - Manufactures and distributes VFD Feed
- Distributors must notify FDA:
  - Prior to the first time they distribute animal feed containing a VFD drug
    - Acknowledgement letter sent to the FDA
  - Within 30 days of any change of ownership, business name, or business address
What about On Farm Feed Manufacturing?

• Will **NOT** need to register as a distributor unless producing feed for commerce or **feed is delivered to site they do not own**
  
  – Example: If they are delivering feed to a site where they own the pigs, but not the site (contract grower), then they will need to register as a distributor with the FDA.
What about “combination drugs”?

• **Combination drugs**
  - An FDA approved label for the combination of different drugs into animal feed, whereby at least one of the antibiotics is classified as a “VFD drug”
    - VFD drug = “Medically important antibiotic”
  - Example: Denagard Plus®
    - Tiamulin (Denagard®)— Not medically important antibiotic
    - Chlortetracycline (CTC) – Medically important antibiotic (VFD Drug)

• **Example: Denagard Plus®**
  - Tiamulin (Denagard®)— Not medically important antibiotic
  - Chlortetracycline (CTC) – Medically important antibiotic (VFD Drug)

• **This combination is considered to be a VFD drug.**
Scenario

- Producer A has 3 x 2,000 head nursery sites all fed out of the same feed mill.

- He feeds the following diets with medications:
  - Diet 1 – 2 weeks of Den/CTC
  - Diet 2 – 2 weeks of Neo/Terra 100
  - Diet 3 – 2 weeks of CTC 400
  - Diet 4 – 2 weeks of Mecadox 50

- How many VFD’s would this producer need for his nurseries?
Scenario

• 3 VFD’s Total
  – 1 Den/CTC – combo product
  – 1 for Neo/Terramycin
  – 1 for CTC
  – 0 for Mecadox (not on the medically important list)
  – All sites are fed out of the same feed mill, so can use the same VFD for all 3 sites, as long as each site is listed on the VFD
What’s involved in a Prescription?

• Veterinarian will need to issue a prescription in order to direct use for “medicated water” when using “medically important” antibiotics.

• **Script should include:**
  – Drug name and active Ingredient
  – Concentration and dosage
  – Route of administration
  – Withdrawal time

• Producer needs to keep treatment records for **1 year** after the animal is treated.
ISUEO Antibiotic Workshops

• ISU Extension will be hosting a series of workshops that will cover these regulations in more detail around the state of IA in the upcoming months.

• **Details such as:**
  – List of medically important and non-medically important antibiotics
  – Which antibiotics can and cannot be used for growth promotion
  – Examples of VFD
  – Different scenarios and how VFD/Prescriptions will need to be written.
  – Frequently Asked Questions

• For more information, please see the signup sheet at registration desk.
Implementation Timeline Summary

• **January 1, 2017** – Implementation date for all medically important antimicrobials for use in or on feed to require a VFD
  
  – **December 2016** – Target for drug sponsors to implement changes to use conditions of products affected by GFI #213
Summary

- FDA Guidance 209, 213, VFD already being implemented
  - No growth promotion of medically important antibiotics
  - More veterinary oversight into antibiotic usage (VFD)
- VFD will be required for all “medically important antibiotics” to be used in feed.
- These regulations will be fully into effect by January 1, 2017
  - We have less than a year to get these changes in place.
Acknowledgements:

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Questions