Changes to Antibiotic Labeling & Veterinary Feed Directive

Craig A. Payne, DVM, MS
Director, Veterinary Extension & CE
University of Missouri
Outline

• How did we get here?
• What changes will occur?
• Getting prepared
• Common questions
Concerns with Antibiotic Use

• Antibiotic residues
• Contribution to antibiotic resistance in humans
National Residue Program

- USDA – Food Safety Inspection Service (FSIS)
- The domestic sampling plan includes:
  - Scheduled Samples
  - Inspector Generated Samples
Scheduled Samples

• Consists of random sampling of tissue from healthy appearing food animals who have passed ante-mortem inspection
Results from 2014 – All Species

• Approximately 6000 samples taken
• 10 violations (0.017%) – 8 of which were found in bob veal calves
Inspector Generated Samples
(High Risk Population for Antibiotic Use)

• Test animals with active lesions
  – Respiratory System (Pneumonia)
  – Reproductive System (Uterine Infection)
  – Musculo-skeletal System (Lame or Swollen Joints)
  – Secretory System (Mastitis)
  – Lymphoreticular (Liver disease, including abscess)
  – Wounds (open sores or lacerations)

• Test animals with apparent injection lesions

• Test animals from previous violators
Results from 2014 – All Species

• Approximately 211,000 samples taken
• Approximately 1150 or 0.05% of samples were confirmed positive for a violative residue
• These carcasses never entered the food supply
ANTIBIOTIC RESISTANCE
from the farm to the table

RESISTANCE All animals carry bacteria in their intestines

Antibiotics are given to animals
Antibiotics kill most bacteria
But resistant bacteria survive and multiply

SPREAD Resistant bacteria can spread to...

animal products
produce through contaminated water or soil
prepared food through contaminated surfaces
the environment when animals poop

EXPOSURE People can get sick with resistant infections from...

contaminated food
contaminated environment

IMPACT Some resistant infections cause...

mild illness
severe illness and may lead to death

Learn more about antibiotic resistance and food safety at www.cdc.gov/foodsafety/antibiotic-resistance.html
FDA Guidance for Industry 152
Finalized 2003

“Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern”

• Discusses the use of antibiotics in herds or flocks for production purposes
• Contains the list of antibiotics used in livestock industry that FDA considers medically important in human medicine
Medically Important Antimicrobials

• Penicillins
• Tetracyclines
  – Chloretracycline
  – Oxytetracycline
• Macrolides
  – Tylosin
  – Tilmicosin
  – Erythromycin
• Lincosamides
  – Lincomycin
• Streptogrammins
  – Virginiamycin
• Aminoglycosides
  – Gentamycin
  – Neomycin
• Sulfonamides
  – Only potentiated sulfonamides are listed in GFI 152 however the FDA-CVM has indicated all sulfas are medically important

Not listed in 152: Ionophores, Bacitracin, Bambermycins, Carbadox, Coccidiostats, Laidlomycin
FDA Guidance for Industry 209
Released in 2010, Finalized 2012

“The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals”

• Specifically addresses use of antibiotics in food producing animals for production or growth-enhancement purposes
Summary of GFI 209

• Begins with trying to build a case that production uses are detrimental to human health

• Transitions to discussing that administration of medically important antimicrobials to entire herd or flocks for production practices poses a qualitatively higher risk to public health (GFI 152)
Recommended Principles from GFI 209

**Principle 1:** The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health.

**Principle 2:** The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation.
FDA Guidance for Industry 213
Released 2012, Finalized December 2013

• “New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209”
Summary of GFI 213

• Defines medically important antimicrobials
  – All drugs listed in GFI 152 Appendix
  – Does not include ionophores

• Describes the process for voluntarily phasing out antibiotics for production purposes

• Discusses the phasing in of veterinary oversight for all therapeutic uses of antibiotics in the feed or water

• Also provides a timeline for implementation – 3 years from the date of publication of the guidance (December 2016)
Summary of Changes

Increased rate of weight gain/improved feed efficiency indications removed from labels:

– Tetracyclines –
  • Chlortetracycline (Aureomycin®)
  • Oxytetracycline (Terramycin®)

– Aminoglycosides
  • Neomycin w/ oxytet combos (Neo-Terramycin®)

– Streptogramins
  • Virginiamycin (V-Max®)
Summary of Changes

A Veterinary Feed Directive (VFD) will be required to:

– Obtain and use antibiotics that are delivered in the feed
– Obtain and use products that already contain an antibiotic
  • Bagged feeds, mineral blocks, milk replacer, etc.

• A prescription will be required to:
  – Obtain and use antibiotics that are delivered in the water
Important Points

• These changes will **NOT** products such as Rumensin®, Bovatec®, Deccox® or Corid®
  – Will be available for production uses
  – VFD not required for use

• A Veterinary Client Patient Relationship (VCPR) is required before a veterinarian can write a VFD or prescription
"Veterinarian-client-patient relationship", the veterinarian has assumed the responsibility for making medical judgments regarding the health of the animal and the need for medical treatment, and the client, owner or owner's agent has agreed to follow the instructions of the veterinarian. There is sufficient knowledge of the animal by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal. Veterinarian-client-patient relationship means that the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal by virtue of an examination or by medically appropriate and timely visits to the premises where the animal is kept. The practicing veterinarian is readily available for follow-up care in case of adverse reactions or failure of the prescribed course of therapy”
Important Points

• Extra-label use is using a drug at a dose, by a route, for a condition or indication, or in a species not on the label

• Extra-label use of feed grade antibiotics is currently illegal and will continue to be illegal

• Chlortetracycline (CTC) example
  • In cattle CTC is labeled for
    – control of anaplasmosis,
    – treatment and control of pneumonia
    – treatment of bacterial enteritis
Important Points

• Length of expiration date on a VFD is not to exceed 6 months if not specified on the antibiotic label

• The producer, veterinarian and distributor will need to keep a copy of the VFD on file for 2 years
Important Points

• Information your veterinarian will need from you to fill out a VFD
  – Production class
  – Approximate number of animals to be fed the medicated feed prior to the expiration date
  – Location of animals
  – If you are using other feed additives
  – Where you will get the medicated feed
Producer Responsibilities
21 CFR Part 558.6

1. Can only feed VFD feed upon receipt of valid VFD from vet
2. Follow VFD exactly, including withdrawal times
3. Do not feed VFD feed past the VFD expiration date
4. Do not transfer VFD feeds to another user
5. Feed only to the species/classes of animals specified on the VFD
6. Do not mix VFD feed with other medicated feeds unless authorized by the VFD
7. No off label or extra-label use
8. Keep VFD records a minimum of 2 years
9. Make records available to FDA for inspection upon request
Common Questions

• What will be the cost of a VFD?
• Are veterinarians ready?
• Will feed mills be able to keep antibiotics in inventory or will it be special order item?
• Will injectable tetracycline and penicillin be impacted by these changes?
• I use feed or water antibiotics in animals that are not considered livestock. Will this impact me?
Common Questions

• Can I load up on CTC before the end of the year to avoid needing a VFD for awhile?
• Will I be able to continue on-farm mixing?
• Can copies of a VFD be sent to multiple distributors?
• Where can I find a list of antibiotics affected?
Drugs Transitioning from Over-the-Counter (OTC) to Veterinary Feed Directive (VFD) Status

Upon completion of their voluntary transition from OTC to VFD, all feed uses of the following drugs, alone and in a combination, will require a VFD as of January 1, 2017, except in cases where a sponsor chooses to voluntarily withdraw the drug application:

### Drugs Transitioning From OTC to VFD Status

<table>
<thead>
<tr>
<th>Established drug name</th>
<th>Examples of proprietary drug name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlortetracycline (CTC)</td>
<td>Aureomycin, CLTC, CTC, Chloratet, Chlorachel, ChlorMax, Chlortetracycline, Deracin, Inchlor, Pennchlor, Pfichlor</td>
</tr>
<tr>
<td>chlortetracycline/sulfamethazine*</td>
<td>Aureo S, Aureomix S, Pennchlor S</td>
</tr>
<tr>
<td>chlortetracycline/sulfamethazine/penicillin*</td>
<td>Aureomix 500, Chlorachel/Pfichlor SP, Pennchlor SP, ChlorMax SP</td>
</tr>
<tr>
<td>hygromycin B</td>
<td>Hygromix</td>
</tr>
<tr>
<td>lincomycin</td>
<td>Lincomix</td>
</tr>
<tr>
<td>oxytetracycline (OTC)</td>
<td>Aureomycin, TM, OXTC, Oxytetracycline, Pennox, Terramycin</td>
</tr>
<tr>
<td>oxytetracycline/neomycin*</td>
<td>Neo-Oxy, Neo-Terramycin</td>
</tr>
<tr>
<td>penicillin*</td>
<td>Penicillin, Penicillin G Procaine</td>
</tr>
<tr>
<td>sulfadimethoxine/ormetoprim*</td>
<td>Rofenaid, Romet</td>
</tr>
<tr>
<td>tylosin</td>
<td>Tylan, Tylosin, Tylovet</td>
</tr>
<tr>
<td>tylosin/sulfamethazine*</td>
<td>Tylan Sufa G, Tylan Plus Sufa G, Tylosin Plus Sulfamethazine</td>
</tr>
<tr>
<td>virginiamycin</td>
<td>Stafac, Virginiamycin, V-Max</td>
</tr>
</tbody>
</table>
## Drugs Transitioning from Over-the-Counter (OTC) to Prescription (Rx) Status

Upon completion of their voluntary transition from OTC to Rx, all uses of the following drugs will require a prescription from a veterinarian as of January 1, 2017, except in cases where a sponsor chooses to voluntarily withdraw the drug application:

### Water Soluble Drugs Transitioning From OTC to Rx Status

<table>
<thead>
<tr>
<th>Established drug name</th>
<th>Examples of proprietary drug name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlortetracycline</td>
<td>Aureomycin, Aureomycin, Chlora-Cycline, Chloronex, Chlortetracycline, Chlortetracycline Bisulfate, Chlortet-Soluble-O, CTC, Fermycin, Pennchlor</td>
</tr>
<tr>
<td>erythromycin</td>
<td>Gallimycin</td>
</tr>
<tr>
<td>gentamicin</td>
<td>Garacin, Gen-Gard, GentaMed, Gentocin, Gentoral</td>
</tr>
<tr>
<td>lincomycin</td>
<td>Linco, Lincomed, Lincomix, Lincomycin, Lincomycin Hydrochloride, Lincosol, Linxmed-SP</td>
</tr>
<tr>
<td>lincomycin/spectinomycin*</td>
<td>Lincomycin S, Lincomycin-Spectinomycin, L-S, Spectinix</td>
</tr>
<tr>
<td>neomycin</td>
<td>Biosol Liquid, Neo, Neomed, Neomix, Neomycin, Neomycin Liquid, Neomycin Sulfate, Neo-Sol, Neosol, Neosol-Oral, Neovet</td>
</tr>
<tr>
<td>oxytetracycline</td>
<td>Agrimycin, Citratet, Medamycin, Oxymarine, Oxymycin, Oxy-Sol, Oxytet, Oxytetracycline, Oxytetracycline HCL, Oxy WS, Pennox, Terramycin, Terra-Vet, Tetravet-CA, Tetroxy, Tetroxy Aquatic, Tetroxy HCA</td>
</tr>
<tr>
<td>penicillin</td>
<td>Han-Pen, Penaqua Sol-G, Penicillin G Potassium, R-Pen, Solu-Pen</td>
</tr>
<tr>
<td>spectinomycin</td>
<td>Spectam</td>
</tr>
<tr>
<td>sulfadimethoxine</td>
<td>Agribon, Albon, Di-Methox, SDM, Sulfabiotic, Sulfadimethoxine, Sulfadived, Sulfamed-G, Sulforal, Sulfasol</td>
</tr>
<tr>
<td>sulfamethazine</td>
<td>SMZ-Med, Sula, Sulmet</td>
</tr>
<tr>
<td>sulfamethoxine</td>
<td>S.O. Solution, Sulfamethoxine Sodium, Sulfamethoxine Solubilized, Sul-Q-Nox, Sulquin</td>
</tr>
<tr>
<td>tetracycline</td>
<td>Duramycin, Polyotic, Solu/Tet, Solu-Tet, Supercycline, Terra-Vet, Tet, Tetra-Bac, Tetracycline, Tetracycline Hydrochloride, Tetramed, Tetrasal, Tetrasol, Tet-Sol, TC Vet</td>
</tr>
</tbody>
</table>

[http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm482106.htm](http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm482106.htm)
According to 2009 FDA data

- 96% of antibiotics used in the livestock industry are administered through the feed and water
- 61% of these antibiotics are considered medically important by the FDA
- 98% of those medically important antibiotics are available OTC