Meat and Milk Drug Residues: Current Dairy Industry Topics

The dairy industry is now under increased drug residue surveillance

Why?

Top Sources of Beef Carcass Drug Residues

#1 Cull Dairy Cows

#2 Veal Calves Sold From Dairies
   Officially listed as “Bob Veal Calves”

2008 Summary Data

- Dairy cull cows accounted for 8% of all cattle slaughtered
- They were responsible for 90% of cattle violative residues from inspector generated samples

Slaughter Violative Residue Comparison

<table>
<thead>
<tr>
<th>Dairy Cattle</th>
<th>Beef Cattle</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.03%</td>
<td>0.0001%</td>
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300X the percentage of violative residues

While the numbers are low, 90% were cull dairy cows
33,865,100 cattle were slaughtered in federally inspected plants
879 carcasses tested positive – 791 were cull dairy cows

Summary of 2008 Dairy Carcass Violative Residue Findings
The table below shows the product percent count for various drugs:

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<thead>
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<td>15.3%</td>
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<td>Desfuroylceftiofur</td>
<td>6.9%</td>
<td>59</td>
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<td>Gentamicin</td>
<td>5.6%</td>
<td>48</td>
</tr>
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<td>Oxytetracycline</td>
<td>3.7%</td>
<td>32</td>
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<td>Sulfamethazine</td>
<td>2.3%</td>
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<td>Neomycin</td>
<td>2.2%</td>
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</tr>
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<td>Tetracycline</td>
<td>1.8%</td>
<td>15</td>
</tr>
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<td>0.8%</td>
<td>7</td>
</tr>
<tr>
<td>Tylosin</td>
<td>0.5%</td>
<td>4</td>
</tr>
<tr>
<td>Dihydrostreptomycin</td>
<td>0.4%</td>
<td>3</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>0.4%</td>
<td>3</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>0.1%</td>
<td>1</td>
</tr>
<tr>
<td>Amikacin</td>
<td>0.1%</td>
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Reasons for the increased number of dairy carcass drug residue violations:

- Increased testing
- More sensitive screening test

What about violative drug residues in milk?

New Milk Testing Program:

- FDA’s Center for Veterinary Medicine (CVM) announced a new program designed to test raw milk for a variety of animal drugs that are used on dairy farms

Their basic assumption is that:

- We do a great job of testing for beta-lactam drugs
- There are other drugs that are used on dairy farms and there is no routine testing program for these drugs
- CVM has seen an increase in animal drug violations associated with tissue residues at slaughter plants
- Many of these tissue residue violations are associated with cows and veal sold from dairy farms
- CVM is concerned that this is indicative of a lack of control at dairy farms which could lead to these drugs being present in milk
From the perspective of the food processors, retailers, restaurants and the consumer any level of violative residue is an unacceptable level.

Human Health Concerns must be addressed

Society trust dairy farmers to produce wholesome milk and beef

We must never violate this trust

How are human health concerns addressed in setting appropriate (label) directions?

- FDA determines safe (label) withdrawal times using safety study data and applies safety factors and conservative assumptions to protect humans from potential effects
  - Safety Data Includes
    - Drug-specific human food safety assessment to determine safe levels
    - Toxicological analysis
    - Acute effects of residue ingestion
    - Chronic effects of residue ingestion
    - Microbiological analysis
      - Effects of bacterial changes and resistance that may impact human health
      - Drug metabolism and excretion, residue profiles, and residue decline in treated animals
  - Thus following label use instructions is very important in protecting human health

How do we prevent residues?

- Carefully follow the proper set of label directions
  - Dose, route of administration, cc’s/injection site, dosing interval, treatment duration, withdrawal times, warnings and cautions
- Keep good treatment records
- Develop and follow science based treatment protocols
  - The prescribing veterinarian is the only one authorized
  - Develop them as a team - veterinarian, owner, management, and employees making cow side treatment decisions
- Watch out for the exceptions
  - Dehydration, kidney failure, liver problems, poor rumen function, etc.
Extra-Label Drug Use (ELDU):

- Giving an animal a drug (OTC or prescription) in a manner different in any way from the manufacturer’s label.
- When OTC drugs are NOT used according to the manufacturer’s label directions they **require a prescription**.

ELDU Label requirements:

- Veterinarian’s label added to the manufacturer’s label on any product OTC or Rx dispensed or prescribed for an extra label use must have:
  - Name and address of veterinarian
  - Animal identification
  - Active ingredients
  - Animal class and health problem
  - Directions for use
  - Withholding time
  - Cautionary statements (residue test, dangers)

**Conditions to Satisfy for ELDU**

- ELDU is permitted only by or under the supervision of a veterinarian, and a valid VCPR is a prerequisite for ALL ELDU.
- ELDU is allowed only for **FDA-Approved** Animal and Human drugs.
- Rules apply to dosage form drugs and drugs administered in water. **ELDU in feed is prohibited.**
- For disease control and treatment and not for production enhancement or convenience
- **No FDA prohibition of a specific ELDU.**

**FSIS RESIDUE VIOLATION INFORMATION SYSTEM**

(Biased Data) – 24 Feb 2009

- All residues are the result of:
  - Extra-label drug use
  - OTC drug use without veterinary supervision

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<tr>
<td>Tilmicosin</td>
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<td>Not a CMEG approved product</td>
</tr>
<tr>
<td>Erythromycin-lysine</td>
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Lactating (adult) dairy cattle are defined by FDA as dairy cattle 20 months of age or older regardless of whether they are milking or dry.

### Prohibited List

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<td>Aminoglycosides</td>
<td>Gentamicin, Kanamycin</td>
<td>Approved for use only according to label. Not for use in females. Dairy Cattle 20 months of age or older. Or in cattle to be processed for veal.</td>
</tr>
<tr>
<td>Thorotrust</td>
<td>None known</td>
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</tr>
<tr>
<td>Phenylbutazone</td>
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<td>None known</td>
</tr>
<tr>
<td>Sulfonamide drugs in lactating dairy cattle unless approved for use at sulfonamide levels</td>
<td>Thiamphenicol, Tetracyclines, Sulfadiazine</td>
<td>Prohibited in poultry</td>
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### The AVMA, AABP, and AVC advocates their members voluntarily refrain from the use of aminoglycosides in food animals

- Amikacin
- Gentamicin
- Kanamycin

### Is this ELDU Legal?

- **Drug:** Baytril®
  - **Label direction:**
    - Single-Dose Therapy: Administer once, a subcutaneous dose of 7.5 - 12.5 mg/kg of body weight (3.4 - 5.7 mL/100 lbs).
    - Multiple-Day Therapy: Administer daily, a subcutaneous dose of 2.5 - 5.0 mg/kg of body weight (1.1 - 2.3 mL/100 lbs). Treatment should be repeated at 24-hour intervals for three days. Additional treatments may be given on days 4 and 5 to animals which have shown clinical improvement but not total recovery.
  - ELDU on dairy farms: Subcutaneous use in calves for the treatment of scours.

**NO** No. Baytril® is a fluoroquinolones which are on the prohibited list. Federal law prohibits the extra-label use of this drug in food-producing animals.

- **Drug:** Banamine® (Flunixin meglumine)
  - **Label Direction:** 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 ml per 100 lbs) of body weight given by slow intravenous administration either once a day as a single dose or divided into two doses administered at 12-hour intervals for up to 3 days. The total daily dose should not exceed 2.2 mg/kg (1.0 mg/lb) of body weight. Avoid rapid intravenous administration of the drug.
  - ELDU on dairy farms: Intramuscular injection.

**NO** No. Injecting Banamine® intramuscularly violates AMDUCA because ELDU cannot be practiced for convenience. The current drug approval is restricted to intravenous administration in cattle. ELDU of this product may lead to violative drug residues as intramuscular injection requires a longer withdrawal period to deplete the drug-related residue.

### How do we prevent residues?

- Carefully follow the proper set of label directions
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    - Develop them as a team - veterinarian, management, employees making cow side treatment decisions
- Watch out for the exceptions
  - Dehydration, kidney failure, liver problems, poor rumen function, etc.
Treatment Record Requirements:
- Uniquely identify all animals
- Maintain all treatment records for a minimum of 2 years after animal leaves the operation
- Treatment records should contain the following information:
  - Identification of animal treated
  - Date treated
  - Product administered
  - Dosage used
  - Route and Location of administration
  - Earliest date animals will have cleared withdrawal time
  - Name of person administering product

What the FDA wants to know if there is a violative residue
- Does the producer know or have a suspicion of how the meat or milk was contaminated?
- Did the producer have a protocol in place to prevent contaminated meat or milk from being shipped?
- Since the positive drug residue incident, has the producer taken steps to prevent future occurrences?
- Review the drug treatment protocol with the producer, at the farm.

Not all carcass residue testing is random
- The following is a list of the pathologies and conditions that warrant Retention and Testing of Carcasses:
  - Mastitis
  - Metritis
  - Peritonitis and surgery — carcasses with active peritoneal inflammation
  - Injection sites
  - Pneumonia

Consequences of FDA Investigations
- Warning Letters
- Inspections
- Consent Decrees - Residue Avoidance System
- Consent Decrees - Permanent Restraint
- Criminal Prosecution

The New FDA Commissioner made the statement in the August 2009 “We will not continue to just send warning letters.”
Dr. Barbara Cassens (SF District Director) hired 40 new investigators in 2009. Will hire 20 new investigators in 2010
It’s all Public Record!

So what’s a Producer and Veterinarian To Do?
- Develop a proactive residue prevention plan
- Written set of treatment protocols
- Incorporate effective products which have a dairy friendly residue risk profile
- Precisely Follow label directions
  - Manufacturers label for OTC and prescription drugs
  - Veterinarian’s label if ELDU
- Train employees
- Keep Good Records — Daily!
- Verify the meat or milk withhold for every animal before it goes into the food supply
- Watch out for the exceptions
  - Dehydration, kidney failure, liver problems, poor rumen function, etc.
Protocols

- **Protocols are an Agreement in Writing**
  - What are the diseases to be treated?
  - What are the treatments allowed?
  - What are the Withdrawals that will be maintained?
  - How do we track treated cow ID's and Withdrawal Times?
  - What drugs are you allowed to have under my script?

- Protocols aren’t made in a vacuum. They are best built between the Veterinarian, Management and Workers, with input by all.

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MAST_G2
(abbreviation for mastitis grade 2)

- Cattle with flakes in milk, signs of clinical mastitis and swelling in the udder
- Before therapy make sure cow has an XMAST<3. Check for previously treated quarter.

- **Treatment**
  - Five Day Protocol
  - Spectramast-LC
  - Meat - 2 days   Milk - 3 days.
  - Evaluate at the end of therapy for additional therapy
  - SPM5QQ.2

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Summary thoughts

- Residue monitoring will certainly become more stringent — with a wider scope.
  - Producers making their own Extra-label decisions may be in for an unexpected outcome.

- Protocols and prescriptions are a legal document between the veterinarian and the herd owner
  - Directions must be followed
  - Meat and Milk Withdrawals must adhered to.
  - Drug or protocol changes are not allowed without the authorization of the veterinarian

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