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RESIDUES? I THOUGHT WE TOOK CARE OF THAT! OR HAVE WE?

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Here is a real headline:
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FDA Takes Action Against New York Dairy Farmer
Proprietor sold animals with illegal drug residues in violation of federal law

"A New York State dairy farmer cited by the U.S. Food and Drug Administration for selling cows that had illegal residues of antibiotics was ordered by the U.S. District Court for the Western District of New York this week to stop offering the animals for slaughter until he complies with federal law. Federal Judge Richard J. Arcara entered a consent decree of permanent injunction on March 25 against Jerald P. Schumacher, the sole proprietor of a farm in Wyoming, N.Y., which sells its dairy cattle to an auction yard in Pavilion, N.Y., to be slaughtered for human consumption. The FDA complaint said Schumacher has sold cows for slaughter for at least 10 years with residues of the antibiotics penicillin and sulfadimethoxine in the animals' edible tissue. The agency also said he illegally gave the cows higher-than-allowed dosages" (From an FDA Press release).

The Food and Drug Administration (FDA) is getting tougher on residue violations in meat and finding that most of those violations are in cull dairy cows and bob veal. Not only do producers face the lost value of that market cow, but their violation becomes public and they could lose the slaughter route for herd removals. In addition, the FDA is considering additional testing for residues in milk. In this presentation, we'll discuss some of the trends in both meat and milk violations, what some of the common reasons are for residues by the kind of drug it is, and what preventive measures and educational resources exist that can keep dairy producers off the violators list and keep that pipeline for market dairy cattle open.

When sending a cow to market, do you know that she does not have a drug or chemical residue in her tissues?

Who are the Players?

The Food and Drug Administration (FDA), through its Center for Veterinary Medicine, regulates the manufacture and distribution of food additives and drugs that will be given to animals. FDA is responsible for investigating veterinary drug residue violations in meats and providing regulatory action when necessary.

The United States Department of Agriculture (USDA), Food Safety and Inspection Service (FSIS) and FDA are responsible for collecting data on tissue residues of animal drugs. FSIS samples carcasses according to the national residue program's domestic sampling plan consisting of the *scheduled sampling plan* and the *inspector-generated sampling plan*. Under the scheduled sampling plan, FSIS inspectors collect random samples from healthy-appearing carcasses that have been passed for consumption to determine prevalence of residues in the national food supply. Under the inspector-generated sampling plan, inspectors select carcasses for sampling based on: (a) symptoms seen in the live animal; (b) abnormalities in the carcass or organs; (c) previous known residue violations by the animal's owner; (d) the animal's herd history; or (e) the fact that an animal is identified as a "high risk" type, such as bob veal.

The Food Safety Reasons

Why do we need to be concerned about drug residues in meat? A recent USDA Office of Inspector General report developed the following table of the most common residues found and highlighted the issues that people might have with their consumption. There are some real health issues associated with some of the drugs that might be found in edible tissues.

Table 1. The most common chemicals found as tissue residues in US market animals and potential effects on people.

CHEMICAL	POTENTIAL EFFECTS ON PEOPLE
Flunixin (e.g. Banamine®)	Fecal blood, gastrointestinal erosions and ulcers, and kidney necrosis (death of tissue)
Penicillin	Allergic-reaction- anaphylaxis (difficulty breathing); nerve damage; severe inflammation of the large intestine; swelling of the lips, tongue, or face; bleeding; diarrhea
Arsenic	Skin lesions, skin cancer; internal cancers; blood vessel diseases; high blood pressure
Copper	Blood cell death; jaundice; kidney dysfunction; death
Ivermectin	Nervous system toxicity

(Adapted from the OIG report -- FSIS National Residue Program for Cattle, March 2010)

How Big a Problem is it?

Through the Washington State Department of Agriculture we were able to get a list of the last 12 months of residue violations in five western states from the FDA (Table 2). The table shows the drug that was found, what class of livestock it was in, and in how many of those livestock it was found. Dairy cows and bob veal have the highest number of residues. Penicillin was the most common drug found in dairy cows followed by the sulfa drugs, flunixin melumine, and the metabolite of ceftiofur (Excenel, Naxcel, Exceed®) - desfuroylceftiofur. There were also tetracycline residues found in dairy cows as well as gentamicin, neomycin and tilmicosin (Micotil®). For Micotil®, the label says specifically: "Do not use in female dairy cattle 20 months of age or older. Use in lactating dairy cattle or sheep may cause milk residues." For gentamicin, "the FDA has not approved gentamicin for use in cattle or scientifically established a withdrawal time for cattle. While the Food Animal Residue Avoidance Databank recommends a minimum preslaughter withdrawal period of 18 months or more for this drug, the AVMA and American Association of Bovine Practitioners have called on veterinarians to avoid extralabel use of aminoglycosides, including gentamicin, in cattle, because of the propensity for

these drugs to be retained in kidney tissue for long periods" (AVMA - JAVMA News http://www.avma.org/onlnews/javma/aug04/040801b.asp.

Table 2. Summary of last 12 months of meat residue violations in AZ, CA, ID, OR, WA, July 2009 – June 2010 (FDA data).

Residue Name	Bob Veal	Bulls/ Stags	Cows Beef	Cows Dairy	Heavy Calves	Heifers	Roaster Pigs	Steers	Total
Ampicillin			1	3					4
Desfuroylceftiofur	1			29					30
Flunixin	1		1	65				1	68
Gentamicin	2			9	2		1	2	16
Ivermectin		2							2
Neomycin	36			6	2			1	45
Oxytetracycline	1			11					12
Penicillin				102					102
Sulfadimethoxine	2			77				1	80
Sulfamethazine				20				5	25
Sulfamethoxazole	2								2
Tetracycline				11					11
Tilmicosin				4		1		1	6
Tylosin	1								1
Total	46	2	2	337	4	1	1	11	404

What are the major reasons for residues violations?

We have been talking about residues for a very long time and quite a few studies have been done to identify what the major reasons are for finding a residue in an animal at slaughter. A summary of these reasons include:

1. Not following label directions for correct treatment
2. Not following label directions for the appropriate withdrawal period
3. Treatment not recorded as a written record—shipped the animal too soon
4. Poor animal identification (don't remember who was treated)
5. Long-term residue following treatment as a calf
6. Extra-label drug use (using a drug not according to label recommendations)

And really, if you think about it, not having proper training in the use of pharmaceuticals is likely the major contributor to residue violations. Although most of the violations last year were for antibiotic residues, some were for anti-inflammatory drugs, such as flunixin (i.e. Banamine®) and a wormer. Let's go through some of the most likely reasons why we might see a meat residue with the specific drugs that popped up on the FDA list.

1) Bob veal with neomycin – The most likely reason for a residue is feeding a medicated milk replacer with neomycin to a calf that is going to slaughter. The medicated milk replacer label should read: "Warning: A withdrawal period has not been established for use in pre-ruminating calves. Do not use in calves to be processed for veal."
2) Dairy Cattle with flunixin – (Banamine®, etc.) The most common reason for a residue from this anti-inflammatory drug is the improper route of administration. The label directs us to administer the injection IV (intravenously) but

many people may give the drug incorrectly in the muscle (IM). When this happens, a much longer withdrawal time is needed before the tissues no longer have a residue. Flunixin is labeled for use in dairy cattle to control fever associated with bovine respiratory disease and endotoxemia. Too often it is used without regard to the need for it. In a study reported last year, investigators in Arizona conducted a clinical trial where they gave it for 3 days to fresh cows to hopefully help with the inflammation that occurs as a result of calving (Shwartz et al., 2009). Not only did it not have any effect on keeping cows milking, it increased body temperature and decreased dry matter intake in those cows compared to saline controls. *The bottom line is to use the drug when it is needed and how it is labeled.*

3) Dairy Cattle with Desfurloylceftiofur (a metabolite of ceftiofur – e.g. Naxcel, Exceed, Excenel,etc.) – The most likely reasons for a meat residue with ceftiofur include an improper dose, duration or route of administration OR an inappropriate withdrawal period. The pre-slaughter withdrawal periods for some of these drugs are: Excede – 13 days, Excene1 3 days, Naxcel 4 days, Spectramast DryCow 16 days, and Spectramast Lactating Cow 2 days.
4) Dairy Cattle with Sulfadimethoxine (Di-methox, Albon) – Different formulations of this drug are available and the ones specifically focused on the correct class of animal need to be used. Meat withdrawal for Albon, if label dosages are followed, is 7 days. Not following the label recommendations can result in a residue.
5) Dairy Cattle with Penicillin – A possible reason is a higher, extra-label dose without using an extended withdrawal time. Also, this drug is sometimes used in intra-uterine infusions and withdrawal times might not be followed.
6) Dairy Cattle with Tetracycline – Most formulations of Oxytetracycline are not to be used in dairy cattle 20 months of age or over. There are also specific requirements for the dose by weight of the animal and not exceeding a specific duration of treatment. Going off-label with this drug with regards to route of administration, dose or duration of treatment could result in a residue.
7) Bull with Ivermectin – A bull may be dewormed with this drug along with the rest of the cattle and then marketed without following the long withdrawal period of 56 days.

The National Milk Drug Residue Data Base is a voluntary industry reporting program. Mandatory reporting is required by State regulatory agencies under the National Conference on Interstate Milk Shipments. From 2009 data, of the over 3.3 million tanker loads, 861 (0.026%) of them were positive for a residue, resulting in the discard of 35 million pounds of milk. The most common class of drug residue found was beta-lactam. Reasons for milk residues include:

1. Accidentally milked treated cow into bulk tank
2. Milked a dry-treated cow into tank
3. Milked a recently purchased, lactating cow into tank that had been treated
4. Treated cows milked last but pipeline not diverted from bulk tank
5. Extra label treatment—shipped milk or cow too soon
6. Milk put in tank before withdrawal period had ended

What can you do?

Education and Training – Participating in Dairy Quality Assurance programs will give you the education you need to understand appropriate drug use. Extensive online educational programs for producers and farm labor (in English and Spanish) exist at the DairyBeef website: http://dairybeef.ucdavis.edu/. Specifically, to avoid a residue when treating an animal:

*Have individual animal identification and specifically identify treated animals.
*Read the drug label.
*Follow the label dose – that means knowing the animal's weight and calculating the specific dose.
*Give the drug through the route indicated on the label – oral, intramuscular, intravenous, subcutaneous, or topical.

*Give the drug for the number of days specified on the label or by your veterinarian.
*Do not market the animal until the entire withdrawal period is complete – after the last dose of the drug, as indicated on the label.

One very important reason for drug residues is the use of the drug off-label (different route, different dose, different duration of use). Extra-label drug use (ELDU) is PROHIBITED except on the order of a veterinarian through a prescription. There must be a valid Veterinary-Client-Patient-Relationship which exists when:
*The licensed veterinarian has assumed clinical responsibility for the animals.
*The owner of the animals has agreed to follow the veterinarian's instructions.
*The veterinarian has sufficient direct knowledge of the animal's condition and care.
*The veterinarian is available for follow-up evaluation.

The law is also clear that ELDU shall not be considered if the purpose is for growth promotion, reproductive performance, or alteration of the cost of therapy and ELDU must not lead to a violative drug residue. Other conditions that must be met before ELDU may be legally considered are:
*A careful diagnosis is made by an attending veterinarian.
*There is no marketable drug specifically labeled to treat the condition diagnosed, or treatment at the dosage recommended by the labeling was found clinically ineffective.
*Assurance that the identity of the treated animal is carefully maintained.
*A significantly extended drug withdrawal is assigned to the animal(s) so that no violative residue occurs.
*If the individual animal cannot be identified for the extended withdrawal time, then the extended withdrawal time must be applied to the entire group.

Feed additives must be used only according to the label instruction. Not even a veterinarian may legally prescribe or use drugs in feed in an extra-label manner. Also, feeding rations containing non-approved combinations of drugs is illegal. This means that concurrent feeding of drugs not approved to be fed to cattle together violates federal regulations. One such scenario relates to "AM/PM" feeding of rations containing feed additives (feeding one drug in the ration in the morning and feeding a different drug in the afternoon) not approved by the FDA to be fed in combination with each other.

Summary

Four things you need to remember about drug use in food animals:
*Drug and chemical residues are of public health concern.
*The livestock industry only gets a bad image when reports of residue violations are made.
*It really is in your financial best interest to reduce condemnations at slaughter and you need to maintain your market channels.
*Scrutiny of our market animals will only increase. We need to have the management practices in place that will eliminate the potential for a drug or chemical residue.

References

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