The Avoidance of Potential Drug Residues and Antimicrobial Resistance

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Take Home Message

✓ The use of veterinary products in beef production can result in residues of those products in the meat.

✓ The development of antimicrobial drug resistant bacteria in the animals which could be transferred from meat to the consumer is a biological possibility but has not occurred.

✓ Feedlot owners are sensitive to the possibility that the use of any veterinary drug could result in a drug residue in beef and they take particular care to ensure that treated animals are suitably identified and that the stated withdrawal period for the drug is followed.

Drug Residues

A residue is any substance which is left behind in the tissues of an animal which has been treated with that substance. Drug residues are most commonly the result of the failure of the elimination of the drug from the edible portions of the animal because insufficient time was allowed between the last treatment and slaughter of the animal. Residues found in beef above tolerable levels can occur because of the permissive and uninformed use of drugs by small segments of the animal industry; failure to adhere to the withdrawal regulations; the extra-label use of drugs for which there may be no stated withdrawal period; and, the lack of original owner identification for animals offered for slaughter.

There is concern about drug residues in beef because their presence in meat can potentially cause a hypersensitivity illness in humans who are hypersensitive to the drug or its metabolites. For example, some people are sensitive to penicillin because of previous exposure to the antibiotic therapeutically and could potentially suffer a hypersensitivity reaction if they consumed meat containing residues of penicillin. However, while the biological and theoretical potential certainly exists, there is no documented evidence that humans have been directly affected by the consumption of beef which may have contained drug residues.
Drug Residues of Concern in Beef Production

The antimicrobials are the drugs used most commonly in beef feedlot production and could potentially be residues in meat. Penicillin, the tetracyclines, trimethoprim-sulfonamides, erythromycin, and other antimicrobials have been used for many years for the treatment of infectious diseases of feedlot cattle especially acute respiratory disease. The incidence of drug residue violations in feedlot cattle is extremely low. Based on surveys done in the US from 1983-1988, antimicrobial residues were found most commonly in cull cows, veal calves, and market hogs. In cull cows the incidence was 46.1%; in feedlot steers and heifers it was 2.9% and 0.5%, respectively. The dominant cause of drug residues is the failure to observe withholding times. In many cases, the individual responsible for the residue was unaware of the correct drug withdrawal time. Feedlot cattle are usually treated for the common diseases during the early part of the feeding period and therefore have from 75 to 200 days to eliminate the drug from the body. In general, violative residues of antimicrobials, hormones and anthelmintics do not constitute a problem in feedlot cattle if the withdrawal periods for the drugs are followed.

The extra-label use of antimicrobials by veterinarians or feedlot personnel is a potential source of drug residues when only the standard withdrawal time is observed. When an antimicrobial is approved for use in a food-producing species, appropriate dosage and withdrawal information is provided on the label and the package insert as part of the approved monograph for that drug.

In some cases, the veterinarian may prescribe or use the drug at variance from the approved specifications. This extra-label use may include using the drug in an unapproved species, or most commonly, using the drug at a dosage other than the approved recommendations. In many cases, antimicrobials are used at higher dosages, and more frequently than the approved label recommendations because empirically the veterinarian feels that lower doses are ineffective.

When antimicrobials are used at extra-label doses it is the responsibility of the user and the veterinarian to extend the withdrawal period to ensure that residues do not occur in the meat and milk of treated animals. The privileges and responsibilities of the veterinarian who prescribes extra-label usage of drugs include the following:

• the veterinarian must be a licensed veterinarian; a
  veterinary/client relationship must have been established;
• the practitioner must have made a diagnosis and indicated the need for treatment;
• the approved label recommendations must have been deemed ineffective for the disease;
• good records must be kept;
• the treated animal(s) should be identified;
• an extended withdrawal time based on sound pharmacokinetic data and principles, including a safety factor must be provided in written form.

A variety of feed additives are used in beef production and raise questions about the potential for residues in beef. Monensin and lasalocid are commonly used growth promotants and when used at recommended levels there are no withdrawal periods and no residues occur. The commonly used coccidiostats such as decoquinate and amprolium are used to control coccidiosis during the first 28 days after arrival in the feedlot and residues do not occur. Tylosin is sometimes used at low levels in the feed to reduce the incidence of hepatic abscesses and there is no withdrawal period and residues do not occur. Chlortetracycline and oxytetracycline are both used as growth promoters and when used at approved levels there is no withdrawal period. Melengesterol acetate (MGA) is a feed additive specifically intended for feedlot heifers to suppress estrus and is not a potential residue problem.

Residue Testing and Avoidance

Routine chemical residue testing of tissue samples of beef carcasses in abattoirs has become part of the food safety and inspection service of many countries. Most residue testing involves random sampling based on a statistical approach developed for the Food Safety and Inspection Service in the US. To detect a violation rate of 1% for a given residue in a given species, a random sampling of 300 animals over a 12 month period nationally yields results at the 95% confidence level.

In Canada, for beef, random surveys in slaughterhouses are conducted for a variety of residues in each fiscal year. These include arsenic, toxic metals such as lead, mercury and cadmium, pesticides, polychlorinated biphenyls, sulfonamides, ivermectin, zeralenone, diethylstilbestrol, and pentachlorophenol. This covers a range of residues which may result from the use of registered veterinary drugs and growth promoters, accidental exposure to agricultural chemicals approved for other uses, as well as environmental contaminants.
Canadian slaughter plants are inspected under the authority of the Meat Inspection Act under the supervision of the Veterinary Inspection Directorate of the Food Production and Inspection Branch of Agriculture Canada. In addition to the collection of planned survey samples, inspectors may also take samples from any animal which they have reason to suspect may have received recent drug treatment, received treatment with unregistered products, or was exposed to toxic chemicals. Such samples are sent for laboratory testing and the suspect carcass is held pending receipt of the test results.

Inspectors may test carcasses randomly or suspect carcasses using the swab test on premises (STOP) test. The STOP is a microbiological assay used only as a screening test. A cotton swab saturated with kidney fluid is placed on a bacterial lawn in an agar plate and incubated overnight. If there is any clear zone of inhibition around the head of the test swab, the result is presumed positive; if there is no zone, the result is presumed negative. If the result is positive, retention of the animal continues while tissue samples are sent to the laboratory for confirmation. The STOP results indicate the presence of antimicrobials, but not which ones or the quantity present. The STOP can easily be used by laboratory workers, veterinarians, farmers, and feed mill operators.

In 1988, in Canada, 1855 beef carcasses were randomly tested and 3948 were tested as suspect. A total of 101 carcasses were condemned for antibiotic residues, with either penicillin or tetracyclines being the most commonly found residues. Despite the widespread use of ivermectin and a test sensitivity of 5 ppb, no residues have yet been found in random survey samples. No residues of commonly used insecticides have been found. For products such as zeranol the residues have been consistently below tolerance levels.

The Live Animal Swab Test (LAST) is available for on-farm screening of urine samples of live animals to detect potential residues before they are sent to market. The Calf Antibiotic and Sulpha Test (CAST) is used to detect violative levels of antibiotics and sulfonamides in veal kidneys. Some on-farm screening tests for the detection of antibiotic residues in milk and urine have been compared. The LAST is reliable in detecting oxytetracycline when the concentration was >4.3 μg/ml but inconsistent in detecting urine oxytetracycline when the concentration was < 4.3 μg/ml. Because of this inconsistency, it failed to accurately predict the antibiotic tissue residues which were at or above tolerance values. The sensitivities of the STOP, the CAST and a laboratory Microbial Inhibitor Test have been compared in testing for 22 antibiotics.
Most violations occur because the instructions on the label were not followed. The use of higher dosages, extended treatment times, or even the use of inappropriate medications without adjusting the known withdrawal times often results in violative residue levels.

In commercial feedlots more than one person may be involved in the treatment of animals and it is easy to forget that a particular animal was treated or that the full withdrawal period may not have been observed. Treated animals must be suitably identified and the information recorded in a master file where it can be retrieved quickly when needed to make a decision about the disposition of an animal. The forced sale of sick or treated animals can often result in non-compliance with withdrawal times.

The role of the veterinarian in drug residue avoidance is to educate the producer about all aspects of the problem and to give high priority to residue avoidance when providing advice to the feedlot personnel and when developing the animal health management protocols which are given to the feedlot. The veterinary recommendations for the use of animal health products must adhere to those which are approved for use in beef cattle. The veterinarian must ensure that there is an easily understood strategy and protocol which is followed for the treatment of sick animals and for the use of other animal health products such as growth promotants and feed additives used on a group basis.

The schedules for the treatment of animals affected with specific disease complexes must include the dose, the route and frequency of administration, alternative medications, and approved withdrawal times. Only those drugs approved for use in cattle should be recommended. When drugs are used extra-label, the withdrawal times can only be estimated on the basis of extrapolation from the pharmacokinetic information available when the drug is used at approved doses.

The Food Animal Residue Avoidance Databank (FARAD) is a single source of large amounts of information on veterinary pharmaceuticals, pharmacokinetics and physicochemical properties of drugs and other chemicals used in livestock production. The primary goal of the Residue Avoidance Program is to reduce the incidence of drug and chemical residues in meat, milk and eggs by means of educational as opposed to regulatory methods. The system utilizes pharmacokinetics models to predict residue depletion times and will be an asset in helping to reduce the number of residue-contaminated animals being sent to market.