Livestock Drug Safety:

Tissue Residues & Human Food Safety

UC DAVIS WIFSS Western Institute for Food Safety & Security

FDA

Overview

Welcome to Tissue Residues and Human Food Safety. This is one, in a series of chapters, on topics related to food animal drug safety. This chapter is designed to give a brief overview of veterinary drugs, drug residues and human food safety in the United States.

This chapter was developed by the Western Institute for Food Safety and Security, or WIFSS, and the UC Davis School of Veterinary Medicine, in partnership with the U.S. Food and Drug Administration (FDA).

Learning Objectives

After reading this chapter, you will be able to:

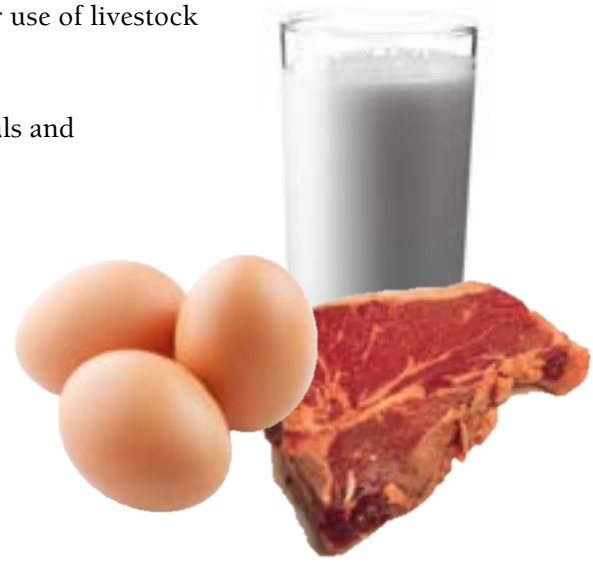
- Describe the relationship between tissue residues and human food safety.
- Recognize important elements of the drug approval process.
- Describe, in general, how tolerance is established as part of the drug approval process.

Drug Use in Food Animal Production

When raising food producing animals, medications and pesticides may be used for a variety of reasons. The most common reasons for use of livestock drugs and pesticides are:

1) Therapeutic, or for the treatment of sick animals
2) To prevent illness in an animal or group of animals and
3) To increase production.

However, when a drug or pesticide is used in a food producing animal there is potential for tissue residues in the edible tissues, or other food products produced, that will be consumed by humans. The Federal register defines edible tissue to include muscle, liver, kidney, fat or skin, milk, eggs and honey. A tissue residue is a concentration of drugs or other chemicals detected in animal tissues that exceeds the legal limit.



Potential Health Effects of Tissue Residues

So what are the potential human health effects of drug residues in food? The presence of drug residues in foods consumed by humans can have acute effects such as allergic or toxic reactions. For instance, it's estimated that 1 in 10 people are allergic to penicillin. Exposure to penicillin residues in this population can cause a range of reactions from rashes to anaphylaxis. Acute toxic reactions can also occur. In Europe, over 1,200 people were hospitalized in France and Spain as a result of ingestion of Clenbuterol residues in the liver of illegally treated animals.

In addition to acute reactions, there can also be chronic health effects from long-term, low level exposure as can happen from continued ingestion of mercury contaminated fish.

Lastly, inappropriate use of antimicrobials may lead to resistant pathogens which can be potentially transmitted to consumers.

Protection against Tissue Residues

How do we protect consumers from drug residues in foods from animals?

Only drugs proven safe and effective are approved by the FDA.

Once a drug is approved and marketed, food products are monitored for residues.

FDA Drug Approval Process

Before a manufacturer can bring a livestock drug to market, they must undergo a rigorous drug approval process. The company must submit data to the Food and Drug Administration proving that the drug is safe for the animal, effective, safe for the environment, and safe for consumers when used according to the manufacture's label instructions.

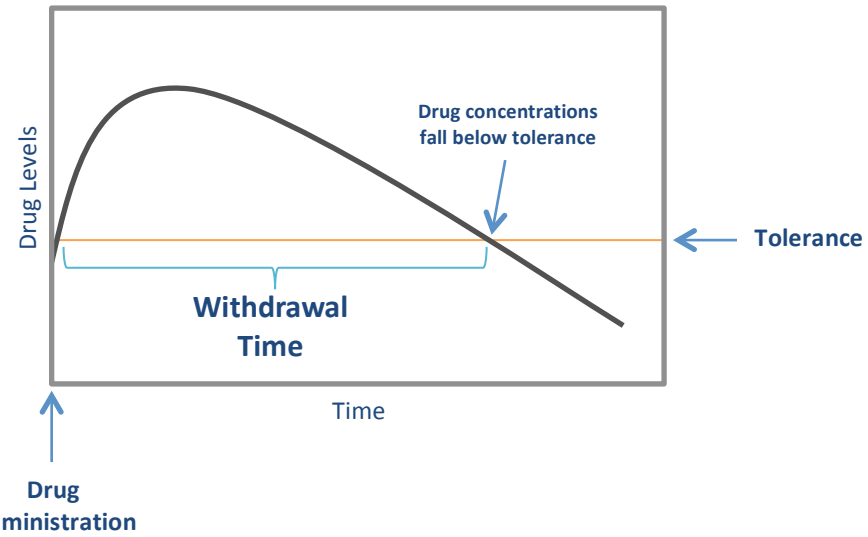
Drug Tolerance

Drug tolerance is the legal concentration of drug residue allowed in foods from food animals. Laboratory animal studies are used to determine safe residue levels for foods from animals that would have no harmful effects on humans even if the food products were consumed daily for an entire lifetime. Once this level is determined, an additional safety factor is added and a tolerance is established for individual tissues or other food items. Tolerances can be set for either the parent compound such as Penicillin or Flunixin, or their breakdown products, such as desfuroylceftiofur, which is a metabolite of ceftiofur.

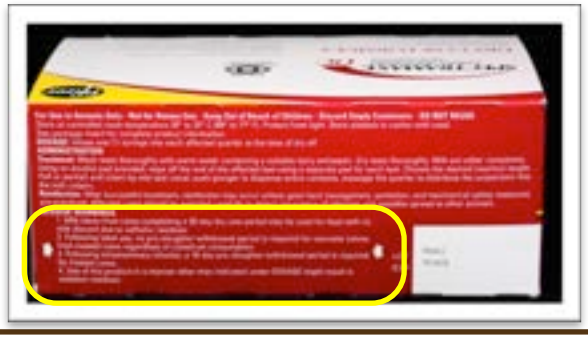
Tolerances for livestock drugs are established by the U.S. Food and Drug Administration (FDA), and tolerances for livestock pesticides are established by the U.S. Environmental Protection Agency (EPA).

Withdrawal Time

Once a tolerance is established, the withdrawal time can be determined. No matter how a drug is administered, it will be absorbed and drug concentrations in the body will initially rise. As the body begins to clear the drug, those drug levels start to fall. The period of time from administration of the drug to when it falls below the tolerance is the withdrawal time.



Every approved livestock drug has a withdrawal time. The withdrawal time only applies when the drug is used according to label directions. Drugs approved for meat producing animals will have a slaughter withdrawal time listed. Drugs approved for milk producing animals, will also have a milk discard time listed.

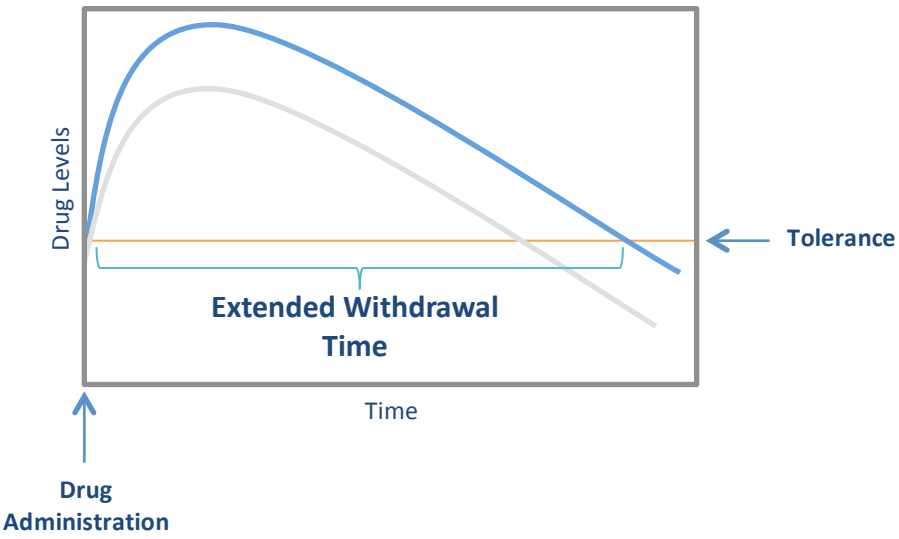


Drug Labels

Label directions describe how the drug should be used and include important information such as: drug name or active ingredients, approved species, route of administration, dose, dosing frequency and withdrawal time.

Extralabel Drug Use

If a producer or veterinarian uses a drug differently from the label directions, also known as off-label or extralabel use, the withdrawal time will change. For example, if a higher than label dose is used, it can dramatically change when the residue levels fall below the tolerance. Because of this, the only way a drug can legally be used off label is when a veterinarian prescribes an extended withdrawal period.



Some drugs cannot be safely used off label or are dangerous enough that they may not be used at all in food animals.

Summary

Because drugs and pesticides are used regularly in food animal production, a potential for tissue residues exists. Drug and pesticide residues in edible tissues and food products pose a significant health risk to humans who consume foods from food animals. In the U.S., an extensive drug approval process and tissue residue monitoring system exists to protect the animals, the environment and consumers. Drug labels contain specific directions for use that, when followed, will prevent tissue residues. These directions include the drug withdrawal time, or the time it takes for a drug to be metabolized down to a safe concentration in food animal tissues. When drugs are used in an extralabel manner, or contrary to the manufacture's label instructions, a veterinarian must prescribe additional directions and an adjusted withdrawal time.