Antibiotic Residues vs. Resistance: What’s the Difference?

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Summary: Antibiotic residues are not the same as antibiotic resistance, but are often confused with each other. Antibiotic residues are molecules that remain in meat from animals that have been treated with antibiotics, with a violative level defined as one that is above what the U.S. Food and Drug Administration (FDA) deems safe. Antibiotic resistance, however, is when bacteria develop the capacity to inactivate or exclude antibiotics, or develop a mechanism to block the inhibitory or killing effects of antibiotics, which can lead to undesirable outcomes for human, animal and environmental health.

To help reduce the potential of the development of antibiotic resistance, the global One Health concept is designed to find a comprehensive solution to the resistance issue by working with all stakeholders to seek solutions that will benefit people, animals and the environment. For their part, U.S. pork producers and swine veterinarians are working together to use antibiotics in a responsible and strategic way to minimize resistance and maximize animal health, animal well-being and food safety. This requires producers to maintain a close relationship with their veterinarians to help ensure FDA-approved antibiotics are used only as needed and according to the label, which will include new regulations on use and record-keeping in 2017.

It Starts with the Label

To avoid contributing to antibiotic resistance or having antibiotic residues in market pigs, following a veterinarian’s direction along with the product label is where producers should start.

All animal health drugs carry specific approvals on the label, which instruct how and when a product is to be used. Labels and package inserts outline dosage, frequency or route of administration, duration of treatment, disease or condition treated, age, class or animal species. Any handling or storage precautions and withdrawal times also are included.

New to product labels, as of Jan. 1, 2017, will be FDA’s requirements for feed-grade and water-based antibiotics. Specifically, those antibiotics that are medically important (to human illness) cannot be used for growth promotion purposes in food-animal production. The products will only be available for therapeutic use—to treat, control or prevent specific disease—and will require veterinary oversight. Feed-grade antibiotics will require a veterinary feed directive (VFD) for each group of pigs and water medications will require a prescription.

Following label instructions, regardless if an antibiotic is an injectable, feed- or water-based product, is key to avoiding violative residues when any hog, including sows, enters the food channel. A producer should consult his/her veterinarian for guidance associated with swine antibiotics and medications.

Understand MRLs, Withdrawal Times and Violative Residues

A top priority for the FDA is to ensure the safety of animal-derived foods for human consumption. During the drug approval process for food-producing animals, FDA sets the drug’s tolerance level—or Maximum Residue Levels (MRLs). Simply put, an MRL is the maximum residue concentration following the administration of a veterinary medicine that is legally permitted or acceptable in food to ensure consumer safety. Marketing animals for food with drug residues above the MRL is illegal and causes the food to be adulterated, and is known as violative residues.

For residues, it’s about how the drug moves through the animal’s body—this is known as pharmacokinetics.
Elimination half-life (T_{1/2}) describes the time it takes for the drug concentration in blood or tissue to decrease by 50 percent. The factors that influence this are:

- Rate of absorption from the site of administration.
- Distribution of the drug from the blood out into the tissue.
- Rate of elimination from the blood.

During the drug approval process, estimates of tissue T_{1/2} are used to calculate the required withdrawal period before a treated hog can be harvested and enter the food chain.

If necessary, to avoid a violative residue, an antibiotic will include a withdrawal period. This constitutes the time between the last dose given to the animal and the time when the residue level in tissues (muscle, liver, kidney and fat) or products is lower than or equal to the MRL. For example, withdrawal studies determine the target organ for a drug. This is the primary organ (often the liver or kidney) that eliminates the drug from the body and will display a residue for the longest period of time.

Further testing and statistical procedures are used to determine a timeline when residues in the target organ in nearly every animal given the drug would fall below the tolerance level. If a violative residue is found in the target organ, the whole carcass is discarded.

Some drugs also have a muscle tolerance level. In this case, if a violative residue is found in an organ, but not in the muscle, the muscle would not be discarded as it would be deemed safe.

It’s important to know that a tolerance level for a drug is determined by using an acceptable daily intake for an average sized person and an estimated annual consumption of the muscle or organ. Withdrawal times are based on the target organ/muscle falling below the tolerance level, not a complete absence of a detectable residue.

**Know that Random Checks Occur**

Until the withdrawal period for an antibiotic has elapsed, the animal or its products must not be used for human consumption. Scientifically random samples at slaughter are collected to test for violative residues as noted.

FDA actively investigates any misuse of veterinary drugs in food animals, and violative residues will prompt follow-up investigations and warning letters to all responsible parties in the animal production and marketing chain. If continued violations occur, FDA can recommend enforcement actions such as injunctions, contempt of injunction and prosecutions. Sows and lightweight roaster pigs, in particular, can present residue challenges because they fall out of the typical marketing cycle and may have different treatment requirements than market hogs. These pigs call for careful planning and veterinary guidance to adhere to withdrawal times and to avoid violative residues.

**Take Steps to Prevent Violative Residues**

Preventing violative drug residues is a basic tenet of responsible animal care and safe food production. Build a good relationship with your veterinarian to ensure the judicious use of antibiotics. Also, implement other management and herd health strategies to prevent and control disease.

The Pork Quality Assurance Plus (PQA Plus) program outlines 10 Good Production Practices, which, together with your veterinarian’s guidance, will help navigate antibiotic use and avoid residue concerns. Here are steps to initiate today:

- Read, understand and follow label directions when giving any medication.
- Identify treated animals. This requires marking or segregating an animal or a group (pens, lots, etc.), as well as tracking them through the production and marketing stages.
- Written records should include identification of the animal(s) treated, treatment date(s), the product used, dosage and who administered it and withdrawal time.
- Animals sometimes lose ear tags, escape pens or accidentally access medicated feeds. Also, treatment records can get lost or destroyed. If there are questions about the residue status of an animal or a group, plan to test live animals before marketing.
- Follow all recommended withdrawal times. This information can be found on the product label, feed tag or package; through your veterinarian; and at pork.org/mrl.
- Verify when the withdrawal time begins, when it’s complete and when it’s safe to market an animal.
- If your veterinarian prescribed antimicrobials in an extra-label manner, discuss your marketing plan for the animal(s) to determine appropriate withdrawal times. Follow the veterinarian’s directions exactly; do not market the animals until the withdrawal time has elapsed.
- When using medicated feed, follow instructions outlined in the veterinary feed directive. Establish a documentation system to ensure that the right feed is delivered to the right pigs. Once treatment is complete, remove all residual feed from bins and feeders.
- Verify that flushing, sequencing and/or physical clean-out occurs at the mill between feed batches to prevent cross-contamination. The same holds true for feed
delivery vehicles. PQA Plus outlines additional steps to prevent cross-contamination during feed processing.

- With water medications, follow the prescription, check the medicator’s accuracy and confirm when the treatment period is finished.
- Minimize environmental exposure through proper handling and disposal of all antibiotics, including any outdated or unused products.
- Educate animal caretakers on the processes to prevent marketing adulterated animals or animals with violative residues. Provide clear instructions and follow-up.

Maximum Residue Limits for U.S. and Exported Pork

With U.S. pork producers exporting 25 percent (or more) of their annual production, understanding MRLs on an international level is critical, as countries sometimes set their own MRLs for pork or pork products. The federal government, along with the U.S. Meat Export Federation, National Pork Producers Council, the American Pork Export Trading Company and others, work to ensure that export customers’ needs are met.

But because the pork export channel begins at the farm, every U.S. producer plays a role in producing safe, nutritious, high-quality pork for the world’s growing population. A close working relationship between producers and veterinarians not only assures animal health and well-being, but also that guidelines for the proper use of antibiotics are met for both U.S. and international consumers.

Note that the withdrawal periods included in this database are based on use as outlined on the product label. Any other use would have to be prescribed by a veterinarian and the withdrawal period extended accordingly. The most up-to-date listing can be found at http://www.pork.org/mrl/

What Is Antibiotic Resistance?

Simply put, antibiotic resistance involves bacteria that develops the capacity to inactivate or exclude antibiotics, or that develops a mechanism to block the inhibitory or killing effects of antibiotics. The bacteria survive, continue to multiply and spread, causing more harm. This process occurs naturally, as any bacteria will eventually try to evolve and survive, but mankind also has played a role.

Antibiotic resistance is both a public health and animal health concern, as everyone wants to maintain the effectiveness of these essential drugs. Farmers, ranchers, veterinarians, medical doctors and consumers all have a role in better understanding and minimizing the risk of antibiotic resistance. That starts with working with your veterinarian to get a proper diagnosis, match the product for the treatment and ensure a complete regimen is administered.

Responsible Use Helps Mitigate Resistance

Responsible antibiotics use in pork production involves evaluating their application to protect animal health, optimizing their effectiveness and minimizing the risk of developing resistance, thereby, protecting public health. Pork producers, veterinarians and animal health experts continuously work to ensure antibiotics are used responsibly on the farm.

As of Jan. 1, 2017, FDA Guidances 209 and 213 will make it illegal for medically important (to human health) antibiotics to be used to promote growth in food animals. Once these new standards go into effect, veterinary oversight will be required when administering antibiotics in feed or water in addition to following the new rules outlined on antibiotic drug labels.

Antibiotics Are One Tool

Antibiotics are just one tool in a producer’s animal health plan that includes veterinary guidance, proper nutrition, clean water, proper air ventilation, temperature management, animal housing maintenance, animal care and even genetics. Vaccination also is key – used at the right time, on the right organisms—as well as heightened biosecurity measures, to reduce the amount of pathogens that animals encounter.

The PQA Plus program outlines numerous steps to establish antibiotic use and herd health strategies. Here are some points to consider:

- Use antibiotics for treatment only when there’s an appropriate clinical diagnosis, which is supported by clinical signs, necropsy, laboratory tests and herd history.
- An accurate diagnosis also includes identification of factors contributing to the cause of the disease. Look at management factors such as ventilation, pig flow, etc.
- Culture and sensitivity results can aid in the selection of antibiotics; also consider herd health history.
- Consider group morbidity and mortality rates when deciding whether or not to initiate herd, group or individual therapy.
- Limit antibiotic treatment to ill or at-risk animals, treating the fewest animals indicated.
Administering antibiotics to prevent disease can mean using fewer antibiotics to prevent disease later. That means fewer antibiotics will be used overall than if treating the same animals following an outbreak. Responsible treatment involves administering antibiotics only when necessary, to the smallest, but proper number of animals feasible and for the least amount of time necessary to prevent disease reoccurrence.

Discuss product options with your veterinarian to select the most appropriate therapy for your herd’s specific situation, as well as any antibiotic resistance implications for your farm and human health. Work with your veterinarian to develop treatment protocols to minimize the development of resistance or cross-resistance. Have a written action plan for antibiotic use, and review it regularly with your veterinarian.

**Principles and Guidelines for Responsible Antibiotic Use**

The National Pork Board has developed the following five principles to guide producers to use antibiotics responsibly:

**Principle 1:** Take appropriate steps to decrease the need for the application of antibiotics.

**Principle 2:** Assess the advantages and disadvantages of all uses of antibiotics.

**Principle 3:** Use antibiotics only when they will provide measurable benefits.

**Principle 4:** Fully implement management practices described for responsible use of animal health products into daily operations.

**Principle 5:** Have a working veterinarian/client/patient relationship and follow the responsible antibiotic use guidelines.