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## Antibiotic Use in Food Animals: FDA's Current Activities

### Issue

The U.S. Food and Drug Administration (FDA), which evaluates human and animal drugs for safety and effectiveness, is concerned that public health may be at risk from certain antibiotic uses in food animals. According to FDA, foods of animal origin may be contaminated with pathogens that cause certain types of foodborne infections, and antibiotic use in animals that produce these foods may render the infections less amenable to treatment, due to antibiotic resistance.

In response, FDA has issued two guidance documents for industry that define judicious use of antibiotics, ask animal drug companies voluntarily to stop labeling antibiotics for production uses, and call for more veterinary oversight. FDA says a voluntary approach is the fastest and most efficient way to tighten control over the use of medically important antibiotics. Regulatory action may require FDA to conduct product-by-product evaluations that could require more time and resources.

Some stakeholders, mainly led by consumer groups, say that use of antibiotics in food animals leads inevitably to drug resistance in foodborne pathogens, and that such use should be curtailed. Other stakeholders, mainly led by industry groups, say that untreatable human infections due to resistance result from misuse of antibiotics in the healthcare system. FDA asserts that concerns about antibiotic-resistant human infections resulting from antibiotic use in food animals are well documented, and FDA generally possesses broad authority to regulate these drugs based on this public health effect.

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An *antimicrobial* is a drug that acts against many pathogens, including bacteria, viruses, fungi, or parasites. An *antibiotic* is an antimicrobial drug that acts against bacteria. Most drugs of concern in this discussion are antibiotics. FDA uses the broader term *antimicrobial* in its publications.

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### Antibiotic Use in Food Animals

FDA has approved three uses (called *label indications*) of antibiotics in food animals: treatment of disease, prevention or control of disease, and growth enhancement. First, livestock and poultry producers use antibiotics to treat sick animals, usually at a high dose for a short period of time. Second, antibiotics may be used, sometimes at a reduced dosage, to prevent disease during times when animals may be more susceptible to infections (for example, after weaning or during transport) or control disease when present in a part of a flock or herd. Lastly, low doses of

antibiotics may be fed to animals over a longer period of time to increase growth rates or improve feed efficiency.

Currently, antibiotics may be dispensed to food animals in several ways. Some types may be purchased over-the-counter (OTC) and used by producers. Antibiotics added to feed must be accompanied by a veterinary feed directive (VFD), a special type of veterinary prescription for this purpose. Veterinarians may prescribe antibiotics used through other routes, such as injection. Although veterinarians may prescribe most drugs “extra-label” (using a drug for a species or indication other than those on the label), restrictions already exist on extra-label use of antibiotics in food animals. Finally, certain types of drugs, including some types of antibiotics, are prohibited for use in food animals under any circumstances.

### FDA's Efforts to Limit Animal Antibiotic Use

The FDA Center for Veterinary Medicine (CVM) oversees the agency's efforts to assure the safety and effectiveness of animal drugs, as required under Section 512 of the Federal Food, Drug, and Cosmetic Act (FFDCA, 21 U.S.C. 360b). CVM issues guidance documents for industry which provide FDA's current thinking on issues. Guidance documents do not necessarily establish legally enforceable responsibilities, but provide recommendations for the industry.

At a July 2009 hearing before the House Committee on Rules, the Obama Administration signaled that it would address the use of antibiotics in food-producing animals. For the first time, an FDA official stated that the use of antimicrobials for growth promotion or feed efficiency was not a judicious use.

In June 2010, FDA released the draft Guidance for Industry #209 (GFI #209), *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. The final version of GFI #209 was released April 2012. In GFI #209, FDA states that a proactive approach is necessary to reduce antibiotic resistance and preserve the effectiveness of medically important antibiotics for humans and animals. FDA offers two principles for the use of antimicrobials.

- (1) *The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health.*
- (2) *The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation.*

First, FDA defines certain uses (indications) as “production uses,” that is, uses intended to hasten growth or improve feed efficiency in animals, rather than to treat or prevent specific diseases. FDA states that production uses are not judicious, that they contribute to public health problems through the development of antibiotic resistance, and that they should be phased out. In addition, FDA states that the use of medically important antibiotics for preventive use is judicious as long as veterinarians are involved in the decision-making process.

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According to FDA’s Center for Veterinary Medicine, halting production uses of antimicrobials “promotes the judicious use of important antimicrobials, which protects public health and, at the same time, ensures that sick and at-risk animals receive the therapy they need.”

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Second, FDA states that judicious uses of antibiotics in food animals (i.e., for disease treatment or prevention) should fall under veterinary supervision. Currently, many antibiotics are approved for OTC use in food animals. FDA believes OTC use should be discontinued.

FDA notes that it considers the antibiotics listed in its 2003 Guidance for Industry #152, *Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern*, as medically important to human health.

Subsequently, FDA provided a roadmap for animal drug sponsors (companies) to follow to abide by the principles in GFI #209. In December 2013, FDA issued Guidance for Industry #213 (GFI #213), *New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*. In GFI #213, FDA asks drug sponsors to work voluntarily with the agency to review existing approvals of antibiotics used in food animals, and to update the evidence for a treatment or preventive use or consider withdrawing the drug. FDA also asked drug sponsors to advise them, within 90 days of the publication of GFI #213, whether they planned to participate. FDA reported in March 2014 that all but one animal drug sponsor affected by GFI #213 have agreed to pursue the goals of the guidance.

FDA plans to reassess, in three years, whether this voluntary approach achieves FDA’s goal, namely, that all approved antibiotics used in food animals have at least one evidence-based treatment or preventive use (indication) in at least one species of food animal, and that all such uses involve either traditional veterinary prescription or a veterinary feed directive (VFD).

In addition to laying out FDA’s approach, GFI #213 provides information about the nature of evidence drug sponsors may use to support a treatment or preventive indication. Also, FDA has published a proposed revision to its VFD regulations so that they are consistent with the proposals in GFIs #209 and #213 (78 *Fed. Reg.* 75515).

## Stakeholder Reaction

Reaction to GFI #213 has been mixed. Trade groups that represent animal drug companies, (e.g., Animal Health Institute, Generic Animal Drug Alliance) and livestock and poultry industry groups (e.g., American Meat Institute, National Chicken Council) have expressed support for GFI #213 for its collaborative approach to judicious use. Other stakeholder groups (e.g., Natural Resources Defense Council, Keep Antibiotics Working) are skeptical of FDA’s voluntary approach, fearing that industry will simply switch from production to preventive indications, resulting in little to no reduction in antibiotic use in food animals.

Some Members of Congress have also publicly expressed concern that GFI #213 is an inadequate response that lacks enforcement mechanisms, or that it does not guarantee the prudent use of antibiotics for preventive indications. Legislation introduced in the 113<sup>th</sup> and previous Congresses, the Preservation of Antibiotics for Medical Treatment Act of 2013 (H.R. 1150), along with a Senate companion bill (S. 1256), would limit the use of medically important antibiotics to treatment in food animals, restrict prevention use, and prohibit production use. The legislation would essentially make mandatory what FDA guidance documents are intended to accomplish.

## Other FDA Actions

In 2009, FDA began to report sales and distribution data on antimicrobials approved for use in food animals as required by the Animal Drug User Fee Amendments of 2008 (ADUFA), which amended the FFCA. FDA reports for 2009-2011 include volume sold and distributed by antimicrobial class and a breakdown by class of the active ingredients. In a July 2012 advance notice of proposed rulemaking, FDA requested comments on its antimicrobial sales and distribution reporting. Comments indicated a desire for more drug *usage* information in order to provide stakeholders with a better understanding of antimicrobial resistance. In September 2013, FDA issued a notice with a request for comment on four additional tables that could be included in its annual ADUFA reports. Future reporting could include antibiotics listed according to medical importance, and then by antibiotic class; by method of administration (feed, water, injection, other); by indication (therapeutic, both treatment and prevention, and production); and lastly, by dispensing method (OTC, VFD, Rx). Potentially, more robust reporting could address some stakeholder concerns about how well FDA’s guidance is implemented over the three-year phase-in period.

For FDA information on judicious use of antimicrobials, see <http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/default.htm>.

**Joel L. Greene**, [jgreene@crs.loc.gov](mailto:jgreene@crs.loc.gov), 7-9877

**Sarah A. Lister**, [slister@crs.loc.gov](mailto:slister@crs.loc.gov), 7-7320