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Testimony of

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INTRODUCTION

Madam Chairwoman and Members of the Committee, I am Joshua Sharfstein, Principal Deputy Commissioner at the Food and Drug Administration (FDA or the Agency) in the Department of Health and Human Services (HHS). Thank you for the opportunity to discuss the important public health issue of antibiotic use in animals.

Preserving the effectiveness of current antimicrobials, and encouraging the continued development of new ones, are vital to protecting human and animal health against infectious microbial pathogens. Approximately two million people acquire bacterial infections in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are associated with bacterial pathogens, displaying resistance to at least one antimicrobial drug. The trends toward increasing numbers of infection and increasing drug resistance show no sign of abating. Resistant pathogens lead to higher health care costs because they often require more expensive drugs and extended hospital stays. The problem is not limited to hospitals. Resistant infections impact clinicians practicing in every field of medicine, including veterinarians.

In my testimony, I will provide background information on antimicrobial resistance, discuss FDA's involvement with the Interagency Task Force on Antimicrobial Resistance, set out a public health framework for assessing the use of antimicrobials in animals, and describe FDA's work with respect to the non-therapeutic use of antimicrobials in food-producing animals.

BACKGROUND

Antimicrobial drugs are used to treat infections caused by microorganisms. The term "antimicrobial" refers broadly to drugs with activity against a variety of microorganisms, including bacteria, viruses, fungi, and parasites (such as malaria). The term "antibacterial" refers to drugs with activity against bacteria in particular. Another term commonly used to describe an antibacterial drug is "antibiotic." This term refers to a natural compound produced by a fungus or another microorganism that kills bacteria that cause disease in humans or animals. Some antibacterial drugs are synthetic compounds, i.e., they are not produced by microorganisms. Though these do not meet the technical definition of antibiotics, they are referred to as antibiotics in common usage.

Antimicrobial resistance is the ability of bacteria or other microbes to resist the effects of a drug. Antimicrobial resistance occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections.

Many factors contribute to the spread of antimicrobial resistance. In some cases, doctors prescribe antimicrobials too frequently or inappropriately. Sometimes patients do not complete the prescribed course of an antimicrobial, making it more likely that surviving microbes will develop resistance. Antimicrobial use in animals has been shown to contribute to the emergence of resistant microorganisms that can infect people. The inappropriate nontherapeutic use of

antimicrobial drugs of human importance in food-producing animals is of particular concern. Through international trade and travel, resistant microbes can spread quickly worldwide.

Antimicrobial agents have been used in human and veterinary medicine for more than 50 years, with tremendous benefits to both human and animal health. Many infections that were fatal or that left individuals with severe disabilities are now treatable or preventable. However, because bacteria are so adept at becoming resistant to antimicrobial drugs, it is essential that such drugs be regulated and used judiciously to delay the development of resistance. Misuse and overuse of these drugs contribute to an even more rapid development of resistance. After several decades of successful antimicrobial use, we have seen and continue to see the emergence of multi-resistant bacterial pathogens, which are less responsive to therapy. Antimicrobial resistant bacterial populations are emerging due to the combined impact of the various uses of antimicrobial drugs, including their use in humans and animals. Many of these pathways are not yet clearly defined or understood. As of today, antimicrobial resistance mechanisms have been reported for all known antibacterial drugs that are currently available for clinical use in human and veterinary medicine. In some cases, strains have been isolated that are resistant to multiple antibacterial agents.

U.S. INTERAGENCY TASK FORCE ON ANTIMICROBIAL RESISTANCE

The U.S. Interagency Task Force on Antimicrobial Resistance was created in 1999 to develop a national plan to combat antimicrobial resistance. FDA co-chairs the task force, along with the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH).

The Task Force also includes the Agency for Healthcare Research and Quality (AHRQ), the Centers for Medicare and Medicaid Services (CMS), the Health Resources and Services Administration (HRSA), the Department of Agriculture (USDA), the Department of Defense, the Department of Veterans Affairs, and the Environmental Protection Agency. In 2001, the U.S. Agency for International Development joined the Task Force to help address global antimicrobial resistance issues.

Public Health Action Plan to Combat Antimicrobial Resistance

In 2001, the Task Force published the "Public Health Action Plan to Combat Antimicrobial Resistance" (Public Health Action Plan or the Action Plan). The Action Plan provides a blueprint for specific coordinated Federal actions to address the emerging threat of antimicrobial resistance. It reflects a broad-based consensus of Federal agencies, which was reached with input from consultants from state and local health agencies, universities, professional societies, pharmaceutical companies, health care delivery organizations, agricultural producers, consumer groups, and other members of the public.

The Action Plan has four major components: surveillance, prevention and control, research, and product development. Highlights of the Action Plan include:

Surveillance. Information and statistics about the emergence and spread of resistant microbes and the use of antimicrobial drugs can help experts interpret trends and identify strategies to prevent or control antimicrobial resistance. CDC is working with state health departments and other Task Force members to design and implement a strategy to coordinate national, regional, state, and local surveillance efforts. In addition, FDA, CDC,

and USDA developed and expanded systems to monitor patterns of antimicrobial resistance among foodborne bacteria in human medicine, in agriculture, and in retail meat.

Prevention and Control. Research shows that controlling the use of antibacterial drugs can help reduce the incidence of antimicrobial resistance. In 2003, FDA partnered with CDC on its launch of its *Get Smart: Know When Antibiotics Work* campaign. The goal of the campaign is to educate consumers and health care professionals on the appropriate use of antibiotics. In partnership with doctors and other medical professionals, CDC has developed clinical guidelines for health professionals on how best to use antimicrobials, and supports pilot projects to identify effective strategies to promote appropriate antimicrobial drug use. FDA has promulgated labeling regulations for the appropriate use of systemic antibacterial drugs in humans. FDA's Center for Veterinary Medicine (CVM) has developed, in conjunction with stakeholders, in-depth antimicrobial prudent use principles for beef cattle, dairy cattle, swine, and poultry producers and veterinarians, and more recently, aquatic veterinarians.

Measures that reduce the need for antimicrobial use also serve to reduce the emergence of antimicrobial-resistant microorganisms. Prevention of bacterial infections through the use of vaccines has effectively eliminated or markedly decreased the problem of resistance in organisms such as *Haemophilus influenzae* type b (virtually eliminated in the United States, while still a problem in other parts of the world) and *Streptococcus pneumoniae*, also known as pneumococcus. Published research has confirmed that the latter pneumococcal vaccine has lowered common infections that are often treated with

antimicrobials. Prevention of viral infections through the use of vaccines can also indirectly help reduce antibiotic use and minimize the emergence of antibiotic-resistant microorganisms. For example, viral infections, such as respiratory infections due to influenza, often lead to unnecessary antimicrobial use and are sometimes complicated by serious secondary infections caused by bacteria such as staphylococcus or pneumococcus. In addition, development of increasingly sensitive diagnostic assays for detection of resistance allows for rational targeted antimicrobial use.

Research. The Action Plan promotes expanding existing research in antimicrobial resistance and related fields in an effort to improve treatments and outcomes. NIH is leading a team of agencies to provide the research community with new information and technologies, including genetic blueprints for various microbes, to identify targets for desperately needed new diagnostics, treatments, and vaccines to combat the emergence and spread of resistant microbes. NIH supports clinical studies to test new antimicrobials and novel approaches to treating and preventing infections caused by resistant pathogens. NIH also continues to support and evaluate the development of new rapid diagnostic methods related to antimicrobial resistance, in conjunction with FDA's Center for Devices and Radiological Health (CDRH). In addition, AHRQ funds various studies on the use of antimicrobial drugs and antimicrobial resistance, including ongoing research on reducing unnecessary prescribing of antimicrobials to children. FDA's Center for Biologics Evaluation and Research (CBER) conducts research that facilitates vaccine development for diseases in which resistance is an issue, such as malaria, staphylococcus (MRSA), and enteric diseases.

Product development. As antimicrobial drugs lose their effectiveness, new products must be developed to prevent, rapidly diagnose, and treat infections. The priority goals and action items in the product development focus area of the Action Plan address ways to:

- Ensure researchers and drug developers are informed of current and projected gaps in the arsenal of antimicrobial drugs, vaccines, and diagnostics, and of potential markets for these products;
- Stimulate development of priority antimicrobial products for which market incentives are inadequate, while fostering their appropriate use;
- Optimize the development and use of veterinary drugs and related agricultural products that reduce the transfer of resistance to pathogens that can infect humans; and
- Facilitate development of effective prophylactic vaccines: in particular, focusing on vaccines against microbes that are known to develop antimicrobial resistance (e.g., MRSA), thereby reducing the need for antimicrobials and the occurrence of antimicrobial resistant strains.

The Task Force met with consultants in December 2007 to discuss suggestions and recommendations for revising and updating the Action Plan. The consultants included both domestic and foreign experts in human veterinary medicine, pharmaceutical and diagnostics manufacturing, animal husbandry, clinical microbiology, epidemiology, infectious disease and infection control, and state and local public health. The Action Plan is being revised and is expected to be released later this year.

A Public Health Approach to Antimicrobial Use in Animals

Antimicrobials used in animal agriculture are indicated for a variety of uses. There are four prominent label indications for use of these antimicrobials: growth promotion/feed efficiency; prevention; control; and treatment. The vast majority of classes of antimicrobials used in animal agriculture have importance in human medicine. A few antimicrobial classes (e.g. ionophores) used in food-producing animals do not appear to impact human medicine.

Protecting public health requires the judicious use in animal agriculture of those antimicrobials of importance in human medicine. I will now review how this principle applies to each use.

Growth promotion/feed efficiency

There is clear evidence that the use of antimicrobials in general selects for resistant organisms. To avoid unnecessary development of resistance under conditions of constant exposure (growth promotion/feed efficiency) to antibiotics, the use of antimicrobials should be limited to those situations where human and animal health are protected. Purposes other than for the advancement of animal or human health should not be considered judicious use. Eliminating these uses will not compromise the safety of food.

Disease prevention; and Control

FDA believes that some prevention indications are necessary and judicious to relieve or avoid animal suffering and death. Important factors in determining whether a prevention use is appropriate include: (1) evidence of effectiveness, (2) evidence that such a preventive use is consistent with accepted veterinary practice, (3) evidence that the use is linked to a specific etiologic agent, (4) evidence that the use is appropriately targeted, and (5) evidence that no

reasonable alternatives for intervention exist. FDA also believes that the use of medications for prevention and control should be under the supervision of a veterinarian.

Treatment

FDA supports the treatment of ill animals according to appropriate veterinary practice within a valid veterinary-client-patient relationship.

Judicious use of antimicrobials in animal agriculture requires a strong commitment to surveillance and research, including monitoring antimicrobial resistance, studying the etiology of resistance, tracking the use of antimicrobials in agriculture, assessing risk in different settings, and evaluating strategies to reduce resistance. Such data will support science-based risk management policies.

Specific Activities by the Center for Veterinary Medicine (CVM)

CVM is addressing potential human health risks associated with the use of antimicrobial drugs in food-producing animals by: 1) using risk assessment methodologies (e.g., Guidance 152) during the new animal drug evaluation process to quantify the human health impact from antimicrobial use in animals, in conjunction with robust monitoring, research, and risk management; 2) actively conducting research to advance our understanding of antimicrobial resistance mechanisms and to support our regulatory decisions; 3) reaching out to stakeholders, including consumer groups, through public meetings to provide educational outreach activities and to strengthen and promote science-based approaches for managing the potential human health risks associated with the use of antimicrobial drugs in food-producing animals; 4) assessing relationships between antimicrobial use in agriculture and subsequent human health

consequences through the National Antimicrobial Resistance Monitoring System (NARMS). CVM is the lead coordinator of NARMS. NARMS is a multi-faceted monitoring system that takes advantage of the expertise and resources of a number of Federal agencies and state public health laboratories. NARMS data provide regulatory officials and the veterinary medical community with critical information to help assess the risk associated with antimicrobial use in food animal production; and 5) participating in international dialogue on the use of antimicrobials in animals, including the World Health Organization (WHO) and the Codex Alimentarius *ad hoc* Intergovernmental Task Force on Antimicrobial Resistance.

CVM continues to collaborate with veterinary and animal producer associations to develop and distribute guidelines on the judicious use of antimicrobial drugs in food-producing animals.

Comments on H.R. 1549

FDA supports the idea of H.R. 1549 to phase out growth promotion/feed efficiency uses of antimicrobials in animals. The current statutory process of withdrawing a new animal drug approval is very burdensome on the agency. FDA recommends that any proposed legislation facilitate the timely removal of nonjudicious uses of antimicrobial drugs in food-producing animals. At the same time, FDA believes that legislation should permit the judicious use of antimicrobials in animals for prevention and control as discussed above.

CONCLUSION

Antimicrobial resistance is an important public health issue that can only be addressed by collaborative efforts of the relevant Federal agencies, state health departments, and the private sector. FDA looks forward to working with Congress on this important public health issue.

Thank you for the opportunity to discuss FDA's activities with regard to antimicrobial resistance. I would be happy to answer any questions.