



RECOMMENDATIONS TO THE FDA REGARDING THE USE OF ANTIBIOTICS IN FOOD ANIMAL PRODUCTION

The American Medical Association, American Association of Pediatrics, American Public Health Association, World Health Organization and other medical and public health organizations recognize the need to reduce the inappropriate use of antibiotics in people, as well as in animal agriculture. It is estimated that up to 70 percent of antibiotics sold in the U.S. are used on industrial farms in healthy food animals, to promote growth and to compensate for the effects of overcrowded and unsanitary conditions.¹ This practice promotes the development of deadly strains of antibiotic-resistant bacteria that can spread to humans.

As a result of the growing problem of antibiotic resistance, on June 3, 2009, the Pew Campaign on Human Health and Industrial Farming provided the U. S. Food and Drug Administration (FDA) with recommendations for a range of proposals that could be carried out to improve the efficacy of vital human antibiotics and reduce the serious health threat of antibiotic resistance. Informed by the results of the Pew Commission on Industrial Farm Animal Production, the recommendations cover the areas of *regulatory clarity* and *expanding surveillance*.

REGULATORY CLARITY

Definitions

The Pew Commission on Industrial Farm Animal Production published several recommendations clarifying antibiotic use definitions to provide reliable estimates of use and facilitate clear policies. Based on the Commission's recommendations, the Pew Campaign on Human Health and Industrial Farming believes appropriate definitions should include:

- *Therapeutic*: use of antibiotic in food animals with microbial diseases diagnosed and documented by a veterinarian;
- *Nontherapeutic*: any use of antibiotic in food animals in the absence of microbial disease or known (documented) microbial disease exposure. This would include use as an additive for growth promotion, feed efficiency, weight gain, routine disease prevention in the absence of documented exposure or other routine purpose; and
- *Prophylactic*: short-term use of antibiotic in animals directly exposed to an infectious agent but before onset of laboratory-confirmed clinical disease as determined by a licensed professional. (This type of use must never be relied upon as a mask for illnesses related to density, nutrition or hygiene.)

These definitions are important because there is considerable dispute over the true nature of antibiotic use in food animal production. With no required farm reporting of antibiotic use, and confidentiality regarding animal feed ingredients, public health officials and policy makers must rely on the agricultural and pharmaceutical industries' and others' rough estimates of use. Agribusiness trade association representatives have testified before Congress that all but six percent of antibiotic use in animal agriculture is therapeutic, which they define as prevention, control and treatment of disease, with or without the supervision and diagnostic input of

veterinarians. In other words, the livestock industry has conflated prophylactic and therapeutic uses. According to industry representatives, the remaining six percent of use is for growth promotion and feed efficiency purposes only, which they recognize as nontherapeutic use.

Should new legislation or regulation be imposed to limit the use of antibiotics for growth promotion or undefined “nontherapeutic purposes” in food animal production, only a small percentage of actual use could be affected if industry interpretation excludes the widespread use of these drugs for routine disease prevention. Curbing this minor form of use would likely have little success in reducing antibiotic resistance.

Therefore, we strongly recommend codifying antibiotic use definitions in line with Pew’s guidelines. Further, any changes to agricultural antibiotic use definitions should be considered in open, official regulatory channels that allow opportunity for public comment.

Guidance #152

In 2003, the Center for Veterinary Medicine (CVM) issued guidance to industry regarding the safety of new antimicrobial drugs in food animals. Guidance #152 states:

FDA believes that human exposure through the ingestion of antimicrobial-resistant bacteria from animal-derived foods represents the most significant pathway for human exposure to bacteria that has emerged or been selected as a consequence of antimicrobial drug use in animals.

By law, prior to approval of any *new* drug, FDA must determine it is safe for both animals and human health. FDA considers an antibiotic new animal drug to be “safe” if it concludes that there is reasonable certainty of no harm to human health from the proposed use of the drug in food-producing animals. FDA also recommends through Guidance #152 a risk assessment approach for evaluating safety as it relates to antibiotic resistance. This guidance is non-binding.

However, most antibiotics currently used in food animal production systems for nontherapeutic purposes were approved before the FDA began giving in-depth consideration to resistance during the drug approval process. FDA has not established a schedule for reviewing existing approvals, although Guidance #152 notes the importance of doing so.

The Pew Campaign on Human Health and Industrial Farming recommends that the discretionary review set out in Guidance #152 be made mandatory, legally enforceable and applied retroactively to previously approved antibiotics. This is one of the most beneficial steps FDA can take to safeguard the efficacy of antibiotics, as it should result in the phase-out of nontherapeutic use of important antibiotics in food animals, and should enable improved knowledge of and response to human antibiotic resistance being caused partially by animal agriculture.

Drug Approvals

In 2004, a CVM internal evaluation questioned the safety of using penicillin in animal feed. However, the report has not yet been released. We ask that the report be made public.

In September 2006, the FDA Veterinary Medicine Advisory Committee (VMAC) met to consider the application for the approval of the first fourth-generation cephalosporin, cefquinome, to be used for disease treatment in food-producing animals. The American Medical

Association, Infectious Diseases Society of America and the American Academy of Pediatrics all opposed its approval because of concerns that it would lead to the reduced efficacy of cephalosporins for treatment of serious human illness, including food-borne *Salmonella*—a disease for which cephalosporins are the treatment of choice. The U.S. Centers for Disease Control and Prevention (CDC) also raised concerns about the approval of this drug. A majority of the VMAC members voted that the sponsor had failed to show cefquinome was safe with respect to antibiotic resistance. FDA has not yet acted and Pew urges the agency to formally reject the application.

In December 2008, after receiving over 300 comments from the animal agriculture industry and production veterinarians, the FDA reversed an earlier ban of extra-label use of cephalosporins in food animals. In July 2008, the FDA had announced the ban based on its determination that extra-label use presents a risk to public health. Pew respectfully urges FDA to reissue the ban of extra-label cephalosporin use based on the body of scientific evidence showing its threat to human health.

Veterinary Medicine and Food Animal Husbandry

In food animal production, local veterinarians often are not involved in all uses of antibiotic on the farm, because they have little to no knowledge of the antibiotic types and dosages being supplied to food animals through the feed that is typically supplied directly to contract growers from vertical integrators with no veterinary oversight. Veterinarians have even less knowledge regarding antibiotic residues that may be fed to poultry and livestock in ethanol distillers grains added to feed. The Pew Commission on Industrial Farm Animal Production viewed this lack of knowledge as hindering animal health, and, ultimately, worker and public health, and recommended enhanced veterinary involvement in all uses of antibiotic.

A January 2009 study by the U.S. Department of Agriculture (USDA) reaffirmed earlier research showing that improved animal husbandry and sanitation at food animal facilities was correlated with reduced use of nontherapeutic antibiotic, as well as enhanced monitoring of zoonotic viruses (animal disease that can transfer to people) and harmful bacteria, all with little negative—or with somewhat positive—economic impact to producers.²

In addition to clarifying antibiotic use definitions, phasing out nontherapeutic use of these drugs in food animal production, and enforcing Guidance #152, the Pew Commission recommended several other steps that FDA could take to lessen the contribution of animal agriculture to the antibiotic resistance public health crisis, including:

- Enforce the Animal Medicinal Drug Use Clarification Act, which allows veterinarians to go beyond label directions for animal drugs, but only when animal health is threatened or lack of treatment may result in suffering or death, and excluding use in animal feed or to enhance production;
- Compel veterinarians to submit prescription and treatment information on food animals to a national database to allow better tracking of antibiotic uses (including uses in feed) as well as better oversight by veterinarians of all antimicrobial uses in food animals; and
- Express to the USDA the need for government assistance to teach producers husbandry methods and best practices that are alternatives to nontherapeutic antibiotic use while also maintaining high productivity.

EXPANDING SURVEILLANCE—INDUSTRIAL FARMS AND FOOD SAFETY

The Pew Campaign on Human Health and Industrial Farming recommends that the FDA require all industrial farm workers to be regularly tested to determine whether they have been colonized with antibiotic-resistant bacteria, and that the CDC be authorized and funded to conduct the testing to ensure objective, standardized procedures and reporting of results.

The food safety challenge in the U.S. is compounded by the growing crisis of antibiotic resistance. Many antibiotic-resistant strains of bacteria include those that cause common food-borne illness. For example, nearly 1.4 million people in the U.S. contract *Salmonella* infections annually, and of those, roughly one-fifth (272,000) of the infections are antibiotic resistant. There are about 2.4 million *Campylobacter* infections in the U.S. annually, and roughly half (more than 1.2 million) of those are resistant to at least one antibiotic.³ A comprehensive examination of food safety in America must include practices creating risk from the beginning of the production chain—on industrial farms—all the way through the production, manufacturing and sales chain to the consumer. Therefore, Pew also recommends:

- Establishing among such agencies as FDA, USDA, CDC and the Environmental Protection Agency (EPA) a permanent interdisciplinary oversight group to improve monitoring and surveillance of antibiotic resistance in the food supply, environment and animal and human populations, including integrating data and coordinating with the National Antimicrobial Resistance Monitoring System (NARMS); and
- Working with EPA, USDA and CDC to develop a comprehensive plan to incorporate monitoring of the farm environment (soils, air and waters) and nearby airsheds and water supplies with the monitoring of antibiotic -resistant microorganisms in food animals.

For more information, contact Laura Rogers, Project Director, Pew Health Group, at (202) 552-2018, or lrogers@pewtrusts.org.

¹ Mellon, Margaret, Charles Benbrook, & Karen Lutz Benbrook. 2001. *Hogging It! Estimates of Antimicrobial Abuse in Livestock*. Cambridge, MA: Union of Concerned Scientists.

² MacDonald, James M. and William D. McBride (January 2009). *The Transformation of U.S. Livestock Agriculture: Scale, Efficiency, and Risks*. Economic Information Bulletin No. (EIB-43), U.S. Department of Agriculture Economic Research Service, pp. 32-35. Available at: <http://www.ers.usda.gov/Publications/EIB43/>.

³ *Salmonella* calculations based on: USDA Economic Research Service, Foodborne Illness Cost Calculator: Salmonella, http://www.ers.usda.gov/Data/FoodborneIllness/salm_Intro.asp; and U.S. Food and Drug Administration, *National Antimicrobial Resistance Monitoring System 2005 Executive report*, at <http://www.fda.gov/cvm/2005NARMSExeRpt.htm> (in 2005, 19.4% of human isolates were resistant, and 6.9% were resistant to at least 5 antimicrobials). *Campylobacter* calculations based on: CDC Campylobacter fact sheet, at http://www.cdc.gov/nczved/dfbmd/disease_listing/campylobacter_gi.html#2; and CDC NARMS, *Human Isolates 2005 Final Report*, at <http://www.cdc.gov/NARMS/annual/2005/NARMSAnnualReport2005.pdf>.