



To define, to promote and to realize the prudent use of antibiotics around the world. NO :29

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**Document:** A proposed framework for evaluating and assuring the human safety of the microbial effects of antimicrobial new animal drugs intended for use in food-producing animals

**Docket No:** 98D-1146

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There is growing recognition and concern that the use of antibiotics in food-producing animals contributes to the development of resistance in bacteria that find their way into food and humans. To protect public health by preserving the long-term effectiveness of antimicrobial drugs for treating human diseases, the Alliance for the Prudent Use of Antibiotics (APUA) supports the FDA's efforts in developing rigorous guidelines for approving and evaluating animal antimicrobial drugs used in food-producing animals. APUA, an international nonprofit organization dedicated exclusively to the proper use of antibiotics and containment of drug resistance, strives to preserve the effectiveness of antibiotics in both human and veterinary medicine. To this end, APUA recommends that the proposed framework be applied to both current and new animal-use antimicrobial drugs along with the following changes:

**The FDA should eliminate the non-therapeutic use of antimicrobial drugs in food-producing animals.**

Chronic subtherapeutic antibiotic usage, such as in growth promotion, poses a major ecological problem that impacts public health. Domestic food-producing animals outnumber humans in the United States by more than five to one, and the majority of these animals are routinely given subtherapeutic doses of antibiotics to promote growth. Repeated low-level exposure to antibiotics (i.e., subtherapeutic doses) disrupts the animal's normal bacterial flora and promotes the growth of antibiotic resistant bacteria. Chronic use (a week or more) of antibiotics, at either subtherapeutic or therapeutic levels, leads to multi-drug resistance in both humans and animals. Antibiotic-resistant bacteria selected in animals can reach humans, where they are propagated by the use of the same antibiotic in humans.

Antimicrobial drugs, regardless of drug "category," should not be used for non-therapeutic purposes in food-producing animals. While it is clear what antimicrobial drugs are currently used in human therapeutics, it may not be clear what new antimicrobial drugs, or derivatives, may someday be used in human medicine. As pharmaceutical companies

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continue discovery efforts, active analogs of animal-use drugs have been found useful in human medicine. Today derivatives of animal-use drugs have been developed as important classes of valued human therapeutics. However, because of years of chronic use as growth promoters, resistant bacteria are already present in the environment which thwart the efficacy of these new antibiotics and transfer resistance traits, in some cases even before the new human therapeutics have been introduced.

**The FDA must prohibit the use of any human-use antimicrobial drugs in food-producing animals if there is evidence of an increase in antimicrobial resistance within the animal population.**

As multi-drug resistance can emerge in as little as 7 days of chronic use of an antimicrobial drug, any rise in resistance levels that is related to antimicrobial drug use in food-producing animals could constitute a public health threat. Thus, the FDA must monitor resistance levels associated with animal-use antimicrobial drugs.

Many pharmaceutical companies monitor animal flora before, during and after the administration of new antimicrobial drugs. These longitudinal data would be invaluable in determining resistance trends and should be available for decision-making purposes. The FDA should require pharmaceutical companies to submit resistance data on a regular basis. These data will be used to determine a conservative threshold of resistance and monitor resistance trends. If antibiotic resistance levels rise above a predetermined point, the use of any human-use drug must immediately be discontinued while further studies are conducted.

In conclusion, the FDA framework must identify and eliminate non-essential antimicrobial drug use and reserve as many of these drugs as possible for proper use in human and veterinary medicine. To accomplish these goals, the FDA must curtail non-therapeutic use of all antimicrobial drugs and closely monitor antimicrobial drug resistance in food-producing animals. Again, APUA applauds the FDA for developing a framework for evaluating new animal-use antimicrobial drugs to protect human safety. APUA would be pleased to work with the FDA to help evaluate and monitor antimicrobial drug resistance patterns.

Sincerely,



Stuart Levy, MD  
President

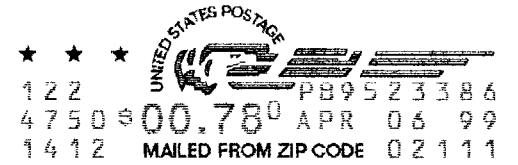


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