

L I V I N G

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March 31, 1999

Dockets Management Branch (HFA-305),
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 98D-1146 - Discussion Paper: "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."

To Whom It May Concern:

These comments are submitted with regard to the Food and Drug Administration's (FDA's) "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" (64 Fed. Reg. 887, Jan. 6, 1999). The proposed Framework (1) describes a pre-approval system under which FDA will consider the potential of new uses of antibiotics in animal agriculture to exacerbate problems of antibiotic resistance in human pathogens, and (2) outlines requirements for post-approval studies and monitoring of resistance levels for new uses of antibiotics in animal agriculture. As discussed below, we are pleased that FDA is beginning to consider antibiotic resistance resulting from antibiotic use in animal agriculture. Nevertheless, the proposed Framework is extremely weak and needs to be substantially revised in order to protect the efficacy of antibiotics vital to human health.

FDA should restrict the use of antibiotics in food-animal production based on concerns about antibiotic resistance.

We support FDA for beginning to consider antibiotic resistance before approving new antibiotics for use in food-animal production. As described in the proposed Framework and in numerous scientific reports, the evolution of antibiotic resistance by bacteria poses a serious threat to human health. In response to heavy use of antibiotics, strains of many disease-causing bacteria are losing their susceptibility to the antibiotics formerly used to treat them. As a result, literally untreatable bacterial infections could become common in the future. Recently, a number of reports by leading experts have urged sharp reductions in uses of antibiotics in agriculture (e.g. WHO 1997, Levy 1998, Witte 1998).

We strongly agree with FDA that uses of antibiotics in animal agriculture should be evaluated and, as appropriate, restricted in order to assure that these uses do not threaten human health by promoting the spread of antibiotic resistance. We strongly advocate that FDA make decisions in favor of protecting

98D-1146

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health when there are tradeoffs between human health and perceived economic advantages for current systems of intensive animal production. Unfortunately, as discussed below, the proposed Framework favors animal agriculture at the expense of human health.

The proposed Framework will only be risk-based if it is applied to existing as well as to new uses of antibiotics.

FDA asserts that the proposed Framework "sets out a conceptual risk-based framework for evaluating the microbial safety of antimicrobial drugs intended for use in food-producing animals." Taking a narrow view, FDA's proposed Framework can be considered a risk-based approach for evaluating new uses of antibiotics in food-animal production, in that FDA's proposed actions are related to the extent of human health risks from particular new uses of antibiotics in animal agriculture.

Taking a broader view of the problem of antibiotic resistance, however, leads to the conclusion that the proposed Framework is not risk-based. More than 40 percent of the total volume of antibiotics in the United States are now used in animal agriculture, and the greatest risk to human health comes from existing rather than new uses of antibiotics in animal agriculture. Yet these existing use of antibiotics in agriculture are virtually ignored by the proposed Framework. We urge FDA to address existing uses of antibiotics in food-animal production, as well as prospective uses. In particular, we urge the agency to implement the March 1999 petition by the Center for Science in the Public Interest, the Environmental Defense Fund, the Union of Concerned Scientists, Food Animals Concerns Trust, and Public Citizen's Health Research Group, to end existing uses of antibiotics in animals feeds consistent with recommendations by the World Health Organization (WHO 1997) and the U.S. Centers for Disease Control and Prevention.

FDA's proposed scheme for categorizing antibiotics does not adequately protect human health.

As part of FDA's proposed Framework, the agency proposes to place antibiotics into one of three categories according to their relative importance in human medicine. FDA would then subject new uses of antibiotics in each of the proposed categories to certain use restrictions and post-approval requirements. Use of antibiotics in Category I, for example, would be subject to far greater restrictions than the use of antibiotics in Category III.

In principle, the establishment of such categories by FDA is a reasonable method to facilitate agency decision-making. As proposed, however, FDA's categorization scheme does not adequately protect against bacterial resistance to antibiotics important to human medicine. FDA's proposed Category I includes antibiotics that are "Essential for the treatment of a serious or life-threatening disease in humans for which there is no satisfactory alternative therapy." In other words, Category I includes antibiotics for which the loss of bacterial susceptibility would likely result in human deaths. Yet, FDA proposes to allow Category I antibiotics to be used in food-animal production, as long as steps are taken to limit the spread of bacterial resistance. But, even limited use of Category I antibiotics will increase the risk that bacteria will evolve resistance to them, thus jeopardizing human lives. Instead of risking the future efficacy of antibiotics critical to human health, we urge that FDA not permit the use of Category I antibiotics in food-animal production.

Similarly, we urge that FDA revise the standards for Category II and III antibiotics. Category II includes antibiotics important for the treatment of human disease, but for which "satisfactory alternative therapies exist." These drugs should be subject to the restrictions and post-approval requirements now proposed for Category I antibiotics. Category III now includes antibiotics that are not a first choice for

treating human infections and drugs that are not used in human medicine. We urge that Category III is subdivided, so that antibiotics used in human medicine are subject to greater restrictions and post-approval requirements than those not used in human medicine.

FDA should require that drug-sales information be submitted to the agency.

The efforts of scientists at FDA and other institutions to correlate the evolution of resistance in bacteria with the use of antibiotics in agriculture are now severely hampered by drug manufacturers' refusal to divulge information on antibiotic sales. Under the proposed Framework, FDA would require that detailed drug sales information be submitted as part of "drug experience reports." Drug sales information is vital to improved understanding of the evolution of antibiotic resistance and to the effectiveness of post-approval monitoring for resistance. We therefore strongly support FDA's proposal to require the submission of drug sales information. We also urge that FDA make drug sales information publicly available to the fullest extent allowed by law, thus allowing researchers and others to have access to it.

Thank you for your consideration.

Sincerely,



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References:

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