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U.S. House of Representatives
Committee on Energy and Commerce
Washington, DC 20515–6115

JOHN D. DINGELL, MICHIGAN
CHAIRMAN

April 18, 2007

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner von Eschenbach:

Pursuant to Rules X and XI of the Rules of the U.S. House of Representatives, the Committee on Energy and Commerce and the Subcommittee on Oversight and Investigations have been conducting an inquiry into the adequacy of the efforts of the Food and Drug Administration (FDA) to protect the American public from the unnecessary risks associated with prescription drugs. We are concerned not only about the risks of drugs prescribed to treat humans but also the human health consequences of drugs, antibiotics in particular, administered to farm animals that later enter the Nation's food chain.

Antibiotic resistance caused by the widespread use of antibiotics in animals is widely recognized as a major health issue. As antimicrobial resistance is driven by antimicrobial use, the sheer volume of pharmaceuticals used in agriculture raises significant public health concerns. Indeed, the U.S. Centers for Disease Control and Prevention (CDC) calls antibiotics resistance "one of the world's most pressing public health problems." In the face of the potentially devastating consequences, many countries have acted to limit the risk. For example, the United Kingdom and Sweden banned the use of penicillin and tetracycline for non-therapeutic growth promotion decades ago.

Nevertheless, antibiotics are still extensively administered in the absence of disease in today's livestock production. The Union of Concerned Scientists estimates that 70 percent of all antibiotics used in the U.S. are used as feed additives for food animals. This continued non-therapeutic use has prompted numerous medical organizations, including the American Medical Association, the American Academy of Pediatrics,

and the Infectious Diseases Society of America, to call for an end to the routine use of medically important antibiotics as feed additives. Scientists and physicians are concerned that if we wait to see irrefutable evidence that a significant amount of antibiotic resistance emerges from the food chain, it will be too late to protect the public health.

At a minimum, great caution should be exercised in the approval of new veterinary applications for antibiotics. That caution is reflected in Guidance #152, which represents FDA's risk assessment approach for evaluating the microbial food safety of the use of a new drug in food-producing animals. The Center for Veterinary Medicine deserves much credit for development of this science-based guidance for the animal drug industry. Nevertheless, questions have been raised about whether it may be time to revise Guidance #152 to reflect changes in diseases and the epidemiology of resistance.

Recent studies raise the possibility that illness other than food-borne disease can result from the transmission of resistant bacteria from animals to humans. For example, new data shows an increase in fluoroquinolone-resistant *Campylobacter jejuni* in humans and animals. Also Antoine Andremont (Groupe Hospital Bichat-Claude Bernard, Paris, France) showed that *Escherichia coli* isolates from urinary tract infections had identical features to *E. coli* in food animals, which suggests that we should look not just at gastrointestinal tract infections, but at other infections, too.

The World Health Organization (WHO), using the "precautionary principle," has developed an antimicrobial drug ranking criteria, different from that contained in Guidance #152, which does not give more importance to food-borne disease. In light of the WHO ranking and the evidence suggested above, some experts suggest it is time to revisit the ranking approach in Guidance #152.

In order to better understand the Agency's position on Guidance #152, we request answers to the following questions:

- Enteric bacteria in animals which cause food-borne illness in man is the most direct link for transmission of resistant bacteria from animals to humans. Nevertheless, non-enteric bacteria in animals may also be transmitted to non-enteric bacteria in humans. Given evidence of this transmission, what is the public health justification for limiting the definition of "critically important" drugs (contained in Guidance #152) to those used to treat enteric pathogens that cause food-borne disease? Why are the criteria for the drug ranking contained in Appendix A of the Guidance #152 different from WHO criteria? Given the WHO ranking, should FDA continue to rely on the food-borne illness link?

- Given the existence of evidence of the transmission of resistant bacteria from animals to humans causing illness other than food-borne disease, does the FDA plan to re-evaluate the criteria contained in Guidance #152 used to classify the importance of drugs? If not, does FDA stand by its Guidance to industry?

Please provide your response to these questions within two weeks of the date of this letter. Should you have any questions relating to this request, please have your staff contact David Nelson or Joanne Royce of the Committee Majority staff at (202) 225-2927, or Alan Slobodin of the Committee Minority staff at (202) 225-3641.

Sincerely,

John D. Dingell
Chairman

Joe Barton
Ranking Member

Bart Stupak
Chairman
Subcommittee on Oversight
and Investigations

Ed Whitfield
Ranking Member
Subcommittee on Oversight
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