

Alexander S. Mathews
President & CEO

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[Docket No. 98D-0969] "Guidance for Industry: Evaluation of the Human Health Impact of the Microbial Effects of Antimicrobial New Animal Drugs for use in Food Producing Animals."

The Animal Health Institute takes this opportunity to comment on the proposed guidance document published November 18, 1998 in the *Federal Register* – AHI is a national trade association representing manufacturers of animal health products – the pharmaceuticals, vaccines and feed additives used in modern food production, and the medicines that keep pets healthy.

We understand that the Center for Veterinary Medicine is publishing this guidance to affirm their authority under the Food, Drug, and Cosmetic Act, specifically Sections 512(d) (1) (A), and 201(u), to require information on the potential development of bacterial resistance as a condition of approval of an antibacterial new animal drug or supplemental new animal drug. These requirements have heretofore been applied only to antibacterials proposed for continuous use in animal feeds under 21 CFR 558.15.

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AHI questions the current basis for, in effect, potentially expanding 558.15 to all uses, including currently approved and marketed products. There is only one recent article (1997) cited in the references with all others being five years or older. Specifically, reference 2 on penicillin use hazards was addressed by the NAS study in the 1980s. Furthermore, the VRE situation with avoparcin is unique to Europe, not the US. Although AHI shares the concern that antibiotic resistance is a *potential* threat to animal and human health, we don't agree that the Agency has justified on a scientific basis the need or public health value of adding such a substantial new burden to the approval process for veterinary therapeutic antibacterial products.

The summary states “FDA now believes it is necessary to evaluate the human health impact of the microbial effects associated with all uses of all classes of antimicrobial new animal drugs intended for use in food-producing animals when approving such drugs.”

Although this guidance document provides “current thinking only about its authority” and “does not provide technical guidance,” it does specify “aspects” that should be evaluated. This includes: (1) The quantity of resistant enteric bacteria formed in the animals intestinal tract following exposure to the antimicrobial new animal drug (resistance) and (2) changes in the number of enteric bacteria in the animals intestinal tract that can cause human illness (pathogen load). The guidance then goes on to state, “In some cases, a pre-approval study or studies may be needed.” It is apparent that to evaluate these aspects of enteric bacteria, additional studies will be required.

The rationale for these new requirements is based on concerns raised by scientific and media reports of antibiotic resistant foodborne pathogens associated with the use of

antimicrobials in food animals. However, while a hazard (resistance) has been identified, the Agency, or other independent organization has not determined the degree of actual risk to human health. The relative risk of an antimicrobial used in food producing animals to public health is dependent on a given resistant foodborne pathogen contaminating a food product and subsequently causing illness. This scenario is highly dependent on the microbial interventions of all critical steps between the farm and the table; therefore, it is difficult to envision how the results of pre-approval studies can be used to accurately predict impact on public health. The role that antimicrobial use in animals plays in this continuum, along with the potential impact on human health, must be determined prior to any new requirements being imposed.

AHI believes measures are in place to protect the public health and can be improved by strengthening the National Antimicrobial Resistance Monitoring System (NARMS). Periodic monitoring of carcasses at slaughter sampling provides the fastest evaluation of a problem in the species tested (*E. coli*, salmonella and campylobacter). The use of the ARS data, based on FSIS samples, will serve as the best and most efficient early warning system. On-farm epidemiological studies may be valuable to provide risk factor analysis, as a follow-up step to the NARMS program, should an animal species, bacteria species and antibiotic MIC shift be identified as a significant concern.

The National Antimicrobial Susceptibility Monitoring Program (61 FR 57732, 57736 and 57737) stated that the data generated is critical because early detection of emerging resistance, identified through the monitoring program, will allow the agency to contain any resistance that does occur, thereby limiting its spread. In fact, the limited data generated by NARMS has found

no evidence of fluoroquinolone resistant salmonella in either man or animals. This program has the potential to detect shifts in susceptibility over time. Therefore, AHI fails to see how adding the additional burden of pre-approval studies can contribute further to protection of the public health.

AHI also believes that current initiatives to develop judicious use principles will help reduce the development of resistance and thereby prolong the useful life of antimicrobials and further protect the public health. We strongly support these efforts.

In summary, AHI believes safeguards are currently in place to adequately protect the public health without requiring additional studies for approving new antimicrobials. Any concern that a public health risk may result from the use of antimicrobials in food producing animals should be investigated with appropriate risk assessment methodology to determine the magnitude of the risk that might exist. If a significant risk is determined, then appropriate risk management measures, encompassing the entire food production chain, can be implemented to assure continued protection of the public health.

Respectfully submitted,



Alexander S. Mathews