



APUA Ecology Program Position Statement

Re: CVM Guidance for Industry #152

Updated: 1/5/04

Summary of Guidance Document

The purpose of this Guidance Document is to outline a suggested approach to risk assessment for use by New Animal Drug Application (NADA) sponsors in demonstrating the microbial food safety of antimicrobial new animal drugs. The Guidance states that “human exposure through ingestion of antimicrobial resistant bacteria from animal-derived foods represents the most significant pathway for human exposure to bacteria that have emerged or been selected as a consequence of antimicrobial resistance.”

Hazard characterization is an initial and independent step in the recommended approach to risk assessment. In general, the purpose of hazard characterization is to determine whether risk assessment is necessary, and, if so, the appropriate targets and parameters for risk assessment. According to the Guidance, hazard characterization should include an assessment of drug-specific information, bacterial resistance information, and data gaps. Sponsors are encouraged to consult with FDA following hazard characterization in order to determine how to proceed.

The Guidance states that qualitative risk assessment should include a Release Assessment (i.e. an estimate of the probability that resistant bacteria are present in animals as consequence of drug use), Exposure Assessment (probability that humans ingest the bacteria in question), and Consequence Assessment (probability that humans exposure results in adverse health consequences). Factors to be considered in Release Assessment include mechanism of action, spectrum of activity, pharmacokinetics, pharmacodynamics, resistance mechanisms, resistance transfer, selection pressure, etc. Exposure is assessed as a function of human consumption of the commodity in question and contamination. Consequence assessment is based on the importance of the drug in question to human medicine.

Once complete, these three qualitative risk estimates are to be integrated in an overall risk estimate. The Guidance also outlines the range of risk management options available to FDA. However, the document is careful to state that risk estimate does not automatically determine approval status; FDA will continue to determine whether or not there is a reasonable certainty of no harm on a case-by-case basis.

Strengths of the Guidance

- The qualitative approach to risk assessment outlined in the Guidance is probably appropriate given the considerable uncertainty surrounding resistance issues.
- FDA’s flexibility with respect to risk management is interesting—essentially, the agency is reserving the right to ignore the outcome of the risk assessment if it deems that other factors are more important. This can be viewed as either a strength or a weakness, depending on how much confidence you happen to have in FDA’s ability to exercise sound judgment. It will be interesting to see how this plays out.

Points of Conflict with the FAAIR Report

- FAAIR Policy Recommendation #4 suggests that “risk assessment procedures should take into account both direct and environmentally mediated human health effects of agricultural antimicrobial use.” Prioritizing ingestion of resistant bacteria in food products as the most significant exposure pathway does not necessarily preclude consideration of indirect or ecologically-mediated transfer of resistance, but the risk assessment approach outlined in the Guidance does not explicitly consider pathways other than ingestion of foodborne bacteria.
- Later, in the same Recommendation, the FAAIR Panel suggests that the precautionary principle should be invoked where data are scarce. When it comes to predicting effects on antimicrobial resistance, data are always scarce. In this respect, the Guidance is not in keeping with the spirit of the FAAIR Recommendations, but neither is US policy with respect to drug regulation.