ANIMAL HEALTH INSTITUTE

Representing manufacturers of animal health products

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January 4, 2001

Dockets Management Branch
Food and Drug Adminstration
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Re: Comments to FDA Docket No. 00D-1677

The Animal Health Institute submits these questions to the Food and Drug Administration Center for Veterinary Medicine docket – " An Approach for Establishing Thresholds In Association With the Use of Antimicrobial Drugs in Food Producing Animals; Availability." AHI is a national trade association representing manufacturers of animal health products – the pharmaceuticals, biologicals, and feed additives used in modern food production and the medicines that keep pets healthy.

The threshold document is intended for discussion at an upcoming workshop sponsored by the agency on January 22-24, 2001. In order for AHI to better understand the concepts discussed in the document and to more effectively prepare for the workshop, it would be very helpful if the agency could clarify certain key terms and relationships being proposed to establish human health impacts and thresholds. Therefore, we respectfully request that the agency provide a response to the following questions:

1. How would the (k-res) proportionality factor be developed? Would it be an analysis of historical data? Would a different (k-res) be developed for each drug and each labeled use? Would currently approved compounds for which concerns exist have a (k-res) developed or only new animal drugs pending approval?

2. In developing H (x) from what time period are the factors that determine the value of Q obtained? Would the Q value essentially be what is calculated in Section 4 of the Vose risk assessment model? Is H (x) expressed in terms in the same manner as in the risk assessment ie: "persons who would have resistant Campylobacter resulting from the consumption of poultry who received Fluoroquinolones"? Is H (x) designed to be some sort of baseline level of human health impact? Would H (x) be determined or calculated generally prior to the approval of a drug product? Would H (x) be calculated for products that were already approved? Is the value 11,000 +or- or 5000 +or- for human health impact as determined by the Vose risk assessment equivalent to H (x)?

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3. T (x) is the unacceptable level of infections in humans. Is T (x) expressed in terms of persons with illness or in some other form like a percentage of resistance? If hypothetically Q=Qt (x) then it appears that T (x) would equal H (x) -- would that then mean that the current level on human health impact was unacceptable? What if T (x) is less than H (x)? How could T (x) be unacceptable? Is there some policy determination necessary to determine the exact level of T (x) that is unacceptable or is it determined purely as a result of Equation 2 (T (x)=(k-res)*Qt (x)?

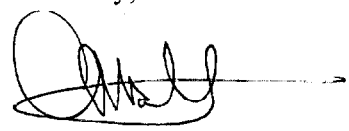
4. Qt (x) appears to be determined by the same basic formula as Q. Is Qt (x) data from a later time period from Q? Generally how would the data to determine Qt (x) be obtained and how would it be related to the data collected to determine Q?

5. The variable (h) can according to the threshold document be potentially obtained in several ways. What is the most likely source of the data to determine (h)? How is (h) different from the "proportion of samples from which resistant bacteria are isolated" used to determine Q and Qt (x)?

6. The variable t (x) appears to be representing a level of resistance prevalence in food either at slaughter or at retail. Can you make clear, conceptually, how the ratio of the current measured prevalence H (x) and the unacceptable prevalence T (x) multiplied by the proportion of resistant isolates (h) independently yields a value for t (x) that establishes a threshold which is related to T (x) or is based on a relationship of resistance prevalence in humans and animals?

7. How can you introduce t (x) into the denominator of the expanded version of the equation T (x)/Q (x)? Is t (x) really a calculated value or is it a result of a policy decision of what is an acceptable level of resistance in animal or food isolates?

Sincerely,



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