

**CORNELL**  
UNIVERSITY

College of Veterinary Medicine

Aquatic Animal Health Program  
Department of Microbiology and Immunology  
Ithaca, New York, 14853-6401Telephone: (607) 253-3365  
Fax: (607) 253-3369

5 September 1997

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
12420 Parklawn Drive, Room 1-23  
Rockville, MD 20857

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Dear Sir or Madam:

I am providing the following comments in response to the FDA "Request for Comments on Development of Options to Encourage Animal Drug Approvals for Minor Species and For Minor Uses (Docket No. 97N-0217)."

My comments will reflect my beliefs with regard to drug approvals in aquatic animals, an area where I consider myself to have considerable experience. They may also be appropriate to other minor animal species.

My comments are as follows:

## 1. Data Submissions:

Historically, those who have submitted data in support of labels have been required to complete considerable original work under GLP conditions. No one would argue against the need to complete high quality work, but there is a need to seriously consider the need to "re-invent the wheel." Recently, there have been discussions within FDA regarding the acceptance of scientific studies that are published in the peer-reviewed literature. I believe the establishment of such a policy (ie. that peer reviewed scientific studies are acceptable) would have a highly significant positive impact on approval of drugs for minor animal species and for minor uses. This would greatly decrease the time and expense associated with repeating studies that have already yielded high quality data. Further, consideration should be made to accept data packages that have been approved in other industrialized countries. Many of these countries have highly credible scientific communities that have conducted excellent work in support of labels for therapeutic compounds. Requiring the work to be redone within the borders of the United States does not make sense.

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## 2. Types of studies:

The following types of studies are currently required:

Target animal safety  
Efficacy  
Human Food Safety  
Environmental Impact

I believe there is an opportunity to achieve a cost savings by combining some of these studies. I would propose the following approach for consideration. Initially conduct a pharmacokinetics study of the compound in the candidate species. The objectives of such a study would be to determine the concentration of drug that could be achieved in tissues (for therapeutic purposes) as well as the elimination kinetics (for human food safety). Concurrently, original studies could be performed and/or the literature could be surveyed to determine the MIC (minimum effective dose) of the drug against selected bacterial pathogens. Knowing that one strives to achieve at least three times the MIC in tissues to establish a therapeutic dose, one could select an appropriate dose based on the results of the pharmacokinetics studies.

At this point, the effort would shift to the collection of efficacy data. I strongly believe that this should be done in the field with actual disease outbreaks. Based on approximately 20 years of experience performing laboratory-based dose titrations in fish, I personally believe such studies to be of very limited value. Even though they are conducted in the laboratory under "controlled" conditions, there are still a number of factors that impact on the results. The conclusions one can draw from laboratory-based dose titrations should be limited to questions of whether the drug provides any therapeutic effect, and that the effect appears to be correlated to dose. Because the laboratory environment is so different from that in the field, I do not believe that one can select an optimum dose based on such studies. Further, I believe that, particularly for fish, laboratory-based dose titration studies in fish are an inappropriate use of animals in research. I believe the pharmacokinetics approach is a far more appropriate and scientifically valid means of determination of the dose.

The field studies are conducted and a determination is made as to the value of the drug. More than one field study could be performed to evaluate the drug for different bacterial pathogens. In addition, disease outbreaks in different species of fish (as per the species grouping concept) could be treated to allow for the broadest "for fish" label to be granted.

The question of environmental impacts has focused on the aquaculture industry. I do not understand why that is so. Drugs are not "dumped into the water." An commercial aquaculturist would go bankrupt if that were the case. The cost of antimicrobials necessary to effect a bath treatment in a pond environment would

far exceed the value of the fish in that culture environment. Bath treatments using antibacterials might only be feasible in systems with very little water volume and fish of very high value. In the commercial aquaculture environment, antibacterial drugs are incorporated into the feed and that medicated feed is fed to the fish. Medicated feed is far too expensive to waste and the aquaculturist that wastes such feed will not remain in business long. I agree that there is some loss of drug to the environment in this process. But is there not a similar loss in land dwelling animals in a terrestrial environment? I believe the granting of a categorical exclusion for terrestrial species should also be extended to include minor species that are aquatic.

Thank you for the opportunity to comment on these issues of minor use animal drugs.

Yours truly,



Paul R. Bowser, PhD  
Professor of Aquatic  
Animal Medicine

**ROUTING AND TRANSMITTAL SLIP**

Date

9/15/97

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**REMARKS**

Please place this  
 in Docket No. 97N-0217  
 ("Comments on Development of  
 Options to Encourage Animal  
 Drug Approvals for minor  
 Species + Minor Uses")  
 Thank you.

DO NOT use this form as a RECORD of approvals, concurrences, disposals, clearances, and similar actions

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Carol Haley

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