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

SUBJECT: Comments on the Discussion Draft "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Use" (Docket No. 97N-0217)

First of all, I wish to thank the Center for Veterinary Medicine (CVM) for their extraordinary efforts to improve our chances of gaining approvals for aquaculture drugs. As part of these efforts, CVM released the Discussion Draft "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Use" (Docket No. 97N-0217). I am very supportive of these proposals and urge quick implementation. My comments on these proposals are presented below:

A. MODIFICATION OF EXTRALABEL PROVISIONS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Will the proposed modification of extralabel provisions and suggested sunset period provide adequate and appropriate temporary relief until approved products are made available, or will it serve as a disincentive to the pursuit of approvals? Should the proposed modifications be extended to include reproductive hormones and implants?

COMMENTS: I support allowing the extralabel use of medicated feeds and reproductive hormones and transplants in aquaculture. I feel that the 10-year sunset clause is an appropriate time period for the extralabel use if it is applied to the start of the approval process for each drug, not a blanket 10-year period for all aquaculture drugs. This clause would offer the incentive to complete the approval process but allow for use of a drug until the drug is approved. I would want some regulatory discretion to evaluate the approval progress if the 10-year period is close to being exceeded for a particular drug and significant progress is continuing. This sunset clause may not work well for water borne chemicals since these compounds usually are not approved in a major species and, therefore, do not have all the human food safety data that CVM requires for establishing a tolerance and granting approval. Since these data are very expensive and take several years to complete, it would be difficult to achieve an approval in 10 years.

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B. REMOVAL OF DISINCENTIVES

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Will the suggested strategies be sufficient to remove the existing direct regulatory disincentives? Are there additional disincentives to gaining approvals that should be removed? How might this be accomplished?

COMMENTS: To remove disincentives, CVM advocates an increase in enforcement resources, the removal of an unapproved drug from the market on the sole basis that it lacks approval for which it is labeled or promoted, and that no critical reviews of original major species data packages will be triggered by a minor use supplemental NADA. These suggested actions are welcome and should help remove some of the disincentives. I am not sure that there are “numerous unapproved drugs and other chemicals marketed for use in aquaculture”, as stated in the Discussion Draft. The mandatory seafood processor HACCP program, if there is any use of unapproved drugs, should significantly curtail such use. I urge CVM to concentrate on the incentives portion of the Discussion Draft.

C. ENHANCEMENT OF EXISTING PROGRAMS FOR DATA DEVELOPMENT

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

- Are there additional existing congressional research funds which could be expanded for minor use research? Would the proposed model program provide a useful supplement to the existing NRSP-7 program? Would the proposed database be useful to parties interested in furthering the approval of minor use products? If so, how might it be developed most cost-effectively?

COMMENTS: Appropriations for the budgets of NRSP-7, Saltonstall-Kennedy Grant Program, and National Coastal Research Institute should be increased and should have earmarked funds for minor drug approvals. In addition, the budgets of two federal laboratories that are dedicated to aquaculture drug approvals (Upper Mississippi Science Center, La Crosse, Wisconsin for public fish culture and Stuttgart National Aquaculture Research Center, Stuttgart, Arkansas for private aquaculture) should be increased to allow the expedited development of data for aquaculture drugs under existing programs and staffs. The NRSP-7 program should include minor use drugs for non-food fish and for production purposes. A minor use data base would be useful but should not be developed at the expense of any of the other proposals.

I agree that a Minor Use Coordinator who organizes research activities for drug applications for each minor species classification is needed. As the National Coordinator for Aquaculture New Animal Drug Applications, I can verify that such a position has been extremely beneficial in attracting pharmaceutical firms, providing liaison between CVM and sponsors, increasing efficiency, reducing duplication, and providing a focal point for queries on aquaculture drug

issues. These positions should also be funded through additional Congressional appropriations earmarked for the respective industries instead of through contributions from various sources.

D. INCENTIVES TO PURSUE MINOR USE DRUG APPROVALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Is the benefit of extended exclusivity, with respect to fostering initial approval, more important than the risk of increased drug costs that could be associated with decreased competition from generic approvals? Would it be a more significant incentive to provide for an extended period of exclusivity for all the claims of the product?

COMMENTS: It is extremely important to create incentives to pursue minor use drug approvals since the lack of return on minor use approvals is the first item that pharmaceutical firms consider when asked about committing any resources to minor drug approvals. Thus, extended exclusivity, tax credits, shorter review periods, and adding residue depletion studies to the significant new data allowed under exclusivity are all important to attracting pharmaceutical firms to aquaculture. Perhaps, exclusivity and shorter review periods could be extended to major drug approvals if the company agreed to develop the drug for minor uses or species. This scenario would create an incentive for the pharmaceutical firm to invest in minor drug uses. It can be a risk that drugs will cost more if there is decreased competition from generic approvals. We must take that chance to ensure that we are able to attract more companies to aquaculture.

E. DATA SHARING BY MAJOR SPECIES NADA HOLDERS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Is it fair to require the sharing of data? How could potential liability be ameliorated under such a data sharing system?

COMMENTS: The Food, Drug, and Cosmetic Act should be amended to allow CVM to consider data from major drug applications when reviewing NADAs for minor uses, once the drug is in the generic classification, has been abandoned or withdrawn. Many times the lack of available data as been a real roadblock to small chemical companies entering the aquaculture market. The requirement to share the data would be fair since the major drug company many times is not interested in minor species drugs and would not be affected. Liability could be ameliorated by placing an appropriate statement on the label of the minor drug use claim.

F. CREATION BY STATUTE OF A "MINOR USE ANIMAL DRUG" PROGRAM

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

- Would a statutory designation of "minor use animal drug" similar to the statutory designation of "human orphan drug" be useful? Are the incentives associated with this

strategy a necessary component of the overall proposed "Minor Use Animal Drug Program"?

COMMENTS: I strongly support a statutory designation of "minor use animal drug" similar to "human orphan drug" designation. As CVM suggested, a work unit should be formed to assume the burden of minor use application review from the Office of New Animal Drug Evaluation (ONADE) so that ONADE is freed to expedite the review of major species drug applications, thus increasing efficiency of the approval process for all applications.

G. CONDITIONAL DRUG APPROVAL FOR MINOR USES INVOLVING NON-FOOD ANIMALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Would the proposed constraints upon conditional approval provide sufficient consumer protection and still provide adequate incentive to pursue a conditional drug approval to final approval? Is the proposed process appropriately restricted to minor uses involving non-food animals?

COMMENTS: Conditional drug approvals for non-food fish should be allowed and should also include gametes, eggs, fry, and fingerlings of food fish because of the inherent withdrawal time associated with these life stages. Previously, CVM had rejected this broad classification because not enough was known about metabolism of aquatic species or the definition of fingerling for each species but this situation has changed. Enough data have been generated on drug metabolism and tissue residue distribution and depletion in fish that CVM should not be concerned about any residues being available to humans under these uses. This is a critical issue since the tolerance is calculated for all minor drug uses the same as for major drug uses: consumption values for major or minor drugs are based on an assumed consumption of animal tissue at 300 grams per day, 365 days a year. This calculation then requires that a complete set of mammalian safety and residue chemistry data be available for all aquaculture drugs, a requirement that may not be met if the drug is not a traditional animal drug (e.g., water borne treatment compounds as chloramine-T). More aquaculture drugs would gain approval if (1) the tolerance could be calculated differently, (2) early life stages of food fish were considered non-food, and (3) drugs could be considered under the non-food fish definition regardless of whether they could have use on later life stages.

H. ALTERNATE APPROVAL STANDARD/EXPERT REVIEW PANELS FOR MINOR USES INVOLVING NON-FOOD ANIMALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

- Will animal caretakers find drugs approved under the proposed alternate standard (with associated restrictions) acceptable? Do the affected industries have the needed expertise and/or will they be willing to fund the expert review panels? Is the proposed process appropriately restricted to minor uses involving non-food animals?

COMMENTS: All aquaculture caretakers would find any drug available to use legally to be acceptable, regardless of the standard under which it was approved. The aquaculture industry has the needed expertise to assess the target animal safety and efficacy data. It is appropriate to restrict this standard to non-food fish only if the gametes, eggs, fry, and fingerlings of food fish are included in the definition of non-food fish. There should be no provision for deletion of a drug from this definition if it has use in later life stages because adequate regulations exist to protect public health.

I. INTERNATIONAL HARMONIZATION

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

- Could non-governmental input facilitate equivalency determinations? Are there sufficient numbers of foreign approvals to justify establishing this program? Should the proposed differences in approval, standards, processes, and data requirements between major and minor species be included in international harmonization activities?

COMMENTS: I support the establishment of a system by CVM to determine whether a foreign country's requirements and systems for animal drug approvals are equivalent. I believe non-governmental input would facilitate equivalency determinations. There are sufficient numbers of foreign aquaculture drug approvals to establish this program, based on results from a recent workshop I coordinated. CVM could advocate that each minor animal industry identify the foreign drug approvals themselves. CVM should include the proposed differences in approval, standards, processes, and data requirements between major and minor species in its international harmonization activities. CVM has been very active in efforts to develop international harmonization activities for aquaculture drugs. CVM is helping to sponsor a second workshop on this subject in February 1998.

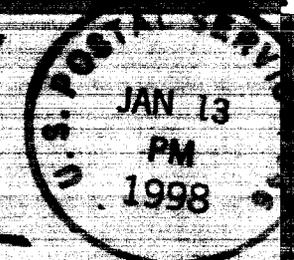
I appreciate the opportunity to comment on these proposals while they are in draft form. I urge the Food and Drug Administration (FDA) accept all the draft proposals and fully consider my comments for changes and additions. I encourage FDA and CVM to implement these proposals as soon as possible to expedite all aquaculture drug approvals. This opportunity to encourage approvals of minor use drugs must be seized and acted upon; we may never have another chance to change the way minor use drugs are approved.

Sincerely,



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