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To:

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From:

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Subject:

Comments on the FDA request for development of ADAA options.

97N-0217

Section III. Agency Request for Comments directed to particular issues:
As it relates to **baitfish and ornamental fish production**:

- * Target Animal Safety - historical record of use in literature or through testing.
- * Food Safety - not an issue.
- * Effectiveness - historical record of use in literature or through testing.
- * Labeling - addressed through model label language with review.
- * Manufacturing - addressed through registration with FDA and accountability for GMPs
- * Environmental impact - historical record of use in literature or through testing.

Will suggested approaches effectuate purposes of ADAA that:

Products be safe and effective?

- * Human safety - Non-diversion of products to food-fish producers could be achieved using a QA program via suppliers.
- * Fish safety - Data from historical use, literature and limited testing if necessary.
- * Consistent product - GMPs as overseen by FDA QA program.
- * Accurate Labeling - Label language developed and reviewed by experts.

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III B. Creating Additional Statutory Authority:

1. Should there be different standards for target animal safety and effectiveness of new animal drugs intended for use in minor species or for minor uses?

Yes: Crop grouping should be allowed (i.e., non-food fish); label extensions from food fish approvals; approval based on historical use, literature reviews; modified animal safety and effectiveness protocols with representative test species.

2. Should there be different standards for human food safety for new animal drugs intended for minor species and for minor uses? a. What should those standards be?

This does not apply to non-food bait and ornamental fish.

3. Should the standards be the same for all minor species & minor uses? Why?

No. There are many variable issues among minor species: food vs. non-food species; mammals, birds, fish, etc.; species diversity within a class; size and quantity of drugs used; mode of access - prescription, feed, over counter, type and purpose of drug; potential human health risks; environmental issues, etc.

4. Should products be labeled to reflect the use of different standards? If not, why not?

Yes - Non-food animal drugs should be labeled as non-food with language "not for use in fish intended for human consumption".

5. If the act were amended to permit FDA to approve new animal drugs for a minor species or minor use under different standards; a. How would appropriate doses be determined?, b. How would residue depletion and withdrawal times for food animals be determined?

a. Historical use, literature sources, modified efficacy testing for now, previously unregistered drugs. b. Residue depletion and withdrawal does not apply to nonfood animals.

6. Would sponsors & users accept conditional approvals & post market surveillance as a trade off for requiring less in the way of premarket target animal safety & effectiveness studies for new animal drugs approved for minor species or minor use? a. Should a drug approved under such a mechanism bear labeling that reflects its conditional status?

Users (i.e., fish producers) would accept almost any mechanism that would make badly needed chemotherapeutants legally available. However, the concern is in what would be included in a post-market protocol? How long could post-market testing be carried out? Exactly what would it involve and at what cost?

a. No - too expensive, confusing to public. What conditions would be required?

7. Should the act be amended to allow FDA to accept foreign reviews or approvals of new animal drugs for minor species or minor uses? a. If so, How should Congress or FDA determine whether the reviews or approvals of a particular country or countries are acceptable as a basis for approval of uses for minor species or for minor uses?

Yes, foreign reviews and approvals should be used.

a. A number of criteria could be used to determine if reviews are suitable: Parallel registration process with the U.S.; comparable criteria; country's history of registration expertise; foreign country's Post-market history for that drug use animal safety, efficacy, etc. Some countries may not require registration for non-food, minor species use based on their drug laws or policy. The basis for this policy could be evaluated by FDA to determine validity for minor uses.

8. Should the current statutory requirement for new animal drug approval for drugs intended for minor species or minor uses or any alternative standards be implemented through primary review process external to the agency? a. If so, how might this process be administered? b. Who should pay for the external reviews?

Yes. With the diversity of minor species and minor use drug, FDA may not have the time or knowledge to become involved with minor species review and development of testing protocols. A panel of recognized and agreed upon experts (agreed upon by FDA and industry or sponsor) could be used to review materials, such as label language, historical use or existing literature dosage recommendations.

a. The process could be administered by the industry or the sponsor preparing a "primary review" submission for label language, review of a minor use drug submission, a proposal for efficacy testing. Industry or sponsor nominates a panel of experts to review materials or a laboratory to complete testing. FDA reviews the protocols and nominees. If agreed upon, industry proceeds with proposal. FDA reviews expert findings or testing results, requests additional information or grants approval.

b. The industry or individual sponsor pays for the primary process.

9. Could determinations of animal safety & effectiveness by expert panels or compendia be used to support drug approvals for minor species or minor uses? a. If so, what information would serve as the basis for such determinations? b. Should determinations of these panels or other information be used to issue monographs or similar standards? c. Who would draft monographs or similar standards and why?

Yes. Determinations of animal safety & effectiveness by experts should be used.

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a. This would vary with the drug, existing approval status with other species, the minor species and minor use being considered, history of use, concentration and volume of drug, to be marketed, marketing limitations, etc.

b.No.

c.What would be purpose of the monographs? The outcome of the expert review and FDA review should be the approval of the drugs.

Administrative and Regulatory Changes:

10.Should there be different standards for manufacturing of drugs for minor species/minor uses?
a. If so, what should those standards be?

Manufacturing of drugs should relate to minimum standards which provide consistency of product, animal safety and efficacy. Animal drugs should not be required to meet human manufacturing standards. Minor species standards for non-food species should not have to meet residue standards.

11. Should products be labeled to reflect the use of different manufacturing standards?

No. If the drug is approved by FDA through an agreed upon process, there is no need to include the standards listed on the label.

12.Would a strategy similar to that used by the agency to facilitate drug approvals for some aquatic species be successful if extended to other minor species? That strategy includes coordination of INAD information collected and generated by end users & a centrally-organized and CVM-operated field education program directed at end users as potential INAD sponsors. a. In which species/uses would such an approach work or not work? Why?

The aquaculture program has great merit and provides positive benefits which could relate to some minor species food animals. However, when dealing with non-food animal minor species, it would not be necessary to establish a separate strategy. Data collected from the food animal sector should be readily transferable to the non-food animal species approvals.

a. The option should be available to any minor species group if they so choose to create a similar process.

Creating Incentives:

13. Would economic incentives, such as tax breaks, grants & periods of market or label exclusivity, encourage the pursuit of approvals or supplemental approvals for labeling modifications for minor species or minor uses? a. If so, What kind of incentives would be most effective? b. Would different kinds of incentives be appropriate for different classes of new animal drugs, such as drugs for hobbyist owned tropical fish as contrasted with production drugs for fish intended for human consumption? c. What incentives would encourage sponsors to pursue approval of a drug for minor species or minor use, using data in public master files (PMF's)?

The primary issue here is the development of an affordable approval process for minor species & uses. It would seem far more simple to provide an affordable process which allows sponsors to invest in the process. Making the process more complex for products with such a small potential market would be counter productive.

a. Reduction on the extensive and expensive approval process for non-food minor species.

b. Yes. Different strategies are certainly appropriate for food vs. non-food minor species animals. Without knowing the specifics of the "incentives" it is impossible to comment. There should be discussion and consultation with each minor species industry to determine workability of options.

c. If the drug in question has a PMF, information should be available for reference for the minor species approval process, avoiding duplication of effort and additional cost.

14. Are there concerns about data in PMF's that make sponsors reluctant to rely on such data? a. What are the concerns? b. How can they be addressed?

This would be based on a case-by-case review of the PMF in question. There may be information in the PMF which does not support the application of a minor species/use application.

15. If producer groups or other organizations were willing to conduct or otherwise fund studies to demonstrate safety and efficacy for new animal drug approvals for minor species/uses, would sponsors be willing to use the data from the studies to support approvals and new or revised

labeling? a. If not, why not?

The purpose for conducting the safety and efficacy studies would be to determine if the drug was suitable for use. If the testing protocol was approved by FDA prior to the testing and there were favorable results, the data could be used by a sponsor as part of the submission packet for minor species/use approval, if that data was released by the group/organization conducting the study. The group/organization doing the testing could also be the sponsor and use the data in their submission packet.

16. Should a program similar to the USDA National Research Support Program #7 (NRSP7), which currently funds studies for minor use therapeutic uses for food & fiber producing animals, be developed for wildlife & zoo animals and/or for production uses?

If non-food, non-fiber animals are to be included, do not create a 'similar' NRSP7 program, but extend the mandate beyond food/fiber production.

17. Should NRSP7 be expanded to cover such issues? Yes.

18. Could and should philanthropic, public interest or other not-for-profit organizations be encouraged to fund research for the development of new animal drugs intended for use in minor species/Uses. a. If so, how & by whom?

It seems reasonable that funding should be made available from any of the resources cited above. There would be a need for independent testing and analysis based on a protocol reviewed and approved by FDA prior to testing.

19. Are there mechanisms other than the new animal drug approval process & extra label uses of animal and human drugs under the AMDUCA that could enhance drug availability for minor species/uses?

Modification of the NADA process through ADAA seems to be the only vehicle for the creation on a new process which could support new drug approvals. Without modification of existing process, non-food animals with multiple species involved and using low volumes of over the counter drug use will not be able to seek approval due to the excessive costs involved.

Extending Existing Legal Authority.

20. Would legislation be desirable to extend the AMDUCA to permit extra label use of:
1. Medicated foods or, 2. reproductive hormones and implants.

Yes. For production of minor species such as aquaculture, there is a need to extend AMDUCA to medicated feeds and reproductive hormones and implants. Some aquaculture industries would collapse if access to reproductive hormones was not made available.

21. What are the pros/cons of approval versus extra label use under AMDUCA?

For farm production of minor species animals, extra label use should be encouraged. Access to drugs considered for approval for minor species can take a long time. Drug availability under a DVM prescription would provide legal access and provide safeguards for use and withdrawal. It would reduce cost and paper work since every farm would not be required to develop an INAD for data collection.