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FDA's Dockets Management Branch
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

To whom it may concern:

I am writing the U.S. Food and Drug Administration in response to the Discussion Draft titled "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Uses" dated 19 December 1997 (Docket No. 97N-0217). I strongly encourage FDA to give serious consideration to the implementation of the majority of the proposals presented. The attached documentation provides individual comments on each of the specific proposals contained in the Discussion Draft.

Based on my experience as National INAD Coordinator for the U.S. Fish and Wildlife Service, implementation of proposals contained in the Discussion Draft is essential to the ultimate success of the drug approval process for minor species and minor uses. Many folks and organizations, including CVM, have worked extremely hard and diligently to get the minor use animal drug approval process to the level it is at today. Yet although it has experienced considerable positive development in the last few years, it desperately needs the "assistance" contained in the Discussion Draft proposals to ensure its success.

Although my comments are made based on my experience(s) as National INAD Coordinator for the USFWS, they are my opinions, and do not necessarily reflect the opinion or the position of the USFWS.

Sincerely,

Dr. David Erdahl
National INAD Coordinator

97N-0217

C85-

**Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Uses: Discussion Draft - Report CVM 97132 - 19
December 1997 - Docket Number 97N-0217**

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Proposals

A. Modification of Extralabel Provisions:

As CVM is well aware, many folk in aquaculture view extralabel drug use as a mechanism (loophole) by which they can avoid having to hold, or participate in, an INAD exemption to use unapproved drugs. For many of these folks, once extralabel drug use becomes an option, it is the only mechanism that they will use. Once this happens, these folks will for all practical purposes be completely disassociated with the INAD/NADA process. And while it is certainly not essential/critical that all aquaculture folks contribute to the process, it is important that some do, and that all realize the importance of INADs and NADAs.

Hence, while I support modification of the extralabel provision, there is little doubt that to a certain extent this provision will most certainly serve as a disincentive to the pursuit of drug approvals. I specifically question the length of the 10 year sunset period. I believe a lot of folks might look at this figure and simply say to themselves "geeeez, we're good to go....no need to worry about INADs/NADAs anymore". Ten years is a long period of time to most folks, and a distance into the future that is often beyond the sight of most. I believe a sunset period of 3 years (maximum) might be more appropriate.....enough to give folks immediate relief, but yet retain their attention as to what remains to be accomplished. If given a 10 year reprieve, I believe most folks will simply "be gone". Based on the reaction of most fish folks to the implementing regulations of AMDUCA 1994 that became effective December 9, 1996 (i.e. "if we can go the extralabel route, the heck with INADs, NADAs, and participating in the approval process), it is imperative that extreme caution be exercised with "carte blanche", or the perception of carte blanche extralabel policy.

I would most certainly support inclusion of reproductive hormones and implants to the extralabel provision.

B. Removal of Disincentives:

Although it is unlikely that the inherent fear and apprehension generated by the drug approval process, particularly for potential pharmaceutical sponsors, will ever go away completely, the proposed removal of disincentives would greatly reduce such concerns. Although I support all three proposed actions, I believe "Changes in the Standard for Regulatory Action" and "Assurance that an Existing Approval Would Not be at Risk" to be most critical. I also believe that extending the period of exclusivity to a sponsor to a minimum of five years would be a simple, straight-forward, and yet very positive action to help entice potential sponsors.

An additional disincentive that would be of benefit would be for FDA to provide some type of assurance to potential sponsors that the "rules" to the approval process would not change over time. I believe many potential sponsors have very bona fide fears that what constitutes a complete approval package today, might not be considered sufficient by FDA next year, or perhaps the year after. If some type of provision could be established that clearly outlines that "approved approval packages" will not be subject to future modification by FDA, it would remove a tremendous disincentive to many potential sponsors.

C. Enhancement of Existing Programs for Data Development:

1. Expand Established Congressional Research Funds

Since this proposal deals with increasing appropriations, why not also request increased appropriations for other federal programs (e.g. USGS/BRD, USFWS, etc.) that have already made a serious commitment to the INAD/NADA process, and are likely operating on limited funding?. Based on their past and present involvement, these folks would (or at least should) best know how to utilize additional funding in order to get the greatest return on investment.

Based on past experience within the federal system, I question the meaning of "earmarked". Earmarked dollars have a long history of going to many places other than those designated in appropriation bills.....and this is particularly

likely to be true if the words "minor" or "minor use" are included in bill language.

2. Establish New Programs Based on the NRSP-7 Model

As I happen to be one of many individuals that have the word "coordinator" as part of their official job title, I am uncertain as to whether the INAD/NADA process is in need of another "coordinator". It seems that now-a-days, we have to have a coordinator for virtually everything, but with everybody coordinating, the question often becomes "so who's doing the work??".

I am also uncertain as if the NRSP-7 program is a good model on which to base another research support program. During the nearly 5 years that I have been involved in the INAD/NADA program, I have never completely understood what NRSP-7 has accomplished, or what it is supposed to have been doing. Rather than establish another program to "support" needed research, why not simply establish/support a program/lab to conduct needed research. Between all the coordinators in place, the FDA folks, the USDA folks, the NRSP-7 folks, etc., etc., prioritizing needed work should not be a problem. All we need are dollars, facilities, and personnel to assign to needed tasks. The progress that has been made by the Stuttgart National Aquaculture Research Center (USDA) is a good example of what can be accomplished by a relatively small, but competent program.

3. Establish a Minor Use Database

Databases, like coordinators, are in vogue. Yet, I believe that databases more often tend to perform, or have the potential to perform useful functions. Currently, there is nothing in existence remotely like the proposed database. The database could be expanded to include all available information with regards to efficacy, target animal safety, etc. etc., so that even the average fish/game farmer-type person would benefit. Although it was proposed as somewhat of a pie-in-the-sky-type proposal, the USFWS National INAD Office has detailed the merits of such a database to its own INAD program and among its own user group.

The most cost effective development approach would simply to be to have this individual as part of the CVM aquaculture/minor use species team, as this

should be a focal point for transfer of all pertinent data.

D. Incentives to Pursue Minor Use Drug Approvals:

As mentioned previously, I believe that extending the period of exclusivity would be a very beneficial incentive to lure new sponsors into the minor use drug approval process. I also do not believe that folks should spend too much time at this point worrying about the potential ramifications of increased drug cost as a result of a lack of generic product competition. The important consideration at this time is simply to get new approvals. We can worry about increasing drug costs later. Either way, I believe most folks would be willing to pay a little more and have needed drugs available, rather than be forced to suffer unnecessary loss of product quality/quantity.

Although I know very little about the orphan drug program, I would have to agree with representatives of this program that tax credits should be a great way to encourage sponsors to seek minor use drug approvals.

I believe that an extended period of exclusivity for all claims of a product would greatly increase the incentive for sponsors to get involved. As stated, much of the data for supplemental labels can very likely be provided by the public sector, and it is only fitting that the original sponsor be the benefactor of value-added labels. This concept would also encourage sponsors to get into the game and submit an NADA for a basic label claim from which they could expect to recoup some return on their investment, and yet be secure in the knowledge that they (with possibly some public assistance) can continue to expand "their" label and increase "their" profits.

I strongly support both of these proposals.

E. Data Sharing by Major Species NADA Holders:

Although it would seem that some sort of "forced/mandatory" data sharing by major species NADA holders with minor use NADA applicants would be beneficial to minor use sponsors, to the lay person, the potential legal ramifications of such action would appear to be significant. As to whether "is it

fair to require the sharing of data?", since when did "fair" really matter? The issue is to protect the public while at the same time promoting availability of approved animal drugs. However, if it can be done.....great.

It would seem liability would simply be split between the minor use sponsor who is defining the "new" label, and CVM who is granting approval (or whatever the current situation is with any typical NADA). Liability protection would obviously have to be granted to major use sponsors, who would be required by law to share their data for other-than-originally-intended purposes.

F. Create a Statutory Category of Minor Use Animal Drugs:

I believe that creating an "official" minor use animal drug category would go a long ways to finally legitimizing the compassionate INAD process that has been implemented by CVM. Although both CVM and aquaculture have worked hard to make this process work, the fact that it has no real basis in law has made it difficult to say the least, particularly for CVM. If a minor use animal drug category were established, it would no longer be necessary for CVM to have to continually attempt to interpret standard INAD regulations as they "might" apply to compassionate INADs.

Although I am uncertain as to whether all the potential incentives associated with this strategy are a necessary component of the process, I believe that the philosophy of "more is better" probably fits this situation. Creation of a minor use animal drug work unit should certainly result in better overall "service" to the minor use drug approval effort.

I support these proposals.

G. Conditional Drug Approval for Minor Uses Involving Non-Food Animals:

I believe that the proposed constraints upon conditional approval would provide needed consumer protection without unduly reducing sponsor incentive. I also believe that the process is appropriately restricted to non-food species.

Although the proposal appears to be well "defined" by a five-year limit and

annual review, it does present a potential route for activity/effort that does not result in an approved label (similar to the extralabel scenario). It also would appear to have the potential for significantly impacting/increasing the workload for CVM, with a portion of this effort being at the best redundant. We must all remember that there is only one acceptable end product to our efforts, and that is approved drugs.....not conditional approvals, not pending approvals, not

temporary drug use loopholes, and not just continued paper progress in the "right" direction.

H. Alternate Approval Standard/Expert Review Panels for Minor Uses Involving Non-Food Animals:

Based on the current lack of approved drugs for minor use species, I doubt that most folks would hesitate in the least at using drugs approved under "alternate" standards. I have no idea if the affected industries have the expertise or money to fund expert review panels, although I rather doubt it. Cost will of course be the number one deciding factor, and that will depend to a large extent on just exactly how much and what quality "reports" CVM mandates. The proposal should definitely be limited to non-food animals.

I do not support this proposal, at least not at this time. I think that it has the potential to do more harm than good to the overall process, particularly with respect to true minor use species such as fish, game birds, etc. Uses described in the proposal including zoo animals and exotic pets could more accurately be described as minor-minor use species. I believe that the paperwork and the required CVM time/dollar commitment generated by this proposal for these minor-minor use species could potentially end up being a significant negative impact for the true minor use species the ADAA was designed to benefit, and the minor use species that to date have driven the process in a forward direction. Regardless, without an alternate approval standard, these minor-minor use species could still go the "conditional approval route" as proposed in proposal "G".

I. International Harmonization:

While international harmonization is an important issue, it is one that goes far beyond minor use species. Regardless of rhetoric, in the near future the only "harmonization/standardization" that is likely to occur is going to be on a case-

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by-case basis, and the creation of a special harmonization program is unnecessary. Use of potential minor use drug approval dollars for support of a broad-based international harmonization program would be a poor utilization of available funds.

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