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January 6, 1998

Center for Veterinary Medicine
Food and Drug Administration
Docket Management Branch (HFA-305)
12420 Parklawn Drive
Rm. 1-23
Rockville, MD 20857

RE: "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Uses" (Docket No. 97N-0217)

The attached document is submitted in response to the referenced document dated December 19, 1997. Two copies of my response are enclosed with the appropriate docket number included on each page.

The concern I have is for the time, cost and effort that it will take to implement the eight major areas listed in the cover letter. The emphasis being placed on downsizing the government and reducing budget expenditures leads to the conclusion that implementation may be difficult in its present form. It will be hard to justify the complete program proposed in the December 19 document for increasing drug availability for minor species and minor uses for veterinary medicine.

Initially the emphasis needs to be placed on a few essential items of significant value to the drug development industry. I believe the items should include the medical record database (Part IV, section C, item 3) as I have proposed it (Attachment I). Additional essential items include adding an Orphan Drug provision for veterinary medicine, eliminating the "opening the file" disincentive and providing some type of exclusivity for the added claim(s).

If I can be of further assistance, please call.

Sincerely,

H. Dennis McCurdy, D.V.M.
Executive Director

97N-0217

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Response to Internet Document

“Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Uses

Dated December 19, 1997

Comments Provided by **H. Dennis McCurdy, D.V.M.¹**
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Response: January 6, 1998

Recommendations: To insure implementation, limit proposals to those having the greatest impact and an optimum return on the investment. The following list is offered in the order of greatest value to reducing drug availability concerns for the minor species and minor use initiative.

1. **Establish a Minor Use Database:** Data concerning the use of drugs for minor species and minor uses in non-food species is essential to safe and effective drug administrations. The proposal in the December 19 document is an excellent aid to this effort, particularly when available to practitioners.

The collection of medical records concerning these applications would be of even greater value. A brief discussion of how what amounts to a continual clinical field trial can be accomplished is found in Attachment I.

The collection and distribution of database facts could be most efficiently handled by a private organization, supported and monitored, as appropriate, by the FDA. Such an effort would entail minimal effort and expense to the Congress and the FDA while providing virtually immediate benefit to practitioners. When sufficient data become available, minimal industry investment could provide for supplemental approvals.

2. **Orphan Drug Provisions for Veterinary Medicine:** “Minor use animal drug development” will provide a significant incentive for industry to seek supplemental claims, particularly if some type of **label claim exclusivity** can be provided. Data to support supplemental claims could be supported by the medical record database proposed in #1 above. Minimal Congressional effort would be involved, and limited additional regulations and staff at the FDA. Amending the NRSP-7 regulations to include non-food animals could provide additional support, as necessary.
3. **Assurance that an Existing Approval Would Not Be at Risk:** This is the most reasonable disincentive of the ones recommended. This disincentive provides

¹ Dr. McCurdy has been developing pharmaceutical products for 23 years, having direct responsibility for 19 new or supplemental product labels mostly for small animals.

industry with a significant impediment to development. This would require no Congressional action and minimal FDA/ CVM action.

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Background: These comments are directed at identifying a path of least resistance to stimulating drug development to fill the drug needs of the veterinary practitioner, particularly for minor species and minor uses. My industry success with the drug approval process leads me to believe we can overcome drug availability concerns addressed by the Animal Drug Availability Act (ADAA) through a cooperative effort involving all interested parties.

A mix of appropriate incentives and a lack of disincentives will help when industry can visualize an opportunity for a reasonable return on investment. My concern is that the December 19 document repeatedly discusses time consuming and expensive options to resolve the issue. Funding and priority concerns, in my opinion, are going to delay action to resolve the problems the ADAA is obligated to address.

The successful approach must consider all alternatives. The problem is too complex and too diverse to fit into the current regulatory approach. Within the context of assuring safe and effective products, any reasonable approach should be fair game. Industry needs an opportunity for a fair return for its investment into product development, but they must also have valid facts, currently unavailable, to make appropriate development decisions.

The process must begin with fair reasonable innovative regulations that will give approved minor species and minor use products the opportunity to compete against the unapproved products. Clearly, the current approach is not working. The cost of enforcement actions against unapproved products that have stood the test of time will be hard to justify. Consider an approval system that will promote the benefits of the approved product against the existing unapproved product.

New methods must involve minimal additional cost in personnel, time and dollars for the Congress and the Food and Drug Administration (FDA) to consider implementation. This will be the focus of the comments provided below.

The centerpiece of my recommendations involves the development of a medical record database. This database would assist all involved in the ADAA by providing essential data that is currently unavailable. Support for this private initiative represents minimal risk or expense to the FDA and will provide industry with data needed to make appropriate decisions concerning seeking minor species and minor species claims. At the same time, data would be available to support such approvals.

* * * * *

General Comments on the December 19 Document:

1. Multiple approval models need to be assessed as an alternative to the current system. Unique requirements for food and non-food animals, minor species and minor uses, *etc.*, present a level of complexity that has made the single model difficult to administer fairly and at the same time reduce drug availability concerns.
2. While the extra-label drug use provisions may not apply to many minor species applications, collecting medical records in a database may provide some insight into the performance of these products under actual field use conditions. Minor uses include drug applications to dogs and cats for certain limited uses. Another example of extra-label potential minor species and minor use applications concerns the dispensing or prescribing of herbal products and alternative medicines.
3. The National Research Support Project #7 (NSRP-7) should be expanded to include all animal species. Though valuable in its present form, this program appears to be quite expensive for the benefit it currently brings to the drug availability issue.
4. Alternatively, or perhaps in addition to NSRP-7, an Orphan Drug provision needs to be available for veterinary medicine, particularly to deal with minor species and minor uses. While their numbers may be few, exotic species are valuable animals and need safety and efficacy data for the products being used. There are minor uses of drugs needed for dogs and cats to meet increasing demands for handling human-related diseases for which no approved animal drugs exist.

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Comments on "Particular Issues on Which FDA Seeks Comment":

1. **Part IV, Section A:** This proposal as presented requires legislative and regulatory action. If it is the best alternative, it should be implemented. It seems like a lot of work for temporary relief for drug availability.
2. **Part IV, Section B:** The proposals presented here would appear to provide significant relief toward stimulating product development. There are significant activities proposed that appear to be expensive and time consuming.
 - **Items 1 and 2:** Additional enforcement resources and changes in the standard for legal action will be helpful, but it may be difficult to justify the cost to deal with products that have been sold for many years, regardless of the fact that they are being sold illegally, particularly in the absence of viable alternatives.

- **Item 3:** Eliminating the risk involved in “opening an NADA” is essential. This is a very strong disincentive as it currently exists. Changing this is an essential action, regardless of the time, effort and expense involved if minor species and minor use claims are to become a viable option for industry to consider proceeding with development.
3. **Part IV, Section C:** Additional funding to reduce industry’s investment is a commendable goal and should be implemented. Expanding the NSRP-7 program is one great idea and will help encourage development. Another approach is the development of a database that was discussed at some length in a separate section above. As proposed above, the database has the greatest opportunity for significantly impacting minor species and minor use drug applications.
 4. **Part IV, Section D:** It is unlikely that increasing exclusivity on an initial drug claim will have any direct impact on a company to promote seeking a supplemental claim for a minor species or minor use. A more profitable approach to industry is an extended exclusivity for all claims.
 5. **Part IV, Section E:** The direct sharing of data from the pioneer company is unlikely under almost any circumstances. This conclusion is based on the obvious reluctance of many companies to publish the results of the basic studies from an initial claim. While liability for such use may be a concern, it is a secondary issue.
 6. **Part IV, Section F:** A statute similar to the human orphan drug, accompanied by incentives, would be very useful in stimulating minor species and minor use product development.
 7. **Part IV, Section G:** Conditional approvals should provide sufficient protection for the animal. It would represent more than what practitioners have now. If the data from the conditional approval evaluations were published, practitioners could use their own judgement in selecting an appropriate product. It is initially appropriate to restrict this to non-food animals.
 8. **Part IV, Section H:** Caretakers should find these drugs acceptable. It is likely that some companies may not have the expertise on staff. It will be hard to convince many of them of the need for an expert review panel, as this is an added expense. Their competitors are operating without an approval. Alternative standards/ expert review panels are an excellent idea, but they will be hard to sell to many companies.
 9. **Part IV, Section I:** International harmonization for minor species and minor uses needs consideration as a tool to reduce drug availability concerns.

ATTACHMENT I: MEDICAL RECORD DATABASE JUSTIFICATION

Support for Minor Species and Minor Use Initiative

Database Recommendation: Part IV, section C, item 3 of the December 19 document suggests the development of a database as a means of addressing minor species and minor use drug availability concerns. Properly constructed and managed, a medical record database could address more than just the minor species and minor use drug availability concerns. Such a database could provide data to address many if not most of the ADAA issues.

The FDA has responded to my protocol (submitted May 1996) to establish such a database by requesting a pilot study (January 1997). A Phase I grant proposal has been submitted to the Small Business Innovation Research (SBIR) program to fund the initiation of a feasibility study. This proposal is currently being directed to the FDA for their consideration, as the FDA is a routine participant in this program. This database proposal represents an opportunity to investigate an innovative alternative to address the minor species and minor use issue at minimal additional cost, as such project proposals have already been funded through a separate budget. Consider the following database proposal features:

- **Summary of Proposed Database Concept:** Practitioners would provide clinical case records on all activities from the initial animal presentation to the hospital/ clinic through post-treatment assessment, much the way data are collected for clinical field trials. When fully implemented, approximately 1% of all practitioners in a balanced distribution across animal species, geographic locations, *etc.*, would provide data on standardized report forms on a continuing basis.

The data will be collected through the most secure electronic data collection system available, using computer submission guidelines provided by the FDA. Accuracy and precision of the data will be monitored/ verified by multiple systems, to include site visits in accordance with Good Clinical Practice requirements for long-duration studies. All identities would be coded to assure confidentiality. The collection system would be monitored by a Practitioner Advisory Board to protect the rights of the practitioner. Only the submitting practitioner will be able to alter the data according to a system acceptable to the FDA.

Practitioners will be compensated from the profits of the sale of the data to industry and other consumers. Additionally, they will receive a free report of their practice's medical performance and a reduced cost for a combined practitioner's report for use in dealing with the unusual cases.

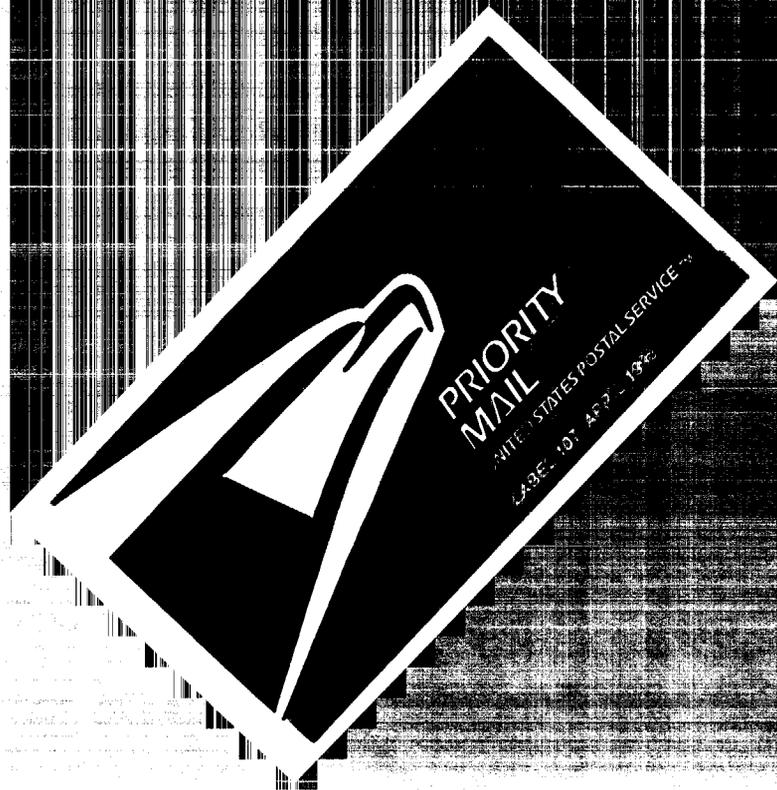
The data will be compiled, for dealing with drug availability concerns, to demonstrate how drugs are being used and for what claims. The data will indicate drug performance, providing clinical use facts on individual products, as well as combination administrations and concurrent therapy.

systems and other animal species at the conclusion of this study.

2. Beyond feasibility, the study will generate interest in quality medical records using a standardized nomenclature and standard report forms, as well as promoting participation in the database. Report forms will be developed to minimize time invested in recording medical facts by employing a “point and click” system for data entry, providing the opportunity for saving a significant amount of time for the practitioner.
3. Phase I involves three recognized dermatologists (two have already agreed to participate) in a pretrial program to resolve computer glitches and system problems with data recording, handling and submission.

4. Phase II will use 10 qualified practitioners (many with “paperless practices” have already indicated an interest in participating) to collect detailed dermatology cases from as wide a range of dermal diagnoses as possible. New cases will be initiated for approximately six months, however, data collection will continue on all cases until those cases have reached their optimum conclusion. On allergy cases, this may be up to 12 months after the case was initiated.
5. At the conclusion of the trial, the data will be compiled into a concise report concerning drug availability and submitted to the FDA for their review. The results of diagnoses with significant case numbers will be analyzed using appropriate statistical methods.
6. Also, the commercial impact of the data will be investigated through the preparation of reports for the product industry and separate reports for practitioners and for academia. Articles will be submitted to refereed journals and presentations prepared for veterinary meetings to promote the expansion of the database. The objective of these efforts is to generate funds to support the continued growth and quality of the database and to keep up with continuing improvements in technology and the increasing data needs of the data users.

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