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Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane – Room 1061
Rockville, MD 20852

Re: Docket/RIN No. 2006N-0067/0910-AF67 – Index of Legally Marketed Unapproved New Animal Drugs for Minor Species

Dear Sir or Madam:

I am writing on behalf of the American Veterinary Medical Association (AVMA), established in 1863 and the largest veterinary medical association in the world. As a not-for-profit association established to advance the science and art of veterinary medicine, AVMA is the recognized national voice for the veterinary profession. The association's more than 74,000 members represent approximately 86% of U.S. veterinarians, all of whom are involved in myriad areas of veterinary medical practice including private, corporate, academic, industrial, governmental, military, and public health services.

The AVMA applauds the passage of the Minor Use and Minor Species Animal Health Act of 2004, and the establishment of the Office of Minor Uses and Minor Species within the Center for Veterinary Medicine. The AVMA and the veterinary profession believe the Act and concomitant regulations to be promulgated by FDA will serve the veterinary profession and the health and welfare of many of their animal patients very well.

The AVMA compliments the FDA on the proposed indexing rules. We recognize the complexity of this new approach for making drugs legally available for non-food minor species conditions where there is little probability that any sponsor would attempt to get full approval through the NADA process. We believe indexing will provide a solution to many health and welfare problems faced by a multitude of minor species.

We offer the following general and specific comments on the proposed rules.

General Comments

The AVMA believes that sponsors that are accustomed to the NADA process for full FDA drug approval and will understand the process required to index a drug. However, we believe that the smaller companies, for whom MUMS indexing is primarily intended and who are likely to be the majority of requestors, are not accustomed to drug safety and efficacy reviews and will find the indexing process overly complex and difficult. We therefore believe and suggest that the FDA consider the greatest flexibility in considering the eligibility requirements, and in the selection and operations of qualified expert panels, and do so on a case-by-case basis. We believe this is important particularly as the agency will have the ability to evaluate the final report of the expert panel before listing an

indexed product, and that the agency will have the ability to remove an indexed drug at any time for due cause. We also encourage the FDA Office of Minor Use and Minor Species to consider implementing education programs for potential requestors and index drug users, once MUMS indexing rules have been finalized.

Chemistry, manufacturing, and control information
The AVMA recognizes that the agency's review requirements for indexing a drug will be much different than for full approval. We believe that, as suggested in the *Federal Register* preamble, it will be sufficient if a requestor illustrates an understanding of current Good Manufacturing Processes (cGMP) for manufacturing MUMS indexed drugs and has established appropriate specifications associated with their application, as one of the requirements for indexing. We believe that all prospective indexing requestors should be required to be registered with FDA, and this information should be publicly accessible, but only on direct request to FDA. However, all drugs granted MUMS indexing status should be updated regularly and easily accessible to the public as suggested in§516.157.

Analysis of Economic Impacts
The FDA has estimated the costs to a MUMS index drug requestor will be approximately $10,000, for each drug considered for indexing. Based on the estimates provided in the *Federal Register* notice, these appear to be reasonable and accurate, unless the process for indexing requires a significantly greater than estimated number of FDA conferences, expert panel members, or panel time spent in evaluation. Acknowledging the possible variation in costs, and that indexing is intended to be an attractive process for marketing evaluated drugs (some of which have very low market returns), we suggest that FDA consider establishing a uniform fee for all indexing requests, after a sufficient period of "testing" the actual economic impacts of indexing drugs. A uniform fee would avoid economic discrimination between different requestors and different drugs, would simplify the process, and would emphasize the primary intent of Congress – a process for increasing the number of legally marketed therapeutic agents for which there is currently little or no economic incentive.

Scope of Use; Early Non-food Life Stages (§ 516.111; § 516.129; 516.133)
The AVMA recognize the provision for allowing indexing for a new animal drug intended for use in an early life stage of a food-producing minor species animal. We believe this is a significant and important provision and concur that there should be reasonable certainty that treated animals will not be consumed by humans or food-producing animals. However, instead of the requestor being required to demonstrate this reasonable certainty, we believe it will be easier if this task is left to the expert panel to determine. The period of time between the restricted use of an indexed drug for an early life stage specified in a MUMS index request (such as gametes, embryos, larvae, etc) and the consumption of a later life stage by humans or animals will, in most cases, greatly exceed the pharmacodepletion of the drug that may result in food or feed residues. Hence, pharmacodynamic evaluation of a specific product in early life stages is best left to the expert panel.

The proposed regulations stipulate the use of MUMS indexed drugs to be "intended for use only in a hatchery, tank, pond, or other similar contained man-made structure". We concur with this confined use of indexed drugs to avoid environmental damage; however the regulations appear to only address animals in an aquatic environment. We seek clarification on whether this intended to apply to only aquatic animals, or if it will apply to all minor species and the early life stages of food/feed producing

terrestrial minors species. We believe there may be instances where indexed drugs should be available for use in terrestrial animals with similar restrictions.

Expert Panels (§516.115; §516.141)
The AVMA recognizes the need for a qualified expert panel to evaluate the target animal safety and effectiveness of a new animal drug under consideration for indexing. We believe that it would be most effective for the qualified expert panel be judged on the collective expertise of the group that is nominated by a requestor, rather than the expertise or credentials of individuals. A panel selected on their collective ability to evaluate published and unpublished information in assessing the safety and efficacy of a product with respect to, for example, the pharmocodynamics of the class of drug being evaluated, cGMPs, and interactions of the active and inactive ingredients of the drug. The panel should also have adequate clinical experience with the disease or condition in question, a full understanding of FDA Guidance 152, and knowledge of the industry in which the drug will be used.

The proposed regulations also suggest that a requestor may provide information to support a categorical exemption from the requirement to prepare an environmental assessment. We would suggest that should the initial information provided by the requestor be inadequate to meet the requirements of a categorical exemption, that environmental assessment is delegated to the expert panel. In such cases we suggest the expert panel should have adequate familiarity with environmental issues related to the drug in question.

The AVMA has some concern that the proposed provisions addressing conflicts of interest may exclude many viable experts from participating in expert panels. Because the drugs under consideration are by definition "minor", it is unlikely there will be a large pool of experts that are sufficiently conversant with a particular product, the particular species, and the particular disease or condition the requestor may be considering for indexing. It is quite likely that in preliminary investigation of a drug potentially suitable for indexing, that a viable expert may have consulted or advised the requestor. It is equally likely that a potential expert may have received a grant and conducted research on the drug, independent of any requestor involvement. We therefore believe the regulations as written may be excessive and exclude a small pool of potentially suitable experts. The FDA may like to consider addressing only obvious and direct financial interest through, for example, full time employment by the requestor or direct investment in the specific product under consideration.

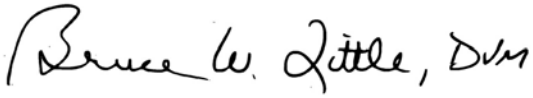
Informal conferences regarding agency administrative actions (§516.123)
The AVMA recognizes the importance of the agency's ability to deny a request for determination of eligibility for indexing, for terminating an investigational exemption, for determining that a qualified expert panel does not meet the selection criteria, for denying a request for addition to the index, or for removing a new animal drug from the index. In such cases FDA will give written notice that specifies the grounds for the initial decision and provides an opportunity for an informal conference for review of the decision. The wording specifically in §516.123(n) "The administrative record of the informal conference specified herein constitutes the exclusive record for decision" suggests that such conferences are not informal and we query why the word "informal" is used.

We note that FDA has 90 days to grant or deny a request for the determination of eligibility of an index drug for a non food-producing animal or 180 days for an index drug request for an early, non-food life

stage of a food producing animal. However, a requestor only has approximately 45 days or less to request, have FDA schedule, and to prepare a written response to an index drug denial by FDA. We believe this may be inadequate time for a requestor to evaluate and adequately prepare the needed information and suggest the time between an FDA denial notice and the informal meeting be at least 90 days.

We hope these comments provide FDA the input sought and look forward to seeing practical and workable regulations in place. Should you need further explanation of any comments offered please feel free to contact Dr. David Scarfe (847-285-6634; dscarfe@avma.org).

Sincerely,



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BWL/ADS