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

Re: Docket No. 2005N-0329 – Designation of New Animal Drugs for Minor Uses and 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 73,000 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 concurs with much of the proposed regulation and believes designation for "minor species" drugs is straight forward. However, we offer comments concerning the designation of "minor uses" in major species (cattle, horses, swine, chickens, turkeys, dogs and cats).

We recognize the complexity of quantitatively defining "minor uses" with respect to diseases that occur infrequently or in limited geographic areas, and FDA's desire to not "establish a test of commercial value" for these drugs. However, we recall the primary intent of Congress was to create realistic incentives for sponsors to seek approval of "minor use" drugs. While recognizing the primary motivation for sponsors to seek approval for any drug, we believe there are several overarching principles or concepts that can be usefully applied to the regulation to ensure Congress' intent is upheld. Perhaps the most important is that, should requirements for "minor use" drug designation and approval be substantially more arduous than that for "minor species" drugs, there will be little to no incentives for developing "minor use" drugs and the objectives of Congress will not be achieved. Indeed, as proposed, the excessive documentation requirements for establishing a justifiable low number of "rare" or "infrequent" diseases in a major species is a strong and distinctive disincentive for any drug sponsor.

We note:

- In enacting the MUMS Act, Congress sought to encourage the development of animal drugs that are currently unavailable to minor species or to major species afflicted with uncommon diseases or conditions (minor uses). FDA's approach to regulating MUMS drugs should be simple and encouraging to sponsors wherever possible.
- The burden of evidence placed upon the sponsor who seeks designation of a minor use drug is disproportionately higher than the burden for a minor species designation. There is a lack of balance between the documentation required of a minor use designation versus a minor species designation. We recognize that minor species are more easily defined, but we urge that FDA seek to balance the burden of evidence of minor use designations to be commensurate with minor species designations.
- When picturing what might constitute a "small number of animals" for minor use in a major species, recall the significant numbers of minor species animals eligible for designation. That is, consider the numbers of animals eligible to be designated under a minor species provision as a benchmark against which to compare numbers of animals to benefit from minor use provisions. Recall that "minor use" drugs are safe and efficacious as demonstrated by approval or conditional approval. Therefore each of the major species can only benefit from a generous interpretation of "small numbers of animals." Furthermore, the checks and balances FDA has for MUMS designated drugs (e.g. ensuring exclusivity of only one drug being designated for a particular claim – Section 516.20 and 516.31; annual evaluation of progress during conditional approval – Section 516.30; the sponsor requirement for assuring availability and distribution of the designated drug Section 516.36; and, the many recourses the agency has for terminating MUMS designation – Section 516.29) more than offset concerns for inappropriate use of "minor use" designation.

The AVMA has examined alternatives of quantitatively defining "minor uses" with respect to diseases that occur infrequently or in limited geographic areas and balancing this determination with the primary intent of the MUMS legislation (to create financial incentives to encourage the development of badly needed "minor use" drugs) but believes it is fraught with complexity that may not be overcome in the near future.

Unquestionably, the AVMA does not believe the system used for human orphan drug determination (a specific number of cases of a specific disease or condition as a percentage of the population) will work for "minor use" animal drugs. For FDA to establish a numeric criterion for designating a "minor use" drug, the only justifiable and defensible approach would be one based on epidemiology. The burden on a sponsor for determining a multitude of constantly changing, highly unreliable and in many cases unavailable epidemiological data that affect a "minor" disease and animal population, needed for determining the probability a drug being used in a small number of animals, may be an unattainable goal and is likely to be a direct disincentive to seeking MUMS designation. It is well established that, unlike human populations, animal population sizes and diseases are highly dynamic and are influenced by consumer demand, market forces and economics, regulatory, and producer, industry, state and federal prevention, control and eradication programs in place at any point in time. The AVMA is well aware of

evolving national programs within the USDA (e.g. Centers for Epidemiology and Animal Health – CEAH); National Center for Animal Health Surveillance – NCAHS; Agriculture Marketing Service – AMS); Economic Research Service – ERS) that seek to estimate both population size of all major species and their diseases. However, these data are collected for reasons other than, and unsuitable for determining “minor disease or conditions”, and the information is incomplete. Simply, on epidemiological grounds currently it is almost impossible to justifiably establish a fixed prevalence (or percentage of the total or sub-population) of a “minor disease” in any animal species without reliable data. We believe the variety of different scenarios presented by FDA in the proposed regulations, clearly illustrates this.

We applaud Congress for giving FDA broad latitude in determining what constitutes a minor use in a major species. However, until sound and justifiable epidemiological data on animal populations and their diseases becomes available it would be inappropriate and ill-advised to attempt to determine the number of animals to which to apply a “minor use” criterion. We therefore propose that, on a case by case basis, FDA utilizes the concept that a “minor use” drug for a major species would, in general, apply if the population (or biomass) of a major species for which the drug is intended, is roughly equivalent to the estimated population (or biomass) of the largest population of a minor species.

In keeping with this concept of applying the intent of Congress and the goal of establishing the expected low use the AVMA therefore believes it would be more practical and useful to recommend that section 516.21 addressing documentation of minor use status be replaced by requiring documentation demonstrating that:

Either:

- The drug is not currently approved for the disease or condition in the major species for which it is intended; *and,*
- It is unlikely the “minor use” designation for a drug will be applicable to a majority of the population of a major species that may be inflicted with the particular disease or condition; *and,*
- The need for a remedial drug for the specific disease or condition has been clearly identified by animal health professionals or an animal industry; *and,*
- If the drug has the same active ingredient as other approved drugs, the environmental safety assessment of the combined active ingredient of all such drugs is shown to be adequate.

Or,

- The return on investment for product does not exceed the development and maintenance costs of the product.

The AVMA is aware that in some circumstances a drug sponsor may seek drug approval for non-economic “philanthropic” purposes and we believe the last criterion would fully recognize and reward sponsors for considering such drugs under MUMS.

The AVMA believes that other principles need to be encompassed in these regulations.

We believe that the agency and sponsors would be best served by separating requirements for companion and food animals. This separation would provide information clearly focused on the information necessary for each group.

We also recognize that the language in Section 516.20 requiring a specific development plan as a prerequisite for designation is an unnecessarily arduous task for a sponsor and may be premature in simply applying for MUMS designation. If the intent of requiring a development plan submission was to dissuade frivolous designation requests, we believe sufficient protection against this exists in Sections 516.29 and 516.30. Consequently we would recommend its removal from Section 516.20.

We also consider the requirements for proof of “minor use” status in Section 516.21 in essence constitutes proving a negative concerning the lack of medical justification, in that a drug developed for one system disease (e.g. a cardiac problem) inevitably would not apply to another diseased system (e.g. muscular). In our opinion such a justification may be impossible and, if not impossible, it is an unnecessary and burdensome requirement.

Furthermore, MUMS drugs require as many incentives as possible and we recommend a 60-day review and response time limit to any designation application be included in Section 516.24. Similarly we recommend a 60-day limit for FDA to update the list of designated MUMS drugs to inform both the public and potential sponsors. In addition, in examining Section 516.29, we believe the 1-year advanced notification for discontinuing the manufacture of a drug is excessive and a 30 – 60 day advance notice may be more appropriate and would be sufficient time for FDA to respond and allow another potential sponsor to step forward.

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) or Dr. Elizabeth Curry-Galvin (847-285-6633; egalvin@avma.org).

Sincerely,

A handwritten signature in black ink that reads "Bruce W. Little, DVM". The signature is written in a cursive, flowing style.

Bruce W. Little, DVM
Executive Vice President

BWL/ADS