



Representing manufacturers of animal health products

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January 26, 2006

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

Re: Docket No. 2005N-0329 – Designation of New  
 Animal Drugs for Minor Uses or Minor Species –Proposed Rule

The ANIMAL HEALTH INSTITUTE (“AHI”) submits the attached comments on the proposed rule to designate certain new animal drugs for minor uses in a major species or any use in minor species. AHI is a national trade association representing manufacturers of animal health – pharmaceuticals, vaccines and feed additives used in modern food production and the medicines that keep pets healthy.

AHI appreciates the FDA’s efforts to facilitate the approval and availability of new animal drugs for needed conditions in major and minor species that may not always be economically viable for companies to pursue. However, AHI believes the proposed rule to be complex, and that this complexity will deter utilization by sponsors. For example, although the definition and requirements to designate a minor species are simple and straightforward, there is a very significant difference in the standards to designate a minor use in a major species. As a result, under the proposed requirements, justification of a minor use indication will be difficult for well established products; let alone for newer or unregistered products for minor use.

The current proposed rule requires economic justification. In reality, many MUMS drugs may never be justified on an economic basis. While sponsors must make a profit to continue to provide benefits to the public, there are still cases where the only “business case” for a drug approval is strictly goodwill, or “just doing the right thing”.

AHI is providing more specific comments on the rule along general and paragraph specific remarks in the attached table.

Sincerely,

Richard A. Carnevale

Enclosure

2005N-0329

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**Comment Form**

				Date: January 26, 2006	Document Docket No. 2005N-0329
Commenter	Section	Paragraph Figure/ Table Line No.	Proposed Change	Comment/ Rationale	
AHI	GENERAL		GENERAL COMMENTS ON PROPOSED RULE	<ul style="list-style-type: none"> <li>AHI recognizes that the agency has determined that "small numbers" needs to be defined for the 7 current major species. In reality, better epidemiologic data than currently exists would be required to establish any meaningful numbers. We would caution the agency that setting numbers that are very low will be a disincentive for development. Therefore, our comments are tempered by this position, and we propose, in the specific affected sections, an alternative approach until meaningful data becomes available. There seems to be a lack of balance with the evidence a company would have to provide for the agency to designate a minor use with that required for a minor species, where in the latter case the exposure to the drug substance on a biomass basis could far exceed the minor use. We recommend that the populations for sheep and other minor species should be kept in mind and considered when numbers for minor use are established.</li> <li>We request that the agency consider separation of the requirements for companion animals from that for food animals, as it is difficult to generalize across the two categories.</li> </ul>	
AHI	516.3	(b) <i>Infrequently</i>	<i>Infrequently ...uncommon or that occurs only sporadically, i.e. on an annualized basis.</i>	Addition of the phrase, <i>i.e. on an annualized basis</i> , adds clarity to the definition, and causes it to be consistent with agency comments on pages 56395 and 56396.	

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AHI	516.3	(b) Minor Use	<p>Minor use means the intended use of a drug in a major species for an indication:</p> <p>(1) <i>that is not currently approved, is not reasonably anticipated to be applicable to a majority of the intended population, and, has been identified as an animal health need by either animal health professionals, producers, and/or the public; or</i></p> <p>(2) <i>for which the annualized commercial return is not reasonably anticipated to exceed the annualized cost incurred in its development and maintenance</i></p>	<p>In response to the agency request for input on "small number of animals", the membership of AHI recognizes that there is currently not enough epidemiological or other source data to establish realistic numbers across the 7 major species at this time. Therefore, the proposed language in the preceding column is AHI's recommended criteria for a practical definition of minor use to enable sponsors to effectively qualify for these claims in keeping with the intent of the Act. The key element of these criteria hinges on the fact that animal drugs have been researched and developed for more than 40 years. It is reasonable to assume that companies have invested in diseases and conditions that yielded the most favourable return on investment, those which likely occur in a large percentage of animal species populations. Therefore, if a claim does not currently appear on any label, it is also reasonable to assume it to be a minor use, unless, on its face, it is obvious it could apply to a majority of a species population(s).</p>
AHI	516.3	(b) Same dosage form (i) Part 520	Combine oral dosage form with feed additives for the purposes of "Same Dosage Form"	<p>As the rule is currently written, it places feed additives at a disadvantage. If a feed additive is designated, an oral dosage form of the same drug, for the same indication, could also get designation and approval, and thus negatively affect the business case and success of the previously designated feed additive. The reverse could also occur. The resulting effect is that this dynamic is a potential disincentive for seeking approval for the MUMS drug/indication.</p>

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AHI	516.3	(b) <i>Same intended Use</i>	Revise the section on "Same Intended Use" to increase clarity and remove barriers to sponsor consideration to development of MUMS drugs/claims.	<p>The current verbiage leaves questions in the following areas:</p> <ul style="list-style-type: none"> <li>• The CVM discussion on the proposed regulation specifies same intended use includes the intended treatment, control or prevention of a disease or condition. The current wording causes us to question whether one sponsor could get a designation for treatment, a second could get control, and a third, prevention, or if designation for one of the three would be protective across treatment, prevention and control, as long as a functionally superior drug did not become available.</li> <li>• Third Principle (page 56398): This method of division of a disease complex by organism is usually not enforceable and/or measurable in a field situation. Thus, if the innovator assesses the business case and/or public need for a MUMS approval for X organism, which is a component of XYZ complex, the information that will be retrievable will usually be associated with the disease complex, not the specific organism, as what is being treated is the complex. Therefore, by allowing division into specific organisms as it applies to a minor use claim, this could also be a disincentive for the first sponsor, since another company could come in behind and take part of the market, which since it is MUMS is already small, for the treatment of the disease complex.</li> </ul>

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AHI	516.21	(b)	Change the requirements for proof of minor use status as specified previously for the definition of Minor Use, Section 516.3	<p>Comments as per previous comment on the definition of Minor Use, section 516.3.</p> <p>In addition, we reinforce the comments that we have made on a general level, that the burden placed on the sponsor for a minor use is disproportionate to the burden for a minor species, and in some cases, even for a regular NADA. For instance, in this specific section, it appears that the agency is requesting that the sponsor prove a negative concerning the lack of medical justification. Please note that even if this could be done in some cases, the sponsor can not predict either the judgement of the individual veterinarian, or movement/evolution of disease. For example, if a drug is indicated for respiratory disease, we, as the sponsor, can maintain the position that it is inappropriate for cardiac disease, but absolute justification of that may be impossible, and is in our opinion, unwarranted and burdensome.</p>
AHI	516.21	(c)	Change the requirements for proof of minor use status as specified previously for the definition of Minor Use, Section 516.3	<p>Comments as per previous comment on the definition of Minor Use, section 516.3</p> <p>In addition, we reinforce that financial assessment and company decisions to market a product are made with variable criteria in individual companies, and are for the most part, confidential. The agency states in the background for this proposed rule that it is not the intention of Congress for FDA to establish a test of commercial value of the drug. We believe that the goal of establishing the expected low use is met with our proposed alternative as stated in previous comments.</p>
AHI	516.23		No change requested	We agree with the verbiage and intent of this section. However, it is our position that the flexibility in timing stated in this section is somewhat negated by the verbiage in 516.21, which implies that the applicant will not be able to apply early in the process due to specifics required for application. (See previous comments on 516.21).
AHI	516.24	(b)	Revision to add a 60 day timeline to the review and response to the sponsor for a designation request.	It is of mutual benefit to the agency and sponsor to commit to timely review and response.
AHI	516.25	(4) (ii)	Revise section (4) as per previous comments on section 516.20 concerning the amount of data required up front just to be designated.	Position previously stated for comments on 516.20
AHI	516.28		Add a 60 day timeline to update the list of designated drugs once a new drug has been designated.	Informing the public and sponsors of new designations will be important for those companies potentially considering the same drug/indication.

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AHI	516.20	(b) (6)	Remove language specifying a specific product development plan as a requirement for designation.	<p>Although the members of AHI recognize that the specific development plan, backed by data, is a vital part of the development of a new animal drug, we feel that this request as a requirement for consideration for designation of a MUMS drug/claim is premature and unrealistic. The agency is, in effect, asking the sponsor to expend a significant amount of time and money prior to even knowing if the sponsor can receive designation. As designation should be considered an incentive, it is partially negated by asking for the specific development plan up front. We understand that the agency will not want frivolous requests. We feel that this is very unlikely, for several reasons:</p> <ul style="list-style-type: none"> <li>• Sponsors are typically resource limited. They will not take the time to put forth a frivolous claim.</li> <li>• Sponsors will not be building their company portfolios with MUMS approvals. That approach would not be viable; therefore, the quantity of requests for designation is not anticipated to be burdensome to the agency.</li> <li>• The proposed rule, in section 516.29 and 516.30 provided the protection of both the agency and the public from frivolous requests. The sponsor will have to be accountable for truthfulness and for reasonable progress as enforced by both the requirements for annual reporting and on designated drugs, with further accountability for conditionally approved drugs. The agency has the right to rescind the designated status if the sponsor has not complied with the requirements. Therefore, if due diligence is not applied by the sponsor in a timely fashion after designation, they will not retain the status, and the door will be opened for another applicant.</li> </ul>
AHI	516.20	(b) (7)	Change the requirements for proof of minor use status as specified previously for the definition of Minor Use, Section 516.3	Comments as per previous comment on the definition of Minor Use, section 516.3
AHI	516.21	(a)	Change the requirements for proof of minor use status as specified previously for the definition of Minor Use, Section 516.3	Comments as per previous comment on the definition of Minor Use, section 516.3

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AHI	516.29	(b)	Change the requirement for 1 year advance notification to 30-60 days.	<ul style="list-style-type: none"> <li>In many instances, the sponsor may not have knowledge 1 year prior to discontinuation.</li> <li>We request clarification on the situation where the agency has withdrawn designation status after notification by the sponsor (sponsor A), but the drug is still being sold, as per the timing of the notification. Could another sponsor (Sponsor B) potentially achieve designation and conditional approval, and thus block any further sale by Sponsor A, even if they still have time left on their notification and drug to be sold? With the current timing of 1 year notification, this could create a significant problem for sponsor A.</li> </ul>	
AHI	516.31	(a)	Clarification/comment requested	As the rule is currently written concerning designation and exclusivity, we interpret this language to still allow a sponsor that does not request MUMS status through designation and/or conditional approval, to move forward with the same drug/indication in parallel with the designated drug if they did not get conditional approval in addition to designation. Although the non-MUMS claim will not get the 7 years, if they get an approval first, they would get 3-5 and effectively block the approval of the designated drug. Please comment.	
AHI	516.31	(a) (2)	Delete "proposes"	We do not agree that the agency should be able to approve another application based on a <i>proposed withdrawal</i> of the currently approved application. This appears to negate the right of the sponsor to any due process.	
AHI	516.52	(d)	Add a 60 day time requirement for updating the list, as per comment on 516.28	As per previous comments on section 516.28	