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Vice President, Regulatory, Scientific, and International Affairs

December 20, 2006

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

**Re: Docket No. 2006N-0067 and RIN number 0910-AF67; Index of  
Legally Marketed Unapproved New Animal Drugs for Minor Species**

The ANIMAL HEALTH INSTITUTE ("AHI") submits these comments to Docket No. 2006N-0067 and RIN number 0910-AF67; Index of Legally Marketed Unapproved New Animal Drugs for Minor Species. AHI is the national trade association representing manufacturers of animal health products -- the pharmaceuticals, biological products and feed additives used in modern food production, and the medicines that keep livestock and pets healthy. As such we have a great interest in proposed regulations to facilitate the availability of drugs for minor use and minor species animals.

We appreciate that the FDA is making available an avenue to provide products for minor species that might not otherwise be suitable for full approval. However, we have concern that the process described in the proposed rule is overly complex and appears to be an alternate approval process. AHI provides the following general and specific comments for your consideration prior to finalization of this regulation. Should you have any questions, please do not hesitate to contact AHI at (202) 637-2440.

Sincerely,



**Richard A. Carnevale, VMD**  
Vice President, Regulatory, Scientific,  
and International Affairs

Enclosure

**Docket No. 2006N-0067: Index of Legally Marketed Unapproved New Animal Drugs for Minor Species**
**Date:**  
December 20, 2006

**Document:**  
Proposed Rule

Commenter	Page No. and/or Section	Proposed Rule Text	Comment / Rationale
AHI	48841-48847 II. Proposed Regulations	General Comments	<p>We appreciate that the FDA is willing to provide an avenue to provide these types of products for minor species. However, we have concern that the process described is overly complex and appears to be an alternate approval process. This is reinforced by the consistent use of regulatory language that, by law, compels compliance with very specific requirements. We suggest an alternative process be considered that would encourage more participation from sponsors. In general, this proposed regulation appears to mirror the approval process. Therefore, there would be more motivation by a requestor to get the product designated and conditionally or fully approved.</p> <p>It is unclear in the preamble what FDA is referencing in terms of statutory criteria. FDA should clarify whether this statement will bind the Expert Panel and the FDA to comparison of the data presented to statutory requirements such as substantial evidence and independent substantiation, for example, one or more adequate and well controlled studies as per 512 (d) (3), as well as target animal safety regulatory requirements under 512 (d) 2), or does this statutory requirement only refer to 572 (d)(2) of the Act. Lastly, we concur with the omission of specific reference to 21 CFR parts 210 and 211, although there are statutory requirements for cGMP that could be interpreted to be in scope and required in full as per 21 CFR parts 210, 211, 225 and 226.</p>
AHI	48843 II. Proposed Regulations F. (4)	Chemistry, manufacturing and control information	<p>We understand the difference in CMC requirement between an NADA and an indexing request. We wish to clarify post-indexing CMC requirements. 516.165 (a) (3) on page 48862 implies that indexed drugs must meet all approved drug CMC requirements. However, 516.165 (c) (3) (iii) implies that CMC changes only need to be reported in the level of detail as required for the original CMC description for initial indexing.</p>

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AHI	48843 II. Proposed Regulations F. (3)	Occupational and user safety	There is no regulatory relief from the statutory requirement for an indexed drug.
AHI	II. Proposed Regulations	Proposed Alternative Process	We propose that the emphasis be removed from each specific product and be focused on the compound(s) [active ingredient(s)] for the safety and effectiveness, similar to the human and veterinary drug DESI panel. This could be accomplished by an expert panel assembled by the government or public sector, and be based on available published information or produced by public agencies. Then the individual or group of manufacturers could provide a statement of assurance of quality for their individual products that would give the user and prescriber basic assurance as to product reliability.
AHI	48849 IV. Analysis of Economic Impacts	Administrative Costs	Estimates of time and cost burden are potentially underestimated, both in the process to gain indexed status and the maintenance requirements. For example, the time for creation of the expert panel by the regulatory professional is estimated to be 8 hours. This does not seem realistic in our experience with contracting with outside experts. In addition, a review by the expert panel is estimated as 80 hours. If a panel is composed of 4 members, this allows only 20 paid hours each for all efforts, including but not limited to travel, research, meetings, and production of the report. Lastly, the example of 12 hours for preparation of a submission is too short. In our experience, depending on the amount of new data vs. referenced data this time commitment could range from approximately 20 hours at the shortest to upwards of 80 hours. In contrast, we are unclear on the 20 hours allotted for the notice of claimed investigational exemption. In conclusion, this section further speaks to the fact that this process is too complex, and translates into unreasonable costs which will potentially inhibit sponsors from utilizing indexing.
AHI	48852 Parts 202,202	Labeling conforming amendment	Addition of indexing references to these parts of the 21 CFR will add very specific statutory requirements to the labeling and advertising process for an unapproved drug.

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AHI	48853 Part 207	Drug Listing conforming amendment	It is unclear whether the unapproved product that has been drug listed will then be subject to product fees under ADUFA.
AHI	48854 Part 510	New Animal Drugs conforming amendments	We are not clear on why the agency is proposing changes to conforming amendments for approved drugs to apply to unapproved indexed drugs.
AHI	48855, 48856 Parts 516.111, 516.129	Scope of Proposal and Content of request	We would like to clarify, providing that the early life stage is sufficiently separated in time from the life stage that is consumed, that requirements for human food safety will be satisfied by existing data (for example, available literature, existing studies and/or extrapolation of data). We additionally request clarification on how close the life stage may be to the consumed life stage in a food animal species before human food safety becomes a greater concern and requires more data, or, it is refused for consideration for indexing.
AHI	48855 Part 516.115	Definitions	<p>Please qualify that the expertise of the panel is a function of the entire panel, rather than each individual member. (516.141(b)(5)- more specific and clearer than the definition)</p> <p>Requestor: We propose that CVM consider the requestor to not necessarily be an individual company. Rather, this could be a range of groups from government to private interests that not only assemble the expert panel but also provide all documentation/ support needed, up to, but not including the manufacturing assurance and process. This could be similar to the Public Master File process that exists today. [Cross reference to 516.141.(c)]</p>
AHI	48855 Part 516.123(b)	Informal conferences	<p>The 30 day time limit for requestor response to an FDA denial is short. We propose that this time be extended to 90 days</p> <p>We request clarification as to the use of “informal” as a descriptor for these meetings. By the content of this section, it appears consistent with formal communications.</p>
AHI	48856 Paste 516.123(n)	Informal conferences	We request clarification as to whether the requestor would have opportunity to read and respond to the minutes within 30 days which is the existing process for conferences.

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AHI	48857 Paste 516.141	Expert panels	We request clarification on qualifications of the expert panel. We would foresee that a combination of several areas of expertise be represented, including pharmacology (especially for the alternative process), plus a clinical expert, a safety (TAS and Toxicology) expert, and a “major user” if that person is available, to address anecdotal evidence.
AHI	48857 Part 516.129 (6)	Content and format of eligibility request	Why is the estimated annual product distribution needed by the agency? Based on the restrictions that are inherent in the definition of minor use, this estimate does not appear to be of pivotal importance to the status of indexing.
AHI	48860 Part 516.155	Labeling of indexed drugs	We understand that indexed drug labeling must be separate from approved or conditionally approved drug labeling. Due to the prohibitive cost of production of small quantities of separately labeled product, the requirement for separate labeling for an indexed drug could be a deterrent for indexing useful drugs that are already approved in major species. We suggest that adequate distinction could be required on existing labeling to provide the indexed claims and information on the approved labeling. For example, a required font, color or alert symbol could be incorporated into the text and graphics. Additionally, we request clarification on the statement that the product can not be utilized extra-label once it is indexed. This could be prohibitive to the veterinarian’s ability to utilize an approved medication off label when needed if it has been also indexed. This could be prohibitive to any use of an established product in the context of an index for minor use.
AHI	48862 Part 516.165	Records and reports	What are the post-approval CMC requirements for an indexed drug? Will they be the same as the current MCSR reporting process or does the agency envision that the manufacturing data be included in the annual DER?
AHI	48859 Part 516.141 (g)	Prevention of conflicts of interest	The proposed regulations are potentially too stringent. The Animal Health Industry is very small, and the extensive detail on conflict of interest appears excessive in the context of the task they are being requested to perform, and will prohibit participation and exclude qualified expertise.