



March 9, 1998

NADA 140-915

John Page III, Ph.D.
Regulatory Affairs Manager,
Novartis Animal Health, US, Inc.
1500 Pinecroft Road, Suite 400
Greensboro, NC 27407

Dear Dr. Page:

We refer to your Drug Experience Report dated January 26, 1998, concerning a promotional piece for Interceptor (Milbemycin oxime), NADA 140-915, titled: "Tough on roundworms ---- Tough on HEARTGARD." It promotes efficacy of Interceptor in comparison with HEARTGARD (HG) Plus (Ivermectin and Pyrantel pamoate), NADA 140-971.

We have reviewed your submission and have the following comments:

1. Tough on roundworms:

The results from different studies are presented and since the materials and methods in these studies are not identical, comparing the efficacy results is unfair. The results from dose confirmation trials are presented for Interceptor, whereas results from the published article are used for HG Plus. In addition, efficacy of HG Plus is misrepresented. The cited 88.2% efficacy of HG Plus against *T. caninum* was from Trial number four, which was the lowest as compared to Trial number six or a combination of these two trials. Despite demonstrated efficacy of HG Plus against *T. leonina* at 99.2% in the cited publication, no mention has been made about its efficacy. In summary, we believe that these two products do not significantly differ with respect to their effectiveness against roundworms as per pre-approval studies and/or cited publication.

2. Tough on hookworms:

The effectiveness of Interceptor against migrating hookworm larvae and the lack of effectiveness of HG Plus in this regard has been mentioned. However, the

approved labeling does not mention effectiveness of either product against migrating hookworm larvae. The promotional piece uses references, quotations, and literature for claims which have no relevance to the approved labeling claims.

In addition, the promotional piece suggests or implies that Interceptor has demonstrated efficacy against a wide variety of hookworms and, therefore, is better than HG Plus which is contrary to the approved labeling. According to the approved package inserts, Interceptor has been approved for control of adult *A. caninum*, only one specie/genus of hookworm, while HG Plus is approved for the treatment and control of three genera/species of hookworms – viz. *A. caninum*, *Uncinaria stenocephala*, and *A. braziliense*. The efficacy of Interceptor in controlling adult *A. caninum* is claimed at 98% in publications, while HG Plus was shown to be greater than 99% efficacious against all three kinds of hookworms in the pre-approval studies.

3. Tough on whipworms:

HG Plus is not approved for the removal and control of *T. vulpis*. This is an irrelevant comparison.

4. Tough on HEARTGARD:

We note that for all other claims, the promotional piece compares Interceptor with HG Plus and not with HG. The phrase "Tough on HEARTGARD" incriminates all HG products. The promotional piece is violative because it uses, quotes, or paraphrases out of context to convey a false or misleading idea. In addition, all HG products are also 100% effective in preventing heartworm disease.

In conclusion, the promotional piece in question compares the effectiveness of Interceptor with HG Plus against various parasites in a manner which is false, lacking in fair balance, or otherwise misleading as stipulated under various subsections of 21CFR part 202.1(e) (6) of the regulations.

We wish to remind you of the commitment you made when you signed the New Animal Drug Application Form V 356 that the labeling and advertising of your product will prescribe, recommend, or suggest its use only in accord with the

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approved labeling. Therefore, we request that you immediately discontinue using this violative promotional piece and in the future, refrain from promoting your product in a false and misleading manner.

Please inform us of your intentions within 30 days of the receipt of this letter.

Sincerely yours,



William C. Keller, DVM
Director, Division of Epidemiology
and Surveillance
Center for Veterinary Medicine