DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL - 7 2006

Ms. Linda Little
Bayer Healthcare, LLC
P.O. Box 390
Shawnee Mission, KS 66201
USA

Re: NADA 140-441
Baytril® (enrofloxacin) antibacterial tablets
B06231 2/14/06
Baytril ad submitted 2/22/06

Dear Ms. Little,

This letter is in reference to your Drug Experience Report (DER) submission dated February 22, 2006, concerning Baytril (enrofloxacin) antibacterial tablets, NADA 140-441. This submission includes a Print Ad identified by Bayer as Lit#B06231. The ad is entitled *"There's a lot to be said for getting things right the first time."*

This advertisement contains unsubstantiated superiority claims for the drug and uses *in vitro* microbial sensitivity data to suggest clinical relevance. In addition, this advertisement contains no risk information about the drug. These violations cause the drug to be misbranded under section 502(n) of the Federal Food, Drug and Cosmetic Act (FFDCA).

Background

Baytril (enrofloxacin) antibacterial tablets are approved for use in the management of diseases associated with bacteria susceptible to enrofloxacin (codified in 21 C.F.R. 520.812). The labeling for Baytril includes, among other information, the following important contraindications, warnings, and precautions:

> **Contraindications**
> Enrofloxacin is contraindicated in dogs and cats known to be hypersensitive to quinolones.
>
> **Dogs:** Based on the studies discussed under the section on Animal Safety Summary, the use of enrofloxacin is contraindicated in small and medium breeds of dogs during the rapid growth phase (between 2 and 8 months of age). The safe use of enrofloxacin has not been established in large and giant breeds during the rapid growth phase. Large breeds may be in this phase for up to one year of age and the giant breeds for up to 18 months. In clinical field trials utilizing a daily oral dose of 5.0 mg/kg, there were no

reports of lameness or joint problems in any breed. However, controlled studies with histological examination of the articular cartilage have not been conducted in the large or giant breeds.

Warnings
In rare instances, use of this product in cats has been associated with Retinal Toxicity. Do not exceed 5 mg/kg of body weight per day in cats.

Precautions
Quinolone-class drugs should be used with caution in animals with known or suspected Central Nervous System (CNS) disorders. In such animals, quinolones have, in rare instances, been associated with CNS stimulation which may lead to convulsive seizures. Quinolone-class drugs have been associated with cartilage erosions in weight-bearing joints and other forms of arthropathy in immature animals of various species. The use of fluoroquinolones in cats has been reported to adversely affect the retina. Such products should be used with caution in cats.

Unsubstantiated Superiority Claims

This advertisement states *"E. coli... has a 20.5% greater sensitivity to Baytril than amoxicillin/clavulanic acid."* This statement is followed by a footnote referencing Aucoin, D, Patient First Therapy: A Rational Approach to Complicated Bacterial Infections, 2005. The reference describes a comparison of *in vitro* microbial sensitivity data contained in a non-clinical study. The clinical relevance of quantitative *in vitro* comparisons of antimicrobials has not been shown. Thus, this statement is misleading because it suggests that this result is clinically significant when this has not been demonstrated by substantial evidence or substantial clinical experience (see 21 C.F.R. § 202.1(e)(6)(vii)). If you want to suggest that Baytril has superior clinical efficacy over amoxicillin/clavulanic acid, such a claim should be based on adequate and well-controlled head-to-head clinical trials. CVM is not aware of any such studies. If you have such studies, please submit them to CVM.

The advertisement also contains the statement *"Broad-spectrum Baytril has not lost efficacy over time."* This statement references Aucoin, D. Fluoroquinolone Update: Reports on Resistance Trends 2002-2005, Insights in Internal Medicine Supplement to Compendium, 2005. The reference describes a comparison of *in vitro* microbial sensitivity data contained in a non-clinical study. The comparison is with regard to the *E. coli* pathogen only. As already noted, the clinical relevance of quantitative *in vitro* comparisons of antimicrobials has not been shown. In addition, this statement broadly suggests that Baytril has not lost efficacy with regard to any microbial pathogen. Therefore, this statement is misleading. If you want to suggest that Baytril, when compared to other drugs, has not lost efficacy over time with regard to a broad range of pathogens, such a claim should be based on adequate and well-controlled head-to-head clinical trials. CVM is not aware of any such studies. If you have such studies, please submit them to CVM.

Omission of Risk Information

This advertisement is accompanied by a brief summary as required under 21 C.F.R. § 202.1(e). However, the advertisement fails to present any of the risk information in the body of the advertisement. In particular, although the advertisement presents several effectiveness claims for Baytril, it fails to include the most serious and frequently occurring risks from the approved labeling. This omission of risk information causes the drug to be misbranded (see 21 C.F.R. § 202.1(e)(5)(iii)).

Conclusion and Requested Action

As discussed above, the advertisement causes the drug to be misbranded under sections 502(n) of the FFDCA because it contains unsubstantiated superiority claims and omits important risk information.

The Center for Veterinary Medicine, Division of Surveillance requests that Bayer Animal Health, LLC, immediately cease dissemination of the Baytril (enrofloxacin) promotional piece described above, and any that may contain similar information. Future promotional materials should adequately address risk information in a balanced manner that is similar in scope and prominence to promotional claims for the product.

Please submit a written response within 30 days of receipt of this letter describing your intent to comply with this request. Please direct your response to me at the Food and Drug Administration, Center for Veterinary Medicine, 7519 Standish Place, Rockville, MD 20855. We remind you that only written communications are official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to see that your promotional materials for Baytril, as well as other Bayer Animal Health products, comply with the requirements of the FFDCA and its implementing regulations.

Sincerely yours,

Mohammad I. Sharar, DVM, M.Sc.
Team Leader, Post-approval Regulatory Review Team, HFV-216
Division of Surveillance
Center for Veterinary Medicine