DEPARTMENT OF HEALTH & HUMAN SERVICES

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REGISTERED MAIL

Food and Drug Administration
Rockville MD 20857

NADA 141-068

Dianne L. Lavenburg, Director
Pharmaceutical Regulatory Affairs
Bayer Corporation
Agricultural Division, Animal Health
P.O. Box 390
Shawnee Mission, KS 66201

Dear Ms. Lavenburg:

We refer to your submissions dated October 12, 1998, and November 2, 1998, concerning the dissemination of promotional materials for Baytril® 100 (enrofloxacin), NADA 141-068. The Division of Epidemiology and Surveillance (DES) has reviewed these materials. We conclude that Bayer, in its promotion of this product, has disseminated information that contain statements or suggestions which causes its product to be misbranded under § 502 (a) of the Federal Food, Drug, and Cosmetic Act (the Act), and in violation of 21 CFR § 514.1 (b)(11) regulation.[1]

The INDICATIONS section of your approved product labeling states that: Baytril® 100 (enrofloxacin) injectable solution is indicated for the treatment of bovine respiratory disease (BRD) associated with *Pasteurella haemolytica*, *Pasteurella multocida*, and *Haemophilus somnus*. The approved product labeling for Baytril® 100 does not contain an indication to treat for *Mycoplasma spp.* or to modulate the function of leukocytes during the BRD process.

Bayer has disseminated promotional materials in such a manner to attach clinical significance to *in vitro* susceptibility data for *Mycoplasma spp.* Bayer has also attached clinical significance to the effect of Baytril® 100 on the function of leukocytes during the BRD process. In the absence of adequate clinical data necessary to substantiate these claims and implications, dissemination of promotional pieces containing these types of claims are deemed false, lacking in fair balance, or otherwise misleading under 21 CFR 202.1-(e)(6)(vii).

Similarly, in the Product Fact Sheet, Bayer has a section entitled, "***Baytril*® 100 Advantages and Benefits**," and under this heading it states: *Baytril*® 100's broad *in vitro* spectrum of action covers a wide range of bacteria and mycoplasmal pathogens. In Bayer's Q & A Booklet introducing Baytril® 100, on page 2 it states: Fluoroquinolone...are known for their ability to destroy a wide range of bacteria and mycoplasma. And in the Technical Manual's introduction on page 2, it states: Baytril 100 has rapid bactericidal activity against Gram-negative and Gram-positive

bacteria and *Mycoplasma spp*. The statements are not preceded or followed by an appropriate qualifying statement as required under 21 CFR 202.1 (e)(6)(vii). Bayer does not have an approved supplemental application providing that activity against *Mycoplasma spp*. has clinical significance.

In the Technical Manual, Bayer has utilized *in vitro* data generated from studies using ciprofloxacin and different species, on page 22, to suggest that the results from these studies may contribute to the efficacy of Baytril 100 by exerting a positive effect on leukocyte function during BRD (pages 2, 5, and 14). This is also implied in Bayer's Q & A Booklet introducing Baytril® 100 on page 4, where fluoroquinolones are stated to modulate leukocyte function during the disease process.

Bayer's activities have resulted in dissemination of false and misleading information about its drug, Baytril® 100. There is lack of substantial clinical evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the promotional materials. We wish to remind you that CRF 530.4 specifically states that extra label uses may not be promoted and 530.41 (a)(10) specifically prohibits extra label use of fluoroquinolones in food-producing animals. We also wish to remind Bayer of the commitment made when it signed the new animal drug application Form FDA 356V that the labeling and advertising will be neither false nor misleading, and that promotional claims will be in accord with those approved.

We request that further distribution of this material be discontinued. We would further request that you carefully review all promotional material prior to release to ensure violative material is not distributed. As we have previously stated, we consider these matters to be potentially serious public health issues and very important Center priorities. Please inform us of your intentions within 15 days of receipt of this letter. If you have any questions, you may contact us at (301) 827-6639.

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[1] These materials include, the Technical Manual B97164, the Question & Answers Booklet BL 8320 and the Baytril®100 Product Fact Sheet.

Sincerely yours,

Vitolis E. Vengris, D.V.M., Ph.D.
Team Leader, Marketed Product Scientific
and Regulatory Review
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