Approval Date: June 6, 1990

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 140-441

B. Sponsor

Mobay Corporation
Animal Health Division
P. O. Box 390
Shawnee, Kansas 66201

C. Proprietary Name

Baytril® Antibacterial Tablets

D. Established Name

enrofloxacin

E. Dosage Form(s), Route(s) of Administration and Recommended Dosage(s)

The optimum oral dose of Baytril® (brand of enrofloxacin) Tablets has been established at 2.5 mg/kg (1.13 mg/lb) of body weight administered twice daily. The three sizes of tablets available can be used as follows:

Weight of Dog	Baytril® (Scored)* Tablet
2.3 kg (5 lb)	1 x 5.7 mg tablet twice daily
9.1 kg (20 lb)	1 x 22.7 mg tablet twice daily
27.2 kg (60 lb)	1 x 68 mg twice daily

* The 5.7 and 22.7 mg tablets are single scored and the 68 mg tablet is double scored for accurate dosing.

The 2.5 mg/kg (1.13 mg/lb) dose administered twice daily should be continued for 2-3 days beyond the cessation of clinical signs to a maximum of 10 days. If no improvement is seen within five days, the diagnosis should be re-evaluated and a different course of therapy considered.

F. Indication

Baytril® (brand of enrofloxacin) Antibacterial Tablets are indicated for the treatment of the following bacterial infections in dogs:

Dermal infections (wounds and abscesses) caused by susceptible strains of *Escherichia coli, Klebsiella pneumoniae* ((*Klebsiella* has been recognized as a significant pathogen associated with nosocomial infections in dogs.(Glickman, L.T. Veterinary Nosocomial (Hospital-Acquired) *Klebsiella* Infections. JAVMA, V.179, No. 12, Dec. 15, 1981, 1389-1392. Kaufman, J. Nosocomial Infections: *Klebsiella* . The

Compendium on Continuing Education, V.6, No. 4, April, 1984, 303-310.)), *Proteus mirabilis* and *Staphylococcus aureus*.

Respiratory infections (pneumonia, tonsilitis, rhinitis) caused by susceptible strains of *Escherichia coli* and *Staphylococcus aureus*.

Urinary cystitis caused by susceptible strains of *Escherichia coli , Proteus mirabilis* and *Staphylococcus aureus*.

G. Effect of Supplement

This supplemental application amends the NADA to remove the contradiction against use in breeding female dogs.

II. EFFECTIVENESS

Well-controlled studies which demonstrated the effectiveness of Baytril® (enrofloxacin) Antibacterial Tablets are discussed in detail in the FOI Summary for the original NADA, 54 FR 3444: January 24, 1989.

III. ANIMAL SAFETY

The safety of Baytril® (enrofloxacin) Antibacterial Tablets was demonstrated in a series of well-controlled studies which are described in detail in the FOI for the original NADA, 54 FR 3444:January 24, 1989.

A seventh pivotal study has been conducted which demonstrates the safety of Baytril Antibacterial Tablets in breeding female dogs.

Study in Female Breeding Dogs (Safety Evaluation for Bay Vp 2674 in Female Breeding Dogs).

A. Stuke and J. Magerkurth of Topeka, Kansas conducted a reproductive safety study in 15 adult female Beagle breed dogs with the 22.7 mg enrofloxacin tablet. The purpose of this study was to evaluate libido and safety in female breeding dogs following multiple treatments with the approved market tablet formulation. Before treatment the dogs were randomly assigned to one of 3 groups. Four dogs served as the non-treated controls, 5 received treatments orally of 2.5 mg/kg (1.13 mg/lb) twice daily for a total of 5 mg/kg (2.27 mg/lb) per day and 6 were treated orally with 7.5 mg/kg (3.40 mg/lb) twice daily for a total of 15 mg/kg (6.80 mg/lb) per day. Each female received treatments for 10 consecutive days at each of 4 stages of reproduction (prior to breeding, early

pregnancy, late pregnancy and lactation). Parameters monitored included number of pups born alive, average number of pups born alive per female, number of dead pups at birth, average number of dead pups per female, verage body weight (birth, 2 and 4 weeks of age), average daily body weight gain, number of pups alive at 2 and 4 weeks and average number of pups alive at 4 weeks of age per female. Blinding was not necessary since the monitored parameters could be measured by objective means. Results of this study (Groups 1,2,3) and the 1987 historical control data for the kennel are presented in Table I.

Table I Comparison of Reproductive Performance with Historical Controls; Groups 1, 2 and 3

Parameter	Historical Controls	Group 1 (Non-Treated Controls)	Group 2 (5 mg/kg/day)	Group 3 (15 mg/kg/day)
Number of Females Whelping	82	4	5	6
Total Number of Pups Born	494	27	38	33
Number of Pups Born Alive	454	27	35	32
Average Number of Pups Born Alive/Female	5.5	6.8	7	5.3
Number of Dead Pups at Birth	40	0	3	1
Average Number of Dead Pups/Female	0.48	0	0.6	0.17
Average Body Weight at Birth (kg)	0.301	0.291	0.267	0.306
Average Body Weight at 2 Weeks (kg)	0.766	0.854	0.777	0.871
Average Body Weight at 4 Weeks (kg)	1.216	1.260	1.277	1.463
Average Daily Gain (gm/day)	32.6	34.3	35.8	41.1
Number of Pups Alive at 2 Weeks	*	24	27	27
Number of Pups Alive at 4 Weeks	411*	24	27	27
Average Number of Pups Alive at 4 Weeks/Female	5.0**	6.0	5.4	4.5

* Data not available
** Parameter evaluated at 6 Weeks for Historical Controls
As shown in the table all the parameters measured were within normal anticipated ranges and are comparable to the historical control results.

An indepth statistical analysis was not essential. The study results were stated as simple averages to allow accurate comparison to the historical control data. The study concluded that no adverse effects occurred upon reproductive parameters nor were there any clinical signs of toxicosis when female breeding dogs are treated with enrofloxacin tablets at doses as high as 3 times the labeled rate for 10 consecutive days at 4 critical stages of reproduction: 30 to 0 days prior to breeding, early pregnancy (between the 10th and 30th days), late pregnancy (between the 40th and 60th days) and during lactation (the first 28 days). This conclusion is further verified when the historical control reproductive data from the colony are used as comparison.

This study was conducted per Good Laboratory Practice Regulations.

IV. HUMAN SAFETY

A. Human Food Safety

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. The drug is labeled for use in dogs, which are nonsfood animals.

B. Human Safety Relative to Possession, Handling and Administration:

The labeling contains an adequate warning statement: "WARNING: Keep out of reach of children."

V. AGENCY CONCLUSIONS

The data submitted in support of this NADA comply with the requirements of Section 512 of the Act and Section 514111 of the implementing regulation. It demonstrates that enrofloxacin is safe and effective when used in accordance with labeling directions for treatment of the following bacterial infections in dogs.

Dermal infections (wounds and abscesses) caused by susceptible strains of *Escherichia coli , Klebsiella pneumoniae , Proteus mirabilis* and *Staphylococcus aureus* .

Respiratory infections (pneumonia, tonsilitis, rhinitis) caused by susceptible strains of *Escherichia coli* and *Staphylococcus aureus* .

Urinary tract infections (cystitis) caused by susceptible strains of *Escherichia coli , Proteus mirabilis* and *Staphylococcus aureus* .

According to the Center's supplemental approval policy (42 FR 64367), this is a Category II change. This supplement provides for the contraindication against use in breeding female dogs. The approval of the supplemental application has no adverse effect on the safety and effectiveness of the new animal drug, for previously approved use. Accordingly, this approval did not required a re-evaluation of the safety and effectiveness data in the parent application.

A differential diagnosis and monitoring of a patient's progress require the professional expertise of a veterinarian in breeding females as well as other dogs. Therefore, the labeling for this product should contain the veterinary prescription legend.

Under section 512(c)(2)(F)(iii) of the Generic Animal Drug and Patent Term Restoration Act of 1988, this Supplemental New Animal Drug Application qualifies for three years of marketing exclusivity, because a new study was required for its approval.

VI. ATTACHMENTS

1. Baytril® Antibacterial Tablets No. 60 package label
2. Baytril® Antibacterial Tablets No. 20 package label
3. Baytril® Antibacterial Tablets No. 5 package label
4. Baytril® Antibacterial Tablets package insert

Copies of these labels may be obtained by writing to the:

Freedom of Information Office
Center for Veterinary Medicine, FDA
7500 Standish Place
Rockville, MD 20855

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.