Date of Approval: December 2, 2005

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 140-929

MICOTIL 300

(tilmicosin phosphate)

To provide user safety information on the product labeling related to the mechanism of toxicity and medical intervention.

Sponsored by:
Elanco Animal Health,
A Division of Eli Lilly & Co.

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1. GENERAL INFORMATION:

a. File Number:	NADA 140-929
b. Sponsor:	Elanco Animal Health A Division of Eli Lilly & Co. Lilly Corporate Center Indianapolis, IN 46285 Drug Labeler Code: 000986
c. Established Name:	Tilmicosin phosphate
d. Proprietary Name:	MICOTIL 300
e. Dosage Form:	Injectable solution
f. How Supplied:	50 mL, 100 mL, and 250 mL glass vials
g. How Dispensed:	Rx
h. Amount of Active Ingredients:	300 mg/mL
i. Route of Administration:	Subcutaneous injection
j. Species/Class:	Cattle (beef and non-lactating dairy), and sheep
k. Recommended Dosage:	10 mg/kg body weight (BW)(1.5 mL per 100 lb BW), administered once
l. Pharmacological Category:	Antimicrobial
m. Indications:	For the treatment of bovine respiratory disease (BRD) and ovine respiratory disease (ORD) associated with *Mannheimia* (*Pasteurella*) *haemolytica*. For the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia* (*Pasteurella*) *haemolytica*.
n. Effect of Supplement:	To provide user safety information on the product labeling related to the mechanism of toxicity and medical intervention.

2. *EFFECTIVENESS:*

The Center for Veterinary Medicine (CVM) did not require effectiveness studies for this supplemental approval. The FOI Summary for the original approval of NADA 140-929 (approved March 24, 1992), and the FOI Summary for a supplemental approval of NADA 140-929 dated December 30, 1996, contain summaries of studies that demonstrate the effectiveness of tilmicosin for the labeled indications in cattle. The FOI Summary for the supplemental approval of NADA 140-929 dated September 4, 2002, contains a summary of studies that demonstrate the effectiveness of tilmicosin for the labeled indication in sheep.

3. *TARGET ANIMAL SAFETY:*

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 140-929 (approved March 24, 1992) contains a summary of target animal safety studies for cattle. The FOI Summary for the supplemental approval of NADA 140-929 dated September 4, 2002, contains a summary of the target animal safety study for sheep.

4. *HUMAN FOOD SAFETY:*

CVM did not require human food safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 140-929 (approved March 24, 1992) contains a summary of human food safety studies for cattle. The FOI Summary for the supplemental approval of NADA 140-929 dated September 4, 2002, contains a summary of the human food safety studies for sheep.

5. *USER SAFETY:*

Human warnings are provided on the product labeling as follows:

HUMAN WARNINGS: Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Do not use in automatically powered syringes. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice or cold pack to injection site while avoiding direct contact with the skin. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000. Avoid contact with eyes.

NOTE TO THE PHYSICIAN: The cardiovascular system is the target of toxicity and should be monitored closely. Cardiovascular toxicity may be due to calcium channel blockade. In dogs, administration of intravenous calcium offset MICOTIL-induced tachycardia and negative inotropy (decreased contractility). Dobutamine partially offset the negative inotropic effects induced by MICOTIL in dogs. β-adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of MICOTIL in dogs. Epinephrine potentiated lethality of MICOTIL in pigs. This antibiotic persists in tissues for several days.

6. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that MICOTIL 300 (tilmicosin phosphate), when administered as a subcutaneous injection, is safe and effective for the treatment of bovine respiratory disease (BRD) and ovine respiratory disease (ORD) associated with *Mannheimia* (*Pasteurella*) *haemolytica*, and for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia* (*Pasteurella*) *haemolytica*.

Labeling continues to restrict this drug to use by or on order of a licensed veterinarian. This decision was based on the following factors: (a) adequate directions cannot be written to enable laypersons to appropriately diagnose and subsequently use this product to treat BRD and ORD, (b) administration by other than approved routes and dosages, or uses in species other than cattle and sheep can cause signs of toxicity, including death, and (c) there is a potential danger to the person administering the product if it is accidentally self injected or to other persons if it is accidentally injected. Because of these effects, extensive warning and caution statements are provided in the labeling which are deemed to be adequate to protect users from accidental injection and to discourage extralabel use.

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

In accordance with 21 CFR 514.106(b)(2)(ix), this is a Category II change which did not require a re-evaluation of safety or effectiveness data in the parent application.

No patents were submitted with this application.

7. ATTACHMENTS:

Facsimile labeling is attached as indicated below.

a. MICOTIL 300 – 50 mL vial label and insert

b. MICOTIL 300 – 50 mL carton

c. MICOTIL 300 – 100 mL vial label and insert

d. MICOTIL 300 – 100 mL carton

e. MICOTIL 300 – 250 mL vial label and insert

f. Client Information Sheet (English)

g. Client Information Sheet (Spanish)