Date of Approval: June 7, 2010

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-299

RESFLOR GOLD

Florfenicol and Flunixin Meglumine (in 2-pyrrolidone and triacetin)
Injectable Solution
Beef and Non-Lactating Dairy Cattle

To add *Mycoplasma bovis* to the list of target pathogens for the bovine respiratory disease treatment indication.

Sponsored by:

Intervet, Inc.

TABLE OF CONTENTS

I. GENERAL INFORMATION:

A. File Number:	NADA 141-299
B. Sponsor:	Intervet, Inc. 56 Livingston Ave. Roseland, NJ 07068 Drug Labeler Code: 000061
C. Proprietary Name:	RESFLOR GOLD
D. Established Names:	Florfenicol and flunixin meglumine (in 2-pyrrolidone and triacetin)
E. Pharmacological Categories:	Antimicrobial and non-steroidal anti-inflammatory drug (NSAID)
F. Dosage Form:	Injectable solution
G. Amount of Active Ingredients:	300 mg florfenicol and 16.5 mg flunixin (27.37 mg flunixin meglumine) per mL
H. How Supplied:	100, 250, and 500 mL glass vials
I. How Dispensed:	Rx
J. Dosage:	40 mg florfenicol/kg body weight (BW) and 2.2 mg flunixin/kg BW once (equivalent to 2 mL/15 kg BW or 6 mL/100 lbs BW)
K. Route of Administration:	Subcutaneous
L. Species/Classes:	Cattle/Beef and non-lactating dairy
M. Indication:	RESFLOR GOLD is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*, and control of BRD-associated pyrexia in beef and non-lactating dairy cattle.
N. Effect of Supplement:	This supplement provides for the addition of *Mycoplasma bovis* to the list of target pathogens for the treatment of BRD and control of BRD-associated pyrexia indication.

II. EFFECTIVENESS:

A. Dosage Characterization:

This supplemental approval does not change the previously approved dosage. The Freedom of Information (FOI) Summary for the original approval of NADA 141-299 dated November 23, 2009, contains dosage characterization information for cattle.

B. Substantial Evidence:

Effectiveness of florfenicol and flunixin meglumine (in 2-pyrrolidone and triacetin) for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni* and control of BRD-associated pyrexia in beef and non-lactating dairy cattle was previously demonstrated in the original approval, and is summarized in the FOI Summary for RESFLOR GOLD (NADA 141-299) dated November 23, 2009.

Effectiveness of florfenicol and flunixin meglumine (in 2-pyrrolidone and triacetin) for treatment of BRD associated with *Mycoplasma bovis* and control of BRD-associated pyrexia was demonstrated by examining treatment success data from cattle enrolled in the BRD treatment study (Study No. C05-126-00) conducted for the original approval of RESFLOR GOLD.

M. bovis isolates were obtained from pre-treatment nasal swabs from all calves enrolled at all four sites, post-treatment nasal swabs from treatment failures in the RESFLOR GOLD and saline control treatment groups at three sites, and lung tissue from one calf that died in the saline control treatment group. Isolates presumptively identified as *M. bovis* were identified to the species level using a polymerase chain reaction (PCR) method.

A total of 66 *M. bovis* isolates were identified from 60 calves across the study. There were numerically more treatment successes than treatment failures in RESFLOR GOLD treated calves that cultured positive for *M. bovis* pre-treatment. In the RESFLOR GOLD treatment group, eight calves cultured positive for *M. bovis* pre-treatment. Six of the eight calves (75%) were treatment successes and two calves (25%) were treatment failures.

These results from Study No. C05-126-00, along with the results previously summarized in the FOI Summary dated November 23, 2009, demonstrate that RESFLOR GOLD, when administered by subcutaneous injection as a single dose of 40 mg florfenicol and 2.2 mg flunixin meglumine/kg body weight, is effective for the treatment of BRD associated with *M. bovis,* and control of BRD-associated pyrexia in beef and non-lactating dairy cattle.

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-299 dated November 23, 2009, contains a summary of target animal safety studies for cattle.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-299 dated November 23, 2009, contains a summary of all toxicology studies.

B. Residue Chemistry:

CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-299 dated November 23, 2009, contains a summary of residue chemistry studies for cattle.

C. Microbial Food Safety:

The impact of the proposed change in indication for RESFLOR GOLD to include a new pathogen, *Mycoplasma bovis*, for the treatment of bovine respiratory disease (BRD) in beef and non-lactating cattle was carefully considered by the Agency. The Agency determined that because there are there are no changes in formulation, dosage, route of administration, or duration of use in this supplement, and the only change is the addition of an organism to the approved indication, the addition of an organism to the previously approved treatment indication should not significantly impact public health, and therefore further evaluation of microbial food safety was not necessary at this time.

D. Analytical Method for Residues:

1. Analytical Method

The FOI Summary for the original approval of NUFLOR Injectable Solution under NADA 141-063 dated May 31, 1996, contains the analytical method summary for florfenicol in cattle. The FOI Summary for the supplemental approval of BANAMINE Injectable solution under NADA 101-479 dated May 5, 1998, contains the analytical method summaries for flunixin in cattle.

2. Availability of Method

The methods are available from CVM, FDA, 7500 Standish Place, Rockville, MD 20855.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to RESFLOR GOLD:

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains material that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.

For customer service or to obtain a copy of the MSDS, call 1-800-211-3573. For technical assistance or to report suspected adverse reactions, call 1-800-219-9286.

VI. 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. The data demonstrate that RESFLOR GOLD, when used according to the label, is safe and effective for treatment of BRD associated with *Mycoplasma bovis*, and control of BRD-associated pyrexia in beef and non-lactating dairy cattle. Additionally, data demonstrate that residues in food products derived from cattle treated with RESFLOR GOLD will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

Labeling restricts this drug to use by or on order of a licensed veterinarian. This decision was based on the following factors: (1) adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this product to treat BRD; and (2) restricting this drug to use by or on order of a licensed veterinarian should help prevent indiscriminate use which could result in violative tissue residues.

B. Exclusivity:

Under Section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval. The three years of marketing exclusivity applies only to the treatment

of BRD associated with *Mycoplasma bovis*, and control of BRD-associated pyrexia in beef and non-lactating dairy cattle indication for which this supplement is approved.

C. Supplemental Applications:

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information:

RESFLOR GOLD is under the following U.S. patent numbers:

U.S. Patent Number	Date of Expiration
6,790,867	January 24, 2023

For current information on patents, see the Animal Drugs @ FDA database (formerly the Green Book) on the FDA CVM internet website.

VII. ATTACHMENTS:

Facsimile Labeling:
A. 100 mL bottle
B. 100 mL carton
C. 100 mL bottle Product Information insert
D. 250 mL bottle with attached, pull-out Product Information insert
E. 500 mL bottle with attached, pull-out Product Information insert