Date of Approval Letter:

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 110-048

VALBAZEN® (albendazole)

"...for the removal and control of a variety of internal parasites common in cattle and sheep."

Sponsored by:
Pfizer, Inc.

I. GENERAL INFORMATION

NADA Number:	110-048
Sponsor:	Pfizer, Inc. 235 East 42d Street New York, New York 10017
Established Name:	albendazole
Trade Name:	VALBAZEN®
Pharmacological category:	antiparasitic
How Supplied:	500- and 1000-mL bottles
Label claim of the Amount of Active Ingredient(s):	11.36% suspension (113.6 mg/mL)
Marketing Status:	over-the-counter
Species:	sheep and cattle
Effect of the Supplement:	The supplement adds sheep uses approved for a less concentrated suspension to labeling for an approved, more concentrated formulation.

II. INDICATIONS FOR USE

For the removal and control of the following parasites in cattle and sheep

Parasite	Cattle	Sheep
Liver Flukes	*Fasciola hepatica*	*Fasciola hepatica, Fascioloides magna*
Tapeworms (heads and segments)	*Moniezia benedeni, M. expansa*	Common Tapeworms (*Moniezia expansa*), Fringed Tapeworms (*Thysanosoma actinioides*)
Stomach Worms (adults and 4th stage larvae)	Brown Stomach Worms, including 4th stage inhibited larvae (*Ostertagia ostertagi*), Barberpole Worms (*Haemonchus contortus, H. placei*), Small Stomach Worms (*Trichostrongylus axei*)	Brown Stomach Worms (*Ostertagia circumcincta*, *Marshallagia marshalli*), Barberpole Worms (*Haemonchus contortus*), Small Stomach Worms (*Trichostrongylus axei*)

Intestinal Worms (adults and 4th stage larvae)	Thread-Necked Intestinal Worms (*Nematodirus spathiger, N. helvetianus*), Small Intestinal Worms (*Cooperia oncophora, C. punctata*)	Thread-Necked Intestinal Worms (*Nematodirus spathiger, N. filicollis*), Cooper's Worm (*Cooperia oncophora*), Bankrupt Worms (*Trichostrongylus colubriformis*), Nodular Worms (*Oesophagostomum columbianum*), Large-Mouth Bowel Worms (*Chabertia ovina*)
Intestinal Worms (adults and 4th stage larvae)	Hookworms (*Bunostomum phlebotomum*), Bankrupt Worms (*Trichostrongylus colubriformis*), Nodular Worms (*Oesophagostomum radiatum*)	
Lungworms (adults and 4th stage larvae)	*Dictyocaulus viviparus*	
Lungworms (adults and larval stages)		*Dictyocaulus filaria*

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

A. *Dosage Form:* suspension

B. *Route of Administration:* oral, as a drench

C. *Recommended Dosage:* 7.5 mg/kg body weight (3.4 mg/lb; sheep) or 10 mg/kg body weight (4.45 mg/lb; cattle).

IV. TARGET ANIMAL SAFETY AND EFFECTIVENESS

Target animal safety and effectiveness data for albendazole in sheep and cattle were accepted under original NADA 140-934 & NADA 110-048.

The increased albendazole concentration is not expected to pose any specific risk hazard to sheep. The actual amount of drug administered to sheep per unit body weight remains unchanged. CVM has concluded that the two formulations should perform in an identical manner when administered to sheep. Accordingly, the sponsor's request for waiver of *in vivo* study requirement has been granted, and no additional studies are required to support the approval of the 11.36% oral suspension of albendazole for sheep.

VI. HUMAN SAFETY

This supplemental NADA did not require new human safety studies. The basic toxicology and residue chemistry studies that support the use of albendazole in cattle and sheep are summarized in the FOI Summaries for the original approvals of albendazole under NADA 110-048 and NADA 140-934. Based on the original NADAs, the following has been assigned to this product:

a. *Acceptable Daily Intake*: The Acceptable Daily Intake (ADI) of 5 µg/kg body weight/day was assigned to cattle and sheep on the basis of the toxicology studies.

b. *Safe Concentrations of Residues:* The safe concentrations of albendazole residues in edible tissues of sheep and cattle were established at 0.6 part per million (ppm) for sheep and cattle muscle, 3.0 ppm for liver, kidney and fat tissue of sheep, 1.2 ppm for cattle liver, 1.8 ppm for cattle kidney, and 2.4 ppm for cattle fat.

c. *Tolerances of Marker Residue:* Residue and metabolism studies established 0.2 ppm and 0.25 ppm as the tolerances for residues of albendazole 2-aminosulfone (the marker residue) in cattle liver (target tissue) and sheep liver, respectively.

d. *Assignment of a muscle tolerance:* A tolerance of 0.05 ppm albendazole 2-aminosulfone is assigned for cattle and sheep muscle following a review of the residue studies conducted with albendazole in those species. The total residue studies conducted with ^{14}C-albendazole show that total residues in muscle are expected to be in the range of 1 ppm to 4 ppm at 1 day after dosing under the approved conditions of use and that those residues deplete to 0.06 ppm or less (10% of the 0.6 ppm muscle safe concentration) by 3 to 4 days after dosing. Because of the rapid depletion of total residues from muscle, muscle tissue was not assayed in any of the non-radiolabeled (withdrawal) residue studies in either NADA 110-048 or NADA 140-934. Likewise, the metabolites present in muscle were not profiled.

   With a minimum of residue data available, the muscle tolerance value is estimated with consideration given to the metabolite profile data in liver of each species and to the capabilities of the determinative analytical method for residues in liver. A concentration of 0.05 ppm of the marker residue is assigned as the muscle tolerance because it represents a conservative estimate of the tolerance, and it is above the 0.025 ppm limit of quantitation of the determinative assay as validated in liver. The 0.05 ppm muscle tolerance makes it possible to identify cattle or sheep that have been marketed within 1 to 3 days after treatment with albendazole. As withdrawal times approaching the preslaughter withdrawal periods of 27 days for cattle and 7 days for sheep, the marker residue is unlikely to be detected in muscle tissue.

VII. AGENCY CONCLUSIONS

The information submitted in support of this application comply with the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 514) and indicate that albendazole oral suspension (11.36%) is safe and effective in sheep for the conditions of the use described in labeling.

Although no new toxicology or residue chemistry studies were submitted with this supplement, CVM has used this opportunity to assign a tolerance of 0.05 ppm albendazole 2-aminosulfone for residues of albendazole in cattle and sheep muscle. The pre-slaughter withdrawal periods of 27 days in cattle and 7 days in sheep remain unchanged.

There is reasonable certainty that the directions for use on labeling can and will be followed in practice. Accordingly, the Agency has concluded that this product shall retain over-the-counter marketing status.

In accordance with 21 CFR 514.106(b)(2), this is a category II change which did not require a reevaluation of the safety and effectiveness data in the parent application.

The Agency has carefully considered the potential environmental effects of this action and has concluded that the action qualifies for a categorical exclusion from the requirement to prepare an environmental assessment in accordance with 21 CFR 25.33(a)(1).

VIII. APPROVED LABELING (attached)

Facsimile label. 1-liter bottle