Date of Approval: January 13, 2026

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)

ANADA 200-831

Defendazole™

(fenbendazole)

Oral suspension

Beef and dairy cattle and goats

Beef and Dairy Cattle – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:

Lungworms: Adult *Dictyocaulus viviparus*;
Stomach worms: Adult brown stomach worms (*Ostertagia ostertagi*), Adult and fourth stage larvae barberpole worms (*Haemonchus contortus* & *H. placei*), and Adult and fourth stage larvae small stomach worms (*Trichostrongylus axei*);
Intestinal worms (Adult and fourth stage larvae): hookworms (*Bunostomum phlebotomum*), thread-necked intestinal worms (*Nematodirus helvetianus*), small intestinal worms (*Cooperia punctata* & *C. oncophora*), bankrupt worms (*Trichostrongylus colubriformis*), and nodular worms (*Oesophagostomum radiatum*).

Goats – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:

Stomach worms (adults): *Haemonchus contortus* and *Teladorsagia circumcincta*.

Sponsored by:

Norbrook Laboratories Ltd.

Executive Summary

Defendazole™ (fenbendazole) 10% oral suspension is approved for the following indications:

Beef and Dairy Cattle – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:
Lungworms: Adult *Dictyocaulus viviparus*;
Stomach worms: Adult brown stomach worms (*Ostertagia ostertagi*), Adult and fourth stage larvae barberpole worms (*Haemonchus contortus* & *H. placei*), and Adult and fourth stage larvae small stomach worms (*Trichostrongylus axei*);
Intestinal worms (Adult and fourth stage larvae): hookworms (*Bunostomum phlebotomum*), thread-necked intestinal worms (*Nematodirus helvetianus*), small intestinal worms (*Cooperia punctata* & *C. oncophora*), bankrupt worms (*Trichostrongylus colubriformis*), and nodular worms (*Oesophagostomum radiatum*).

Goats – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:
Stomach worms (adults): *Haemonchus contortus* and *Teladorsagia circumcincta*.

The reference listed new animal drug (RLNAD) is safe-guard® (fenbendazole) 10% oral suspension sponsored by Intervet, Inc. under NADA 128-620. This is the first generic fenbendazole 10% oral suspension for beef and dairy cattle and goats.

Bioequivalence

The sponsor conducted one *in vivo* blood-level study in cattle to show that Defendazole™ 10% oral suspension is bioequivalent to safe-guard® 10% oral suspension. No serious adverse events were reported during the study.

Human Food Safety

Under the NADA for safe-guard®, the Food and Drug Administration (FDA) previously established the acceptable daily intake and tolerances for fenbendazole, and these values also apply to Defendazole™.

The sponsor conducted one tissue residue study in cattle that supports assigning Defendazole™ the same withdrawal period in cattle that was previously established for safe-guard®. Therefore, FDA has assigned an 8-day withdrawal period to Defendazole™ when administered orally to cattle.

The sponsor conducted two tissue residue studies in goats that support assigning Defendazole™ the same withdrawal period in goats that was previously established for safe-guard®. Therefore, FDA has assigned a 6-day withdrawal period to Defendazole™ when administered orally to goats.

The sponsor conducted one bioequivalence study in cattle that supports assigning Defendazole™ the same milk discard time that was previously established for safe-guard®. Therefore, FDA has assigned a 48-hour milk discard time to Defendazole™ when administered orally to dairy cattle.

FDA determined that there is reasonable certainty of no harm from fenbendazole residues in edible tissues of treated cattle and goats when Defendazole™ is used according to the labeling.

Conclusions

Based on the data submitted by the sponsor for the approval of Defendazole™, FDA determined that the drug is safe and effective when used according to the label.

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I. GENERAL INFORMATION

A. File Number

ANADA 200-831

B. Sponsor

Norbrook Laboratories Ltd.
Carnbane Industrial Estate
Newry, County Down
BT35 6QQ, United Kingdom

Drug Labeler Code: 055529

C. Proprietary Name

Defendazole™

D. Drug Product Established Name

fenbendazole

E. Pharmacological Category

Antiparasitic

F. Dosage Form

Oral suspension

G. Amount of Active Ingredient

100 mg/mL (10%)

H. How Supplied

1 L and 5 L bottles

I. Dispensing Status

Over the counter (OTC)

J. Dosage Regimen

Beef and Dairy Cattle: 2.3 mg/lb (5 mg/kg) body weight.

Goats: 2.3 mg/lb (5 mg/kg) body weight.

K. Route of Administration

Oral

L. Species/Classes

Beef and dairy cattle and goats

M. Indications

Beef and Dairy Cattle – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:

Lungworms: Adult *Dictyocaulus viviparus*;
Stomach worms: Adult brown stomach worms (*Ostertagia ostertagi*), Adult and fourth stage larvae barberpole worms (*Haemonchus contortus* & *H. placei*), and Adult and fourth stage larvae small stomach worms (*Trichostrongylus axei*);
Intestinal worms (Adult and fourth stage larvae): hookworms (*Bunostomum phlebotomum*), thread-necked intestinal worms (*Nematodirus helvetianus*), small intestinal worms (*Cooperia punctata* & *C. oncophora*), bankrupt worms (*Trichostrongylus colubriformis*), and nodular worms (*Oesophagostomum radiatum*).

Goats – 2.3 mg/lb (5 mg/kg) body weight for the treatment and control of:
Stomach worms (adults): *Haemonchus contortus* and *Teladorsagia circumcincta*.

N. Reference Listed New Animal Drug

safe-guard®; fenbendazole; NADA 128-620; Intervet, Inc.

II. BIOEQUIVALENCE

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, allows for an abbreviated new animal drug application (ANADA) to be submitted for a generic version of an approved new animal drug (RLNAD). The ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. Effectiveness, target animal safety and human food safety data (other than tissue residue data) are not required for approval of an ANADA. If bioequivalence is demonstrated through a clinical endpoint study in a food-producing animal, then a tissue residue study to establish the withdrawal period for the generic product is also required.

For this ANADA, one *in vivo* blood-level study was conducted to demonstrate product bioequivalence using the generic and RLNAD fenbendazole 10% oral suspension. The *in vivo* blood-level study was conducted in 36 healthy cattle. The pivotal parameters to evaluate bioequivalence are the observed maximum plasma drug concentration (C_{MAX}) and area under the concentration-time curve (AUC) from time 0 to the last sampling time before the first unquantifiable concentration after C_{MAX}. Bioequivalence was demonstrated between the Defendazole™ (fenbendazole) 10% oral suspension and the RLNAD safe-guard® (fenbendazole) 10% oral suspension by the average bioequivalence approach as described in the Statistical Methods section below. The study information is summarized below.

A. Blood-level Bioequivalence Study in Cattle

Title: A Pharmacokinetic Study to Determine the Plasma Levels of Fenbendazole in Cattle Following the Oral Administration of a Formulation of Fenbendazole 10% Oral Suspension (Norbrook Laboratories Limited, Product Code: OD-FEN-040) and Safe-

guard (fenbendazole) Suspension 10% (Intervet Inc., NADA 128-620). (Study No. 019/17)

Study Dates: January 8, 2018 to April 1, 2019

Study Locations:

In-life phase: Northern Ireland

Bioanalytical testing: Ireland

Study Design:

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence data for the generic Defendazole™ (fenbendazole) and the RLNAD safe-guard® (fenbendazole) in fed cattle.

Study Animals: Thirty-six steers (castrated male cattle) 6 to 14 months of age, weighing between 253 and 392 kg.

Experimental Design: A randomized, masked, two-period, two-sequence, single-dose crossover study conducted according to Good Laboratory Practice for Nonclinical Laboratory Studies and Organization for Economic Cooperation and Development Principles of Good Laboratory Practice.

Drug Administration: Each animal received 5 mg per kg of body weight of either the generic or RLNAD fenbendazole oral suspension according to their randomized treatment sequence (generic/RLNAD or RLNAD/generic).

Measurements and Observations: The plasma concentrations of fenbendazole were measured using a validated bioanalytical method. Pharmacokinetic parameters were determined for each animal individually in each period. Animal observations were made throughout the study for assessment of general health and adverse events.

Statistical Methods:

The laboratory study was conducted as a randomized, masked, two-period, two-sequence, two-treatment, single-dose crossover design using 36 steers with a 28-day washout between periods. The study was conducted in two sets (18 animals per set) with staggered schedules due to limited housing capacity at the animal facility. Appropriate randomization of animal to sequence and pen/treatment order was performed. Primary variables evaluated were C_{MAX} and AUC. Time to maximum concentration (T_{MAX}) was summarized and evaluated clinically.

A mixed-effect model was used to evaluate bioequivalence. The model included fixed effects of treatment, sequence and period, and random effects of set and subject nested within sequence*set (sequence by set interaction). Prior to the analysis, C_{MAX} and AUC were natural logarithm transformed. Bioequivalence is established because the back-transformed estimated upper and lower bounds of the 90% confidence interval for geometric mean ratios (generic/RLNAD) of both C_{MAX} and AUC are contained within the acceptance limits of 0.80 to 1.25.

Results:

As seen in the table below, C_{MAX} and AUC fall within the prescribed bounds (Table II.1). The mean values of T_{MAX} obtained for the generic article and RLNAD were summarized.

Table II.1. Bioequivalence Evaluation

Parameter	Generic Mean	RLNAD Mean	Ratio◊	Lower 90% CI	Upper 90% CI
AUC (ng/mL)*hour	2512.2†	2621.2†	0.96	0.89	1.03
C_{MAX} (ng/mL)	83.7†	89.2†	0.94	0.87	1.01
T_{MAX} (hours) (SD)‡	19.9 (5.0)‡	18.5 (4.1)‡	NE	NE	NE

† Geometric mean
‡ Arithmetic mean and standard deviation (SD)
◊ Ratio = Generic/Reference
CI = confidence interval
NE = not estimated

Adverse Reactions:

There were no serious adverse events reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic Defendazole™ (fenbendazole) 10% oral suspension and the RLNAD safe-guard® (fenbendazole) 10% oral suspension are bioequivalent in cattle.

III. HUMAN FOOD SAFETY

A. Acceptable Daily Intake and Tolerances for Residues

The acceptable daily intake (ADI) for total residues of fenbendazole is 40 µg/kg of body weight per day. The tolerances established for the RLNAD apply to the generic product. A tolerance of 0.8 parts per million (ppm) is established for fenbendazole (the marker residue) in cattle liver (the target tissue), and a tolerance of 0.22 ppm is established for fenbendazole sulfoxide (the marker residue) in cattle milk. A tolerance of 0.8 ppm is established for fenbendazole (the marker residue) in goat liver (the target tissue), under 21 CFR 556.275.

B. Withdrawal Periods

The following withdrawal periods and milk discard time are assigned to fenbendazole suspension when used according to label directions in cattle and goats:

Cattle: 8-day withdrawal period and 48-hour milk discard time
Goats: 6-day withdrawal period

The studies that supported assignment of the withdrawal periods and milk discard time are summarized below:

Withdrawal Period in Cattle:

Title: A Study to Determine and Compare the Levels of Fenbendazole in Bovine Liver 6 Days Following the Oral Administration of a Formulation of Fenbendazole 10% Oral Suspension (Norbrook Laboratories Limited, Product Code: OD-FEN-040) and Safe-guard® (fenbendazole) Suspension 10%, (Intervet Inc., NADA 128-620). (Study No. 014/21)

Study Dates: October 22, 2021 to March 01, 2022

Study Locations:

In-life phase: Northern Ireland

Analytical phase: Northern Ireland

Study Design:

Objective: The objective of this Good Laboratory Practice (GLP) study was to compare the liver fenbendazole concentrations between cattle treated orally with the generic fenbendazole suspension and cattle treated orally with safe-guard® (NADA 128-620).

Study Animals and Group Assignment: Twenty-four beef cattle (12 males and 12 females), weighing 279 kg to 340 kg prior to dosing, were used in this study. Cattle were assigned to one of two groups. Group A consisted of six steers and six heifers treated with the generic fenbendazole suspension. Group B consisted of six steers and six heifers treated with safe-guard® (NADA 128-620).

Drug Administration: Cattle in Group A were treated with the generic fenbendazole suspension once orally at a dose rate of 20 mg fenbendazole/kg body weight. Cattle in Group B were treated with safe-guard® (NADA 128-620) once orally at a dose rate of 20 mg fenbendazole/kg body weight.

Sampling and Analysis: Cattle were slaughtered at six days following drug administration. Liver samples were collected and analyzed for fenbendazole by high pressure liquid chromatography (HPLC) with Ultraviolet (UV) detection.

Results: Mean (± standard deviation (SD)) fenbendazole concentrations in liver samples from cattle in Group A (generic fenbendazole suspension) and Group B (safe-guard®; NADA 128-620) were 0.108 (± 0.0365) ppm and 0.0974 (± 0.0471) ppm, respectively.

Liver fenbendazole concentrations were analyzed using an upper tolerance limit approach. The fenbendazole concentrations from cattle in Group B (safe-guard®; NADA 128-620) were confirmed to be normally distributed by the Shapiro-Wilk test. The 99th percentile upper tolerance limit with 95% confidence for the liver fenbendazole concentrations from Group B (safe-guard®; NADA 128-620) was calculated to be 0.285 ppm. The individual liver fenbendazole concentrations from cattle in Group A (generic fenbendazole suspension) were compared to this upper tolerance limit. None of liver fenbendazole concentrations from Group A (generic fenbendazole suspension) exceeded the upper tolerance limit for Group B (safe-guard®; NADA 128-620).

Conclusions: The data from Study 014/21 indicate that the generic fenbendazole suspension is as safe as the RLNAD with respect to fenbendazole residues in edible cattle tissues. Therefore, the data support assigning the generic fenbendazole suspension the withdrawal period previously assigned to the RLNAD for cattle: 8-day withdrawal period.

Withdrawal Period in Goats:

The following two studies supported the withdrawal period in goats:

1. **Title:** A Study to Determine and Compare the Levels of Fenbendazole in Caprine Liver 5 Days Following the Oral Administration of a Formulation of Fenbendazole 10% Oral Suspension (Norbrook Laboratories Limited, Product Code: OD-FEN-040) and Safe-guard® (fenbendazole) Suspension 10%, (Intervet Inc., NADA 128-620). (Study No. 015/21)

   Study Dates: November 03, 2021 to April 28, 2023

   Study Locations:

   In-life phase: Northern Ireland

   Analytical phase: Northern Ireland

   Study Design:

   Objective: The objective of this GLP study was to compare the liver fenbendazole concentrations between goats treated orally with the generic fenbendazole suspension and goats treated orally with safe-guard® (NADA 128-620).

   Study Animals and Group Assignment: Twenty-four goats (12 males and 12 females), weighing 31.5 kg to 96 kg prior to dosing, were used in this study. Goats were assigned to one of two groups. Group A consisted of six males and six females treated with the generic fenbendazole suspension. Group B consisted of six males and six females treated with safe-guard® (NADA 128-620).

   Drug Administration: Goats in Group A were treated with the generic fenbendazole suspension once orally at a dose rate of 20 mg fenbendazole/kg body weight. Goats in Group B were treated with safe-guard® (NADA 128-620) once orally at a dose rate of 20 mg fenbendazole/kg body weight.

   Sampling and Analysis: Goats were slaughtered at five days following drug administration. Liver samples were collected and analyzed for fenbendazole by the HPLC-UV method.

   Results: Mean (±SD) fenbendazole concentrations in liver samples from goats in Group A (generic fenbendazole suspension) and Group B (safe-guard®; NADA 128-620) were 0.229 (± 0.115) ppm and 0.375 (± 0.268) ppm, respectively.

2. **Title:** A Study to Determine and Compare the Levels of Fenbendazole in Caprine Liver 5 Days Following the Oral Administration of a Formulation of Fenbendazole 10% Oral Suspension (Norbrook Laboratories Limited, Product Code: OD-FEN-

040) and Safe-guard® (fenbendazole) Suspension 10%, (Intervet Inc., NADA 128-620). (Study No. 014/24)

Study Dates: August 28, 2024 to December 19, 2024

Study Locations:

In-life phase:	Northern Ireland
Analytical phase:	Northern Ireland

Study Design:

Objective: The objective of this GLP study was to compare the liver fenbendazole concentrations between goats treated orally with the generic fenbendazole suspension and goats treated orally with safe-guard® (NADA 128-620).

Study Animals and Group Assignment: Twenty-eight goats (14 males and 14 females), weighing 36.3 kg to 79.2 kg prior to dosing, were used in this study. Goats were assigned to one of two groups. Group A consisted of seven males and seven females treated with the generic fenbendazole suspension. Group B consisted of seven males and seven females treated with safe-guard® (NADA 128-620).

Drug Administration: Goats in Group A were treated with the generic fenbendazole suspension once orally at a dose rate of 20 mg fenbendazole/kg body weight. Goats in Group B were treated with safe-guard® (NADA 128-620) once orally at a dose rate of 20 mg fenbendazole/kg body weight.

Sampling and Analysis: Goats were slaughtered at five days following drug administration. Liver samples were collected and analyzed for fenbendazole by the HPLC-UV method.

Results: Mean (±SD) fenbendazole concentrations in liver samples from goats in Group A (generic fenbendazole suspension) and Group B (safe-guard®; NADA 128-620) were 0.393 (± 0.383) ppm and 0.247 (± 0.120) ppm, respectively.

Studies 015/21 and 014/24 summarized above were conducted based on the same study design using the same dosing regimen and slaughter timepoint. To this end, the data from these studies were combined to support assignment of the withdrawal period in goats. The data from studies 015/21 and 014/24 were analyzed using the upper tolerance limit approach. The liver fenbendazole concentrations from goats treated with safe-guard® (NADA 128-620) were not normally distributed, and therefore, were natural logarithm (log) transformed. The natural log-transformed concentrations were confirmed to be normally distributed by the Shapiro-Wilk test. The 99th percentile upper tolerance limit with 95% confidence for the natural log-transformed fenbendazole concentrations from goats treated with safe-guard® (NADA 128-620) was calculated to be 0.638 ppm, which was back-transformed to 1.89 ppm. None of the fenbendazole concentrations from goats treated with the generic fenbendazole suspension exceeded this upper tolerance limit.

Conclusions: The data from studies 015/21 and 014/24 indicate that the generic fenbendazole suspension is as safe as the RLNAD with respect to fenbendazole residues in edible goat tissues. Therefore, the data support assigning the generic fenbendazole suspension the withdrawal period previously assigned to the RLNAD for goats: 6-day withdrawal period.

Milk Discard Time in Cattle:

Title: A Pharmacokinetic Study to Determine the Plasma Levels of Fenbendazole in Cattle Following the Oral Administration of a Formulation of Fenbendazole 10% Oral Suspension (Norbrook Laboratories Limited, Product Code: OD-FEN-040) and Safe-guard® (fenbendazole) Suspension 10%, (Intervet Inc., NADA 128-620). (Study No. 019/17)

See Section II. Bioequivalence for a description of this study.

Results: Plasma concentrations of fenbendazole were greater than the limit of quantitation of the analytical method for the duration of the milk discard time assigned to the RLNAD. In addition, the data from study 019/17 demonstrated bioequivalence between the generic fenbendazole suspension and the RLNAD.

Conclusion: The data from study 019/17 support assigning the generic fenbendazole suspension the milk discard time previously assigned to the RLNAD for cattle milk: 48-hour milk discard time.

C. Analytical Method for Residues

The validated analytical method for analysis of residues of fenbendazole is on file at the Center for Veterinary Medicine, CPK1, 5001 Campus Drive, College Park, MD 20740. To obtain a copy of the analytical method, please submit a Freedom of Information request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

IV. USER SAFETY

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

WARNINGS: NOT FOR USE IN HUMANS. KEEP OUT OF REACH OF CHILDREN. The Safety Data Sheet (SDS) contains more detailed occupational safety information.

V. AGENCY CONCLUSIONS

The data submitted in support of this ANADA satisfy the requirements of section 512(c)(2) of the FD&C Act. The data demonstrate that Defendazole™, when used according to the label, is safe and effective for the conditions of use in the General Information Section above.

Additionally, data demonstrate that residues in food products derived from beef and dairy cattle and goats treated with Defendazole™ will not represent a public health concern when the product is used according to the label.