Approval Date: April 20, 2007

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-333

SUPERIORBUTE POWDER

(phenylbutazone)

Indications: For the relief of inflammatory conditions associated with the musculoskeletal system in horses

Sponsored by:

Superior Equine Pharmaceuticals, Inc.

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1. GENERAL INFORMATION:

a. File Number:	ANADA 200-333
b. Sponsor:	Superior Equine Pharmaceuticals, Inc. 1547 West 110 N Pleasant Grove, UT 84062 Drug Labeler Code: 27053
c. Established Name:	Phenylbutazone
d. Proprietary Name:	SUPERIORBUTE
e. Dosage Form:	Powder
f. How Supplied:	Each 115 gram container provides 100 g of phenylbutazone
g. How Dispensed:	Rx
h. Amount of Active Ingredients:	1 gram of phenylbutazone per scoop (1/4 tablespoon)
i. Route of Administration:	Oral
j. Species/Class:	Equine
k. Recommended Dosage:	Into grain ration, mix 1 to 2 scoops (equal to 1/4 to 1/2 tablespoon) of SUPERIORBUTE Powder per 500 pounds of body weight, but not to exceed 4 scoops (equal to 1 tablespoon) or 4 grams per horse daily.
l. Pharmacological Category:	Non-steroidal anti-inflammatory drug (NSAID)
m. Indications:	For the relief of inflammatory conditions associated with the musculoskeletal system in horses.
n. Pioneer Product:	Phenylbutazone Tablets; phenylbutazone; NADA 091-818; IVX Animal Health, Inc.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Superior Equine Pharmaceuticals, Inc. was granted approval of a suitability petition allowing them to submit an ANADA for a different dosage form of an approved product with the stipulation that *in vivo* bioequivalence of the generic product to the pioneer product be demonstrated to support safety and effectiveness of the generic product. Additionally, a palatability study was required.

A. Blood-Level Bioequivalence Study

One blood-level bioequivalence study was conducted to determine the comparative bioavailability of the generic powder formulation and pioneer tablet formulation of phenylbutazone.

Investigator: Sierra Biomedical (Sbi), A Charles River Company; 26416 Old Julian Highway; Ramona, CA

Objective: The objective of this study was to determine the comparative blood-levels of Superior Equine Pharmaceuticals' phenylbutazone powder (generic) and IVX Animal Health, Inc.'s phenylbutazone tablets (reference) in a two-period crossover study in horses.

Summary: The design of this study is a comparative bioavailability study using healthy adult horses in a single-dose, two-period, two-treatment crossover design with randomization of experimental units to two sequences. Twenty-four horses (12 males and 12 females) were randomly assigned in equal numbers to either of two treatment sequences (6 male, 6 female each sequence) separated by a 14-day washout interval; Superior Equine Pharmaceuticals' phenylbutazone powder test article followed by IVX Animal Health, Inc.'s phenylbutazone tablets pioneer product or vice-versa. Venous blood samples for plasma phenylbutazone analysis were collected at 0 hour and at 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 18, 24, 36, and 48 hours after treatment.

Results: The area under the curve was calculated using the trapezoidal rule from time 0 out to the last sampling time associated with quantifiable drug concentrations (AUC). The natural logarithm of AUC was computed and used as the variable for analysis. The maximum concentration measured for all time periods (CMAX) was determined and the natural logarithm of CMAX was computed and used as the variable for analysis.

The criteria for determining bioequivalence, as described in CVM's Bioequivalence Guidance is to construct a 90% confidence interval about the difference of the two means, generic minus pioneer, based on the log scale of AUC and CMAX and then take the anti-log of the confidence limits multiplied by 100. The resulting bounds should be between 80.00% and 125.00%. As seen in Table 1 below both AUC and CMAX fall within those bounds.

TABLE 1. Comparative Bioequivalence Criteria for the Test and Reference Products

Variable	Superior Mean	IVX Mean	Lower Bound	Upper Bound
AUC (μg/mL)	468.7*	464.1*	91.35%	110.54%
CMAX (μg/mL)	34.5*	33.4*	90.70%	116.94%
TMAX (hours)	4.08†	4.96†	NA	NA

* Geometric Mean
† Arithmetic Mean

The variable time to maximum concentration (TMAX) is permitted to be interpreted by clinical judgment. In this case, there is no reason to expect the difference in TMAX will affect the efficacy of the drug, since both AUC and CMAX fall within acceptable limits and the product is administered as a single dose. Therefore, the study objective to determine the bioequivalence of the generic phenylbutazone powder and pioneer phenylbutazone tablets was achieved.

B. Palatability Study

One palatability study was conducted to determine the palatability of phenylbutazone powder.

Investigator: Sierra Biomedical (Sbi), A Charles River Company; 26416 Old Julian Highway; Ramona, CA

Objective: The objective of this study was to determine the palatability of Superior Equine Pharmaceuticals' phenylbutazone powder in horses.

Summary: The design of the study is a two-period, two-sequence, two-treatment crossover design. Twenty healthy adult horses (10 males and 10 females) were randomly assigned in equal numbers to either of two treatment sequences (5 male, 5 female each sequence) separated by a 2 day washout interval. Each period was five days in length. The horses were fed twice a day resulting in 10 feedings per horse per period. In the first period, the horses in Sequence A received 2 grams of phenylbutazone per day with half given in the morning and half given in the afternoon for two days. The last three days the horses received 1 gram of phenylbutazone per day with half given in the morning and half given in the afternoon. The horses in Sequence B received the grain ration in the same manner as in Sequence A but without the addition of the test article. In the second period, the feeding pattern was reversed. Consumption was measured on a scale of 0 to 4 but analyzed as consumed completely versus not consumed completely.

Results: In the study there were 200 dependent feedings without the test article, 80 dependent feedings at 2 grams and 120 dependent feedings at 1 gram. The feedings are dependent since each horse contributed 20 feedings. The medicated feed when fed at 1 gram was consumed completely 92.5% (111/120) of the time; when fed at 2 grams was consumed completely 87.5% (70/80). The unmedicated feed was consumed completely 93.0% (186/200) of the time.

In the study each horse was fed 20 times; 10 with unmedicated feed, 6 with 1 gram of phenylbutazone powder, and 4 with 2 grams of phenylbutazone powder. Seventeen of the 20 horses (85%) completely consumed all their unmedicated feed; fifteen of the 20 horses (75%) completely consumed all their 1 gram medicated feed; and sixteen of the 20 horses (80%) completely consumed all their 2 gram medicated feed.

Since all the above palatability percentages were greater than 70%, the palatability of Superior Equine Pharmaceuticals' phenylbutazone powder in horses was achieved. See the comparative consumption profile in Table 2.

TABLE 2. Comparative Consumption Profile for the Test Product and Non-medicated Feed

Medicated vs. Non-medicated	No. of Horses That Completely Consumed All Feed	No. of Horses That Did Not Completely Consume All Feed	Total Number of Horses and in Parenthesis Total Number of Feedings per Horse
Non-medicated	17 (85%)	3 (15%)	20 (10)
Medicated, 1 gram	15 (75%)	5 (25%)	20 (6)
Medicated, 2 grams	16 (80%)	4 (20%)	20 (4)

3. HUMAN SAFETY:

This drug is intended for use in horses, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

Human Warnings are provided on the product label as follows: "Keep this and all medications out of the reach of children. Dispense in tight, child resistant containers."

4. AGENCY CONCLUSIONS:

This ANADA filed under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that SUPERIORBUTE Powder, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as indicated below:

Generic labeling for ANADA 200-333: Package labeling; Package insert

Pioneer labeling for NADA 091-818: Package labeling; Package insert