Approval Date: February 2, 2006

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 100-094

POULTRYSULFA Soluble Powder
(sodium sulfamethazine, sodium sulfamerazine, sodium sulfaquinoxaline)

For treatment of coccidiosis and acute fowl cholera in
chickens and turkeys

Sponsored by:

Alpharma Inc.

FREEDOM OF INFORMATION SUMMARY

1. General Information:

a. File Number:	NADA 100-094
b. Sponsor:	Alpharma, Inc. One Executive Drive Fort Lee, NJ, 07024 Drug Labeler Code: 046573
c. Established Names:	Sodium sulfamethazine, sodium sulfamerazine, and sodium sulfaquinoxaline
d. Proprietary Name:	PoultrySulfa
e. Dosage Form:	Soluble Powder
f. How Supplied:	Packet (195 grams)
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	78 grams sodium sulfamethazine 78 grams sodium sulfamerazine 39 grams sodium sulfaquinoxaline
i. Route of Administration:	Oral
j. Species/Class:	Chickens and turkeys
k. Recommended Dosage:	Acute Fowl Cholera – Turkeys and chickens: Provide medicated water (.04% solution) for 2-3 days. Coccidiosis – Turkeys: Provide medicated water (.025% solution) for 2 days, then plain water for 3 days, then medicated water (.025% solution) for 2 days, then plain water for 3 days, then medicated water (.025% solution) for 2 days. Coccidiosis – Chickens: Provide medicated water (.04% solution) for 2-3 days, then

plain water for 3 days, then medicated water (.025% solution) for 2 days.

l. Pharmacological Category: Anticoccidial/Antimicrobial

m. Indications: Acute Fowl cholera – TURKEYS AND CHICKENS: As an aid in the control of acute fowl cholera caused by *Pasteurella multocida* susceptible to sulfamethazine, sulfamerazine and sulfaquinoxaline.

Coccidiosis – TURKEYS: As an aid in the control of coccidiosis caused by *Eimeria meleagrimitis* and *E. adenoeides* susceptible to sulfamethazine, sulfamerazine, and sulfaquinoxaline.

Coccidiosis – CHICKENS: As an aid in the control of coccidiosis caused by *Eimeria tenella* and *E. necatrix* susceptible to sulfamethazine, sulfamerazine, and sulfaquinoxaline.

2. TARGET ANIMAL SAFETY:

Sulfamethazine, sulfamerazine and sulfaquinoxaline were evaluated within the scope of the National Academy of Sciences/National Research Council (NAS/NRC) Drug Efficacy Study Implementation (DESI) program. They were evaluated as safe to the target animal on the basis of published literature and labeling revisions by FDA for the claims and species listed in the Federal Register, Vol 49, No. 130, July 5, 1984.

3. DRUG EFFECTIVENESS:

Sulfamethazine, sulfamerazine and sulfaquinoxaline were evaluated with in the scope of the National Academy of Sciences/National Research Council (NAS/NRC) Drug Efficacy Study Implementation (DESI) program. They were evaluated as probably effective on the basis of published literature and labeling revisions. Consequently, they were moved to the effective category by FDA for the claims and species listed in the Federal Register, Vol 49, No. 130, July 5, 1984. The label revisions requested by NAS/NRC were: (1.) Each disease claim should be properly qualified as appropriate for use in (name of disease) caused by pathogens (genus, species) sensitive to sulfamethazine, sulfamerazine and sulfaquinoxaline. If the disease claim cannot be qualified, the claim must be dropped.
(2.) The claim for coccidiosis should be properly qualified by listing the species for each respective host. (3.) The claim for infectious coryza in chickens and turkey should be supported by data or it should be deleted. (4.) The labeling should warn that treated animals must actually consume enough medicated water to provide a therapeutic dose.

(5.) The labeling should state the desired oral dose per unit of animal weight per day for each species as a guide of effective use.

Thereafter, the sponsor complied with the evaluation of NAS/NRC and FDA's conclusions in the following manner: (1.) Two diseases have been properly qualified as being caused by pathogens sensitive to sulfamethazine, sulfamerazine and sulfaquinoxaline for chickens and turkeys. (coccidiosis and acute fowl cholera) (2.) The claim for coccidiosis in chickens is caused by *Eimeria tenella* and *E. necatrix* and the claim for coccidiosis in turkeys is caused by *Eimeria meleagrimitis* and *E. adenoeides* is properly listed on the label. (3.) The claim for infectious coryza has been deleted from the labeling. (4.) The label carries the following statement concerning water: Treated animals must actually consume enough medicated water to provide a therapeutic dose. (5.) The label contains appropriate direction for use to make a .04% solution by adding one packet to 1 gallon of water for the treatment of acute fowl cholera and .025% by adding one packet to 1.6 gallons for the treatment of coccidiosis. Published dosages for poultry aare expressed as concentrations in drinking water.

FDA has concluded that NADA's for drug products containing more than one sulfonamide will comply with the Center for Veterinary Medicine's combination drug policy (21 CFR 514.1(b)(8)(v) without submission of data from studies that compare the combination of sulfonamides with individual sulfonamides. Because all sulfonamides have the same mechanism of action, each individual sulfonamide can be expected to contribute to the total effect of the combination drug. Sponsors of pending NADA's for sulfonamide products containing two or more sulfonamides had to submit bioavailability data demonstrating sulfonamide blood levels (serum or plasma of blood) of 8-mg percent or more. In the alternative, the sponsor could submit the results of clinical study demonstrating the effectiveness of the combination drug against one disease claim on the label in one of the labeled species. The sponsor chose to submit a clinical study for the control of acute fowl cholera in turkeys.

A clinical study was performed at Health Management Services, Tulare, CA, where the efficacy of POULTRYSULFA was demonstrated in turkeys for control of infection due to *Pasteurella multocida*. Eighty birds, 12 weeks of age, were inoculated with the pathogenic organism. One half of the flock was administered POULTRYSULFA in drinking water at a concentration of 0.04% immediately after inoculation. Medication continued for 5 days. The other half did not receive any medication during the entire study period. Observation continued 10 days post challenge.

Each group was monitored for mortality, weight gain, and lung scores. There was a significant difference in mortality and weight gain between the two groups. Group I (untreated) experienced a mortality rate of 53% (21 out of 40 birds). Group II (treated) experienced a 10% mortality rate (4 out of 40 birds). Group I showed an average loss of 0.4 kg for each surviving bird compared to an average gain of 0.57 kg for birds in Group II.

The average lung scores for birds dying during the study were similar in both groups. Group I lung scores were 2.1 while Group II were 2.2 (0= normal, 3= severe). All surviving birds were sacrificed on day 10 and their lungs scored. There was no significant differences in the scores for both groups (Group I= 0.1, Group II= 0.0).

The results of this study demonstrated that 0.04% of POULTRYSULFA for 2-3 days is effective for the control of acute fowl cholera in turkeys and chickens.

4. HUMAN SAFETY:

Studies to Establish the Withdrawal Time:

A tissue residue study using a triple sulfonamide combination (40% sodium sulfamethazine, 40% sodium sulfamerazine and 20% sodium sulfaquinoxaline) in broiler chickens. Study Nº. 8933c.

1. Study Author: John W. Byrd, MS

2. Study Completion Date: June 1, 1990

3. Performing Laboratory: Southwest Bio-Labs, Inc.
Las Cruces, NM 88005

4. Animals Used: Forty-four 3-day-old Cornish Rock broiler chickens (22 M and 22F), weighing 161.04±25.98 g were acquired for the study. At the time of dosing, broilers weighed 1.5±0.4 kg and were 41 days of age.

5. Route of drug administration: Orally in drinking water.

6. Time and duration of dosing: The PoultrySulfa was administered in the drinking water for five consecutive days. Drinking water solutions were prepared daily as a 0.04% solution.

7. Results:

Table Mean concentration (ppm) of sulfamethazine (SMZ) + sulfamerazine (SMR) and sulfaquinoxaline (SQ) in the liver of chickens following treatment with medicated drinking water containing 0.04% PoultrySulfa for five days.

Withdrawal (hr)	Liver residues (ppb)	
	SMZ + SMR*	SQ
4	1692.11±427.07	11939.52±1551.18
72	52.57±8.01	74.94±10.11
96	31.73±12.18	41.42±27.70
120	18.69	13.19

144	<LOD**	<LOD
168	<LOD	<LOD
192	<LOD	26.70±6.17

* SMZ + SMR are measured as a single entity
** LOD (SMZ + SMR) = 15 ppb; LOD (SQ) = 10 ppb

A tissue residue study using a triple sulfonamide combination (40% sodium sulfamethazine, 40% sodium sulfamerazine and 20% sodium sulfaquinoxaline) in turkey poults. Study Nº· 8908t.

1 Study Author: John W. Byrd, MS

2. Study Completion Date: October 1989

3. Performing Laboratory: Southwest Bio-Labs, Inc.
Las Cruces, NM 88005

4. Animals Used: Twelve 1-day-old Nicholas Broad Breasted White turkey poults (6 M and 6 F), weighing 145.75 g were acquired for use in the study. At the time of dosing, broilers weighed 1.2±0.2 kg and were 34 days of age.

5. Route of drug administration: Orally in drinking water.

6. Time and duration of dosing: PoultrySulfa was administered in the drinking water for five consecutive days. Drinking water solutions were prepared daily as a 0.04% solution.

7. Results:

Table Mean concentration (ppm) of sulfamethazine (SMZ) + sulfamerazine (SMR) and sulfaquinoxaline (SQ) in the liver of chickens following treatment with medicated drinking water containing 0.04% PoultrySulfa for five days.

Withdrawal (hr)	Liver residues (ppb)	
	SMZ + SMR*	SQ
4	1243.40±963.93	5737.50±2469.92
48	31.75±8.27	348.65±226.06
96	<LOD	26.55±10.25
144	<LOD	<LOD
192	<LOD	<LOD

* SMZ + SMR are measured as a single entity

** LOD (SMZ + SMR) = 15 ppb; LOD (SQ) = 10 ppb

Withdrawal period calculations were made using a statistical tolerance limit algorithm applied to the depletion data for sulfaquinoxaline, the residue depleting most slowly in the livers of chickens and turkeys. A 14-day withdrawal period is assigned for the use of Triple Sulfa in both chickens and turkeys. The 14-day withdrawal period is consistent with the withdrawal period calculations and is protective of the public health.

F. Regulatory Method

The regulatory analytical method for detection of residues of the drug is a multiresidue thin layer fluorometric scanning densitometry procedure. This method is found in the Analytical Chemistry Laboratory Guidebook (Residue Chemistry) USDA/FSIS/Science & Technology, Winter,1991.

G. Tolerances for Residues:

The codified tolerance for negligible residues of sulfaquinoxaline in uncooked edible tissues of chickens and turkeys is 0.1 pmm (21 CFR 556.685).

The codified tolerance for negligible residues of sulfamethazine in uncooked edible tissues of chickens and turkeys is 0.1 ppm (21 CFR 556.670).

Using the official analytical method, residues of sufamethazine and sulfamerazine co-elute and cannot be quantified individually. There are no products containing only sulfamerazine approved for use in chickens and turkeys. Therefore, a tolerance for sulfamerazine residues in chickens and turkeys tissues is not established at this time.

Regulatory Method for Residues:

The analytical method of detection for sulfas in tissue uses a thin layer-densitometric procedure. The method is found in the Official Methods of Analysis of the Association of Official Analytical Chemists, 16th Edition, 1997. The method is available from the Center for Veterinary Medicine, Food and Drug Administration, HFV-199, 7500 Standish Place, Rockville, Maryland 20855.

5. AGENCY CONCLUSIONS:

This NADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of the act and demonstrates that POULTRYSULFA Soluble Powder, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENT:

Labeling: (Packet) 195 grams