Approval Date: September 16, 1999

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION

NADA number: 140-908

Sponsor: Lloyd, Inc.
P.O. Box 86
604 West Thomas Avenue
Shenandoah, IA 51601

Generic name: Sulfamethazine USP

Trade name: Veta-Meth™ (sulfamethazine)

Marketing status: OTC

2. INDICATIONS FOR USE

For use in beef and nonlactating dairy cattle for the treatment of diseases caused by sulfamethazine-sensitive organisms such as bacterial pneumonia and bovine respiratory disease complex (shipping fever complex) (Pasteurella spp.), colibacillosis (bacterial scours) (E. coli), necrotic pododermatitis (foot rot) (Fusobacterium necrophorum), calf diphtheria (Fusobacterium necrophorum), acute mastitis (Streptococcus spp.), acute metritis (Streptococcus spp.) and coccidiosis (E. bovis, E. zurnii).

3. PRODUCT INFORMATION

A. Dosage Form: Tablets

B. Route of Administration: Oral

C. Recommended dosage:

Initial Dose-- Administer as a single dose at the rate of 1 1/2 grains (100 mg) per pound body weight or 5 grams per each 50 pounds the first day. Follow within 24 hours with a maintenance dose.
Maintenance Dose-- Dose at the rate of 3/4 grain (50 mg) per pound body weight or 5 grams for each 100 pounds. The maintenance dose may be given once each 24 hour period but not to exceed 5 days.

4. EFFECTIVENESS

Sulfamethazine was the subject of a final rule, and was published in the FEDERAL REGISTER of June 11, 1982 (47 FR 25320-25323). The final rule amended the animal drug regulations (1) to indicate those portions which reflect the National

Academy of Science-National Research Council, Drug Efficacy Study Implementation (DESI) evaluation of the product and (2) to specify the conditions of use for which approval of similar products need not include certain types of efficacy data, but may require submission of bioequivalence or similar data.

Lloyd's NADA 140-908 was submitted and reviewed prior to the 1988 implementation of the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) and was designated the DESI "me-too" status for approval purposes. Lloyd's product has been shown to be bioequivalent to the pioneer product, Sulmet® Oblets, American Cyanamid Company, NADA 122-271. The study satisfied the requirements annotated in CVM's bioequivalency study Guidelines dated 1985.

Bioequivalence study. Date of the study: October, 1987

Twenty healthy cattle, 10 steers and 10 heifers, ranging from 425 pounds to 590 pounds were used. An initial dose of 100 mg/Lb body weight was given followed with four single daily doses of 50 mg/Lb body weight which were given at 24 hour intervals after the initial dose. Dosages for both groups were equal and based on individual body weight values determined at the beginning of each phase. Blood samples were drawn immediately prior to drug administration, 6 hours after the first dose and at 12 hour intervals for 108 hours after the last dose of drug.

Values of each drug in Phase 1 and Phase 2 were pooled for each time point. The mean values for sulfamethazine for Veta-Meth and Sulmet were:

	Drug 1 (Sulmet)	Drug 2 (Veta-Meth)
0	0.00	0.00
6	12.5	12.3
24	13.7	14.5
48	13.0	12.6
72	11.6	12.2
96	11.8	11.5
108	16.6	16.4
120	11.4	11.1
132	6.73	6.78
144	3.40	4.07
156	1.23	1.49
168	0.342	0.533
180	0.124	0.197
192	0.058	0.072
204	0.029	0.042
Total time	102.5	103.6

The following pharmacokinetic measures were found:

	Drug 1 (Sulmet)	Drug 2 (Veta-Meth)
Cmax (mg/dl)	16.6	16.4
Tmax (h)	108	108
Cmin (mg/dl)	11.8	11.5
t 1/2 (h)	8.58	8.55
AUC (mg/dl)	102.5	103.6
Plasma Sulfmethazine 108 hour post final dose (mg/L)	0.3	0.4

Analysis of variance was conducted on total time measures for the following parameters: plasma sulfamethazine concentrations; packed cell volume; slopes, intercepts, and half-lives derived from regression lines during the useful elimination phase. T-tests were performed on all time periods relative to sulfamethazine. No significant differences in the concentration of sulfamethazine were found in plasma of animals receiving Lloyd's brand of sulfamethazine (Veta-Meth) tablets and animals receiving American Cyanamid brand of sulfamethazine (Sulmet) tablets when averaged over both phases of the experiment.

5. TARGET ANIMAL SAFETY

The pioneer product, American Cyanamid's Sulmet, NADA 122-271, was approved as safe and effective for use as labeled on June 11, 1982. The demonstration of bioequivalence to that product established that no additional target animal safety studies were required for Veta-Meth™ tablets.

6. HUMAN FOOD SAFETY

The bioequivalence study in cattle as previously described, demonstrates that the Lloyd's brand of sulfamethazine tablets is bioequivalent to the American Cyanamid Co. pioneer product (NAS/NRC approved and codified 6/11/82), as determined by CVM's 1985 bioequivalency guidelines. For purposes of determining bioequivalency, a variety of factors were compared between the two products. These factors include: point-to-point blood level comparisons, area under the blood level curve, Cmax, Cmin, and the elimination rate constants. There were no significant statistical differences detected between treatment periods or between treatments. Therefore, Lloyd's Veta-Meth™ Tablets were approved based upon CVM's 1985 Bioequivalency Guidelines. As a result, the withdrawal period for Veta-Meth Tablets has been established at the same time as the pioneer product, i.e.,10 days.

7. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Act and demonstrate that Veta-Meth™ Tablets (5 g, 15 g,and 25 g) when used under its proposed conditions of use is safe and effective for its labeled indications.

The sponsor submitted bioequivalency data for cattle which demonstrated biological equivalence to the approved pioneer product. This bioequivalency blood level study was accepted in lieu of tissue depletion. Therefore, for human food safety considerations, when bioequivalence is demonstrated through blood level studies, the DESI "me-too" product is assigned the same withdrawal period as the reference product. The withdrawal period for cattle is 10 days for beef cattle and nonlactating dairy cattle. The tolerance for sulfamethazine is established at 0.1 part per million (negligible residue) in the uncooked edible tissue of cattle . (21 CFR 556.670).

The agency finds that the labeled use of Veta-Meth™ Tablets is biologically equivalent to other approved uses of sulfamethazine and will not result in residues above the published tolerance. Thus, the approval of this DESI “me-too” new animal drug application will not adversely affect the human health. If the agency decides to take an action against sulfamethazine due to concern regarding the carcinogenicity of this compound, the application together with all other approved applications for sulfamethazine, will be subject to that action.

Sulfamethazine tablets are marketed as an over-the-counter product. Over-the-counter sulfamethazine products are currently on the market for use in food animals. Adequate directions for use have been written for the layman, and the conditions for use prescribed on labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine (CVM) has concluded that this product be granted over-the - counter marketing status.

8. APPROVED PRODUCT LABELING (Attached)

5 g, 15 g and 25g labels for 50 tablet bottles