Approval Date: December 10, 1993

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 130-435

B. Sponsor

I.D. Russell Company, Laboratories
1301 Iowa Avenue
Longmont, CO 80501

C. Proprietary Name

OXYTET SOLUBLE

D. Established Name

oxytetracycline hydrochloride

E. Dosage Form

Soluble Powder

F. Dispensing Status

OTC

G. Dosage Regimen

Swine	Bacterial enteritis and bacterial pneumonia: 10 mg/lb body weight
Breeding Swine	Leptospirosis: 10 mg/lb body weight D.
NOTES	
Duration of Treatment:	Swine: Up to 5 days

H. Route of Administration

Oral - Drinking Water

I. Indication

Swine: For the control and treatment of bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* susceptible to oxytetracycline. For the control and treatment of bacterial pneumonia caused by *Pasteurella multocida* susceptible to oxytetracycline.

Breeding Swine: Leptospirosis (reducing the incidence of abortion and shedding ofleptospira) caused by *Leptospira pomona* susceptible to oxytetracycline.

J. Effect of Supplement

This supplement provides for use of this product in swine.

II. EFFICACY

The purpose of this supplemental application is to add certain claims for swine to the label of an existing product. Bioequivalency of this product was established in earlier submissions to the Center for Veterinary Medicine. For details demonstrating the efficacy of this product, please refer to the Freedom of Information Summary provided as the basis of approval for NADA 130-435, as published in the **FEDERAL REGISTER** of August 14, 1985 (**50 FR 32694**).

SPECIAL ISSUES

The safety and efficacy of this product are based on the National Academy of Science/ National Research Council (NAS/NRC) review of oxytetracycline soluble powder published in the **FEDERAL REGISTER** of May 5, 1970 (**35 FR 7089**). The NAS/NRC concluded, and the Food and Drug Administration (FDA) concurred, that the product is effective in swine for use in the treatment of bacterial enteritis, bacterial pneumonia and leptospirosis when each disease claim is properly qualified as, "appropriate for use in (name of disease) caused by (name of pathogens) sensitive to oxytetracycline". Other qualifying label revisions have been incorporated into the labeling for the product.

III. ANIMAL SAFETY

The safety of oxytetracycline hydrochloride soluble powder to the target species is established under the conditions outlined in the NAS/NRC review of the product with reference to indictions for use, route of administration, recommended dosages and limitations of use, as specified in **35 FR 7089**. Therefore, to assure target animal safety, oxytetracycline hydrochloride soluble powder is to be used in accordance with NAS/NRC recommendations, and is not to be used for more than 5 consecutive days in swine.

IV. HUMAN SAFETY

A. Safe Concentration of Residues:
The tolerance established by the Food and Drug Administration FDA) by regulation (21 CFR 556.500) for residues of oxytetracycline in edible tissue of treated swine is:

a. In edible tissues of swine: (1) 0.1 parts per million in uncooked edible tissues

B. Residue Depletion Studies:
A study was designed and conducted to ascertain the rate of elimination of oxytetracycline (OTC) from edible tissues of swine treated with OXYTET SOLUBLE. The study was performed to assess the elimination rate of OTC relative to the tolerance of O. 10 parts per million of OTC residues in uncooked edible tissues of treated swine.

(a) Name and Address of Investigator:
Colorado Animal Research Enterprises, Inc.
6200 E. County Road 56
Ft. Collins, CO 80524

Study Director: Dan C. Ronning

b. Description of Animals Used:

Thirty (30) near-market-age production swine (15 males, 15 females) were administered OXYTET SOLUBLE. Three of the pigs in each medicated group were included as substitutes for any pig which might be removed from the study due to unforeseen circumstances. The weight of the males at the beginning of the study ranged from 124 to 144 lbs. and the weight of females ranged from 122 to 146 lbs.

c. Route of Administration:

Oral administration via voluntary consumption of medicated tap water to provide 10 mg/lb body weight per day.

d. Time and Duration of Dosing:

The daily doses were determined on an individual pig basis and administered at approximately 24-hour intervals for 5 consecutive days.

e. In accordance with the above parameters the 30 pigs were treated for 5 consecutive days at medication rates which provided intake levels of 10 mg oxytetracycline hydrochloride per pound body weight daily. At the end of the medication period, 2 medicated male pigs and 2 medicated female pigs each were sacrificed at intervals of 24, 48, 72, 96, 120, and 144 hours after withdrawal of the drug and 1 non-medicated male and 1 non-medicated female each were sacrificed at 24 and 120 hours after withdrawal of the drug. Loin muscle and kidney tissue were carefully collected for oxytetracycline residue analysis.

The study was conducted in compliance with standards established by FDA's Good Laboratory Practice Regulations (21 CFR 58).

The microbiological analysis of loin muscle and kidney tissues collected during the first part of the study at 24, 48, 72, 96, 120 and 144 hours following final treatment revealed samples of all loin muscle samples from 24 through 120 hours had no OTC residues (i.e. less than detection limit) with the exception of one detectable, nonquantifiable residue of OTC at 24 hours: consequently, samples of loin muscle at the 144 hour sampling were not assayed for OTC levels. Additionally, the residue data on loin muscle were not statistically analyzed.

Data on residues of OTC in kidney samples were used to calculate the withdrawal time. Kidney residue values obtained from the 24, 48, and 72 hour (at least 3 valid points at each timepoint) sample times above the LOQ of O. 1 ppm OTC were used for withdrawal time calculations. Due to variabilities in the dosing solution assays, a correction factor of 1.07 was multiplied against each residue value. The following kidney residue values (all values multiplied by 1.07) were used in the withdrawal time calculation:

OTC LEVEL (ppm)	WITHDRAWAL TIME POINT -24 hours	WITHDRAWAL TIME POINT -48 hours	WITHDRAWAL TIME POINT -72 hours
	0.254	0.122	0.119
	0.205	0.133	0.124
	0.408	0.198	0.170
	0.215		

Statistical analysis of the above kidney residue data using 99% tolerance limit with 95% confidence, calculated a withdrawal time of 13 days to be necessary to allow OTC residues to deplete to less than 0. 1 ppm tolerance for market-size swine administered 10 mg oxytetracycline/lb. body weight for 5 days.

Oxytetracycline levels in loin muscle and kidney tissue samples were determined by the method described under "Regulatory Methods" below.

f. Regulatory Methods

The regulatory analytical method for detection of residues of oxytetracycline is a microbiological test using *Bacillus cereus* suspension. The method is as published by the Food and Drug Administration: "Antibiotic Residues in Milk, Dairy Products and Animal Tissues: Methods, Reports and Protocols", revised October 1968, reprinted December 1974.

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Act and demonstrate that I.D. Russell's product, Oxytet Soluble, when used under its proposed conditions of use is safe and effective in swine.

The sponsor submitted residue data for swine which calculated a withdrawal time of 13 days to be necessary to allow oxytetracycline residues to deplete to less than 0.1 ppm tolerance for market-size swine. This supplement is approved under DESI "me-too" pipeline provision and therefore the sponsor had to submit a residue study to satisfy human food safety requirements.

Oxytetracycline Soluble Powder for use in food-producing animals is currently on the market as an over-the-counter product. Adequate directions for use have been written for the layman, and the conditions for use prescribed in labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine (CVM) has concluded that this product retains over-the-counter marketing status.

Under the Center's supplemental approval policy (21 CFR 514.106 (b)(2)(v)(vii)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not require a re-evaluation of the human food or target animal safety data in the parent application.

This approval does not qualify for an exclusivity period under any of the provisions of section 512 (c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, (21 U.S.C. 360b (c)(2)(F) (iii) because the supplemental application does not contain reports of new clinical or field investigations (other than bioequivalence or residue studies) and, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) essential to the approval and conducted or sponsored by the applicant.

VI. ATTACHMENTS

1. 2.46 oz packet

2. 9.87 oz packet

3. 3.09 lb pail

Copies of these labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.