DATE OF APPROVAL LETTER: NOVEMBER 29, 2000

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 130-435

Oxytet Soluble (oxytetracycline HCl)

"removal of withdrawal period for turkeys and swine"

Sponsored by:
Alpharma, Inc.

I. GENERAL INFORMATION:

NADA: 130-435

Sponsor: Alpharma Inc.
One Executive Drive
Fort Lee, New Jersey 07024

Generic Name: Oxytetracycline HCl

Trade Name: OXYTET SOLUBLE & TETRAVET-CA

Marketing Status: OTC

Effect of the Supplement: Removal of withdrawal period for turkeys and swine.

II. INDICATIONS FOR USE:

Chickens: 200 to 400 mg for control of infectious synovitis caused by *Mycoplasma synoviae,* susceptible to oxytetracycline.
400 to 800 mg for control of respiratory disease (CRD) and air sac infections caused by *Mycoplasma gallisepticum* and *Escherichia coli,* susceptible to oxytetracycline.
400 to 800 mg for control of fowl cholera caused by *Pasteurella multocida,* susceptible to oxytetracycline.

Turkeys: 200 to 400 mg for control of hexamitiasis caused by *Hexamita meleagridis,* susceptible to oxytetracycline.
400 mg for control of infectious synovitis caused by *Mycoplasma synoviae,* susceptible to oxytetracycline.
25 mg/lb body weight in GROWING TURKEYS for control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis), susceptible to oxytetracycline.

Swine: 10 mg/lb body weight FOR THE CONTROL AND TREATMENT OF THE FOLLOWING DISEASES IN SWINE – Bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis*, susceptible to oxytetracycline. FOR BREEDING SWINE: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona,* susceptible to oxytetracycline.

III. DOSAGE:

A. *Dosage Form*: This supplemental NADA provides for a revised withdrawal period in turkeys and swine.

B. *Route of Administration*: Oral, in water

C. *Recommended Dose*: See indications above.

IV. EFFECTIVENESS

No further effectiveness data were required.

V. ANIMAL SAFETY

No further target animal safety data were required.

VI. HUMAN FOOD SAFETY:

A. TOLERANCES

Tolerances are established in 21 CFR 556.500 for the sum of residues in tissues of beef cattle, beef calves, non-lactating dairy cattle, dairy calves, swine, sheep, chickens, turkeys, catfish, lobsters, and salmonids as follows: 2 ppm in muscle, 6 ppm in liver, 12 ppm in fat and kidney.

B. WITHDRAWAL TIME

1. The residue data supporting the original approval of NADA 130-435 for turkeys were used to recalculate the withdrawal period based on the revised tissue tolerances.

   The residue depletion data were analyzed using a statistical tolerance limit algorithm to calculate the withdrawal period for the upper 99^{th} percentile of the population with 95% confidence. For each of the edible tissues, the calculated withdrawal period for the 99^{th} percentile upper tolerance limit was less than the nominal zero withdrawal period of 6 hours. Therefore, the residue depletion profile for each of the edible tissues is consistent with a zero withdrawal.

Table 6B1: Residues (ppm) of oxytetracycline in the edible tissue of turkeys treated with oxytetracycline HCl soluble powder in the drinking water at a dose of 25 mg/lb body weight for 14 days.

Withdrawal (hrs)	Liver	Muscle	Skin/Fat
0	1.89±0.42	0.90±0.19	0.57±0.32
4	1.24±0.35	0.69±0.13	0.41±0.19
8	0.90±0.25	0.53±0.15	0.37±0.25
12	0.65±0.26	0.43±0.24	0.39±0.13
18	0.52±0.31	0.44±0.09	0.43±0.26
24	0.36±0.25	0.28±0.12	0.22±0.19

2. The kidney residue data supporting the original approval of NADA 130-435 for swine were used to recalculate the withdrawal period based on the revised kidney tolerance, 12 ppm.

   The residue depletion data were analyzed using a statistical tolerance limit algorithm to calculate the withdrawal period for the upper 99th percentile of the population with 95% confidence. For kidney, the calculated withdrawal period for the 99th percentile upper tolerance limit was less than the nominal zero withdrawal period of 12 hours, consistent with a zero withdrawal.

   Table 6B2: Residues (ppm) of oxytetracycline in kidney tissue of swine treated with oxytetracycline HCl soluble powder in the drinking water at a dose of 10 mg/lb for 5 days.

Withdrawal (hr)	Residues (ppm)
24	0.27±0.09
48	0.15±0.04
72	0.14±0.03

C. REGULATORY METHODS

The regulatory method for determination of oxytetracycline in tissues is a microbiological assay procedure using *Bacillus cereus* var. *mycoides* (ATCC 11778) suspension and is found in the FDA publication "Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports, and Protocols" revised October 1968, reprinted December 1974.

VII. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 514) to demonstrate that OXYTET SOLUBLE (oxytetracycline HCl), is safe and effective for use in chickens, turkeys, and swine for the approved indications, when administered in water at the approved dose.

Tolerances are established in 21 CFR 556.500 for the sum of residues in tissues of beef cattle, beef calves, non-lactating dairy cattle, dairy calves, swine, sheep, chickens, turkeys, catfish, lobsters, and salmonids as follows: 2 ppm in muscle, 6 ppm in liver, 12 ppm in fat and kidney. The preslaughter withdrawal time for chickens, turkeys, and swine is zero.

The Agency has concluded that this product shall retain over-the-counter marketing status because adequate directions for use have been written for the layman and the conditions for use prescribed on the label are likely to be followed in practice.

In accordance with 21 CFR 514.106(b)(2), this is a Category II change which did not require a reevaluation of the safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under section 512(c)(2)(F)(ii) of the FFDCA, this approval for food-producing animals does not qualifies for marketing exclusivity.

VIII. APPROVED PRODUCT LABELING (attached)

A. Facsimile label – OXYTET Soluble 2.46 oz, 9.87 oz, 3.09 lb packets
B. Facsimile label – TETRAVET-CA 3.91 lb packet