Approval Date: July 10, 1993

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 038-200

B. Sponsor

Fermenta Animal Health Company
10150 North Executive Hills Blvd.
Kansas City, Missouri 64153

C. Proprietary Name

OXY WS (TM) Soluble Antibiotic; MEDAMYCIN ® Soluble Antibiotic

D. Established Name

oxytetracycline hydrochloride

E. Dosage Form

Soluble powder

F. Dispensing Status

OTC

G. Route of Administration

Oral via drinking water

H. Indication

CHICKENS
Control of infectious synovitis caused by *Mycoplasma synoviae* - 200 to 400 mg oxytetracycline HCl per gallon drinking water (5.0-13.4 mg/lb body weight per day). Control of chronic respiratory disease (CRD) and air sac infections caused by *M. gallisepticum* and *Escherichia coli* and fowl cholera caused by *Pasteurella multocida* 400 to 800 mg oxytetracycline HCl per gallon drinking water (10.0-26.8 mg/lb body weight per day).

TURKEYS
Control of hexamitiasis caused by *Hexamita meleagridis* - 200 to 400 mg oxytetracycline HCl per gallon drinking water (1.6-16.8 mg/lb body weight per day). Control of infectious synovitis caused by *M. synoviae* 400 mg oxytetracycline HCl per gallon drinking water (3.2-16.8 mg/lb body weight per day). In growing turkeys, control of complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis) - 25 mg/lb body weight daily.

I. Effect of Supplement

The effectiveness oxytetracycline HCl soluble powder was reviewed by the National Academy of Sciences/National Research Council Drug Efficacy Study Implementation (NAS/NRC DESI) and has been deemed effective when labeled as specified in the Indications and Recommended Dosage section of the summary.

II. EFFECTIVENESS

The effectiveness of OXY WS(TM) (MEDAMYCIN®) Soluble Powder (oxytetracycline HCl) was reviewed by the National Academy of Sciences/National Research Council Drug Efficacy Study Implementation (NAS/NRC DESI) and has been deemed effective when labeled as specified in the Indications and Recommended Dosage sections presented above (35 FR 7089, May 5, 1970).

Studies in the original NADA demonstrated the bioequivalence of Pfizer's Terramycin ® Soluble Powder and Fermenta's OXY WS (TM) (MEDAMYCIN®) Soluble Antibiotic in chickens. To support a formula modification, this supplemental NADA contains another bioequivalence study in chickens.

A crossover bioequivalence and palatability study using 148 Hubbard Rock-Cornish chicks (74 males, 74 females) approximately eight weeks of age was conducted at the Fort Collins, Colorado research facility of Fermenta Animal Health Company by Dr. J. Szanto. The chicks were divided into two groups, 120 medicated and 28 unmedicated controls. Pfizer's Terramycin Soluble Powder Concentrate and Fermenta's OXY WS (TM) (MEDAMYCIN®) Soluble Antibiotic were administered in the drinking water for 14 consecutive days at an approximate concentration of 800 mg oxytetracycline HCl per gallon.

Weight gains were measured on days O, 5, 9 and 13 during the study. Water consumption was monitored daily from day -7 through day 13 for each animal group and feed consumption was monitored daily from day -14 through day 13 for each animal group. Blood samples were collected on days 5, 9 and 13.

The combined (male and female) average daily weight gains per bird for each medicated group was as follows: Fermenta OXY WS (TM) (MEDAMYCIN®) , 66 g/bird; Pfizer Terramycin ® , 65 g/bird; unmedicated control, 56 g/bird. The combined average water consumption for the medicated groups was 310 mL for the Fermenta product, 306 mL for the Pfizer product and 279 mL for the unmedicated controls. The feed conversion rate (feed/gain) was identical for the two medicated groups (2.4); the unmedicated controls feed conversion rate was 2.6. Combined (male and female) average blood levels of oxytetracycline were 0.174 ppm for Fermenta OXY WS (TM) (MEDAMYCIN®) and 0.169 ppm for the Pfizer product.

The blood concentration data show no difference between the two medicated groups. All parameters examined (feed consumption, drinking water consumption, feed conversion rate, serum drug levels) are indicative of complete comparability between the reference drug product (Pfizer) and Fermenta's OXY WS (TM) (MEDAMYCIN®).

III. TARGET ANIMAL SAFETY

The animal safety of oxytetracycline hydrochloride soluble powder is recognized under the conditions outlined in the NAS/NRC DESI review of the product with reference to the indications for use, route of administration, recommended dosages and limitations of use as specified in 35 FR 7089, May 5, 1970. Therefore, to assure 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 14 consecutive days in chickens or turkeys.

IV. HUMAN FOOD SAFETY

Residue Depletion Studies

The following studies establish a withdrawal time when residues of oxytetracycline hydrochloride are at or below the established tolerances in edible tissues when given the Fermenta product at the recommended label doses.

Forty large white turkey poults, approximately 14 weeks of age (36 medicated, 4 unmedicated controls) were used to determine the tissue residue depletion rate of oxytetracycline HCI. OXY WS (TM) (MEDAMYCIN®) was administered in the drinking water continuously for 14 consecutive days at a final drug concentration to deliver 25 mg oxytetracycline HCI per pound body weight. Blood, skin/fat, liver and muscle tissue samples collected at 0, 4, 8, 12, 18 and 24 hours after withdrawal of medicated water were analyzed for residues of oxytetracycline by microbiological assay. Blood samples were collected from all birds just prior to euthanasia. The control birds were negative for detectable levels of oxytetracycline at time 0 and 24 hours post drug withdrawal. The average tissue concentrations were less than 1 ppm for all time points.

	Average Tissue Residues (ppm)					
Tissue	0*	4	8	12	18	24*
Skin/fat	0.376	0.726	0.451	0.253	0.352	0.287
Muscle	0.348	0.208	0.155	0.136	0.069	0.030
Liver	0.786	0.555	0.363	0.354	0.226	0.206
Blood	0.198	0.126	0.093	0.065	0.005	0.018

* Control tissue below the Method Detection Limit.
The residue depletion study in turkeys supports a four day withdrawal period.

Thirty-two Hubbard Rock-Cornish chicks (24 medicated, 8 unmedicated controls), approximately 8 weeks of age were used to determine the tissue residue depletion rate of oxytetracycline HCI. OXY WS (TM) (MEDAMYCIN®)
Soluble Antibiotic was administered ad libitum via the drinking water for 14 consecutive days at an approximate drug concentration of 800 mg oxytetracycline HCl per gallon. Muscle, liver, and skin/fat tissue samples collected at 0, 1, 2, 3, 4 and 5 hours post withdrawal of the medicated drinking water were analyzed for residues of oxytetracycline by microbiological assay. The control birds were negative for detectable levels of oxytetracycline at time 0 and 5 hours post medication. The average tissue concentrations were less than the 1 ppm tolerance at all time points.

	Average Tissue Residues (ppm)					
Tissue	0*	1	2	3	4	5*
Skin/fat	0.330	0.293	0.451	0.253	0.352	0.287
Muscle	**	**	**	**	**	**
Liver	0.535	0.462	0.556	0.406	**	**

*Control tissue below the Method Detection Limit.

**All sample replication values below Limit of Quantitation-

This residue depletion study supports a zero day withdrawal period in chickens-

D. Analytical Method for Residues.

The regulatory analytical method for detection of residues of oxytetracycline is a microbiological test using *Bacillus cereus* spore suspension- The method, "Antibiotic Residues in Milk, Dairy products, and Animal Tissues: Methods, Reports, and Protocols" , Revised October, 1968, Reprinted December, 1974, is published by the Food and Drug Administration. The method was fully validated by the Research Laboratory and the analytical limits developed by the laboratory were well below the published tolerance levels. The results of the residue depletion studies presented in this summary demonstrate that the residues are below the established tolerances in edible tissues (**21 CFR 556.500**) after a four day withdrawal period in turkeys and a zero withdrawal in chickens.

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Act and demonstrate that Fermenta's product, Oxytetracycline Soluble Powder, when used under its proposed conditions of use is safe and effective in turkeys and chickens.

The sponsor submitted bioequivalency data for chickens which demonstrated biological equivalence to the approved pioneer product. This supplement is approved under DESI "me-too" pipeline provision and therefore the sponsor had to submit residue studies to satisfy human food safety requirements. The withdrawal period for turkeys is 4 days, and there is no withdrawal period for chickens. The tolerance for oxytetracycline has been previously established in edible tissues of chickens and turkeys:

- 3 parts per million in uncooked kidney
- 1 part per million in uncooked muscle, liver, fat, and skin.

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 reevaluation 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. ATTACHMENT

Oxytetracycline HCl Soluble Antibiotic Amended Supplement to NADA 038-200

1. ATTACHMENT 3 - Facsimile Labeling

   - LABEL DESCRIPTION
   - DESIGN CODE

2. **OXY WS (TM) Soluble Antibiotic**

   - 3.8 oz Packet

- 50 x 3.8 oz Packets
- 15.2 oz Packet
- *25* x 15.2 oz Packets
- 4.74 lb Pail 23.7 lb Pail

3. **TechAmerica(TM) MEDAMYCIN®Soluble Antibiotic**
   - 3.8 oz Packet
   - 50 x 3.8 oz Packets
   - 15.2 oz Packet
   - 25 x 15.2 oz Packets
   - 4.74 lb Pail 23.7 lb Pail

Copies of applicable 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.