Date of Approval: December 7, 2007

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-281

AVIAX II

Semduramicin
Type A Medicated Article
Broiler Chickens

"For the prevention of coccidiosis caused by *Eimeria tenella, E. acervulina, E. maxima, E. brunetti, E. necatrix,* and *E. mitis"*

Sponsored by:

Phibro Animal Health

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I. GENERAL INFORMATION:

A. File Number:	NADA 141-281
B. Sponsor:	Phibro Animal Health 65 Challenger Road 3d floor Ridgefield Park, NJ 07660 Drug Labeler Code: 066104
C. Proprietary Name:	AVIAX II
D. Established Name:	Semduramicin
E. Pharmacological Category:	Anticoccidial
F. Dosage Form:	Type A medicated article
G. Amount of Active Ingredient:	22.7 g (5%) semduramicin per pound (as semduramicin sodium biomass)
H. How Supplied:	40 lb (18.2 kg) bags
I. How Dispensed:	OTC
J. Dosage:	22.7 g/ton (25 ppm)
K. Route of Administration:	Oral, via feed
L. Species/Class:	Broiler chickens
M. Indication:	For the prevention of coccidiosis caused by *Eimeria tenella, E. acervulina, E. maxima, E. brunetti, E. necatrix,* and *E. mitis*

II. EFFECTIVENESS:

A. Dosage Characterization:

AVIAX (NADA 140-940), a Type A medicated article containing 5.13% semduramicin sodium (in the crystalline formulation) is approved in broiler chickens at a feeding level of 22.7 g of semduramicin per ton of Type C finished broiler feeds. The same feeding level of semduramicin (22.7 g/ton) was used for approval of the mycelial formulation (semduramicin sodium biomass) of the product. The FOI for the original approval of NADA 140-940, dated March 10, 1994, contains dosage characterization information for broiler chickens.

B. Substantial Evidence:

The effectiveness of AVIAX II (semduramicin, as semduramicin sodium biomass), was compared with AVIAX (semduramicin, as semduramicin sodium) for the prevention of coccidiosis caused by *Eimeria tenella*, *E. acervulina*, *E. maxima*, *E. brunetti*, *E. necatrix*, and *E. mitis* in broiler chickens in a pivotal mixed-species clinical end-point bioequivalence (battery) study. Production performance of broiler chickens fed diets containing AVIAX II or AVIAX were further evaluated in both a pivotal floor-pen performance study and in a commercial field study. These studies are summarized as follows.

1. Battery Effectiveness Study

a. Title: "Broiler Coccidiosis Battery Effectiveness Test"
(Study # 211S-60-96-184)

b. Study Director:

Beverly A. George, Ph.D.
Colorado Quality Research, Inc.
Wellington, CO

c. Study Design:

1) Objective: To compare the effects of AVIAX II (semduramicin, as semduramicin sodium biomass) and AVIAX (semduramicin, as semduramicin sodium) Type A medicated articles when fed at 22.7 g of semduramicin/ton (25 ppm) for the prevention of coccidiosis in broiler chickens following infection with mixed *Eimeria* species.

2) Study Animals: 320 twelve-day-old Ross x Arbor Acres broiler chickens (160 males and 160 females)

3) Housing: 32 cages of 10 birds per cage, with four cages of each sex per treatment group

4) Treatment groups: There were four treatment groups: (1) a non-infected, non-medicated control; (2) an infected, non-medicated control; (3) AVIAX-fed infected birds; and (4) AVIAX II-fed infected birds.

5) Establishment of Infection: Birds in the infected treatments were each dosed *per os* on Day 2 with a one-mL inoculum that contained 30,000 oocysts of *Eimeria acervulina*, 10,000 oocysts of *Eimeria maxima*, 10,000 oocysts of *Eimeria brunetti*, 25,000 oocysts of *Eimeria mitis*, 20,000 oocysts of *Eimeria necatrix*, and 10,000 oocysts of *Eimeria tenella*. The non-infected control group received 1 mL distilled water *per os*.

6) Route of Administration: AVIAX and AVIAX II were administered orally, mixed with feed, and fed continuously for 8 days, starting on Day 0.

7) Test Duration: 8 days

8) Dosage Used: The Type A medicated articles were mixed in feed to supply 22.7 g of semduramicin per ton of feed (25 ppm).

9) Pertinent Variables Measured: The primary decision variables were improvement in body weight gain in treated birds compared with infected, non-medicated controls, and the reduction in lesion scores in the upper intestine, middle intestine, lower intestine, and cecum upon necropsy, six days after inoculation with the mixed *Eimeria* species. Intestinal lesions were scored using the method of Johnson and Reid (*Experimental Parasitology*, 28:30-36, 1970).

10) Statistical Analysis: The data were analyzed by analysis of variance using a general linear mixed model.

d. Results:

Table 1 Means of Weight Gain and Lesion Scores

Variable	Noninfected-Nonmedicated	Infected-Nonmedicated	AVIAX	AVIAX II
Weight gain, g	245[a]	114[b]	182[c]	174[c]
Lesion scores				
Upper	0.00 [a]	1.18[b]	0.26[ac]	0.49 [c]
Middle	0.00 [a]	2.54 [b]	0.95 [c]	1.13 [c]
Lower	0.00 [a]	1.67 [b]	0.30 [c]	0.19 [ac]
Cecum	0.00 [a]	2.20 [b]	0.22 [c]	0.27 [c]
Mortality, % (# of dead birds / # of birds per group)				
All causes[d]	0	3.75 (3/80)	0	5.00 (4/80)
Coccidiosis[d]	0	1.25 (1/80)	0	1.25 (1/80)

[abc] Least squares means in the same row with different superscripts are different ($P \leq 0.05$).
[d] Statistical analysis was not performed.

e. Conclusions:

Results of this replicated, controlled comparative study demonstrate that semduramicin, as semduramicin sodium biomass, (mycelial formulation) is as effective as semduramicin sodium (crystalline formulation) for the prevention of coccidiosis caused by a mixed infection of *Eimeria* species.

2. Floor Pen Performance Study

a. Title: "Broiler Floor Pen Performance Trial" (Study # 2311S-60-96-201)

b. Study Director:

Greg F. Mathis, Ph.D.
Georgia Poultry Research, Inc.
Athens, GA

c. Study Design:

1) Objective: To compare the performance (feed efficiency and weight gain) of broiler chickens fed diets containing either AVIAX II (mycelial formulation) or AVIAX (crystalline formulation).

2) Study Animals: 1,440 day-old Ross x Cobb broiler chickens (720 males and 720 females)

3) Housing: 24 commercial floor pens with 30 males and 30 females per pen

4) Treatment groups: The two treatments, AVIAX II and AVIAX, were assigned to the pens in a randomized complete block design using pairs of adjacent pens as a blocking factor.

Coccidial infection was presumed to be induced in both groups by exposure of birds to dirt floors and used litter; the litter was not examined for the presence of *Eimeria* species.

5) Route of Administration: AVIAX II and AVIAX were administered continuously through the feed.

6) Dosage Used: The Type A medicated articles were mixed in feed to supply 22.7 g of semduramicin per ton of feed (25 ppm).

7) Test Duration: 42 days

8) Pertinent Variables Measured: Feed consumption, weight gain, feed conversion, and % mortality were evaluated on Day 42 of the study.

9) Statistical Analysis: The data were analyzed by analysis of variance using a general linear mixed model.

d. Results:

Table 2 Performance comparison between semduramicin formulations

Variable	AVIAX	AVIAX II
Feed consumption, kg	4.029	4.148
Weight gain, kg	2.161	2.160
Feed/gain	1.870	1.925
Total mortality, %	6.67	5.56
Coccidiosis mortality, %	0.0	0.0

*The means in the table are least squares means.

e. Conclusions:

f. The means for the variables listed in the table above showed similar results for AVIAX II (mycelial formulation), and AVIAX (crystalline formulation), indicating similar performance of broiler chickens fed the two Type A medicated articles.

3. Commercial Field Comparison Study

a. Title: "Safety and Efficacy Evaluation of Mycelial Semduramicin in Broiler Chickens under Commercial Conditions" (Study # USD 119-003)

b. Study Director:

Karen Christensen, M.S.
O.K. Industries, Inc.
Fort Chaffee, AR

c. Study Design :

1) Objective: To compare the safety and effectiveness of AVIAX II (mycelial formulation) and AVIAX (crystalline formulation) when fed at 22.7 g/ton (25 ppm) in broiler chickens under conditions of commercial management and natural exposure to coccidia.

2) Study Animals: 72,000 day-old Ross x Hubbard broiler chickens (males and females, straight run)

3) Housing: Four identically constructed commercial broiler houses with 18,000 birds per house

4) Treatment Groups: AVIAX II, 22.7 g/ton (25 ppm), and AVIAX, 22.7 g/ton (25 ppm), were randomly assigned to each of the four houses. All diets throughout the 54-day study period contained the growth promoter virginiamycin.

5) Route of Administration: AVIAX II and AVIAX were administered continuously through the feed for 46 days.

6) Test Duration: 46 days, followed by an 8 day withdrawal period

7) Dosage Form: Type A medicated article

8) Pertinent Variables Measured: Feed consumption, weight gain, feed conversion, and % mortality were evaluated after a 46-day semduramicin treatment followed by an 8-day withdrawal period.

9) Statistical Analysis: The data were analyzed by descriptive methods.

d. Results:

Table 3 Commercial comparison between semduramicin formulations

Variable- Live production results	**AVIAX**	**AVIAX II**
Number of birds placed/house [1]	18,000	18,000
Live birds at end of trial/house[2]	17,270	17,328
Live birds weight, lb/house[3]	106,360	106,420
Average live weight per bird, lb[4]	6.158	6.142
Livability, %[5]	95.9	96.3
Feed consumption/house, lb[6]	217,378	219,430
Feed consumption per bird, lb[7]	12.59	12.66
Feed conversion ratio[8]	2.044	2.062
Total mortalities, %[9]	4.05	3.73
- Culled birds, %	0.83	0.69
- Dead birds, %	3.22	3.04

[1] Average of two houses fed AVIAX and two houses fed AVIAX II. Number was determined by the hatchery

[2] Average number of live birds per house at the end of the trial

[3] Average of two houses fed AVIAX and two houses fed AVIAX II

[4] (Live birds weight, lb/house)/(Live birds at end of trial/house)

[5] 100*(Live birds at end of trial/house)/ (Number of birds placed/house)

[6] Average of the difference between the sum of the net weight of the feed delivered minus the sum of the net weight of the feed weighback per house

[7] (Feed consumption/house, lb)/(Live birds at end of trial/house)

[8] (Feed consumption/house, lb)/(Live birds weight, lb/house)

[9] 100*[(Number of birds placed/house- Live birds at end of trial/house)]/(Number of birds placed/house)

Variable – Processing Results	AVIAX	AVIAX II
Estimated catching count, birds/house[10]	17,290	17,358
Number of carcasses condemned, farm/house[11]	18.5	17
Number of carcasses condemned, plant/house[12]	26	29
Total weight of parts condemned, lb/house[13]	892	875
% of production condemned* – farm[14]	0.53	0.51
% of production condemned* – plant[15]	0.57	0.59

[10] Estimated count by catching crews and recorded on the Poultry Condemnation Certificate as "NO. HEAD IN LOT."

[11] Average # condemned carcasses attributed to the farm per house (i.e. tuberculosis, leukosis, septicemia, toxemia, synovitis, tumors, bruises, airsacculitis, and inflammatory process).

[12] Average # condemned carcasses attributed to the processing plant per house (i.e. cadavers, overscald, contamination, no viscera, and plant rejects).

[13] Average weight of parts that were condemned per house.

[14] 100*(**[**(Live birds weight, lb/house/est. catching count) x (number of carcasses condemned, farm/house)] + [(weight of parts condemned)/2)]**)**/weight of live birds at end of trial

[15] 100*(**[**(Live birds weight, lb/house/est. catching count) x (number of carcasses condemned, plant/house)] + [(weight of parts condemned)/2)]**)**/weight of live birds at end of trial

* For calculation of percent condemnations, half of the total weight of parts was attributed to the farm, and half to the plant, and was recorded as such on the Poultry Condemnation Certificate.

e. Conclusions:

The means for the variables listed in the table above showed similar results for the two semduramicin Type A medicated articles, suggesting similar production performance of broiler chickens fed the two semduramicin Type A medicated articles.

III. TARGET ANIMAL SAFETY:

A. 1X, 2X, 3X Floor Pen study in nonchallenged broiler chickens

1. Title: "Aviax (semduramicin) Target Animal Safety Study in Broiler Chickens" (Study # 2411S-60-96-194)

2. Study Director:

   Terry N. Terhune, D.V.M., Ph.D.
   Health Management Services,
   Tulare, CA

3. Study Design

   a. Objective: To evaluate the safety of semduramicin, as semduramicin sodium biomass (mycelial formulation, mSEM) fed at 1X, 2X, and 3X of the recommended concentration (25 ppm) in broiler chickens

   b. Study Animals: 1440 (720 males, 720 females) healthy day-old Peterson X Arbor Acres broiler chicks

   c. Housing: 48 floor pens in a conventional California style commercial poultry building, with 12 pens per treatment group (15 males and 15 females per pen)

   d. Treatment Groups: nonmedicated control, 25 ppm (or 22.7 g/ton) mSEM, 50 ppm (or 45.4 g/ton) mSEM, and 75 ppm (or 68.1 g/ton) mSEM. No concomitant drug therapy was used.

   e. Dosage Form: Type A medicated article

   f. Route of Administration: Semduramicin, as semduramicin sodium biomass, was administered continuously through the feed.

   g. Test Duration: 42 days, without interruption

   h. Pertinent Measurements/Observations: Pens were observed twice daily to monitor the health and environment of the birds. A gross necropsy was performed on all mortalities and culls to confirm the sex, determine the cause of death, and to definitively rule out coccidiosis as an etiology. Feed consumption was quantified throughout the study. Feed weighbacks (in kilograms) were performed at the end of each of the starter (Day 21), grower (Day 37), and finisher (Day 42) periods for each pen. On Day 0, Day 21, and Day 42, blocks of pens were chosen in successive order and the pens of birds in each block were weighed by sex and recorded in successive order. Performance measurements were made on study Days 21 and 42. At study termination, birds were appropriately euthanized and discarded.

4. Statistical analysis:

   Data were analyzed with a mixed model procedure. A repeated measures mixed general linear model which included the fixed effects of sex, treatment, day of study, and all interactions, the random effects of block, block by sex, block by treatment, block by sex by treatment, and block by sex by day of study was used to analyze pen-sex group average body weight. A general linear mixed model which included the fixed effect of treatment and the random effect of block was used to analyze feed consumption, feed conversion, and percent mortality. Percent mortality was transformed to the arcsine-square root scale before analysis and after analysis the least squares means were back-transformed for presentation.

5. Results: Results are summarized in Table 4

No clinical signs of toxicity and no significant differences in specific performance variables were reported for birds administered the recommended level of 25 ppm semduramicin, as semduramicin sodium biomass, in the diet as compared to untreated birds. Neurologic signs typical of ionophore toxicity (leg weakness and ataxia) were also not observed at the 50 ppm and 75 ppm doses. However, the 50 ppm and 75 ppm doses significantly reduced weight gain, feed consumption, and feed conversion at study Days 21 to 42 and 0 to 42. Mortality was three percent or less in all treatment groups and was not affected by the dietary concentration of mycelial semduramicin.

Table 4 Performance of broiler chickens fed various levels of semduramicin (mycelial formulation)

Time Interval Variable	Dietary semduramicin concentration 0 ppm	25 ppm	50 ppm	75 ppm
Study Days 0 to 21				
Weight gain, g	687 [a]	700 [a]	616 [b]	434 [c]
Feed Consumption, g	1070 [a]	1074 [a]	998 [b]	904 [c]
Feed conversion, g feed/g gain	1.557 [a]	1.536 [a]	1.620 [a]	2.088 [b]
Mortality, %	0.8 [a]	0.6 [a]	0.6 [a]	0.5 [a]
Study Days 21 to 42				
Weight gain, g	1527 [a]	1523 [a]	1285 [b]	884 [c]
Feed Consumption, g	3088 [a]	3066 [a]	2753 [b]	2000 [c]
Feed conversion, g feed/g gain	2.023 [a]	2.015 [a]	2.146 [b]	2.270 [c]
Mortality, %	1.3 [a]	1.1 [a]	0.4 [a]	0.2 [a]
Study Days 0 to 42				
Weight gain, g	2214 [a]	2223 [a]	1901 [b]	1318 [c]
Feed Consumption, g	4209 [a]	4191 [a]	3771 [b]	2915 [c]
Feed conversion, g feed/g gain	1.902 [a]	1.887 [a]	1.986 [b]	2.217 [c]
Mortality, %	3.0 [a]	2.5 [a]	1.7 [a]	0.9 [a]

[a, b, c]Means in same row with different superscripts are significantly different ($P \leq 0.05$).

6. Conclusions: The recommended level (25 ppm) of semduramicin, as semduramicin sodium biomass, fed continuously in the feed, is safe for use in broiler chickens.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

For the summary of the general toxicology studies, please refer to the FOI for the original approval of semduramicin sodium under NADA 140-940.

Microbiological Acceptable Daily Intake (ADI)

An assessment of the effects of semduramicin residues present in edible tissues of chicken on human intestinal flora was presented following the step-by-step approach recommended in FDA Guidance for Industry (GFI) #159. It was concluded that (1) semduramicin does have antimicrobial activity on bacterial groups of the human intestinal flora; (2) 100% of semduramicin residues present in edible chicken tissues will pass through the colon and retain 100% of their microbiological activity; (3) there is scientific justification to eliminate the need for determining a microbiological ADI for the endpoint "increase in the population(s) of resistant bacteria in the human colon"; and (4) a microbiological ADI was determined for the endpoint "disruption of the colonization barrier".

Of the two endpoints of human health concern mentioned above, a microbiological ADI for semduramicin residues was determined for "disruption of the colonization barrier" following the recommendations in FDA GFI #159 "Studies to evaluate the safety of residues of veterinary drugs in human food: general approach to establish a microbiological ADI". The microbiological ADI for disruption of the colonization barrier was determined to be 22.5 µg/kg bw/day or 1.35 mg/person/day.

The study performed for determining the microbiological ADI for disruption of the colonization barrier was the following:

Semduramicin: Minimum Inhibition Concentration (MIC) with Bacteria Representative of the Human Intestinal Flora

Study Number: USD 119-078

Study Director: Robert J. Carman, Ph.D.

Test Facility: TechLab, Inc., Blacksburg, VA

Report Date: June 19, 2006

The study was conducted using semduramicin crystalline product and followed the methodology recommended by the Clinical and Laboratory Standards Institute (formerly NCCLS) for the agar dilution method. In a subsequent study (# USD119-107), the antibacterial activity of semduramicin mycelial (biomass product) was demonstrated to be comparable to the activity of semduramicin crystalline. This conclusion validated the data from the MIC study performed with the crystalline product.

Frozen feces from ten healthy male and female volunteers were used in the study. MIC values were obtained by testing semduramicin against ten isolates of the recommended bacterial groups of the human intestinal flora. MIC_{50} (MIC at

which 50% of the isolates tested were inhibited) values were calculated for each bacterial group and used to calculate the MIC_{calc} for semduramicin following the recommendations in FDA GFI #159. Three bacterial groups were not considered for the calculation of the MIC_{calc} because they were inherently resistant to semduramicin. These bacterial groups were *Bacteroides*, *E. coli* (both with MIC_{50} >32 µg/mL), and *Fusobacterium* (MIC_{50} >8 µg/mL). The calculated MIC_{calc} was 6.143 µg/g.

The MIC_{calc} was applied to the formula recommended in FDA GFI #159 for the calculation of the microbiological ADI for disruption of the colonization barrier as follows:

$$\text{Microbiological ADI} = \frac{6.143\ \mu g/g \times 220\ g}{1 \times 60\ kg\ person} = 22.5\ \mu g/kg\ bw/day$$

The sponsor submitted scientific arguments to dismiss the necessity of determining a microbiological ADI for the endpoint "increase in the population(s) of resistant bacteria in the human colon." It was determined that, although resistance to semduramicin may occur by *in vitro* induction, it would be a rare event. The precise mechanisms of resistance to semduramicin are unknown. In addition, at this time, there are no approved ionophores for systemic use in humans. Therefore, this endpoint was not considered for setting a microbiological ADI.

Consequently, the microbiological ADI for semduramicin mycelial residues is 22.5 µg/kg bw/day or 1.35 mg/person/day. Since this ADI is higher than the general toxicological ADI, the final ADI for semduramicin mycelial is the general toxicological ADI, which is 3 µg/kg bw per day or 0.18 mg/person/day.

The following are the revised safe concentrations for semduramicin residues in edible tissues calculated using the current consumption values:

TISSUE	SAFE CONCENTRATION
Muscle	600 ppb
Liver	1800 ppb
Skin/Fat	3600 ppb
Fat	3600 ppb

B. Residue Chemistry:

1. Summary of Residue Chemistry Studies

a. Total Residue and Metabolism Study

Total residue and metabolism data were described in the FOI summary for semduramicin sodium (NADA 140-940, FOI dated March 10, 1994).

b. Comparative Metabolism Study

Comparative metabolism data was described in the FOI summary for semduramicin sodium (NADA 140-940, FOI dated March 10, 1994).

c. Residue Depletion Study

Semduramicin Concentration in Liver of Broiler Chickens Consuming Feed Medicated with the Mycelial Premix Formulation of Semduramicin.

Study Number: 2511S-60-235

Study Director: Terry N. Terhune, D.V.M., Ph.D.

Test Facility: Health Management Services, Tulare, CA

Study Dates: December 13, 1996 to July 29, 1997

A statement describing adherence to Good Laboratory Practice Regulations (21 CFR 58) is provided.

One hundred sixty, one day old Peterson x Arbor Acre chickens (80 males, 80 females), were allocated to two pens per sex, each pen containing 40 birds. Eighty test birds (40 males, 40 females) were administered feed containing 22.7 g/ton semduramicin mycelial for 42 days. Eighty control birds (40 males, 40 females) received nonmedicated feed throughout the study. Twenty-four control birds (12 males, 12 females) were sacrificed at 6 hours (practical zero withdrawal). Twelve test birds (6 males, 6 females) were sacrificed at each of the following times after the medicated feed was withdrawn: 6 (practical zero withdrawal), 12, and 18 hours. Livers from six control birds (three males and three females) and six test birds (three males and three females) collected at each withdrawal time were homogenized and analyzed for parent semduramicin using a validated HPLC method.

Mean concentration of semduramicin (ppb) in livers of chickens fed 25 ppm semduramicin mycelial for 42 days.

Withdrawal Period	Males (n=3)	Females (n=3)
6 hours	155	77.8
12 hours	45.9	48.0
18 hours	38.3	40.9

Limit of quantitation = 35 ppb

Residues of parent semduramicin in liver are well below the tolerance of 400 ppb. The data confirm zero withdrawal.

2. Target Tissue and Marker Residue Assignment

The target tissue is liver. The marker residue is parent semduramicin.

3. Tolerance Assignments

The tolerances for parent semduramicin are 400 ppb in liver and 130 ppb in muscle (21 CFR 556.597).

4. Withdrawal Times

The withdrawal period for semduramicin mycelial is zero.

C. Microbial Food Safety:

Microbial food safety information for semduramicin mycelial (biomass) was evaluated. The microbial food safety assessment was based on both a *hazard characterization* and *qualitative risk assessment*, which included a *release assessment* to describe the probability that use of semduramicin mycelial will result in the emergence of resistant bacteria or resistance determinants in treated food animal species under proposed conditions of use; an *exposure assessment* to describe the likelihood of human exposure to resistant bacteria or resistance determinants through consumption of edible products from treated food animals; and a *consequence assessment* to describe potential human health consequences arising from exposure to defined resistant bacteria or resistance determinants by considering the human medical importance of semduramicin or similar drugs used in the treatment of human infectious diseases.

To support their microbial food safety assessment, the sponsor conducted a study (sponsor's study # USD119-107) titled, "Evaluation of potential microbiological effects of mycelial semduramicin sodium on bacteria of human health concern." The purpose of the study was to determine whether semduramicin mycelial and any impurities in the biomass product had any antibacterial activity, particularly against food-borne pathogens of public health interest. The study demonstrated that the (original) crystalline semduramicin and (new) mycelial (biomass) form of semduramicin have comparable activities against tested microorganisms, which included *Escherichia coli*, *Salmonella* species, *Campylobacter* species, and some Gram-positive organisms as part of the control, and further indicated that the impurities in the product had no additional noteworthy antimicrobial activity. More importantly, as expected, semduramicin, an ionophorous agent, had no remarkable activity against Gram-negative microorganisms tested, and activity against selected Gram-positive control organisms was minimal.

Based upon the Agency's evaluation of all information submitted by the sponsor, it is reasonably determined that the overall risk estimation associated with the product's proposed conditions of use is **low**, integrated from individual rankings of low for the *release assessment*, high for the *exposure assessment*, and low for the *consequence assessment* (note: at this time, there are no ionophorous antibacterial agents used systemically in humans). This risk estimation is compatible with the proposed use of semduramicin mycelial in feed for broiler chickens for coccidiosis control.

D. Analytical Method for Residues:

The requirement for a regulatory method was waived based on the policy that existed when semduramicin sodium was approved and when the tissue residue depletion study was conducted. A regulatory method was not required because total residues of semduramicin and its metabolites were well below the safe concentration in all edible tissues at zero withdrawal time.

A validated analytical method for detection of residues of semduramicin is available from the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

V. USER SAFETY:

CVM reviewed the labeling approved under NADA 140-940 and the Material Safety Data Sheet (MSDS) for semduramicin sodium to determine whether user safety concerns were appropriately addressed in the labeling. As a result of this review, the product labeling contains the following information regarding safety to humans handling, administering, or exposed to AVIAX II:

"Precautions such as the following should be considered: avoid contact with skin, eyes, or mucous membranes; dust masks or respirators, safety glasses, gloves, and protective clothing should be worn; dust-arresting equipment and adequate ventilation should be utilized; personal hygiene should be observed; wash before eating or leaving a work site; be alert for signs of allergic reactions- seek prompt medical attention if such reactions are suspected."

VI. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data demonstrate that AVIAX II, when used according to the label, is safe and effective for the prevention of coccidiosis in broiler chickens caused by *Eimeria tenella, E. acervulina, E. maxima, E. brunetti, E. necatrix,* and *E. mitis.* Additionally, data demonstrate that residues in food products derived from broiler chickens treated with AVIAX II will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

B. Exclusivity:

Under section 512(c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval.

C. Patent Information:

The sponsor did not submit any patent information with this application.

VII. ATTACHMENTS:

Facsimile labeling:
Type A medicated article
Type C medicated feed