Date of Approval: October 13, 2023

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-336

AIVLOSIN®

(62.5% w/w tylvalosin as tylvalosin tartrate)

Granules for solution

Female swine intended for breeding
(replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows)

This supplement provides for the addition of female swine intended for breeding (replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows) to the classes approved for the control of porcine proliferative enteropathy and control of swine respiratory disease indications, and provides for removal of the precaution “Not for use in lactating or pregnant females or females intended for breeding” from the labeling.

Sponsored by:

ECO LLC

Executive Summary

This supplemental approval of AIVLOSIN® (62.5% w/w tylvalosin as tylvalosin tartrate) water soluble granules provides for the addition of female swine intended for breeding (replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows) to the classes approved for the control of porcine proliferative enteropathy and control of swine respiratory disease indications, and provides for the removal of the precaution "Not for use in lactating or pregnant females or females intended for breeding" from the labeling. AIVLOSIN® is an antimicrobial drug that is administered to pigs continuously in the drinking water for 5 consecutive days.

Safety and Effectiveness
FDA did not require systemic margin of safety or effectiveness studies for this supplemental approval. Previous studies, which are described in the Freedom of Information (FOI) Summaries for the original and supplemental approvals of AIVLOSIN®, demonstrate the systemic safety and effectiveness of the drug in swine when used according to the labeling.

The sponsor conducted a reproductive safety study to assess the safety of AIVLOSIN® when administered to sows continuously throughout their reproductive cycle. Healthy, multiparous, commercial purebred and crossbred sows, ranging in age from approximately 1.5 to 4.5 years old, were enrolled in the study. Sows in the treated group received AIVLOSIN® in their drinking water at an inclusion rate of 150 parts per million of tylvalosin (3X the approved inclusion rate). Sows in the control group were given non-medicated water. The treatment period started at the expected onset of estrus and lasted through at least two complete estrous cycles, breeding, gestation, farrowing, and lactation, until piglets were weaned at 21 days post-farrowing. The duration of the treatment period was 174 to 195 days, depending on the farrowing date. Sows were bred by artificial insemination beginning on their third or fourth estrus during the treatment period, using semen from the same boar.

Sows generally remained healthy throughout the study, and the administration of AIVLOSIN® did not affect their feed consumption or body weight. Sows treated with AIVLOSIN® drank less water on the first day of treatment compared with what they drank before the drug was added to their water. Water intake recovered in most treated sows in 1 to 3 days. When starting AIVLOSIN®, sows should be monitored to ensure they continue to drink adequate amounts of water.

There were no adverse events or abnormalities in piglets attributed to the administration of AIVLOSIN® in the sows. There were no significant differences between treated and control groups for conception rate, farrowing rate, 1-day survival rate, 5-day survival rate, or 21-day survival rate (weaning index). AIVLOSIN® also did not negatively affect piglet growth or viability.

Human Food Safety
FDA evaluated the microbial food safety of tylvalosin for this supplemental approval using an updated hazard characterization and qualitative risk assessment. FDA identified *Campylobacter* as the primary hazard, which was used in the qualitative risk assessment. The assessment described the drug's antimicrobial characteristics with

respect to (1) promoting the emergence or selection of antimicrobial resistant bacteria of public health in or on treated swine; (2) the relative consumption quantities and bacterial contamination rates for food commodities derived from treated swine; and (3) its importance in human clinical medicine. Results from these components were integrated into an overall risk estimation of high for the intended uses of AIVLOSIN® in breeding female swine. The risk estimation of high is compatible with the Agency's recommended risk management strategies, which include the use of the drug only in groups of swine in buildings experiencing an outbreak of porcine proliferative enteropathy or swine respiratory disease.

The FOI Summaries for the original and supplemental approvals of AIVLOSIN® contain summaries of the information used to assess human food safety. There is no change to the previously established withdrawal period; it remains zero-day.

User Safety
The labeling for AIVLOSIN® describes the precautions people should take when handling the drug and preparing the medicated drinking water.

Conclusions
Based on the data submitted by the sponsor for the approval of AIVLOSIN®, FDA determined that the drug is safe and effective when used according to the labeling.

Table of Contents

I. GENERAL INFORMATION 5
II. EFFECTIVENESS 6
A. Dosage Characterization 6
B. Substantial Evidence 6
III. TARGET ANIMAL SAFETY 6
A. Reproductive Safety Study 7
IV. HUMAN FOOD SAFETY 12
A. Microbial Food Safety 12
B. Toxicology 13
C. Residue Chemistry 13
D. Analytical Method for Residues 13
V. USER SAFETY 13
VI. AGENCY CONCLUSIONS 14
A. Marketing Status 14
B. Exclusivity 14
C. Supplemental Applications 14
D. Patent Information 14

I. GENERAL INFORMATION

A. File Number

NADA 141-336

B. Sponsor

ECO LLC
344 Nassau St.
Princeton, NJ 08540

Drug Labeler Code: 066916

C. Proprietary Name

AIVLOSIN®

D. Drug Product Established Name

62.5% w/w tylvalosin as tylvalosin tartrate

E. Pharmacological Category

Antimicrobial

F. Dosage Form

Granules for solution

G. Amount of Active Ingredient

62.5% w/w tylvalosin as tylvalosin tartrate

H. How Supplied

160 g and 400 g sachets

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

50 ppm tylvalosin continuously in drinking water for five (5) consecutive days

K. Route of Administration

Oral

L. Species/Class

Female swine intended for breeding (replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows)

M. Indications

Control of porcine proliferative enteropathy (PPE) associated with *Lawsonia intracellularis* infection in groups of swine intended for slaughter and female swine intended for breeding in buildings experiencing an outbreak of PPE. Not for use in male swine intended for breeding.

Control of swine respiratory disease (SRD) associated with *Bordetella bronchiseptica, Glaesserella (Haemophilus) parasuis, Pasteurella multocida, Streptococcus suis*, and *Mycoplasma hyopneumoniae* in groups of swine intended for slaughter and female swine intended for breeding in buildings experiencing an outbreak of SRD. Not for use in male swine intended for breeding.

N. Effect of Supplement

This supplement provides for the addition of female swine intended for breeding (replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows) to the classes approved for the control of porcine proliferative enteropathy and control of swine respiratory disease indications, and provides for removal of the precaution “Not for use in lactating or pregnant females or females intended for breeding” from the labeling.

II. EFFECTIVENESS

A. Dosage Characterization

This supplemental approval does not change the previously approved dosage regimen. The Freedom of Information (FOI) Summary for the original approval of NADA 141-336 dated July 6, 2012, and a supplemental approval dated July 19, 2017, contain dosage characterization information for use of the drug in swine when administered at 50 ppm tylvalosin in drinking water for 5 consecutive days.

B. Substantial Evidence

CVM did not require effectiveness studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-336 dated July 6, 2012, and supplemental approvals dated July 19, 2017, and January 7, 2021, contain a summary of studies that demonstrate effectiveness of the drug in swine when administered at 50 ppm tylvalosin in drinking water for 5 consecutive days.

III. TARGET ANIMAL SAFETY

CVM did not require systemic margin of safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-336 dated July 6, 2012, contains a summary of the study that demonstrates an adequate margin of systemic safety of the drug in swine when administered at 50 ppm tylvalosin in drinking water for 5 consecutive days.

The following study was conducted to demonstrate the reproductive safety of AIVLOSIN® (62.5% w/w tylvalosin as tylvalosin tartrate) water soluble granules in female

swine intended for breeding when administered at 50 ppm tylvalosin in drinking water for 5 consecutive days.

A. Reproductive Safety Study

Title: AIVLOSIN® (Tylvalosin) Water Soluble Granules: Target Animal Reproductive Safety Study in Female Pigs. (Study No. TAS.US.180583)

Study Dates: November 27, 2018, to March 12, 2021

Study Location: Tranent, East Lothian, Scotland, United Kingdom

Study Design:

Objective: To assess the reproductive safety of AIVLOSIN® (62.5% w/w tylvalosin as tylvalosin tartrate) water soluble granules when administered to sows continuously throughout the reproductive cycle.

Study Animals: Twenty-eight healthy, multiparous (parity 2 to 9; average of 3.7 and 4.6 for the control and treated groups, respectively) Purebred Landrace and Yorkshire (Large White)/Landrace crossbred sows were enrolled in the study. Sows were approximately 1.5 to 4.5 years old and weighed approximately 239 kg to 392 kg (526 lbs. to 862 lbs.) at enrollment. Sows were acclimated to the test facility for at least 27 days prior to treatment initiation (Study Day [SD] 1). Sows were housed individually from SD -9 until 3 to 5 days prior to their expected farrowing date, and then in individual farrowing crates until the end of the study (21 days post-farrowing). All sows received a non-medicated feed ration adjusted throughout the study to accommodate different phases of the reproductive cycle.

Experimental Design: This was a randomized, masked, controlled reproductive safety study. The study was conducted in accordance with Organization for Economic Co-operation and Development (OECD) Good Laboratory Practices (GLP).

On SD -9, sows were randomly allocated to individual pens and pens were subsequently randomized to one of two treatment groups as shown in Table III.1. Sows were bred by artificial insemination (AI) beginning at on-study estrus 3 or 4, using semen from the same boar. Prior to farrowing, sows were randomly assigned to farrowing crates; sows remained in the same treatment group. After farrowing, routine procedures were performed and medications (i.e., iron, toltrazuril) were administered to piglets at appropriate times.

Table III.1. Treatment Groups

Treatment Group (TG)*	Dosage Level	Number of Sows
TG 1 (0X)	0 ppm tylvalosin	14
TG 2 (3X)	150 ppm tylvalosin	14

* Multiples of the approved tylvalosin inclusion rate in drinking water in parentheses

Drug Administration: The test article (TA) was AIVLOSIN® (62.5% w/w tylvalosin as tylvalosin tartrate) water soluble granules administered in drinking water targeting an inclusion rate of 150 ppm tylvalosin (3X the approved inclusion rate). Non-medicated water was used as the control article. Water was offered *ad libitum* to each sow via an individual gravity flow drinking system. Fresh batches of water were prepared for each treatment group daily. Daily samples from each batch of water prepared were assayed to confirm the actual concentration of tylvalosin or to confirm that tylvalosin was not present.

Treatment began at the expected time of estrus (on-study estrus 1). Medicated and non-medicated water were provided continuously over the course of two additional estrous cycles, at the time of breeding, through gestation, farrowing, and lactation, until piglets were weaned at 21 days post-farrowing. The treatment period was 174 to 195 days depending on farrowing date.

Measurements and Observations: Data collected for each sow at the time of farrowing included the end of farrowing (date and time), total number of piglets born, total number of piglets born alive, number of mummified piglets, number of stillborn piglets, and sex of piglets. Confirmation of lactation was recorded for each sow at 5- and 21-days post-farrowing.

Additional data recorded for each litter included veterinary inspection at 24-hours and 21-days post-farrowing to confirm sex, assess piglet health status, and document the presence of abnormalities; piglet mortality within 24 hours; number of piglets alive at 5- and 21-days post-farrowing; and piglet body weight within 24-hours, and at 7-, 14-, and 21-days post-farrowing.

The following other measurements and observations were made for piglets: general health observations (including suckling behavior and locomotion) twice daily post-farrowing.

The following other measurements and observations were made for each sow throughout the study:

1. General health observations twice daily from arrival to the test site through the end of the study.

2. Estrus observations were conducted for one or two estrous cycles (depending on arrival date) prior to treatment and then for two on-study estrous cycles prior to breeding.

3. Feed consumption and water consumption were recorded daily for each sow from SD -9 to the end of the study.

4. Sow body weight was generally measured at weekly intervals during the study.

Gross necropsies were conducted on animals that died or were euthanized during the study. A histopathological evaluation of select tissues was conducted at the pathologist’s discretion.

Statistical Methods: The following reproductive variables were analyzed.

Sow variables: conception rate (number of sows that achieved pregnancy / number of sows artificially inseminated); and farrowing rate (number of pregnant sows that had at least one live piglet / number of sows that achieved pregnancy). The experimental unit of analysis was the individual sow for sow variables. Conception and farrowing rates were analyzed using Fisher's Exact test.

Litter variables: total number of piglets born per sow (including stillborn and mummified); total number of piglets born alive per sow; percentage of mummified piglets [(number of piglets mummified / total number of piglets born) x 100]; percentage of stillborn piglets [(number of piglets stillborn / total number of piglets born) x 100]; sex ratio [(number of male piglets, including stillborn, born per litter / total number of piglets born per litter) x 100], intersex piglets were judged as not being male; 1-day survival rate [(number of piglets alive 1 day after birth / number of piglets born alive) x 100]; 5-day survival rate [(number of piglets alive 5 days after birth / number of piglets born alive) x 100]; 21-day survival rate (weaning index) [(number of piglets alive 21 days after birth / number of piglets born alive) x 100]; and average live piglet weight per litter. The experimental unit of analysis was the litter for litter variables.

Farrowing parameters and piglet survival rates were analyzed using a Wilcoxon Rank Sum test. Average live piglet weights were analyzed by a repeated measures analysis of covariance (RMANCOVA), with treatment, time and treatment-by-time terms in the model as fixed effects, litter size as the covariate, and animal within treatment as the subject in the repeated statement (MIXED procedure in SAS software version 9.4, SAS Institute Inc., Cary, NC). No adjustment was made for multiple comparisons.

All statistical tests and pairwise comparisons between treatment groups were two-sided based on a significance level of 0.10.

Results:

Test Article Administration: Sows in the tylvalosin treated group had reduced water consumption at the beginning of treatment (SD 1) when compared to pre-treatment observations. The water consumption recovered in 1 to 3 days in 13 sows. One sow continued to reject the medicated water and was removed from the study. Reduced water consumption, and therefore reduced tylvalosin consumption during this period of time, had no impact on the study results because sows were exposed to the TA for at least one additional estrous cycle before being bred.

From approximately SD 70 to SD 170, the average water consumption for treated sows was lower than the average water consumption for control sows. There were no clinical signs related to water consumption in treated sows during this time period (e.g., dehydration). From SD 70 to 150, the average water consumption was 12.5 kg/sow/day (control) and 9.6 kg/sow/day (treated). Two control sows drank excessive volumes of water (relative to the other control sows and published literature) from

approximately SD 70 to approximately SD 150. The average water consumption for each of these sows was 32.0 kg water/day and 24.8 kg water/day for this time period. These two sows likely increased the average water consumption for the control group during this time period. Median water consumption from SD 70 to SD 150 was similar between treatment groups (control: 9.2 kg/sow/day; treated: 8.6 kg/sow/day).

From SD 151-170, the average water consumption was 11.8 kg/sow/day (control) and 8.5 kg/sow/day (treated). Median water consumption for SD 151-170 was 11.2 kg/sow/day (control) and 8.5 kg/sow/day (treated). The difference in water consumption between treatment groups during this time period likely reflects differences in farrowing dates and an inherent increase in water consumption to support lactation.

Daily medicated water assays were within defined specifications (135 ppm to 165 ppm tylvalosin) for > 90% of the treatment period. Tylvalosin was not detected in daily samples of water provided to sows in the control group.

Sow Health: Sows generally remained healthy prior to breeding and throughout gestation. Feed consumption and body weight were not affected by treatment.

After treatment initiation and prior to breeding, two control sows were removed from the study and euthanized. One sow had a suspected gastric ulcer and the other sow was euthanized due to a suspected impaction. Data from these sows was not included in the analysis.

After treatment initiation, three treated sows were removed from the study and euthanized. One removal was considered to be related to the TA: this sow refused to drink the medicated water at the start of treatment, became clinically dehydrated, and was euthanized on SD 12 (prior to breeding). Water consumption data from this sow was included in the analysis. The other sow removals were not considered TA-related. Relevant data from these sows were included in the analysis of conception rate and farrowing rate. One treated sow failed to conceive following AI on two estrous cycles. This sow had signs consistent with a chronic-active pericarditis/pleuritis on post-mortem examination. The reproductive tract was normal. This instance of conception failure was determined not to be related to the TA because conception rate for the treated group (92.3%) was within the range expected in the U.S. (88-92%). One treated sow had delayed farrowing, was unable to deliver piglets following administration of oxytocin, and was euthanized. The dystocia was determined not to be related to the TA as the sow had predisposing factors (e.g., parity, heavy body weight) that likely contributed to the dystocia.

One control sow and two additional treated sows (not including the sow described above that was removed for dystocia) had difficulty farrowing and required intervention to deliver at least one piglet; these events were determined not to be related to the TA because of the distribution across both treatment groups and the presence of other contributing factors (e.g., parity, heavy body weight). Anomalous (delayed) birth of a stillborn piglet was noted in two treated sows; this was determined not to be a TA effect as other factors likely contributed, such as parity or

heavy body weight. Post-farrowing complications in sows included mastitis (one control sow) and metritis (three control sows and three treated sows). Mastitis and metritis were not considered TA related because these are not uncommon events and incidence was similar across both groups.

Piglet Health: There were no adverse events or abnormalities in piglets attributed to TA administration in the sows.

Reproductive Variables: There were no significant differences between treatment groups for conception rate, farrowing rate, 1-day survival rate, 5-day survival rate, or 21-day survival rate (weaning index). Results for average piglet weights indicate that the TA did not have a negative effect on piglet growth or viability.

As shown in Table III.2., the median total number of piglets born alive per sow in the treated group was significantly lower compared to the control group. This was determined not to be related to the TA. The results for this variable reflect the percent of stillborn piglets which was numerically, but not significantly higher in the treated group compared to control. The proportion of piglets born alive (100 x number of live piglets / total number of piglets born to each sow) was not significantly different in the treated group (median 85.7%) compared to the control group (median 89.2%). The total number of piglets born per sow was numerically, but not significantly different between groups.

Table III.2. Results for reproductive variables in Study TAS.US.180583

Variable	**TG 1 (0X) median (range)**	**TG 2 (3X) median (range)**	**P value***
Total number piglets born per sow	24.0 (15.0-28.0)	21.0 (9.0-28.0)	p = 0.16
Total number piglets born alive per sow	20.0 (13.0-23.0)	16.0 (8.0-24.0)	p = 0.069†
Mummified piglets, %	0 (0-14.8)	0 (0-9.1)	p = 0.79
Stillborn piglets, %	7.0 (0-37.5)	10.5 (0-35.7)	p = 0.69

* p-value from Wilcoxon Rank Sum test for comparison between TG1 and TG2
† p-value indicates statistical significance at 0.10 level.

The piglet sex ratio of each litter, expressed as percentage of male piglets per litter, was significantly higher in the treated group (median 60.9%) compared to the control group (median 44.6%; p = 0.004). Results for piglet sex ratio were not considered clinically relevant, and do not represent a safety concern because there were no sex-linked adverse events.

Conclusion: This study demonstrates the reproductive safety of AIVLOSIN® administered at 50 ppm continuously in drinking water for 5 consecutive days in female swine intended for breeding (replacement gilts, gestating replacement gilts,

gestating sows, lactating sows, and weaned sows). Sows should be monitored when starting treatment to ensure they continue to drink adequate amounts of water.

IV. HUMAN FOOD SAFETY

A. Microbial Food Safety

Microbial food safety (antimicrobial resistance) information for tylvalosin was evaluated using an updated hazard characterization and qualitative risk assessment procedure employed for the original approval. Several potential foodborne pathogens of public health concern were evaluated for the role they could play in foodborne disease. *Campylobacter* was identified as the primary hazard, and was used in the qualitative risk assessment.

The qualitative risk assessment procedure involved conducting 1) a *release assessment* to describe the probability that tylvalosin and its use in swine will result in the emergence of macrolide-resistant bacteria or macrolide resistance determinants in treated swine under proposed conditions of use; 2) an *exposure assessment* to describe the likelihood of human exposure to macrolide-resistant bacteria or macrolide resistance determinants through consumption of edible products from treated swine; and 3) a *consequence assessment* to describe potential human health consequences arising from exposure to macrolide resistant bacteria or macrolide resistance determinants by considering the human medical importance of macrolides used in the treatment of human infectious diseases.

It was determined that the risk of development of transferable macrolide resistance elements from this use of tylvalosin in swine is low. This decision is supported by data from animal studies that have shown tylvalosin administration does not cause substantial changes in tylvalosin susceptibility within *Campylobacter* spp. Also, changes have not been demonstrated among *Enterococcus* spp., and due to pre-existing macrolide resistance, this is of less significance.

The combination of a high consumption rate and a low contamination rate resulted in a medium probability of human exposure to *Campylobacter* in pork. It was determined that expansion of the total consumption estimate was not needed if the restriction against use in lactating and pregnant female swine and female swine intended for breeding was removed.

Macrolides are ranked as *critically important* drugs in human medicine; therefore, by default, the consequence assessment yields a high ranking, and the overall risk estimation derived was high. The conditions of use and labeled restriction of use only for groups of swine in buildings experiencing an outbreak are compatible with the Agency's risk management strategies associated with a product having an overall risk estimation of high.

Decision Statement:

The Agency's integration of the degree of risk derived from the three individual assessments (low, medium, and high) gave an overall risk estimation of high. The conditions of use are compatible with the Agency's risk management strategies for a

Category 1 drug, corresponding to the estimated high risk. Further, post-approval monitoring may be achieved from the testing of surrogate antimicrobials (erythromycin and azithromycin) in the current National Antimicrobial Resistance Monitoring System.

B. Toxicology

Reassessment of the codified acceptable daily intake (ADI) or safe concentrations was not needed for this supplemental approval. The codified ADI for total residue of tylvalosin is 47.7 µg/kg body weight per day, as listed under 21 CFR §556.748. The safe concentrations for total residue of tylvalosin in individual edible tissues of swine are 2.9 ppm for muscle, 8.6 ppm for liver, 17.3 ppm for kidney, and 17.3 ppm for fat. The FOI Summary for the original approval of NADA 141-336, dated July 6, 2012, contains a summary of all toxicology studies and information.

C. Residue Chemistry

CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-336, dated July 6, 2012, contains a summary of residue chemistry studies for swine.

This supplement does not result in any changes to the previously established withdrawal period. The withdrawal period remains zero-day. Refer to the FOI Summary for the original approval of NADA 141-336, dated July 6, 2012.

D. Analytical Method for Residues

Because a tolerance for tylvalosin in swine is not required, an official analytical method for monitoring tylvalosin residues in swine is not necessary.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to AIVLOSIN®:

USER SAFETY WARNINGS:
NOT FOR USE IN HUMANS.
KEEP OUT OF REACH OF CHILDREN.

May cause skin irritation. Tylvalosin tartrate has been shown to cause hypersensitivity reactions in laboratory animals.

People with known hypersensitivity to tylvalosin tartrate should avoid contact with this product. In case of accidental ingestion, seek medical advice.

When handling AIVLOSIN® Water Soluble Granules and preparing medicated drinking water, avoid direct contact with the eyes and skin. Wear a dust mask, coveralls and impervious gloves when mixing and handling this product. Eye protection is recommended. In case of accidental eye exposure, wash eyes immediately with water and seek medical attention. If wearing contact lenses, immediately rinse the eyes first, then remove contact lenses and continue to rinse the eyes thoroughly and seek medical

attention. Avoid eating, chewing gum and smoking during handling. Wash contaminated skin.

The Safety Data Sheet contains more detailed occupational safety information.

To report adverse effects in users, to obtain more information or obtain a Safety Data Sheet, call Pharmgate Animal Health LLC. at 1-833-531-0114.

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 (FD&C Act) and 21 CFR part 514. The data demonstrate that AIVLOSIN®, when used according to the label, is safe and effective for the effect of supplement in the General Information Section above. Additionally, data demonstrate that residues in food products derived from species treated with AIVLOSIN® will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product may be dispensed only by or on the order of a licensed veterinarian (Rx marketing status). This decision was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this drug product, and because restricting this drug product to use by or on the order of a licensed veterinarian is critical for assuring the safe and appropriate use of this drug product in animals in order to mitigate the potential for development of bacterial resistance to antimicrobial drugs.

B. Exclusivity

This supplemental approval for AIVLOSIN® qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the FD&C Act because the supplemental application included a safety study. This exclusivity begins as of the date of our approval letter and only applies to use of AIVLOSIN® for the currently approved indications (control of porcine proliferative enteropathy and control of swine respiratory disease) in female swine intended for breeding (replacement gilts, gestating replacement gilts, gestating sows, lactating sows, and weaned sows).

C. Supplemental Applications

This supplement is a Category II supplement as defined in (21 CFR 514.106(b)(2)). This supplemental approval did not require a reevaluation of certain safety or effectiveness data in the application.

D. Patent Information

For current information on patents, see the Green Book Reports in the Animal Drugs @ FDA database.