

2007-141-259
Freedom of Information Act

Date of Approval:

APR 13 2007

FREEDOM OF INFORMATION SUMMARY

APPLICATION FOR CONDITIONAL APPROVAL

Application Number 141-259

AQUAFLOL-CA1

Florfenicol
Type A medicated article
Catfish

“for the control of mortality in catfish due to columnaris disease due to
Flavobacterium columnare”

Sponsored by:

Schering-Plough Animal Health Corp.

2007.141.259

FOIS 1

TABLE OF CONTENTS

I. GENERAL INFORMATION:..... 1

II. EFFECTIVENESS:..... 2

 A. Reasonable Expectation of Effectiveness: 2

 B. Conditional Dose: 2

III. TARGET ANIMAL SAFETY:..... 2

IV. HUMAN FOOD SAFETY: 2

 A. Toxicology: 2

 B. Residue Chemistry: 3

 C. Microbial Food Safety: 3

 D. Analytical Method for Residues: 3

V. USER SAFETY: 3

VI. AGENCY CONCLUSIONS:..... 4

 A. Marketing Status: 4

 B. Exclusivity: 4

 C. Patent Information: 5

VII. ATTACHMENTS:..... 5

I. GENERAL INFORMATION:

- A. Application Number:** 141-259
- B. Sponsor:** Schering-Plough Animal Health Corp.
556 Morris Ave.
Summit, NJ 07901

Drug Labeler Code: 000061
- C. Proprietary Name(s):** AQUAFLOR-CA1
- D. Established Name(s):** Florfenicol
- E. Pharmacological Category:** Antimicrobial
- F. Dosage Form(s):** Type A medicated article
- G. Amount of Active Ingredient(s):** 500 g (1.1 lb) of florfenicol per kg
(227.27 g per lb)
- H. How Supplied:** 2 kg (4.4 lb) foil laminate pouches
(12 x 16 inches)

16 kg (35.2 lb) fiber board drum
(8 x 2.0 kg pouches)
- I. How Dispensed:** VFD
- J. Conditional Dose:** 10 mg florfenicol/kg of fish/day for
10 consecutive days
- K. Route(s) of Administration:** Oral
- L. Species/Class(es):** Catfish
- M. Indication(s):** For the control of mortality in catfish due to
columnaris disease associated with
Flavobacterium columnare.

II. EFFECTIVENESS:

A. Reasonable Expectation of Effectiveness:

Flavobacterium columnare is the bacterial pathogen associated with columnaris disease in fish. This disease is a common cause of morbidity and mortality in catfish. *F. columnare* is a long, thin Gram-negative rod. The bacteria are thought to enter the fish through breaks in the skin and the gills. During an outbreak, bacteria may be transmitted fish to fish by direct contact or through the water. Systemic infections may appear as a sudden onset of mortality in a population of fish. Total mortality may exceed 70%.

Based on information reviewed by CVM, florfenicol appears effective for controlling mortality associated with columnaris disease in freshwater-reared salmonids. The pharmacokinetic profile of florfenicol in various species of fish has been reported in the published literature. The florfenicol minimum inhibitory concentrations (MIC) ranged from 0.5 to 1.0 µg/mL for 22 isolates of *F. columnare* collected in Mississippi.

The MIC and pharmacokinetic information demonstrate a reasonable expectation of effectiveness for the use of AQUAFLO-CA1 (florfenicol) for the control of mortality in catfish due to columnaris disease associated with *F. columnare*.

B. Conditional Dose:

The conditional dose for the indication “for the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*” is 10 mg florfenicol/kg of fish/day for 10 consecutive days. The safety data presented in this document and the data to demonstrate a reasonable expectation of effectiveness provide data to establish this conditional dose.

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this conditional approval. The FOI Summary for the original approval of NADA 141-246 dated October 24, 2005, contains a summary of target animal safety studies for catfish.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this conditional approval. The FOI Summary for the original approval of NADA 141-246 dated October 24, 2005, contains a summary of all toxicology studies.

B. Residue Chemistry:

CVM did not require residue chemistry studies for this conditional approval. The FOI Summary for the original approval of NADA 141-246 dated October 24, 2005, contains a summary of residue chemistry studies for catfish.

C. Microbial Food Safety:

CVM evaluated microbial food safety information for AQUAFLO-CA1 for the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare* using a qualitative risk assessment procedure. This risk assessment procedure involved conducting 1) a release assessment to describe the probability that the antimicrobial new animal drug and its use in animals will result in the emergence and dissemination of resistant bacteria or resistant determinants in the food animal under the proposed conditions of use, 2) an exposure assessment to describe the likelihood of human exposure to the resistant bacteria or resistance determinants through consumption of edible products from treated animals, and 3) a consequence assessment to describe the potential human health consequences of exposure to the defined resistant bacteria or resistance determinants by considering the human medical importance of florfenicol in the treatment of human infectious disease.

The outcome of the release assessment was determined to be **medium**. The outcome of the exposure assessment was determined to be **low**, and the outcome of the consequence assessment was determined to be **medium**. These outcomes were integrated into an overall risk estimation of **medium** for florfenicol under the proposed conditions of use. Risk management strategies associated with an overall risk estimation of **medium** are compatible with the proposed use of florfenicol.

D. Analytical Method for Residues:

The FOI Summary for the original approval of NADA 141-246 dated October 24, 2005, contains the analytical method summaries for florfenicol in catfish.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to AQUAFLO-CA1:

“Avoid inhalation, oral exposure, and direct contact with skin or eyes. Operators mixing and handling AQUAFLO-CA1 should use protective clothing, gloves, goggles and NIOSH-approved dust mask. Wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse thoroughly with water. If irritation persists, seek medical attention. Not for human consumption. Keep out of reach of children. The Material Safety Data Sheet (MSDS) contains more detailed occupational

safety information. For a copy of the MSDS sheet, call 1-800-770-8878. For more information or to report adverse effects, call 1-800-224-5318.”

CVM looked at the material safety data sheet to conclude that user safety concerns have been appropriately addressed in the labeling.

VI. AGENCY CONCLUSIONS:

The data submitted in support of this application satisfy the requirements of section 571 of the Federal Food, Drug, and Cosmetic Act. The data demonstrate that AQUAFLO-CA1, when used according to the label, is safe and has a reasonable expectation of effectiveness for the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*. Additionally, the data demonstrate that residues in food products derived from catfish treated with AQUAFLO-CA1 will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

AQUAFLO-CA1 is conditionally approved for one year from the date of approval and is annually renewable for up to four additional one-year terms. This drug may be dispensed only under a valid Veterinary Feed Directive (VFD). Any animal feed bearing or containing this VFD drug will be fed to animals only by or on a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice. In addition, veterinary feed directives issued for this drug are not refillable.

Labeling restricts this drug to use by or on the order of a licensed veterinarian. The decision to restrict this drug to use by or on the order of a licensed veterinarian was based on the following factors: (a) adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this product, (b) restricting this drug to use by or on the order of a licensed veterinarian should help prevent indiscriminate use which could result in violative tissue residues, and (c) the rate of emergence of florfenicol-resistant organisms may be reduced by the involvement of veterinarians in product use. Because the drug will be administered in feed, the drug will be marketed as a VFD drug.

B. Exclusivity:

AQUAFLO-CA1 in the dosage form and for the intended uses conditionally approved by FDA under application number 141-259 qualifies for seven years of exclusive marketing rights beginning as of the date of conditional approval. This new animal drug qualifies for exclusive marketing rights under section 573(c) of the Federal Food, Drug, and Cosmetic Act (the act) because it has been declared a designated new animal drug by FDA under section 573(a) of the act.

C. Patent Information:

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

VII. ATTACHMENTS:

Facsimile Labeling:

AQUAFLOr-CA1 (florfenicol) Type A Medicated Article Label 2 kg
AQUAFLOr-CA1 (florfenicol) Type A Medicated Article Label 8 x 2 kg
AQUAFLOr-CA1 Type C Catfish Medicated Feed Label
AQUAFLOr-CA1 (florfenicol) Type A Medicated Article VFD Form

NDC 0061-1355-04

2 kg (4.4 lb)

Aquaflor®-CA1

(Florfenicol)

Type A Medicated Article
For Use in Catfish Feeds Only

Conditionally approved by FDA
pending a full demonstration of effectiveness
under application number 141-259

Active Drug Ingredient: Florfenicol 500 g per kg (227.27 g per lb)

Description: Each kg of Aquaflor®-CA1 contains 500 g (1.1 lb) of florfenicol in a palatable base.

Do Not Feed Undiluted



Schering-Plough

Copyright © 2007, Schering-Plough Animal Health Corp., Summit, NJ 07901, USA. Made in Ireland. All right reserved.

XXXXXXXX 2/07

7

NDC 0061-1355-04

2 kg (4.4 lb)

Aquaflor®-CA1 (Florfenicol)

Conditionally approved by FDA
pending a full demonstration of effectiveness
under application number 141-259

Type A Medicated Article
For Use In Catfish Feeds Only

Do Not Feed Undiluted

CAUTION: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive (VFD) issued by a licensed veterinarian in the course of the veterinarian's professional practice. Extra-label use of this drug in or on animal feed is strictly prohibited.

Active Drug Ingredient: Florfenicol 500 g per kg (227.27 g per lb)
Inert ingredients: Lactose and Povidone.

Description: Each kg of Aquaflor®-CA1 contains 500 g (1.1 lb) of florfenicol in a palatable base.

Indication: For the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*.

Caution: The effects of Aquaflor®-CA1 on reproductive performance have not been determined. A dose-related decrease in hematopoietic/lymphopoietic tissue may occur. The time required for the hematopoietic/lymphopoietic tissues to regenerate was not evaluated.

RESIDUE WARNING: Feeds containing Aquaflor®-CA1 must be withdrawn 12 days prior to slaughter.

IMPORTANT: Must be thoroughly mixed in feeds before use.

Mixing Instructions for Incorporation: For making Type C Medicated Feed for catfish: a) Aquaflor®-CA1 is added to other feed ingredients in the mixer, b) the medicated feed is mixed thoroughly to assure homogeneity, c) the mixture is extruded and pellets are dried, d) the pellets are dry-mixed or coated with a predetermined amount of fish or vegetable oil, and e) at the completion of mixing, the product is transferred to a storage tank for packaging or transport.

Recommended Aquaflor®-CA1 Inclusion Rates for Preparation of Type C Medicated Feed

Feeding Rate	Florfenicol Concentration In Feed	Amount of Aquaflor®-CA1 per Ton	Biomass of Fish Medicated per Ton of Feed per 10-day Treatment Period
% Biomass	Grams/ton	lbs	lbs
0.5	1,816	8.00	40,000
1.0	908	4.00	20,000
2.0	454	2.00	10,000
3.0	300	1.32	6,666
5.0	182	0.80	4,000

Feeding Directions: Feed as the sole ration for 10 consecutive days. Aquaflor®-CA1 medicated feed should only be administered once disease associated with *Flavobacterium columnare* has been appropriately diagnosed. Feeding fish at a percent of biomass and corresponding florfenicol concentration included in the table above will deliver 10 mg florfenicol per kg of fish.

Caution: Feed containing Aquaflor®-CA1 shall not be fed to catfish for more than 10 days. Following administration, fish should be reevaluated by a licensed veterinarian before initiating a further course of therapy. The expiration date for VFD for Aquaflor®-CA1 must not exceed 15 days from the date of prescribing. VFD for Aquaflor®-CA1 shall not be refilled.

WARNING: Avoid inhalation, oral exposure, and direct contact with skin or eyes. Operators mixing and handling Aquaflor®-CA1 should use protective clothing, gloves, goggles and NIOSH-approved dust mask. Wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse thoroughly with water. If irritation persists, seek medical attention. Not for human consumption. Keep out of reach of children. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. For a copy of MSDS sheet, call 1-800-770-8878. For more information or to report adverse effects, call 1-800-224-5318.

STORAGE CONDITIONS: Store at 2-30°C (36-86°F).

For customer service, call 1-800-521-5767.

Aquaflor® is a registered trademark of Schering-Plough Animal Health Corporation.

 Schering-Plough

Copyright © 2007, Schering-Plough Animal Health Corporation, Summit, NJ 07901, USA.
Made in Ireland. All rights reserved. XXXXXXXX Rev. 2/07



NDC 0061-1355-04

8 x 2.0 kg
16 kg (35.2 lb)

Aquaflor®-CA1

(Florfenicol)

Type A Medicated Article
For Use in Catfish Feeds Only

Conditionally approved by FDA
pending a full demonstration of effectiveness
under application number 141-259

Active Drug Ingredient: Florfenicol 500 g per kg (227.27 g per lb)

Description: Each kg of Aquaflor®-CA1 contains 500 g (1.1 lb) of florfenicol in a palatable base.

Do Not Feed Undiluted



Schering-Plough

Copyright © 2007, Schering-Plough Animal Health Corp., Summit, NJ 07901, USA. Made in Ireland. All right reserved.

XXXXXXXX 2/07

NDC 0061-1355-04

8 x 2.0 kg
16 kg (35.2 lb)

Aquaflor®-CA1 (Florfenicol)

Conditionally approved by FDA
pending a full demonstration of effectiveness
under application number 141-259

Type A Medicated Article
For Use In Catfish Feeds Only

Do Not Feed Undiluted

CAUTION: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive (VFD) issued by a licensed veterinarian in the course of the veterinarian's professional practice. Extra-label use of this drug in or on animal feed is strictly prohibited.

Active Drug Ingredient: Florfenicol 500 g per kg (227.27 g per lb)
Inert ingredients: Lactose and Povidone.

Description: Each kg of Aquaflor®-CA1 contains 500 g (1.1 lb) of florfenicol in a palatable base.

Indication: For the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*.

Caution: The effects of Aquaflor®-CA1 on reproductive performance have not been determined. A dose-related decrease in hematopoietic/lymphopoietic tissue may occur. The time required for the hematopoietic/lymphopoietic tissues to regenerate was not evaluated.

RESIDUE WARNING: Feeds containing Aquaflor®-CA1 must be withdrawn 12 days prior to slaughter.

IMPORTANT: Must be thoroughly mixed in feeds before use.

Mixing Instructions for Incorporation: For making Type C Medicated Feed for catfish: a) Aquaflor®-CA1 is added to other feed ingredients in the mixer, b) the medicated feed is mixed thoroughly to assure homogeneity, c) the mixture is extruded and pellets are dried, d) the pellets are dry-mixed or coated with a predetermined amount of fish or vegetable oil, and e) at the completion of mixing, the product is transferred to a storage tank for packaging or transport.

Recommended Aquaflor®-CA1 Inclusion Rates for Preparation of Type C Medicated Feed

Feeding Rate	Florfenicol Concentration in Feed	Amount of Aquaflor®-CA1 per Ton	Biomass of Fish Medicated per Ton of Feed per 10-day Treatment Period
% Biomass	Grams/ton	lbs	lbs
0.5	1,816	8.00	40,000
1.0	908	4.00	20,000
2.0	454	2.00	10,000
3.0	300	1.32	6,666
5.0	182	0.80	4,000

Feeding Directions: Feed as the sole ration for 10 consecutive days. Aquaflor®-CA1 medicated feed should only be administered once disease associated with *Flavobacterium columnare* has been appropriately diagnosed. Feeding fish at a percent of biomass and corresponding florfenicol concentration included in the table above will deliver 10 mg florfenicol per kg of fish.

Caution: Feed containing Aquaflor®-CA1 shall not be fed to catfish for more than 10 days. Following administration, fish should be reevaluated by a licensed veterinarian before initiating a further course of therapy. The expiration date for VFD for Aquaflor®-CA1 must not exceed 15 days from the date of prescribing. VFD for Aquaflor®-CA1 shall not be refilled.

WARNING: Avoid inhalation, oral exposure, and direct contact with skin or eyes. Operators mixing and handling Aquaflor®-CA1 should use protective clothing, gloves, goggles and NIOSH-approved dust mask. Wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse thoroughly with water. If irritation persists, seek medical attention. Not for human consumption. Keep out of reach of children. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. For a copy of MSDS sheet, call 1-800-770-8878. For more information or to report adverse effects, call 1-800-224-5318.

STORAGE CONDITIONS: Store at 2-30°C (36-86°F).

For customer service, call 1-800-521-5767.

Aquaflor® is a registered trademark of Schering-Plough Animal Health Corporation.



Copyright © 2007, Schering-Plough Animal Health Corporation, Summit, NJ 07901, USA.
Made in Ireland. All rights reserved. XXXXXXXX Rev. 2/07



**BLUEBIRD FEED COMPANY
BLUEBIRD CATFISH FEED
Medicated Type C Feed**

FOR USE IN CATFISH ONLY

**Conditionally approved by FDA
pending a full demonstration of effectiveness
under application number 141-259**

Indication

For the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*.

Active Drug Ingredient

Florfenicol..... 182 to 1816 g/ton*

Guaranteed Analysis

Crude Protein (Min).....%
Crude Fat (Min).....%
Crude Fiber (Max).....%
Phosphorus (Min).....%

Ingredients

Each ingredient must be named in accordance with the names and definitions adopted by the Association of American Feed Control Officials (AAFCO).

Feeding Directions

“Feed as a sole ration at a rate of ___% biomass daily for 10 consecutive days. Feeding at this rate will deliver 10 mg florfenicol per kg of fish”**.

Caution

Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive (VFD) drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian’s professional practice.

Extra-label use of this product in or on animal feed is strictly prohibited.

Feed containing florfenicol shall not be fed to catfish for more than 10 days. Following administration, fish should be reevaluated by a licensed veterinarian before initiating a further course of therapy. The expiration date for VFD for Aquaflor-CA1 (florfenicol) must not exceed 15 days from the date of prescribing. VFD for Aquaflor-CA1 shall not be refilled.

A dose related decrease in hematopoietic/lymphopoietic tissue may occur. The time required for the hematopoietic/lymphopoietic tissues to regenerate was not evaluated.

The effects of florfenicol on reproductive performance have not been determined.



RESIDUE WARNING: Feeds containing florfenicol must be withdrawn 12 days prior to slaughter.



Storage Conditions: Store in a cool, dry place. Avoid excessive moisture and heat.

Manufactured By: Bluebird Feed Mill, Robin, IN 46813

NET WEIGHT 50 lbs (22.7 kg)

Lot No. _____



*Final printed label must bear a single drug concentration.

**Feed according to the veterinarian instructions on the VFD.

2/07

20

Aquaflor®-CA1 Veterinary Feed Directive



Conditionally approved by FDA
pending full demonstration of effectiveness
under application number 141-259

Client: _____	Veterinarian: _____
Address: _____	Address: _____
_____	_____
Phone: _____	Phone: _____
Fax: _____	Fax: _____
E-mail: _____	E-mail: _____

Catfish to be Treated: Number, Total Weight (Biomass): _____
Farm Location: Farm Address, Pond Identification (Pond Number, etc.): _____

Indications: For the control of mortality in catfish due to columnaris disease associated with *Flavobacterium columnare*.

Mix into Type C Medicated Feed to Provide: Check one: 182 g/ton 300 g/ton 454 g/ton 908 g/ton 1816 g/ton

Amount of Final (Type C) Feed: _____ (Pounds or Tons) **Feeding Rate:** _____ % Biomass

Feeding Directions: Feed as the sole ration for 10 consecutive days. Feeding at this rate will deliver 10 mg florfenicol per kg of fish.

Feeding Rate	Florfenicol Concentration in Feed	Amount of Aquaflor®-CA1 per Ton	Biomass of Fish Medicated per Ton of Feed per 10-day Treatment Period
% Biomass	Grams/ton	lbs	lbs
0.5	1,816	8.00	40,000
1.0	908	4.00	20,000
2.0	454	2.00	10,000
3.0	300	1.32	6,666
5.0	182	0.80	4,000

Special Instructions

Date of Treatment: _____ (Month/Day/Year)
Expiration Date of VFD: _____ Month/Day/Year (Not to exceed 15 days from date of prescribing.)
Veterinarian's Signature: _____ **Date:** _____
License Number and State: _____

Caution: Federal law limits this drug to use under the professional supervision of a licensed veterinarian. Animal feed bearing or containing this veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive (VFD) issued by a licensed veterinarian in the course of the veterinarian's professional practice. Extra-label use (i.e., use of this VFD feed in a manner other than as provided by the VFD drug approval) is strictly prohibited.

Feed containing Aquaflor-CA1 shall not be fed to catfish for more than 10 days. Following administration, fish should be reevaluated by a licensed veterinarian before initiating a further course of therapy. The expiration date for VFD for Aquaflor-CA1 must not exceed 15 days from the date of prescribing. VFD for Aquaflor-CA1 shall not be refilled. A dose related decrease in hematopoietic/lymphopoietic tissue may occur. The time required for the hematopoietic/lymphopoietic tissues to regenerate was not evaluated. The effects of florfenicol on reproductive performance have not been determined.

RESIDUE WARNING: Feeds containing Aquaflor®-CA1 must be withdrawn 12 days prior to slaughter.

Warning: Avoid inhalation, oral exposure, and direct contact with skin or eyes. Operators mixing and handling Aquaflor®-CA1 should use protective clothing, gloves, goggles and NIOSH-approved dust mask. Wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse thoroughly with water. If irritation persists, seek medical attention. Not for human consumption. Keep out of reach of children. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. For a copy of MSDS, call 1-800-770-8878. To obtain more information or to report adverse effects, call 1-800-224-5318.

For customer service, call 1-800-521-5767.

Aquaflor® is a registered trademark of Schering-Plough Animal Health Corporation.
 Copyright © 2007, Schering-Plough Animal Health Corporation, Summit, NJ 07901, USA
 Made in Ireland. All rights reserved. 02/07 SPAH-AQF-51



White Copy- Supplier

Canary Copy- Client

Pink Copy- Veterinarian