



I-010697-P-0076-EF

APR 04 2008

U.S. Department of the Interior
Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief
4050 Bridger Canyon Road
Bozeman, MT 59715

Re: Request to complete the Effectiveness technical section for AQUAFLO

Dear Dr. Erdahl:

Based on the information in your submission dated October 4, 2007, and the information contained in investigational new animal drug (INAD) file 010697, the Division of Therapeutic Drugs for Food Animals considers the Effectiveness technical section for AQUAFLO (florfenicol) Type A medicated article for the control of mortality due to streptococcal septicemia associated with *Streptococcus iniae* in hybrid striped bass (*Morone chrysops* x *M. saxatilis*) when administered at a dose of 10 mg florfenicol/kg of fish/day for 10 consecutive days to be complete.

We will make a final decision on whether we can approve your application after we have reviewed all of the data for all applicable technical sections submitted in support of an Administrative New Animal Drug Application (NADA), NADA, or supplemental NADA, and any other information available to us, as a whole, and determined whether the requirements for approval set forth in the Federal Food, Drug, and Cosmetic Act have been met.

If you submit correspondence relating to this letter, you should reference this letter by date and the principal submission identifier found at the top of this letter. If you have any questions about this letter, please contact me at 240-276-8341 or Dr. Donald Prater, Leader, Aquaculture Drugs Team at 240-276-8343.

Sincerely,

A handwritten signature in cursive script that reads "Cindy L. Burnsteel DVM".

Cindy L. Burnsteel, DVM
Acting Director, Division of Therapeutic
Drugs for Food Animals
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

Enclosure:
Freedom of Information Summary (Effectiveness section)

Freedom of Information Summary (Effectiveness section)

II. EFFECTIVENESS**A. Dose Characterization**

Florfenicol has been shown to have a spectrum of activity against both Gram-positive and Gram-negative bacteria. The pharmacokinetic profile of florfenicol in various species of finfish has been reported in the published literature. Additionally, the published literature reports the use of florfenicol to treat a variety of bacterial diseases in finfish using a dose of 10 mg florfenicol/kg of fish/day for 10 days.

Dosage characterization trials were conducted under field conditions to evaluate florfenicol to control mortality due to septicemia in hybrid striped bass associated with *Streptococcus iniae*. Florfenicol was administered at a dose of 10 mg/kg of fish/day for 10 consecutive days. The trials did not include another treatment group for comparison. During most trials, mortality in the treated fish decreased significantly once treatment began, decreased to low levels by the end of the treatment period, and remained low following treatment.

B. Substantial Evidence

The data summarized in this section are publicly available and contained in Investigational New Animal Drug file 010697. The data were compiled by the U.S. Department of the Interior, Fish and Wildlife Service, Aquatic Animal Drug Approval Partnership Program.

1. Field Study

- a. "The Efficacy of Florfenicol-Medicated Feed to Control Mortality of Fingerling Hybrid Striped Bass Caused by Bacterial Streptococcal Septicemia, Causative Agent *Streptococcus iniae*" (Study Number FLOR-01-EFF-02.b)
- b. Investigator: Vaughn E. Ostland
Kent SeaTech Corporation
Mecca, CA

c. Study Design:

- 1) **Objective:** To evaluate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of fish/day for 10 consecutive days to control mortality due to streptococcal septicemia associated with *S. iniae* in hybrid striped bass.
- 2) **Study Animals:** Approximately 600 fingerling hybrid striped bass (*M. chrysops* x *M. saxatilis*)
- 3) **Treatment Groups:** The study included two treatment groups with three replicates of each treatment. Each replicate was a tank of fish. Treatments were assigned to tanks using a completely randomized study design.
- 4) **Drug Administration:** Florfenicol was administered in a commercial salmonid feed at a dose of either 0 or 10 mg/kg of fish daily. Study feeds were fed for 10 consecutive days.
- 5) **Measurement and Observations:** *S. iniae* was identified on cultures of brain and kidney tissue collected from two fish seven days before the start of the treatment period. The clinical signs observed were consistent with streptococcal septicemia. Approximately 100 fish were randomly transferred to each study tank. The study included a 10-day treatment period and a 7-day post-treatment period. Dead fish (mortalities) were counted and recorded twice daily. Two apparently healthy fish were collected for examination from each tank on Days 11 and 17. A low-grade, subclinical infection with *Ambiphyra* spp. and *Trichodina* spp. parasites were found on the gills and skin on both fish on both days. Fish behavior and appetite were observed throughout the study, but were not recorded. Medicated feed samples were collected on Days 1, 4, and 10 of the study for analysis of florfenicol concentration. Water temperature, pH, and dissolved oxygen concentration were measured and recorded once or twice daily. Water hardness, pH, total ammonia, and alkalinity were measured in samples from one of the study tanks on Days 2, 4, and 10.
- 6) **Statistical Analysis:** Mortality was analyzed using a mixed model with treatment group, day, and the interaction between treatment group and day as fixed effects, and tank within treatment as a random effect.

d. Results: Mortality results are included in the following table.

Table 1. Mortality results for a field effectiveness study in hybrid striped bass with a 10-day treatment period and 7-day post-treatment period.

Florfenicol Dose (mg/kg of fish)	Percent Cumulative Mortality 7 days post-treatment
0	36.7 (110/300)
10	29.3 (88/300)

The treated and untreated control groups differ significantly in the cumulative percent mortality ($P=0.0039$) after seven days post-treatment.

The mean florfenicol dose was 9.8 mg/kg of fish/day. Mean water hardness, alkalinity, pH, and ammonia were 89 mg/L, 153 mg/L, 7.1 and 5.72 mg/L, respectively. The mean water temperature was 30.4°C. The mean dissolved oxygen concentration was 12.6 mg/L.

- e. Adverse Reactions: No adverse reactions were reported in this study.
- f. Conclusion: Results of this study demonstrate the effectiveness of florfenicol for the control of mortality due to streptococcal septicemia associated with *Streptococcus iniae* in hybrid striped bass (*M. chrysops* x *M. saxatilis*) when administered at a dose of 10 mg florfenicol/kg of fish/day for 10 consecutive days.

2. Field Study

- a. "The Efficacy of Florfenicol-Medicated Feed to Control Mortality of Hybrid Striped Bass *Morone chrysops* x *M. saxatilis* Caused by Bacterial Strep, Causative Agent *Streptococcus iniae*" (FLOR-01-EFF.3-19)
- b. Investigator: Vaughn E. Ostland
Kent SeaTech Corporation
Mecca, CA
- c. Study Design:
 - 1) Objective: To evaluate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of fish/day for 10 consecutive days to control mortality due to streptococcal septicemia, associated with *S. iniae* in hybrid striped bass.
 - 2) Study Animals: Approximately 300 subadult hybrid striped bass (*M. chrysops* x *M. saxatilis*)
 - 3) Treatment Groups: The study included two treatment groups with three replicates of each treatment. Each replicate was a tank of fish. Treatments were assigned to tanks using a completely randomized study design.

- 4) **Drug Administration:** Florfenicol was administered in a commercial salmonid feed at a dose of either 0 or 10 mg/kg of fish daily. Study feeds were fed for 10 consecutive days.
- 5) **Measurement and Observations:** Four moribund fish from the reference population were examined. Based on gross observations, bacteriology, and histopathology, streptococcal septicemia was diagnosed. Test fish were randomly transferred into each of 6 test tanks. The study included a 10-day treatment period and a 7-day post-treatment period. Dead fish (mortalities) were counted and recorded twice daily. Post-treatment mortality was recorded for 7 days. One fish was collected for examination from each tank on the last day of the treatment period. The medicated feed was assayed to confirm the florfenicol concentration. Water temperature and dissolved oxygen concentration were measured and recorded at least once daily. Medicated feed samples were collected on Days 1, 5, and 10 of the treatment period for analysis of florfenicol concentration. Water hardness, pH, and alkalinity were measured on Days 4 and 11.
- 6) **Statistical Analysis:** Mortality was analyzed using a mixed model with treatment group, day, and the interaction between treatment group and day as fixed effects, and tank within treatment as a random effect.
- d. **Results:** Mortality results are included in the following table.

Table 2. Mortality results for a field effectiveness study in hybrid striped bass with a 10-day treatment period and 14-day post-treatment period.

Florfenicol Dose (mg/kg of fish)	Percent Cumulative Mortality 14 days post-treatment
0	52 (78/150)
10	19.3 (29/150)

The treated and untreated control groups differ significantly in the cumulative percent mortality ($P=0.0001$) after 14 days post-treatment.

The mean florfenicol concentration in the feed samples was 830 mg/kg and the mean florfenicol dose was 8.3 mg/kg of fish/day. Mean water hardness, alkalinity, and pH were 66 mg/L, 92 mg/L, and 6.7, respectively. The mean water temperature was 26.6 °C. The mean dissolved oxygen concentration was 13.3 mg/L.

- e. **Adverse Reactions:** No adverse reactions were reported in this study.

- f. Conclusion: Results of this study demonstrate the effectiveness of florfenicol for the control of mortality due to streptococcal septicemia associated with *Streptococcus iniae* in hybrid striped bass (*M. chrysops* x *M. saxatilis*) when administered at a dose of 10 mg florfenicol/kg of fish/day for 10 consecutive days.



U.S. Fish & Wildlife Service
Aquatic Animal Drug Approval Partnership Program



4050 Bridger Canyon Road
Bozeman, MT 59715

phone: (406) 587-9265 / fax: (406) 582-0242
www.fws.gov/fisheries/aadap

October 04, 2007

Dr. Joan Gotthardt
Director, Division of Therapeutic Drugs
for Food Animals
Document Control Unit, HFV – 199
Center for Veterinary Medicine
7500 Standish Place, MPN-2
Rockville, MD 20855

Dear Dr. Gotthardt:

The purpose of this submission is to request that the effectiveness technical section for the following claim be considered complete: "Use Aquaflor[®] administered at a concentration of 10 mg florfenicol per kg of fish per day for 10 consecutive days to control mortality of hybrid striped bass caused by *Streptococcus iniae*." As per previous CVM guidance, you informed us that to complete the effectiveness technical section data requirements for this claim, we were required to provide CVM with the following information:

1. Draft label claim language,
2. Draft language for the dose characterization portion of the effectiveness claim,
3. All other information we are aware of pertaining to the effectiveness of florfenicol to control mortality in hybrid striped bass caused by *S. iniae*, and
4. Effectiveness Freedom of Information Summaries.

The requested information is provided below. Please note that we also request that this letter be included in the efficacy technical section in support of a New Animal Drug Approval for florfenicol, and that the letter be filed in the U.S. Fish and Wildlife Service's Investigational New Animal Drug (INAD) file #10-697. Additional data (Final Study Reports) to support this request have been previously submitted to CVM. Please reference Study Numbers FLOR-01-EFF-02b (Supportive effectiveness study - CVM response letter dated August 15, 2003; INAD 010-697 P 0032) and FLOR-01-EFF.3-19 (Pivotal effectiveness study – CVM response letter dated December 09, 2005; INAD 010697-P 0041). We refer to your file number 010697-P 0041 dated April 19, 2007.

1. Draft label claim language:

For the control of mortality in hybrid striped bass due to *Streptococcus iniae*.

2. Dose Characterization:

A dosage of 10 mg florfenicol/kg fish body weight/d for 10 d was selected as the therapeutic dosage for this label based on (1) the fact that Aquaflor[®] is currently approved in the U.S. at the above described dosage, and (2) results from a number of studies have shown this dosage to be effective against a wide variety of host/pathogens, such as:

A. Channel Catfish *Ictalurus punctatus* and Enteric Septicemia, Causative Agent *Edwardsiella ictaluri* or Columnaris Disease, Causative Agent *Flavobacterium columnare*

- a. Florfenicol medicated feed was administered to channel catfish to control mortality caused by *E. ictaluri*. Treatment groups included fish fed florfenicol at dosages of (1) 10 mg/kg body weight, (2) 20 mg/kg body weight, and (3) 40 mg/kg body weight, as well as (4) negative controls, and (5) positive controls. All groups were fed for 10 d. At the end of the 7-d post-treatment period, mean cumulative mortality in the treatment groups 1- 5 were 0%, 1.25%, 1.25%, 2.5%, and 57.5%, respectively.

Gaunt, P., R. Endris, L. Khoo, T. Leard, S. Jack, T. Santucci, T. Katz, S.V. Radecki, and R. Simmons. 2003. Preliminary assessment of the tolerance and safety of florfenicol against *Edwardsiella ictaluri* administered in feed to channel catfish. *Journal of Aquatic Animal Health* 15:239 – 247.

- b. Gaunt, P.S., R.G. Endris, L. Khoo, R. Howard, A.L. McGinnis, and T.D. Santucci. 2004. Determination of dose rate of florfenicol in feed for control of mortality in channel catfish *Ictalurus punctatus* (Rafinesque) infected with *Edwardsiella ictaluri*, etiological agent of enteric septicemia. *Journal of World Aquaculture Society* 35:257 – 267.
- c. Gaunt, P., Gao D, Sun F, and Endris R,. Efficacy of florfenicol administered in feed to channel catfish to control mortality associated with *Flavobacterium columnare*. In press.

B. Sunshine Bass and *S. iniae*

- a. Florfenicol medicated feed was administered to sunshine bass (female white bass *Morone chrysops* x male striped bass *M. saxatilis*) to control mortality caused by *S. iniae*. Treatment groups included fish fed florfenicol at dosages of 0, 5, 10, 15, and 30 mg active drug/kg body weight. All groups were fed for 10 d. At the end of the 7-d post-treatment period, mean cumulative survival in the control group was 4.2%, 69.2% in the 5 mg/kg treated group,

86.7% in the 10 mg/kg treated group, and 94.2% in the 15 and 30 mg/kg treated groups.

Darwish, A. 2007. Laboratory efficacy of florfenicol against *Streptococcus iniae* infection in sunshine bass. *Journal of Aquatic Animal Health* 19:1 – 7.

C. Hybrid Striped Bass and *S. septicemia*

- a. Florfenicol use will continue under INAD 10-697 at the Kent SeaTech Corporation's Hybrid Striped Bass farm in Mecca, CA. Since 2004, a total of 182 florfenicol field effectiveness trials have been conducted at this facility to control mortality in hybrid striped bass caused by streptococcus septicemia. Additional trials will be conducted in the future until Aquaflor® is approved for this claim.
- b. Gaunt P., A. McGinnis, W. Baumgartner, A. Camus, J. Steadman, J. Cao, and R. Endris. Determination of the dose rate of florfenicol in feed for control of mortality in Nile tilapia (*Oreochromis niloticus*) infected with *Streptococcus iniae*. In press.

D. Tilapia and *S. iniae*

- a. Gaunt, P., A. McGinnis, W. Baumgartner, A. Camus, J. Cao, and R. Endris. 2005. Assessment of florfenicol efficacy against *Streptococcus iniae* *in vitro* and *in vivo* in Nile tilapia (*Oreochromis niloticus*). Presented at Aquaculture America 2005, January 17 – 20, 2005 New Orleans, Louisiana.
- b. Mark Gaikowski and the staff at the USGS Upper Midwest Environmental Sciences Center are working with the sponsor on a study to evaluate the effectiveness of florfenicol to control mortality in tilapia caused by *S. iniae* (personal communication, Mark Gaikowski, UMESC, LaCrosse, WI and Dr. Richard Endris, Schering-Plough Animal Health Corporation, Summit NJ). The studies are currently being conducted at a private hatchery in Minnesota in support of a label expansion for Aquaflor®.

E. Salmonids and Furunculosis, Causative Agent *Aeromonas salmonicida* or Coldwater Vibriosis, Causative Agent *Vibrio salmonicida*

- a. Inglis, V., R.H. Richards, K.J. Varma, I.H. Sutherland, and E.S. Brokken. 1991. Florfenicol in Atlantic salmon, *Salmo salar* L., parr: tolerance and assessment of efficacy against furunculosis. *Journal of Fish Diseases* 14:343 – 351.
- b. The efficacy of 10 mg florfenicol/kg body weight administered for 10 consecutive days to Atlantic salmon *S. salar* to control natural infections of furunculosis (causative agent, *A. salmonicida*) on five Norwegian farms was

evaluated. During the 10 d period following therapy there was an associated rapid decline in mortality caused by furunculosis.

Nordmo, R., K.J. Varma, I.H. Sutherland, and E.S. Brokken. 1994. Florfenicol in Atlantic salmon, *Salmo salar*, L.: Field evaluation of efficacy of furunculosis in Norway. *Journal of Fish Diseases*. Vol. 17, no. 3, pp. 239 – 244.

- c. Aquaflor® premix was incorporated into an extruded feed and administered to 12 pens of Atlantic salmon *S. salar* at a dosage of 10 mg florfenicol/kg fish body weight for 10 d to control mortality caused by *A. salmonicida*. Eight pens served as non-treated controls. Fish in the florfenicol-medicated pens demonstrated an immediate, substantial, and sustained drop in mortality rates when compared to the negative control pens.

Sheppard, M.E., M.J. Beattie, and C.K. Johnson. 1994. Efficacy of Aquaflor premix against furunculosis in Atlantic salmon smolts in British Columbia. *Bulletin of the Aquaculture Association of Canada*. No. 94(2):51 -53.

- d. Nordmo, R., J.M.H. Riseth, K.J. Varma, I.H. Sutherland, and E.S. Brokken. 1998. Evaluation of florfenicol in Atlantic salmon, *Salmo salar* L.: efficacy against furunculosis due to *Aeromonas salmonicida* and cold water vibriosis due to *Vibrio salmonicida*. *Journal of Fish Diseases* 21(4):289 – 297.
- e. The efficacy of 10 mg florfenicol/kg body weight administered for 10, 13, or 16 d to Atlantic salmon *S. salar* to control mortality caused by experimentally induced furunculosis. The cumulative mortality of fish treated with florfenicol was strikingly lower than the mortality of fish in the control groups.

Samuelsen, O.B., B. Hjeltnes, and J. Glette. 1998. Efficacy of orally administered florfenicol in the treatment of furunculosis in Atlantic salmon. *Journal of Aquatic Animal Health* 10:56 – 61.

- f. The efficacy of florfenicol medicated feed to control mortality of fingerling coho salmon, *Oncorhynchus tshawytscha*, caused by furunculosis (causative agent, *Aeromonas salmonicida*). USFWS Final Study Report Number FLOR-01-EFF.3-22 (see CVM response letter dated February 11, 2002 INAD 10697-H-0006).
- g. The efficacy of florfenicol medicated feed to control mortality of fingerling fall Chinook salmon, *Oncorhynchus kisutch*, caused by furunculosis (causative agent, *Aeromonas salmonicida*). USFWS Final Study Report Number FLOR-01-EFF-01 (see CVM response letter dated August 26, 2005 INAD 10697- H-0056).

- F. Salmonids and Bacterial Coldwater Disease, Causative Agent, *F. psychrophilum* or Columnaris Disease, Causative Agent, *F. columnare*
- a. Rangdale, R.E., R.H. Richards, and D.J. Alderman. 1997. Minimum inhibitory concentrations of selected antimicrobial compounds against *Flavobacterium psychrophilum* the causal agent of rainbow trout fry syndrome. *Aquaculture* 158(3-4):193 – 201.
 - b. The efficacy of florfenicol medicated feed to control mortality of fingerling steelhead trout *Oncorhynchus mykiss* caused by bacterial coldwater disease, causative agent *Flavobacterium psychrophilum*. USFWS Final Study Report Number FLOR-01-EFF-06 (see CVM response letter dated July 01, 2005 I-010697-G-0049, 0050, 0051, 0052, 0053, 0054, and 0055).
 - d. The efficacy of florfenicol medicated feed to control mortality of fingerling steelhead trout *Oncorhynchus clarki lewisi* caused by bacterial coldwater disease, causative agent *Flavobacterium psychrophilum*. USFWS Final Study Report Number FLOR-01-EFF-12 (see CVM response letter dated July 01, 2005 I-010697-G-0049, 0050, 0051, 0052, 0053, 0054, and 0055).
 - e. The efficacy of florfenicol medicated feed to control mortality of fingerling cutthroat trout *Oncorhynchus clarki lewisi* caused by bacterial coldwater disease, causative agent *Flavobacterium psychrophilum*. USFWS Final Study Report Number FLOR-01-EFF-04 (see CVM response letter dated July 01, 2005 I-010697-G-0049, 0050, 0051, 0052, 0053, 0054, and 0055).
 - f. The efficacy of florfenicol medicated feed to control mortality of fingerling cutthroat trout *Oncorhynchus clarki lewisi* caused by bacterial coldwater disease, causative agent *Flavobacterium psychrophilum*. USFWS Final Study Report Number FLOR-01-EFF-03 (see CVM response letter dated July 01, 2005 I-010697-G-0049, 0050, 0051, 0052, 0053, 0054, and 0055).
 - g. The efficacy of florfenicol medicated feed to control mortality of fingerling fall Chinook salmon, *Oncorhynchus kisutch* caused by columnaris, causative agent *Flavobacterium columnare*. USFWS Final Study Report Number FLOR-01-EFF-08 (see CVM response letter dated July 01, 2005 I-010697-G-0049, 0050, 0051, 0052, 0053, 0054, and 0055).
- G. Cod and Vibriosis, Causative Agent *Vibrio anguillarum*
- a. Samuelson, O.B., and O. Bergh. 2004. Efficacy of orally administered florfenicol and oxolinic acid for the treatment of vibriosis in cod (*Gadus morhua*). *Aquaculture* 235:27 – 35.

- b. Seljestokken, B., O. Bergh, G.O. Melingen, H. Rudra, R. Hetlelid Olsen, and O.B. Samuelsen. 2006. Treating experimentally induced *Vibrio (Listonella anguillarum)* in cod, *Gadus morhua* L., with florfenicol. *Journal of Fish Diseases* 29(12):737 – 742.

3. All Other Information:

We know of no other studies that are being conducted to evaluate the effectiveness of florfenicol to control mortality in hybrid striped bass caused by *S. iniae*.

4. Effectiveness FOI Summary:

FOI Summaries for Study Number FLOR-01-EFF-02b and FLOR-01-EFF.3-19 are appended to the letter.

The current sponsor of INAD #10-697 is Dr. David Erdahl, Branch Chief, Aquatic Animal Drug Approval Partnership Program, U.S. Fish and Wildlife Service, 4050 Bridger Canyon Road, Bozeman, MT 59715. We would like to thank you in advance for your time and consideration with respect to the above-described request. If you have questions, please contact Dr. Erdahl at (406) 994-9904.

Sincerely,



Dr. David Erdahl
AADAP Program – Branch Chief

Enclosures: 3 copies of the journal abstracts and FOI summaries referenced in this letter

Results: Mortality results are included in the following table.

Table 6. Mortality results for a field effectiveness study in coho salmon with a 10-day treatment period and 7-day post-treatment period.

Florfenicol Dose (mg/kg body weight)	Percent Cumulative Mortality
0	30.3 (331/1,092)
10	11.1 (145/1,306)

Conclusion: Results of this study support the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of body weight/day for 10 consecutive days to control mortality in coho salmon, *Oncorhynchus kisutch*, due to furunculosis caused by *Aeromonas salmonicida*. Although the clinical signs were those associated with furunculosis, the presence of an additional pathogen could have affected the level of mortality due to the predominant etiologic agent.

4. The following two studies demonstrate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of body weight/day for 10 consecutive days for the control of mortality in hybrid striped bass associated with streptococcal septicemia caused by *Streptococcus iniae*.

a. Study Number FLOR-01-EFF-02.b

Title: The Efficacy of Florfenicol-Medicated Feed to Control Mortality of Fingerling Hybrid Striped Bass Caused by Bacterial Streptococcal Septicemia, Causative Agent *Streptococcus iniae*

Investigator: Vaughn E. Ostland

Study Location: Kent SeaTech Corporation
Mecca, CA

General Design of the Study:

1. **Purpose:** To evaluate the effectiveness of florfenicol administered in feed at a dose of 10 mg florfenicol/kg of body weight/day for 10 consecutive days to control mortality in hybrid striped bass due to streptococcal septicemia, caused by *Streptococcus iniae*.
2. **Animals:** 600 fingerling hybrid striped bass
3. **Test article/controls:** Trial feeds were prepared with a commercial feed to deliver 0 and 10 mg florfenicol/kg body weight daily.
4. **Study Design:** Two moribund fish from the reference population were examined. Based on gross observations, bacteriology, and histopathology,

streptococcal septicemia was diagnosed. Beta-hemolytic Gram-positive cocci were recovered from the kidneys and brains of both fish. Test fish were randomly transferred into each of 6 test tanks. Untreated control and florfenicol-medicated groups were tested in triplicate. Trial feeds were fed for 10 consecutive days. Mortalities were counted twice daily. Fish behavior and appetite were observed throughout the study, but were not recorded. Post-treatment mortality was recorded for 7 days. Two apparently healthy fish were collected for examination from each tank on Days 11 and 17. The medicated feed was assayed to confirm the florfenicol concentration.

5. Parameters Measured: Mortality and water quality.

Results: Mortality results are included in the following table.

Table 7. Mortality results for a field effectiveness study in hybrid striped bass with a 10-day treatment period and 7-day post-treatment period.

Florfenicol Dose (mg/kg body weight)	Percent Cumulative Mortality
0	36.7 (110/300)
10	29.3 (88/300)

Statistical Analysis: Mortality was analyzed using a mixed model with treatment group, day, and the interaction between treatment group and day as fixed effects, and the tanks within treatment as a random effect. There was a statistically significant decrease in mortality in the treated group as compared to the untreated control group (P=0.0039).

Conclusion: Results of this study demonstrate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of body weight/day for 10 consecutive days to control mortality in hybrid striped bass, *Morone chrysops* X *M. saxatilis*, due to streptococcal septicemia caused by *Streptococcus iniae*.

b. Study Number FLOR-01-EFF.3-19

Title: The Efficacy of Florfenicol-Medicated Feed to Control Mortality of Hybrid Striped Bass *Morone chrysops* x *M. saxatilis* Caused by Bacterial Strep, Causative Agent *Streptococcus iniae*

Investigator: Vaughn E. Ostland

Study Location: Kent SeaTech Corporation
Mecca, CA

General Design of the Study:

1. Purpose: To evaluate the effectiveness of florfenicol administered in feed at a dose of 10 mg florfenicol/kg of body weight/day for 10 consecutive

streptococcal septicemia was diagnosed. Beta-hemolytic Gram-positive cocci were recovered from the kidneys and brains of both fish. Test fish were randomly transferred into each of 6 test tanks. Untreated control and florfenicol-medicated groups were tested in triplicate. Trial feeds were fed for 10 consecutive days. Mortalities were counted twice daily. Fish behavior and appetite were observed throughout the study, but were not recorded. Post-treatment mortality was recorded for 7 days. Two apparently healthy fish were collected for examination from each tank on Days 11 and 17. The medicated feed was assayed to confirm the florfenicol concentration.

5. Parameters Measured: Mortality and water quality.

Results: Mortality results are included in the following table.

Table 7. Mortality results for a field effectiveness study in hybrid striped bass with a 10-day treatment period and 7-day post-treatment period.

Florfenicol Dose (mg/kg body weight)	Percent Cumulative Mortality
0	36.7 (110/300)
10	29.3 (88/300)

Statistical Analysis: Mortality was analyzed using a mixed model with treatment group, day, and the interaction between treatment group and day as fixed effects, and the tanks within treatment as a random effect. There was a statistically significant decrease in mortality in the treated group as compared to the untreated control group ($P=0.0039$).

Conclusion: Results of this study demonstrate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of body weight/day for 10 consecutive days to control mortality in hybrid striped bass, *Morone chrysops* X *M. saxatilis*, due to streptococcal septicemia caused by *Streptococcus iniae*.

b. Study Number FLOR-01-EFF.3-19

Title: The Efficacy of Florfenicol-Medicated Feed to Control Mortality of Hybrid Striped Bass *Morone chrysops* x *M. saxatilis* Caused by Bacterial Strep, Causative Agent *Streptococcus iniae*

Investigator: Vaughn E. Ostland

Study Location: Kent SeaTech Corporation
Mecca, CA

General Design of the Study:

1. Purpose: To evaluate the effectiveness of florfenicol administered in feed at a dose of 10 mg florfenicol/kg of body weight/day for 10 consecutive

days to control mortality in hybrid striped bass due to streptococcal septicemia, caused by *Streptococcus iniae*.

2. Animals: 300 subadult hybrid striped bass.
3. Test article/controls: Trial feeds were prepared with a commercial feed to deliver 0 and 10 mg florfenicol/kg body weight daily.
4. Study Design: Four moribund fish from the reference population were examined. Based on gross observations, bacteriology, and histopathology, streptococcal septicemia was diagnosed. Beta-hemolytic Gram-positive cocci were recovered from the kidneys and brains of all four fish. Test fish were randomly transferred into each of 6 test tanks. Untreated control and florfenicol-medicated groups were tested in triplicate. Trial feeds were fed for 10 consecutive days. Mortalities were counted twice daily. Post-treatment mortality was recorded for 14 days. One fish was collected for examination from each tank on the last day of the treatment period. The medicated feed was assayed to confirm the florfenicol concentration.
5. Parameters Measured: Mortality, fish behavior, appetite, and water quality.

Results: Mortality results are included in the following table.

Table 8. Mortality results for a field effectiveness study in hybrid striped bass with a 10-day treatment period and 14-day post-treatment period.

Florfenicol Dose (mg/kg body weight)	Percent Cumulative Mortality
0	52 (78/150)
10	19.3 (29/150)

Statistical Analysis: Mortality was analyzed using a mixed model with treatment group, day, and the interaction between treatment group and day as fixed effects, and the tanks within treatment as a random effect. There was a statistically significant decrease in mortality in the treated group as compared to the untreated control group (P=0.0001).

Conclusion: Results of this study demonstrate the effectiveness of florfenicol administered in feed at a dose of 10 mg/kg of body weight/day for 10 consecutive days to control mortality in hybrid striped bass, *Morone chrysops* X *M. saxatilis*, due to streptococcal septicemia caused by *Streptococcus iniae*.

cc: Document Control Unit, I-010697-G-0049, G-0050, G-0051, G-0052, G-0053, G-0054, G-0055

SStorey/Aquaculture Drugs Team/June 20, 2005

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Laboratory Efficacy of Florfenicol against *Streptococcus iniae* Infection in Sunshine Bass

AHMED M. DARWISH*

U.S. Department of Agriculture, Agricultural Research Service, Harry K. Dupree Stuttgart National Aquaculture Research Center, Post Office Box 1050, 2955 Highway 130 East, Stuttgart, Arkansas 72160, USA

Abstract.—An experimental feeding trial was performed to evaluate the efficacy of florfenicol (FFC) in controlling *Streptococcus iniae* infection in sunshine bass (female white bass *Morone chrysops* × male striped bass *M. saxatilis*). Five dosage levels of FFC in medicated feed were administered daily: 0, 5, 10, 15, and 30 mg of active ingredient/kg of fish body weight. Treatment was started within 22–24 h postchallenge by waterborne exposure to virulent *S. iniae*. The FFC medication was continued for 10 consecutive days, followed by a 25-d posttreatment observation. At the conclusion of the experiment, FFC treatment significantly increased the survival of *S. iniae*-challenged sunshine bass from 4.2% in the nonmedicated (positive control) group to 69.2% in the 5-mg/kg dosage group, 86.7% in the 10-mg/kg group, and 94.2% in the 15- and 30-mg/kg groups. Survival was significantly higher in the 15- and 30-mg/kg treatment groups than in the 5-mg/kg treatment group; differences among the 10-mg/kg and higher dosage groups were not significant. Survival curve analysis using a log-rank test indicated no significant difference between curves for the 10- and 15-mg/kg groups but a significant difference between curves for the 5- and 10-mg/kg groups. At the end of the experiment, no carriers were detected in any challenged group receiving an FFC-medicated diet, but the bacterium was recovered from the nonmedicated challenged survivors of the infection. The results of the experiment suggest that the optimum therapeutic daily dose of FFC is between 10 and 15 mg/kg body weight for 10 d.

Production of sunshine bass (female white bass *Morone chrysops* × male striped bass *Morone saxatilis*) has been the fastest growing segment of the U. S. aquaculture industry over the past decade and has spread to several countries in Europe and Asia (Harrell and Webster 1997; Hiney et al. 2002). However, the expansion of sunshine bass production has been plagued by infections of *Streptococcus iniae*, a bacterium that also affects many other economically important cultured fish species (Plumb 1999a). Estimated annual losses of about US\$2 million have made *S. iniae* the most costly and threatening pathogen to the sunshine bass industry in the USA (Li et al. 2004). *Streptococcus iniae* is a Gram-positive coccus that is nonmotile, catalase negative, fermentative in glucose, and nonspore-forming (Plumb 1999a).

Proper husbandry and health management practices, such as good water quality, low levels of stress, vaccination, etc., are essential, but when an epizootic is in progress, antibiotics can be the only viable option to averting catastrophic mortalities. Florfenicol (FFC) is a broad-spectrum antibiotic that acts by binding to the 50S ribosomal RNA, thereby inhibiting bacterial protein synthesis (Plumb 1999b). Presently, there are no approved antibacterial agents for use in the

husbandry of striped bass or their hybrids. Florfenicol has been approved for controlling susceptible bacterial infections of aquacultured fish in Japan (yellowtail *Seriola quinqueradiata*, red seabream *Pagrus major*, coho salmon *Oncorhynchus kisutch*, horse mackerels *Trachurus* spp., rainbow trout *O. mykiss*, sweetfish *Plecoglossus altivelis*, tilapias *Oreochromis* spp., Japanese eel *Anguilla japonica*), South Korea (yellowtail, Japanese eel), Norway (Atlantic salmon *Salmo salar*), Canada (Atlantic salmon), and the United Kingdom (Atlantic salmon; Gaunt et al. 2004). Most recently, the U.S. Food and Drug Administration (FDA) approved FFC for treating enteric septicemia of catfish in channel catfish *Ictalurus punctatus*, thus making it the third antibiotic available for treating food fish in the USA. The potential of expanding the approval of FFC to encompass sunshine bass is therefore more promising than exploring other antibiotics that have not been approved.

There is currently no published information on the efficacy of FFC in controlling *S. iniae* infection in sunshine bass. The objective of this study was to determine the efficacy of FFC in controlling *S. iniae* infection in this species.

Methods

In Vitro Sensitivity

Antimicrobial agent.—A stock solution of FFC (Sigma-Aldrich, St. Louis, Missouri) was made by

* E-mail: adarwish@spa.ars.usda.gov

Preliminary Assessment of the Tolerance and Efficacy of Florfenicol against *Edwardsiella ictaluri* Administered in Feed to Channel Catfish

P. GAUNT*

*Mississippi State University, College of Veterinary Medicine,
Thad Cochran National Warmwater Aquaculture Center,
Post Office Box 197, 127 Experiment Station Road,
Stoneville, Mississippi 38776, USA*

R. ENDRIS

*Schering-Plough Animal Health Corporation,
1095 Morris Avenue, Union, New Jersey 07083, USA*

L. KHOO¹ AND A. T. LEARD²

*Mississippi State University, College of Veterinary Medicine,
Thad Cochran National Warmwater Aquaculture Center,
Post Office Box 197, 127 Experiment Station Road,
Stoneville, Mississippi 38776, USA*

S. JACK

*Mississippi State University, College of Veterinary Medicine,
Post Office Box 6100, Mississippi State, Mississippi 39762-6100, USA*

T. SANTUCCI

*Mississippi State University, College of Veterinary Medicine,
Thad Cochran National Warmwater Aquaculture Center,
Post Office Box 197, 127 Experiment Station Road,
Stoneville, Mississippi 38776, USA*

T. KATZ³

*Schering-Plough Animal Health Corporation,
1095 Morris Avenue, Union, New Jersey 07083, USA*

S. V. RADECKI

150 North County Road 3, Ft. Collins, Colorado 80524, USA

R. SIMMONS

*Schering-Plough Animal Health Corporation,
1095 Morris Avenue, Union, New Jersey 07083, USA*

Abstract.—A tolerance study was conducted to determine the palatability of florfenicol to channel catfish *Ictalurus punctatus*. Four tanks of fish (20 fish/tank) were assigned to each of five treatments distinguished by the amount of florfenicol given in feed per kilogram of body weight, namely, 0, 10, 20, 40, or 100 mg. Fish were fed at a rate of 2.5% of body weight per day for 10 consecutive days. On day 11, all surviving fish were euthanatized, counted, and weighed as a group. Florfenicol-medicated feed was palatable to fish at doses of 10, 20, 40, and 100 mg for 10 consecutive days.

* Corresponding author: gaunt@cvm.msstate.edu

¹ Present address: University of Pennsylvania, School of Veterinary Medicine, New Bolton Center, 382 West Street Road, Kennett Square, Pennsylvania 19348, USA.

² Present address: Merial, 115 Transtech Drive, Athens, Georgia 30601-1649, USA.

³ Present address: PRA International, 4 Industrial Way West, Eatontown, New Jersey 07724, USA.



English Title: Determination of dose rate of florfenicol in feed for control of mortality in channel catfish *Ictalurus punctatus* (Rafinesque) infected with *Edwardsiella ictaluri*, etiological agent of enteric septicemia.

Personal Authors: Gaunt, P. S., Endris, R. G., Khoo, L., Howard, R., McGinnis, A. L., Santucci, T. D., Katz, T.

Author Affiliation: College of Veterinary Medicine, Thad Cochran National Warmwater Aquaculture Center, Mississippi State University, 127 Experiment Station Road, Stoneville, MS 38776, USA.

Document Title: Journal of the World Aquaculture Society, 2004 (Vol. 35) (No. 2) 257-267



Abstract:

A dose titration study was conducted to determine the appropriate dosage of florfenicol in feed to control mortality in channel catfish *Ictalurus punctatus* associated with enteric septicemia of catfish caused by *Edwardsiella ictaluri*. Six tanks (20 fish/tank) were assigned to each of the following treatment: (1) not challenged with *E. ictaluri* and fed unmedicated feed; (2) challenged with *E. ictaluri* and fed unmedicated feed; (3) challenged and fed 5-mg florfenicol/kg body weight (kg bw); (4) challenged and fed 10-mg florfenicol/kg bw; or (5) challenged and fed 15-mg florfenicol/kg bw. Treatment was initiated the day after inoculation, and feed was administered by hand at 2.5% body weight for 10 consecutive days. Feeding activity was scored for all groups and was noted to be significantly less than the challenged, unmedicated group. Cumulative mortality in the challenged untreated group was 60%. The mortality in the unchallenged untreated group was 0%, and in the 5-, 10-, 15-mg florfenicol/kg bw group was 2.5%, 0.8%, and 2.5%, respectively. The mortality in each challenged, treated group and the non-challenged control group was significantly less than the challenged, unmedicated controls ($P < 0.0001$ for each contrast). There were no pairwise statistically significant contrasts among the florfenicol treated groups and the non-challenged control group. All 600 fish in the study were necropsied, cultured for bacteria, and examined by gross pathology. No specific lesions that could be associated with the antibiotic were observed. The efficacy of the 10 mg/kg dosage was confirmed in a separate dose confirmation study. In this study, fish in 30 tanks (20 fish/tank) were infected with *E. ictaluri* by immersion. Two days post-inoculation, fish in 15 tanks were hand-fed unmedicated feed, and 15 tanks were hand-fed medicated feed at a dosage of 10-mg: florfenicol/kg bw at 2.5% body weight for 10 d. Feeding activity was scored and was noted to be significantly less than the challenged, unmedicated group. Cumulative mortality in the florfenicol group (14%) was significantly less than cumulative mortality in the untreated group (87.3%) ($P < 0.0001$). All 600 fish were submitted for bacterial culture, necropsied, and examined for gross pathology, and once again, no specific lesions that could be associated with the antibiotic were observed. The minimum inhibitory concentration of florfenicol against *E. ictaluri* in both studies was 0.25 µg/mL. Florfenicol was palatable, safe, and efficacious for control of mortality due to infection by *E. ictaluri* in catfish.

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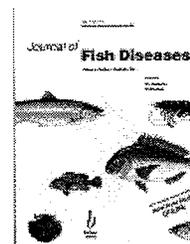
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Abstract

Florfenicol in Atlantic salmon, *Salmo salar* L., parr: tolerance and assessment of efficacy against furunculosis

V. INGLIS¹ & R. H. RICHARDS¹ K. J. VARMA², I. H. SUTHERLAND² & E. S. BROKKEN²

¹Institute of Aquaculture, University of Stirling, Stirling, Scotland²Schering-Plough Animal Health, Kenilworth, New Jersey, USA

V. Inglis, Institute of Aquaculture, University of Stirling, Stirling FK9 4LA, Scotland.

Abstract

Abstract. The efficacy of florfenicol against laboratory-induced infection with *Aeromonas salmonicida* was tested in Atlantic salmon, *Salmo salar* L., parr. Medication at three dose levels in the feed was started 24 h after bath challenge with *A. salmonicida*. The specific mortality rate in the unprotected infected control group was 75% compared with 5, 13 and 17% when florfenicol was given at dose levels of 20, 10 and 5 mg per kg body weight per day, respectively. Florfenicol was palatable to the fish at doses in excess of effective therapeutic levels and feeding for 10 days at 100 mg per kg, or for prolonged periods



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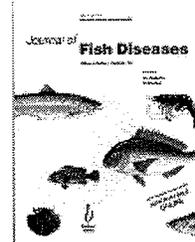
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Abstract

Florfenicol in Atlantic salmon, *Salmo salar* L.: field evaluation of efficacy against furunculosis in Norway

R. NORDMO,¹ K. J. VARMA,² I. H. SUTHERLAND³ & E. S. BROKKEN²

¹VESO Vikan AkvaVet, Allusstrand, Norway²Schering-Plough Animal Health, Union, New Jersey, USA³Cotgreen, North Berwick, Scotland

Dr K. J. Varma. Schering-Plough Animal Health, P.O. Box 3182, Union. NJ 07083, USA.

Abstract

Abstract. The efficacy of florfenicol in the control of natural outbreaks of furunculosis in Atlantic salmon, *Salmo salar* L. was evaluated on five Norwegian farms during the summer of 1992. A total of 115 245 first- or second-generation fish received florfenicol with feed at a dose rate of 10mgkg⁻¹ body weight daily for 10 consecutive days. Comparisons were made with similar pens of fish medicated with the preferred treatment for each location. In the 10 days following introduction of therapy, all treatments were associated with a rapid decline in mortality caused by infection with *Aeromonas salmonicida*. Florfenicol-medicated salmon had a lower specific mortality than those given oxolinic acid, flumequine or a trimethoprim and sulphadiazine combination. No adverse reactions to treatment



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Abstract

Evaluation of florfenicol in Atlantic salmon, *Salmo salar* L.: efficacy against furunculosis due to *Aeromonas salmonicida* and cold water vibriosis due to *Vibrio salmonicida*

Nordmo, Holth Riseth, Varma, Sutherland & Brokken

¹VESO Vikan AkvaVet, Alhusstrand, Namsos, Norway ²Schering-Plough Animal Health, Union, New Jersey, USA ³Easter Rubislaw, Edinburgh, Scotland

Correspondence to: **Correspondence** Dr R Nordmo, VESO Vikan AkvaVet, Alhusstrand, N-7800 Namsos, Norway

Abstract

Two replicated controlled trials were conducted to determine the efficacy of florfenicol against *Aeromonas salmonicida* and *Vibrio salmonicida* infections in Atlantic salmon, *Salmo salar* L., smolts kept in 25‰ salt water. Infection with *A. salmonicida* was treated with florfenicol, oxolinic acid, oxytetracycline, trimethoprim/sulphadiazine or flumequine, whereas the *V. salmonicida* infection was treated with florfenicol or oxolinic acid only. *A. salmonicida* infection was induced by the introduction of cohabitant fish previously inoculated intraperitoneally.



Minimum inhibitory concentrations of selected antimicrobial compounds against *Flavobacterium psychrophilum* the causal agent of rainbow trout fry syndrome (RTFS)

R.E. Rangdale^{a,*}, R.H. Richards^a, D.J. Alderman^b

^a Institute of Aquaculture, Stirling University, Stirling, FK9 4LA, UK

^b CEFAS Weymouth Laboratory, The Nothe, Barrack Road, Weymouth, Dorset, DT4 8UB, UK

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Abstract

The in vitro susceptibilities of 48 isolates of *Flavobacterium psychrophilum*, the causal agent of rainbow trout fry syndrome (RTFS), to the major fish farming antimicrobial agents and to a selection of other antimicrobials were assessed using a broth microdilution method. These data were used along with previous published antibiograms for *F. psychrophilum*, drug serum and tissue levels and reports clinical effect in an attempt to predict the probable therapeutic efficacy. The results indicated that resistance to the most commonly used antimicrobial compounds was significant, but that doxycycline, sarafloxacin, enrofloxacin and florfenicol showed potential as candidate compounds for in vivo trials. © 1997 Published by Elsevier Science B.V.

Keywords: *Flavobacterium psychrophilum*; *Cytophaga psychrophila*; Rainbow trout fry syndrome (RTFS); Antimicrobial susceptibility; Bacterial resistance

1. Introduction

Rainbow trout fry syndrome (RTFS) is a serious bacterial disease affecting hatchery reared rainbow trout (*Oncorhynchus mykiss* Walbaum) fry and fingerlings in many parts of Europe. The aetiologic agent of this disease is *Flavobacterium psychrophilum*

* Corresponding author. Tel: +44-01305-206640; fax: +44-01305-206600; e-mail: r.e.rangdale@cefass.co.uk.

COMMUNICATIONS

Efficacy of Orally Administered Florfenicol in the Treatment of Furunculosis in Atlantic Salmon

OLE B. SAMUELSEN¹

Department of Pharmacology, University of Bergen
Armauer Hansens Hus, N-5021 Bergen, Norway

BRIT HJELTNES AND JOHAN GLETTE

Institute of Marine Research, Department of Aquaculture
Post Office Box 1870, Strandgaten 229, N-5024 Bergen, Norway

Abstract.—This study was performed to determine the efficacy of orally administered florfenicol to treat experimentally induced furunculosis in Atlantic salmon *Salmo salar* held in seawater. A strain of the causative bacterium, *Aeromonas salmonicida* subsp. *salmonicida*, sensitive to florfenicol was used. In two trials, cohabitation challenges were performed by introducing six (trial 1) or eight (trial 2) fish—challenged in advance by an intraperitoneal injection of 2.2×10^4 colony-forming units—to eight aquaria, each containing 40 healthy fish. The treatment groups in both trials consisted of three groups receiving medication at 10, 13, and 16 d, respectively, postchallenge and one control group. An unchallenged, unmedicated group was used to determine the natural mortality in the population. The recommended therapeutic dose of 10 mg florfenicol/kg fish daily for 10 d was used. A higher mortality rate was observed in both trials for challenged unmedicated control fish than for unchallenged fish. In both trials, the cumulative mortality of fish treated with florfenicol was strikingly lower than the mortality of fish in the control groups. The mortality for the two untreated control groups was quite different; the lower mortality rate occurred in the group with the lower number of cohabitants. The mortality rates of the treated groups in trial 1 differed only slightly from each other, whereas in trial 2, the group starting medication at 10 d had a substantially lower mortality rate than the group starting medication at 16 d postchallenge.

Vaccination and improved management practices have reduced the problem with bacterial diseases in the culture of Atlantic salmon *Salmo salar* in Norway. However, when outbreaks occur, antimicrobial therapy is essential to treat the infection. With the emergence of bacterial strains resistant to the most used antibacterials like the quinolones, oxytetracycline, and the trimethoprim:sulfadiazine combination (Barnes et al. 1990; Inglis et al. 1991a; Høie et al. 1992), it would be highly desirable for the fish culturist to have ad-

ditional treatment options available. Florfenicol is a synthetic antibacterial agent with a chemical structure and a spectrum of antibacterial activity similar to those of thiamphenicol. Both florfenicol and thiamphenicol are chloramphenicol analogs where the *p*-nitro group on the aromatic ring is substituted with a sulfonylmethyl group. Florfenicol and thiamphenicol are not associated with the toxic side effects of chloramphenicol, and bacteria resistant to chloramphenicol and thiamphenicol due to production of the enzyme acetyltransferase, which inactivates the drugs, are susceptible to florfenicol (Martinsen et al. 1993).

In vitro investigations with florfenicol have demonstrated potent activity against several bacteria pathogenic to fish including *Aeromonas salmonicida* strains resistant to the other approved antibacterial agents in aquaculture (Fukui et al. 1987; Inglis and Richards 1991; Inglis et al. 1991b; Martinsen et al. 1993). Due to lower susceptibility of *Yersinia ruckeri*, florfenicol may be less effective in the treatment of *Y. ruckeri* infection in fish (Martinsen et al. 1993). Pharmacokinetic studies have shown florfenicol to be well absorbed in Atlantic salmon held in seawater with a bioavailability of 96.5% (Martinsen et al. 1993).

Efficacy studies of antibacterial agents in fish held in seawater are limited. The efficacy of florfenicol against an experimentally induced infection of *A. salmonicida* in Atlantic salmon parr was shown by Inglis et al. (1991b). In a field study, florfenicol was found to be significantly better than oxolinic acid, flumequine, and trimethoprim-sulfadiazine with respect to reducing both total and *A. salmonicida*-specific mortality in Atlantic salmon held in seawater (Nordmo et al. 1994). Elston et al. (1995a) found orally administered furfloxacin and flumequine to be effective against furunculosis in seawater-adapted Atlantic salmon.

¹ Corresponding author: ole.samuelson@ikb.uib.no



Efficacy of orally administered florfenicol and oxolinic acid for the treatment of vibriosis in cod (*Gadus morhua*)

Ole Bent Samuelsen*, Øivind Bergh

Department of Aquaculture, Institute of Marine Research, P.O. Box 1870 Nordnes, N-5817, Bergen, Norway

Received 1 March 2003; received in revised form 31 May 2003; accepted 15 June 2003

Abstract

This study was performed to determine the efficacy of orally administered oxolinic acid and florfenicol in the treatment of experimentally induced vibriosis in cod *Gadus morhua*. The *Vibrio anguillarum* strain HI-610 was used. This strain has minimum inhibitory concentration (MIC) values of 0.016 mg/l against oxolinic acid and 0.5 mg/l against florfenicol. Ten groups of 40 fish each were challenged by bath, 8.5×10^6 cells/ml for 1 h. Three days following challenge, medication with oxolinic acid or florfenicol was introduced in eight of the groups. The dosages used were 10 or 20 mg/kg day for both antibacterials and administered at days 1, 2, 4, 6, 8 and 10 following initiation of treatment for oxolinic acid and daily for 10 consecutive days for florfenicol. Among challenged unmedicated fish, the mortality started at day 3 post-challenge reaching a final cumulative mortality of 87.5% at day 22 when the experiment was terminated. In the medicated groups, the majority of deaths occurred from days 3 to 5 post-challenge reaching final cumulative mortalities of 34% and 28%, respectively, for the fish treated with 10 and 20 mg/kg of oxolinic acid and 31% and 20%, respectively, for the fish treated with 10 and 20 mg/kg of florfenicol. Survival of medicated fish in all groups were significant ($p < 0.005$) greater than survival of challenged unmedicated fish. No significant difference ($p > 0.1$) in survival was however found between groups with parallel treatment or between groups given different drugs, dosages or medication regimens. Twenty-four hours following last medication, fish ($n = 5$) given a daily dosage of 10 mg/kg of florfenicol had mean plasma and muscle concentrations of 5.0 ± 1.6 mg/l and 4.6 ± 0.9 mg/kg, respectively. Corresponding values for fish given 20 mg/kg day of florfenicol were 6.5 ± 1.3 mg/l (plasma) and 7.0 ± 2.7 mg/kg (muscle). The plasma and muscle concentrations for fish treated with

* Corresponding author. Present address: Department of Pharmacology, University of Bergen, Armauer Hansens Hus, 5021 Bergen, Norway. Tel.: +47-55-974615; fax: +47-55-974605.

E-mail address: ole.samuelsen@imr.no (O.B. Samuelsen).



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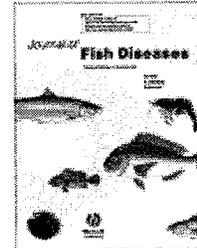
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Abstract

Treating experimentally induced vibriosis (*Listonella anguillarum*) in cod, *Gadus morhua* L., with florfenicol

B Seljestokken¹, Ø Bergh¹, G O Melingen², H Rudra¹, R Hetlelid Olsen¹ and O B Samuelsen¹

1 Department of Aquaculture, Institute of Marine Research, Nordnes, Bergen, Norway

2 Schering-Plough Animal Health, Eiksmarka, Norway

O B Samuelsen, Department of Pharmacology, Armauer Hansens Hus, 5021 Bergen, Norway
(e-mail: ole.samuelsen@imr.no)

Abstract

This study was performed to determine the efficacy of orally administered florfenicol in the treatment of experimentally induced vibriosis (*Listonella anguillarum*) in cod, *Gadus morhua*. The *L. anguillarum* strain HI-610 was used. This strain has a minimal inhibitory concentration value of 0.5 mg L⁻¹ against florfenicol. Fifteen groups of 40 fish each were challenged by bath with 1.7 × 10⁵ CFU mL⁻¹ for 1 h. Three days following challenge, medication with florfenicol was introduced in 12 of the

EFFICACY OF AQUAFLOR™ PREMIX AGAINST FURUNCULOSIS IN ATLANTIC SALMON SMOLTS IN BRITISH COLUMBIA

- 1) Sheppard, M.E., DVM. Moore-Clark Co. (Canada) Inc.
#303-909 Island Highway, Campbell River, B.C., Canada
Tel. (604)-287-9242, Fax. (604)-287-3216
- 2) Beattie, M.J., DVM. Atlantic Veterinary College, University of PEI, Canada
- 3) Johnson, C.K., DVM. Schering-Plough Animal Health, Union, NJ., USA

Abstract

An efficacy and field safety trial of a 50% florfenicol premix (AQF) was conducted under commercial aquaculture conditions during a furunculosis epizootic. The *Aeromonas salmonicida* affecting the Atlantic salmon smolts (*Salmo salar*) demonstrated neither *in vitro* nor *in vivo* susceptibility to various antibiotics. The AQF premix was incorporated into an extruded feed, and was administered to 12 pens at 0.5% body weight / day delivering a daily dose of 10 mg florfenicol / kg fish for 10 days. Eight pens served as negative controls. The AQF pens demonstrated an immediate, substantial and sustained drop in mortality rates when compared to the negative control pens. Seven days following the cessation of the treatment, the mean weekly mortality rates in the AQF pens dropped to 0.05% while the control pen mortalities remained at 1.45%. Appetites of the fish remained vigorous throughout the trial period.

Introduction

Aeromonas salmonicida infections are common in Atlantic salmon (*Salmo salar*) populations under various physiological and environmental conditions (1). The infections can progress to a clinical disease status called furunculosis. The economic losses associated with furunculosis outbreaks in Atlantic salmon are often substantial and highly significant (2, 3). Despite improvements in salmonid husbandry practices, occasions arise where antimicrobial therapy is essential in the containment of outbreaks and to minimize fish mortalities.

It is generally accepted that *Aeromonas salmonicida* can become non-responsive to certain chemotherapeutants (4). To date, the limited availability of effective and safe antibiotic compounds in Canada has contributed to the global, competitive disadvantage facing the Canadian aquaculture industry in terms of fish survival, production performance, and ultimately in the cost of production of farmed salmon internationally (5, 6). The Canadian finfish aquaculture industry requires alternative antimicrobials to help control inevitable bacterial infections and epizootics.