

Project Title: Effectiveness Research Leading to Approvals for Controlling Mortality in Coolwater and Warmwater Finfish due to *Aeromonas* Infections with Terramycin 200 for Fish® (oxytetracycline dehydrate) and Aquaflor® (florfenicol) [Termination Report]

Key Word(s): Aquaculture Drugs

Total Funds Committed: \$150,000

Initial Project Schedule: September 1, 2008 to July 31, 2012

Current Project Year: September 1, 2015 to August 31, 2016

Participants: Mark P. Gaikowski, USGS, Upper Midwest Environmental Sciences Center, Wisconsin

Extension Liaison: Joseph E. Morris, Iowa State University

Industry Liaison: Mark Willows, Binford Eagle Fisheries, North Dakota

Reason for Termination: Project objectives completed and funds have been terminated.

Project Objectives

1. Identify the etiologic agent (*Aeromonas* spp.) from isolates collected from disease outbreaks in the NCR and characterize the disease syndrome before conducting any effectiveness studies.
2. Have active, established Investigational New Animal Drug (INAD) exemptions or work with the sponsors of publicly disclosable INADs for Terramycin 200 for Fish® and Aquaflor®.
3. Develop draft pivotal effectiveness study protocols with the concurrence of the two drug sponsors (Phibro Animal Health=PAH for Terramycin 200 for Fish® and Schering- Plough Animal Health=SPAH for Aquaflor®).
4. Submit the draft pivotal effectiveness study protocols through established INADs for Terramycin 200 for Fish® and Aquaflor® for protocol concurrence from the CVM before beginning the effectiveness studies.
5. Conduct pivotal effectiveness studies on Terramycin 200 for Fish® and Aquaflor® according to Good Clinical Practice and the CVM concurred protocols.
6. Analyze the effectiveness data and prepare draft final study reports for Terramycin 200 for Fish® and Aquaflor® no more than four months after the studies are completed.
7. Submit the respective draft study reports to PAH and SPAH for their review.
8. Submit the final study reports through established INADs for Terramycin 200 for Fish® and Aquaflor® to CVM for acceptance no more than two months after PAH and SPAH have completed their reviews of the draft study reports.
9. Ensure that all questions and concerns about the final study reports are answered no more than one month after receiving comments from CVM.
10. If CVM accepts the data as proving effectiveness for the aeromonad infections encountered in the NCR, provide the acceptance letter and effectiveness studies to PAH and SPAH so that they can pursue supplemental NADA approvals for their respective drug products.

Project Summary

The efficacy of Terramycin 200 for Fish®- or Aquaflor®-medicated feed therapy to control mortality associated with motile aeromonad infections was evaluated in muskellunge and walleye under field conditions at Spirit Lake Fish Hatchery, a state walleye, northern pike, and muskellunge hatching and rearing station production facility in Spirit Lake, IA. The hatchery historically experiences rising mortality rates due to motile aeromonad septicemia as the water temperature rises in early July. Parameters evaluated included daily mortality, clinical observations, feed consumption, and water chemistry measurements..

Technical Summary and Analysis

Field efficacy trials were initiated at Spirit Lake Fish Hatchery following presumptive diagnosis of motile aeromonad infection in muskellunge (*Esox masquinongy*) fingerlings in 2011 and in walleye (*Sander vitreus*) fingerlings in 2012. In both trials, fingerlings were indiscriminately removed from the culture facility source tanks and randomly transferred to test system tanks. Fifty-eight fingerlings were transferred to each of 18 tanks in the test system consisting of 38 L (10 gal) fiberglass tanks. The test tanks were individually plumbed and received the same culture water as the source tanks. Fingerlings were offered non-mediated control diet, Aquaflor®-medicated diet (equivalent to 15 mg per kg of body weight per day [mg/kg BW/d] florfenicol), or Terramycin 200®-medicated diet (equivalent to 87.5 mg/kg BW/d oxytetracycline dihydrate). Each treatment was given to six test tanks for 10 days followed by 14 days of observation during which only the non-medicated diet was offered.

Survival of muskellunge fingerlings fed Aquaflor®-medicated feed (less than 17%) was not significantly different at 14 days post-treatment than that of non-medicated controls (16.2%). Survival of muskellunge fingerlings fed Terramycin 200®-medicated feed (greater than 32%) was significantly greater than that of non-medicated controls (figure 1; $p < 0.05$). Efficacy of either medicated feed for walleye could not be determined, because all walleye tanks received a DIQUAT concurrent treatment wrongly and inadvertently administered by hatchery personnel.

The etiological agents were identified as mostly *Aeromonas allosaccharophila* in the muskellunge and mostly *A. veronii* in the walleye with 1 occurrence of *A. media*, 1 occurrence of *A. salmonicida*, 2 occurrences of *A. sobria*, 1 occurrence of *Actinobacter* sp., 1 occurrence of *Klebsiella oxytoca*, 3 occurrences of *Pseudomonas* sp., and 12 occurrences of *Plesiomonas shigelloides*. This work was conducted under INAD numbers 11-902 and 11-366. The protocols had concurrence with the two drug sponsors and CVM, and the study was conducted following good clinical practices. Study reports were not submitted to CVM or the drug sponsors, because (1) efficacy for either drug could not be determined during the walleye trials for the reasons previously mentioned, (2) Aquaflor® was not efficacious reducing mortality in infected muskellunge, and (3) although the reduction in muskellunge mortality with Terramycin 200® was statistically significant, the reduction (~15%) was considered marginal. These data would not support the supplemental NADA approvals for either drug.

Principal Accomplishments

Efficacy could not be evaluated in walleye because of the inadvertent concurrent DIQUAT treatment. Although the reduction in muskellunge mortality with Terramycin 200® was statistically significant, the reduction (~15%) was considered marginal.

Impacts

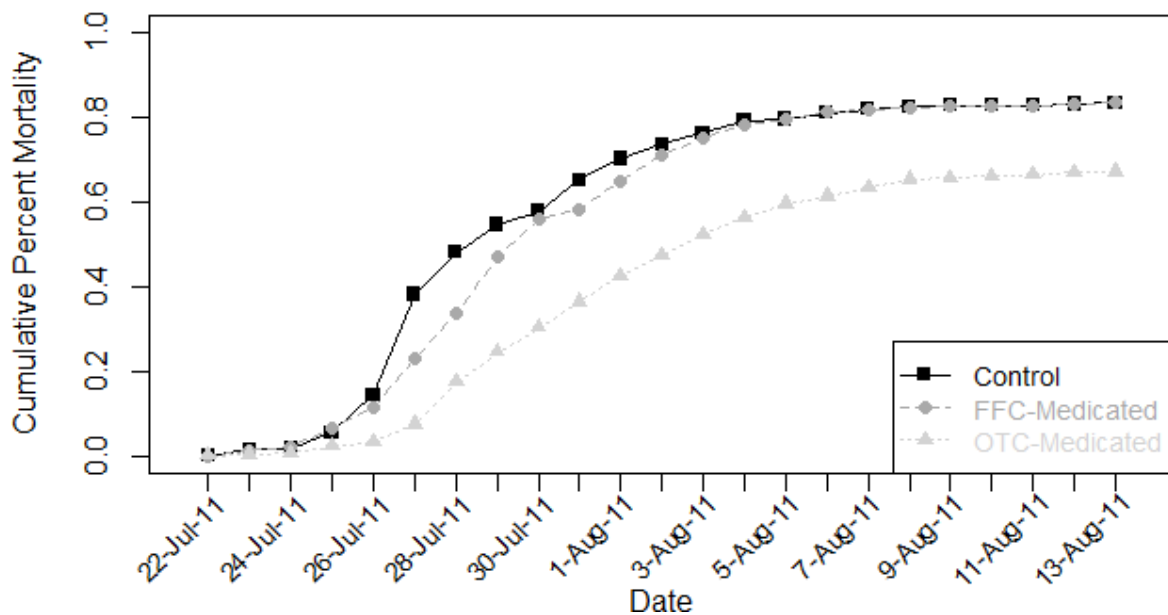
Because of the reason listed previously, these data will not support the supplemental NADA approvals for Terramycin 200® (oxytetracycline) or Aquaflor® (florfenicol) either drug.

Recommended Follow-Up Activities

None.

Technical Update

Cumulative Percent Mortality in Muskellunge



Cumulative percent mortality in muskellunge. Cumulative percent mortality of muskellunge offered non-medicated control feed, FFC-medicated feed at a nominal dose of 15 mg FFC/kg bodyweight/d, or OTC-medicated feed at a nominal dose of 82.5 mg OTC/kg BW/d for 10 days. Mortality was associated with motile aeromonad