

Finding of No Significant Impact (FONSI)

For AQUAFLO (Florfenicol) 50% Type A Medicated Article

Fed at a Dose Up to 15 mg florfenicol/kg body weight/day For Control of Mortality Associated with Bacterial Diseases in Freshwater-Reared Finfish In Recirculating Aquaculture Systems

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The Center for Veterinary Medicine has considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment. Therefore, an Environmental Impact Statement will not be prepared.

Intervet Inc. has prepared the attached Environmental Assessment (EA) dated August 15, 2013, in support of a supplemental new animal drug application (NADA) for the use of AQUAFLO (florfenicol) 50% Type A Medicated Article at a dose up to 15 mg/kg BW/day in freshwater-reared finfish in recirculating aquaculture systems (RAS).

AQUAFLO is currently approved for use in ponds and flow-through systems at a dose of 10 mg/kg/day for 10 consecutive days in freshwater-reared salmonids for control of mortality due to (1) coldwater disease associated with *Flavobacterium psychrophilum* and (2) furunculosis associated with *Aeromonas salmonicida*, as codified in 21 CFR 558.261. It is also approved for use at a dose up to 15 mg/kg/day for 10 consecutive days in (3) catfish for control of mortality due to enteric septicemia associated with *Edwardsiella ictaluri*, and (4) freshwater-reared warmwater finfish for columnaris disease associated with *Flavobacterium columnare*, and (5) streptococcal septicemia associated with *Streptococcus iniae*, also codified in 21 CFR 558.261.

Florfenicol is also approved for use in swine and cattle as codified under 21 CFR 520.955 and 522.955, respectively.

The EA addresses the potential environmental impacts from use of AQUAFLO in RAS, describing the proposed use of the product, the chemical characteristics of florfenicol, its fate in the environment, and effects to aquatic and terrestrial organisms. In particular, it evaluates the potential environmental impacts of florfenicol in receiving waters as a result of use in, and discharge from, RAS for freshwater-reared finfish. The EA consists of (1) a summary of the scientific literature relevant to the proposed use, pharmacokinetics, and environmental fate and effects of florfenicol; (2) estimates of predicted environmental concentrations (PECs) for typical and worst-case exposure scenarios; (3) initial screening and

refined risk characterizations for freshwater organisms; and (4) supporting tables and figures.

Risks from short-term (acute) and long-term (chronic) exposures for aquatic organisms, microorganisms, terrestrial plants (cress, wheat, cabbage, and mustard), and earthworms were evaluated. Effects on terrestrial plants and earthworms are not expected. Risks to sediment-dwelling organisms were not addressed in the EA because florfenicol and its metabolites are not likely to adsorb significantly to sediment. The primary interest is with aquatic surface water exposures.

Aquatic toxicity studies on florfenicol were conducted in seven (7) species for acute assessments and eight (8) species for chronic assessments. The initial screening PECs and risk quotients (RQs) are presented in the EA for low, typical and high density scenarios when 50% of the fish in a RAS facility are treated with AQUAFLOL at the same time. Refined PECs and RQs are also presented in the EA that account for metabolism in the fish and environmental fate processes that would potentially remove florfenicol from the system water prior to discharging in effluent (i.e., removal with biosolids, degradation, etc.).

Overall, it was found that the introductory environmental (effluent) concentrations from some aquaculture facilities expected to use florfenicol could potentially result in adverse effects to sensitive populations of cyanobacteria, algae, vascular plants, and aquatic invertebrates. Receiving water concentrations for most of these RAS facilities are expected to be well below the effluent concentrations predicted in the EA due to subsequent dilution and degradation of florfenicol. However, because many states do not allow the discharge of toxic substances in toxic amounts and limit the use of mixing zones in receiving waters, it is inappropriate to always account for dilution and/or degradation within receiving waters when evaluating risks for all facilities that may use AQUAFLOL.

Therefore, based on the risk characterizations in the EA, it was determined that risk mitigation was needed to insure that the discharge of florfenicol from its use in RAS facilities will not adversely impact aquatic life in surface waters. Acute and chronic water quality criteria or "benchmark" values were therefore derived for florfenicol using the available aquatic toxicity database and the U.S. Environmental Protection Agency Tier II methodology developed for the Great Lakes System. The complete procedures used to derive these benchmark concentrations are described in the EA. The acute benchmark value is 20.6 mg/L. The chronic benchmark value is 0.23 mg/L. Consistent with EPA regulations in 40 CFR 122.44(d) that allow effluent permitting authorities to use information from FDA on a pollutant, these benchmark values can be used by the appropriate National Pollutant Discharge Elimination System (NPDES) authority to establish the need for and, when necessary, set appropriate effluent discharge limits for florfenicol on a facility-by-facility basis taking into account site-specific conditions (e.g., dilution in receiving water) and other factors in conformance with applicable State and Federal water quality regulations.

The FONSI is based on inclusion of the following risk mitigation language on the AQUAFLOL animal drug label:

LIMITATIONS AND CAUTIONS FOR ALL USES

Before using this drug for the first time, you must inform the appropriate National Pollutant Discharge Elimination System (NPDES) permitting authority of your intentions and of the following information. Acute and chronic water quality benchmarks for the protection of freshwater aquatic life have been derived by FDA for florfenicol following EPA guidance for calculating Tier II water quality criteria for the Great Lakes System (40 CFR 132, App. A). The acute benchmark value (Secondary Maximum Concentration) is 20.6 mg/L (equivalent to one-half of the Secondary Acute Value). The chronic benchmark value (Secondary Continuous Concentration) is 0.23 mg/L (equivalent to the Final Plant Value). The NPDES authority may require an NPDES permit before you can discharge Aquaflor[®]. The water quality benchmark concentrations are not discharge limits, but may be used by the NPDES authority to derive such limits for the permit. Additional environmental information on Aquaflor[®] and the benchmark values are available in an environmental assessment posted at <http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/EnvironmentalAssessments/ucm300656.htm>.

Based on the information presented in the EA, and inclusion of the specified language described above on the AQUAFLOR product label, no significant environmental impacts are expected from the proposed use of AQUAFLOR (florfenicol) in freshwater-reared finfish in recirculating aquaculture systems.

{see appended electronic signature page}

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Food and Drug Administration

Electronic Signature Addendum for Submission ID

Signing Authority (Role)	Letter Date
Steven Vaughn (Office Director)	9/5/2013

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