Finding of No Significant Impact (FONSI)

For

AQUAFLOR (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

Freshwater Ponds and Flow-Through Water Systems

Intervet, Inc.
(d/b/a Merck Animal Health)
Summit, NJ

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 impact on the quality of the human environment and, therefore, an Environmental Impact Statement will not be prepared.

Intervet, Inc. is requesting approval of a supplemental New Animal Drug Application (NADA) for the use of AQUAFLOR (florfenicol) 50% Type A Medicated article for control of mortality in freshwater-reared finfish due to (a) enteric septicemia associated with *Edwardsiella ictaluri* (b) columnaris disease associated with *Flavobacterium columnare*, and (c) streptococcal septicemia associated with *Streptococcus iniae*. AQUAFLOR may be fed at a dose up to 15 mg florfenicol/kg body weight/day for 10 consecutive days.

Florfenicol is already approved for use at a dose of 10 mg/kg/day for 10 consecutive days in (1) catfish for control of mortality due to enteric septicemia associated with *E. ictaluri*, (2) freshwater-reared salmonids for control of mortality due to coldwater disease associated with *Flavobacterium psychrophilium*, and (3) freshwater-reared salmonids for control of furunculosis associated with *Aeromonas salmonicida*, as codified in 21 CFR 558.261. It is also approved for use in swine and cattle as codified under 21 CFR 520.955 and 522.955, respectively.

In support of the application, Intervet, Inc. has provided an Environmental Assessment (EA) signed December 12, 2011, which addresses the potential environmental impacts from use of AQUAFLOR in pond and flow-through aquaculture systems. A copy of the EA is attached.

The EA describes the proposed use of the product, the chemical characteristics of florfenicol, its fate in the environment, and effects to aquatic and terrestrial organisms. It especially examines the potential environmental impacts of florfenicol in receiving waters as a result of use in, and discharge from, ponds and flow-through water systems (i.e., raceways) 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.

Risk from short-term (acute) and long-term (chronic) exposure for aquatic organisms, microorganisms, terrestrial plants (cress, wheat, cabbage, and mustard), and earthworms is 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 both the typical and worst-case scenarios. Refined PECs and RQs are also presented which account for metabolism, degradation, partitioning to sediments in ponds, and the percentage of fish that may be treated with AQUAFLOR at one time.

Based on the results of acute risk characterization for pond and flow-through raceway management systems, there is no anticipated risk to fish (*Oncorhynchus mykiss* and *Lepomis macrochirus*), invertebrates (*Daphnia magna)*, and diatoms (*Navicula pelliculosa*) as representative ecological species. There are observed effects on some aquatic microorganisms. This includes algae (*Pseudokirchneriella subcapitata*), duckweed (*Lemna gibba*), and cyanobacteria (*Anabaena flos-aquae*). Under the typical scenarios for both ponds and flow-through raceways, cyanobacteria was the only species that had an RQ>1, with an RQ of 1.5. Under the pond worst-case scenario, all three representative species had RQ>1, with RQ values of 1.5, 2.0, 6.5, respectively. Under the raceway worst-case scenario, algae, duckweed, and cyanobacteria had RQ values of 3.5, 4.6, and 15, respectively. But the potentially affected species have rapid population growth, resulting in short recovery times once the florfenicol exposure is removed. Therefore, any effect would be transient and not expected to be significant. In addition, as a result of using AQUAFLOR in ponds, most, if not all, of the effects on these organisms are expected to be confined to the ponds themselves because discharges are so infrequent.

A chronic risk assessment was not needed for ponds because discharge for the ponds is not expected to occur as part of daily agricultural practices. Based on the results of chronic risk characterization for flow-through raceway systems, there is no anticipated risk to representative fish (*Pimephales promelas*), invertebrates (*Chironomus riparius*) or diatoms (*N. pelliculosa*). There are observed effects on the same aquatic microorganisms described above for acute risk characterization. Under the typical scenario, cyanobacteria was the only species that had an RQ>1 (RQ=1.6). Under the worst-case scenario, algae, duckweed, and cyanobacteria had RQ>1, with RQ values of 2.2, 4.3, 15, respectively. Again, these affected sensitive species have rapid population growth, resulting in short recovery times once the florfenicol exposure is removed. Therefore, any effect would be transient and not expected to be significant.

Chronic risk characterization under the worst-case scenario for flow-through raceway systems also resulted in RQ>1 for daphnids (*D. magna;* RQ=1.1) and rotifers (*Brachionus calcyflorus;* RQ=2.2). These RQ values were calculated using the no observed effects concentration (NOEC) for the most sensitive endpoint, reproduction. This worst-case scenario is defined by using the following very conservative assumptions: 1) simultaneous treatment of 50% of the facility, 2) a high fish density of 50 kg/m^3, and 3) a low flow rate of 3 L/s in a system containing three raceways in a

single series. Because disease outbreaks may be expected under these assumptions, this worst case scenario is not expected to occur in practice. For example, high fish density would not be expected with low flow rates. It is also anticipated that for up to 33% of florfenicol to be transiently bound to solids and feces under optimal conditions and potentially removed from the water column. This will further reduce the water PEC and subsequently the RQ values stated above by approximately 33%. Therefore, while RQ values are slightly greater than 1 under the worst-case scenario for representative aquatic animals evaluated in the EA, this scenario will not likely occur and significant environmental impacts on these organisms is not anticipated.

Overall, ecological effects on aquatic organisms in receiving waters are not expected because the release of florfenicol from ponds or flow-through raceway facilities will be short-lived and, in the use of ponds, relatively rare. Florfenicol is an antibiotic so it is expected to have some impact on microorganisms including cyanobacteria such as *A. flos-aquae*. However, because florfenicol is algalstatic (i.e., does not actually kill algae), a rapid recovery in microorganism populations is expected after exposure to florfenicol is removed. Further, there is expected to be a wide range of algae sensitivity to florfenicol and many, algal species will likely not be affected by florfenicol under the expected exposure conditions. Because there is functional redundancy in algal communities, even if sensitive species are affected, the overall productivity of the phytoplankton is likely to remain relatively constant.

Because of the wide range of species and rearing conditions considered in the EA, the document is considered sufficient to be used in support of future proposed actions on supplemental NADAs for use of AQUAFLOR for additional indications and fish species beyond those discussed in the EA, provided that the dose rate does not exceed 15 mg florfenicol/kg bw/day, the duration of feeding does not increase, and the fish species are reared in ponds or flow-through culture systems.

Based on the information in the EA, no significant environmental impacts are expected from the proposed use of florfenicol in freshwater-reared finfish in ponds and flow-through production systems.

{see appended electronic signature page}

Steven D. Vaughn, DVM
Director, Office of New Animal Drug Evaluation, HFV- 100

Electronic Signature
Addendum for Submission ID N-141246-C-0031-B1

Signing Authority (Role)	Letter Date
Steven Vaughn (Office Director)	2/24/2012

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