FINDING OF NO SIGNIFICANT IMPACT

for

Oxytetracycline-medicated Feed

for

Control of Mortality Associated with Bacterial Diseases

in Freshwater-reared Finfish

United States Geological Survey
Upper Midwest Environmental Sciences Center

The Center for Veterinary Medicine has carefully 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.

The Upper Midwest Environmental Sciences Center of the United States Geological Survey (USGS) has prepared the attached Environmental Assessment (EA) dated July 27, 2007, in support of the approval of a new animal drug application (NADA) and/or a supplemental NADA providing for label claims for the use of oxytetracycline-medicated feed in freshwater aquaculture at a the upper treatment dose regimen of 82.5 mg/kg bodyweight per day for 10 days. Use is indicated for control of mortalities associated with (1) columnaris disease (*Flavobacterium columnare*) in all freshwater-reared finfish; (2) bacterial hemorrhagic septicemia (*Aeromonas liqufaciens*) and pseudomonas disease (*Pseudomonas*) in scaled warm freshwater-reared finfish; (3) bacterial hemorrhagic septicemia (*Aeromonas liqufaciens*), furunculosis (*Aeromonas salmonicida*), and pseudomonas disease (*Pseudomonas*) in cool freshwater-reared finfish; and (4) bacterial coldwater disease (*Flavobacterium psychrophilium*) in freshwater-reared salmonids.

The EA examines the potential environmental impacts of oxytetracycline in receiving waters (both freshwater and brackish-water) as a result of use in, and discharge from, intensive freshwater aquaculture facilities using flow-through water systems. In support of a NADA or supplemental NADA for the proposed uses of oxytetracycline-medicated feed in freshwater, a drug sponsor should submit or reference the USGS technical section complete letter, EA and this Finding of No Significant Impact.

The assessment consists of (1) a summary of the scientific literature relevant to the present uses, potential impacts, and environmental fate and effects of oxytetracycline; (2) a risk characterization for certain freshwater aquaculture uses based on data from the scientific literature, results of a USGS survey detailing the projected use of oxytetracycline at public and private aquaculture facilities, and facility use data generated under public-disclosable INAD 9332 issued to the U.S. Fish and Wildlife Service; and (3) tables, figures, and appendixes which include projected and actual hatchery use data, a semi-quantitative fate evaluation using the WASP-6 model, hatchery discharge estimates, and summaries of key toxicity studies.

The EA contains an extensive discussion of the stability, mobility, and environmental fate of oxytetracycline in aquatic system including the potential for this compound to undergo hydrolysis, photodecomposition, chelation, and adsorption to soil, sediment and particles in the water column. Limited biodegradation and bioaccumulation data are also presented. Oxytetracycline sorbs to a dissolved organic matter (DOM) and variety of solids including suspended hatchery biosolids (e.g., fish feed and fish feces), inorganic suspended solids, and sediment. It is biologically available when unchelated and in the freely-dissolved form, but is largely biologically unavailable when sorbed to either organic or inorganic solids, or associated with DOM. Environmental fate modeling predicts that the large majority of oxytetracycline administered at an aquaculture facility will be discharged to receiving waters attached to hatchery solids or deposited into the facility's settling pond, if one is present, and subsequently buried.

Ecotoxicity data for oxytetracycline are available for a wide variety of aquatic receptors including multiple species of fish, invertebrates, algae, and bacteria. Data indicate that microorganisms (i.e., bacteria, algae) present in aquatic ecosystems are generally much less tolerant of oxytetracycline exposures than are fish and invertebrates. Median effect concentrations (EC_{50} values) for bacteria and algae generally range from 0.2 to 4 mg/L for exposures up to 7 days, while those for fish and invertebrates (e.g., *Daphnia magna*) are generally at or above 75 mg/L. Chronic toxicity data are limited, but in a 21-d reproduction study on *Daphnia magna*, the EC_{10} and EC_{50} values were 7.4 and 46.2 mg/L, respectively.

Extensive risk characterizations are presented in the EA using the available toxicity data and Environmental Introduction Concentrations (EICs) calculated based on facility use data generated under the U.S. Fish and Wildlife Service's public-disclosable INAD 9332. The methodology for estimating EICs conservatively assumes that all oxytetracycline in the water column is present in the freely-dissolved, bioavailable form. The 95th percentile EIC value thus represents a "reasonable worst-case" effluent discharge concentration and the one generally most appropriate for assessing risks. The 95th percentile EIC was 19.1 µg/L and represented the 792nd highest EIC out of 834 total INAD data points. This compared to a median EIC (i.e., 50th percentile value for all facilities) of 2.1 µg/L.

Risk quotients determined for acute and chronic effects are less than 1.0 for green algae, aquatic macrophytes, aquatic invertebrates, and fish species whether based on the median or 95th percentile EIC, thus it is expected that the proposed uses of oxytetracycline in aquaculture will not cause significant impacts on these receptors. Bacteria and blue-green algae (which are also considered cyanobacteria) are the only taxonomic groups which have risk quotients greater than one when using the 95th percentile EIC for assessment. Factors which mitigate risks to populations of bacteria and sensitive algae are discussed in the EA within the individual subsections of Section 8. These factors include the following:

- Long-term exposures in receiving waters will be at concentrations considerably reduced from the EIC values (i.e., effluent discharge concentrations) used for the risk quotient calculations due to dilution after discharge;

- Exposures will be reduced as oxytetracycline becomes biologically unavailable by sorption to suspended particles in the receiving waters, by chelation with divalent cations present in water, and as oxytetracycline undergoes biotic and abiotic degradation in the receiving waters;

- Discharges of oxytetracycline will be relatively small, isolated and intermittent; therefore, it is unlikely that there will be significant long-term effects on the numbers and types of microflora/fauna present at any location;

- Algae and bacteria have the ability to quickly repopulate after a temporary depletion;

The conservative nature of the methodology used to estimate the EICs in the revised EA is such that these concentrations did not take into account the environmental fate (e.g., dilution, adsorption, degradation) of oxytetracycline prior to, or after, discharge to receiving waters. For example, removal in settling ponds prior to discharge was not accounted for even though modeling showed that this removal will be significant. Dilution following discharge was also not factored into the calculations. Given that these factors will significantly mitigate both the temporal and spatial distribution of oxytetracycline in receiving waters, it is concluded that any adverse effects on bacteria or algal populations will not be widespread, persistent, or significant in nature.

The information available is adequate to support a conclusion that use of oxytetracycline in intensive freshwater aquaculture in finfish under a dose regimen up to 82.5 mg/kg bodyweight per day for 10 days is not expected to have a significant impact on the environment.

February 20, 2008
Date

Director, Office of New Animal Drug Evaluation, HFV-100

Attachment: Environmental Assessment Dated July 27, 2007