

FINDING OF NO SIGNIFICANT IMPACT
for
HALAMID AQUA
(Chloramine-T Powder for Immersion)
for
Control of Mortality in All Freshwater-reared Finfish Due to
Bacterial Gill Disease and External Columnaris Disease

Axcentive SARL

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 April 2007, in support of a new animal drug application (NADA) for the use of HALAMID AQUA (Chloramine-T Powder for Immersion; active ingredient chloramine-T trihydrate) as a waterborne therapeutant in freshwater aquaculture. Use is to control mortality in freshwater-reared finfish due to bacterial gill disease and in freshwater-reared finfish due to external columnaris disease. For each therapy, treatments will be administered in water as either a continuous-flow immersion bath or as a static bath for as long as 60 minutes at concentrations up to 20 mg/L on consecutive or alternate days, as many as three times.

The USGS EA examines the potential environmental impacts of chloramine-T in receiving waters as a result of use in, and discharge from, intensive freshwater aquaculture facilities using flow-through water systems. Potential effects from uses of chloramine-T in estuarine or marine environments (e.g., on shellfish or on fish in net pens) are not addressed in the EA. Effects due to use in extensive aquaculture (i.e., large ponds with no or little water flow) or recirculating systems have also not been evaluated. The EA also summarizes proprietary data submitted independently by Axcentive SARL and found to be adequate and reliable.

The assessment consists of (1) a summary of the scientific literature relevant to the present uses, potential impacts, and environmental fate and effects of chloramine-T (including information on degradation products); (2) a risk characterization for certain freshwater aquaculture uses based on data from the scientific literature and results of a recent USGS survey detailing the projected use of chloramine-T at public and private aquaculture facilities; and (3) tables, figures, and appendixes which include toxicity data and risk results, relevant exposure and fate models, hatchery schematics, projected hatchery use data, and hatchery discharge estimates.

Data from an extensive USGS survey of 100 public and private aquaculture facilities in 25 states were used to determine the present and projected use of chloramine-T for fish

culture. Of those surveyed, 60 hatcheries reported that they already used or plan to use chloramine-T once approved. Hatcheries that use chloramine-T could be expected to discharge less than 40 days per year (an average of 10 therapies per year and an average of 3.7 treatments per therapy).

Survey data were used in the EA to estimate environmental introduction concentrations (EICs) of chloramine-T for typical (average daily) and worst-case (lowest annual) internal water flow scenarios. Average effluent discharge concentrations were estimated over 1, 5, and 21-day periods taking into account the number and frequency of expected treatments at each facility. Median estimated EICs for all hatcheries that were expected to use chloramine-T ranged from 0.40 mg/L for a 1-day period to 0.09 mg/L for a 21-day period based on typical flow rates, and from 0.40 (1-day) to 0.12 (21-day) mg/L based on low flow rates. The 95th percentile EIC values were generally within a factor of two of the median EIC values.

Environmental fate data in the EA indicate that aqueous chloramine-T can remain unchanged, release its chlorine as aqueous free chlorine, or donate its chlorine directly to produce ammonia chloramines or other chlorinated organic-N or non-N compounds. Chloramine-T is a mild chlorinating agent which produces p-toluenesulfonamide (p-TSA) as its primary degradation product through dechlorination. The rate at which chloramine-T decomposes in natural water can vary from hours to days or weeks, depending on specific chemical, biological, and physical factors; however, it is not expected to produce free chlorine at concentrations of concern at the proposed treatment and effluent discharge concentrations.

Ecotoxicity data in the EA show that most species of microorganisms (i.e., bacteria, algae), zooplankton, and fish have a similar sensitivity to chloramine-T. Effects of short-term exposures on sensitive fish (e.g., channel catfish, rainbow trout) and invertebrates (e.g., *Daphnia magna*; *Ceriodaphnia dubia*) have been observed at concentrations in the low mg/L (ppm) range, while effects on two sensitive algal species have been reported at levels approximately 10 times lower. Acute toxicity data for several fish species indicate that chloramine-T toxicity increases with decreasing pH, although the magnitude of the effect varies greatly. Limited data for aquatic invertebrates support this trend. Chronic studies on *Daphnia magna* and the fathead minnow did not show significantly enhanced toxicity with extended exposures to chloramine-T, producing a no observable effect concentration (NOEC) of 1.1 mg/L in both studies.

Using available ecotoxicity data, both initial and refined risk characterizations were conducted in the EA. It was found that the introductory concentrations from a majority of aquaculture facilities expected to use chloramine-T could potentially result in adverse effects to sensitive populations of algae, invertebrates, and fish species. Receiving water concentrations for most of these facilities are expected to be well below the introductory concentrations predicted in the EA due to subsequent dilution and degradation of chloramine-T. However, many states do not allow the discharge of toxic substances in toxic amounts, therefore, it is inappropriate to automatically account for dilution and/or degradation within receiving waters when evaluating risk for all facilities.

Based on the risk characterizations in the EA, it was determined that risk mitigation was needed to insure that the discharge of chloramine-T from its use in aquaculture will not adversely impact aquatic life in surface waters. Therefore, an acute water quality criterion or "benchmark" value was derived for chloramine-T using the available toxicity database and U.S. Environmental Protection Agency Tier II methodology developed for the Great Lakes System. The complete procedure used to derive this benchmark concentration is

described in the EA. The acute benchmark value is 0.13 mg/L. It should be protective of aquatic life when the receiving water pH is at or above pH 6.5. This benchmark 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 on a facility-by-facility basis using site-specific conditions (e.g., pH, receiving water dilution) in conformance with applicable State and Federal water quality regulations.

Although the risk characterizations in the EA indicate a potential for chronic effects on certain aquatic life (i.e., sensitive algal species) at some of the hatchery sites expected to use chloramine-T, there are several reasons why a chronic water quality benchmark is not believed to be necessary to mitigate these potential risks. These reasons are summarized and discussed briefly in Section 8.7 of the EA. They include the fact that most exposures to chloramine-T will not be chronic in nature and information which indicates that the chronic water quality benchmark, if one were derived, would not likely be significantly lower than the acute water quality benchmark.

The FONSI is based on inclusion of the following risk mitigation language on the HALAMID AQUA 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. A water quality benchmark for the protection of freshwater aquatic life has been derived by FDA. The acute benchmark is 0.13 mg/L, which is equivalent to the Secondary Maximum Concentration (one-half of the Secondary Acute Value). The NPDES authority may require an NPDES permit before you can discharge chloramine-T. The water quality benchmark concentration is not a discharge limit, but it may be used by the NPDES authority to derive one for the permit. The acute benchmark should be protective of aquatic life when the receiving water pH is at or above pH 6.5. Additional environmental information on chloramine-T and the benchmark value are available in an environmental assessment posted at <http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/EnvironmentalAssessments/ucm300656.htm>

ENVIRONMENTAL WARNING

Chloramine-T may be hazardous to aquatic life, including invertebrates and algae. Do not release the undiluted product directly into natural waterways.

Improper storage and disposal of chloramine-T could potentially result in releases that cause adverse effects on aquatic life, therefore appropriate storage and disposal instructions are needed on the drug label. This FONSI is based on inclusion of the following storage and disposal statements on the HALAMID AQUA label. These statements differ slightly from those described in the USGS EA, but are consistent with their intent to reduce potential releases of chloramine-T to the environment.

STORAGE:

- Store in a manner designed to prevent spills that may result in discharge to surface waters.
- Exercise due caution to prevent damage or leakage from the container.

DISPOSAL:

- Implement procedures for properly containing, cleaning, and disposing of any spilled material.
- Contact your State Environmental Control Agency, or the Hazardous Waste Representative at the nearest EPA Regional Office for guidance on disposal of unused product, empty containers, and spilled materials,
- Do not allow undiluted product to escape into sewage or surface water.
- Empty containers should be cleaned of residual drug before disposal or return. Follow label warnings even after container is emptied because empty containers can still contain drug residues.

In addition, because effects due to the use of HALAMID AQUA in extensive aquaculture (i.e., large ponds with no or little water flow) and recirculating aquaculture systems (those which have little discharge) have not specifically been evaluated to date, the FONSI is based on inclusion of the following statements on the product label:

- Do not use in earthen ponds or systems that cannot be flushed after treatment.
- If used in recirculating systems, bypass biofilter during treatment and flushing. Effects on biofilter and water quality have not been evaluated. Ensure that drug is flushed from the system after treatment.

Conclusion

The information available is adequate to conclude that the proposed use of HALAMID AQUA in intensive aquaculture for treatment of freshwater-reared finfish via continuous flow-through or static bath exposures (at concentrations up to 20 mg/L for as long as 60 minutes on consecutive or alternate days, for as many as three times) is not expected to have a significant impact on the environment.

Date

Steven D. Vaughn, DVM
Director, Office of New Animal Drug Evaluation, HFV-100
Center for Veterinary Medicine
U.S. Food and Drug Administration

Attachment: USGS Environmental Assessment for chloramine-T dated April 2007

Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Steven Vaughn (Office Director)	2/13/2014

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.