



INAD 004000 G 0096

Dave Erdahl, Ph.D.
National INAD Coordinator
USFWS Fish Technology Center
4050 Bridger Canyon Road
Bozeman, Montana 59715

FEB 4 2003

Dear Dr. Erdahl:

We refer to your submission dated October 22, 2002, to your investigational new animal drug (INAD) file for the use of chloramine-T to control mortality in freshwater-reared salmonids caused by bacterial gill disease when administered as a 60 minute static or flow-through bath at a concentration of 12-20 mg/L on 3 consecutive or alternate days. You requested review of the target animal safety and effectiveness sections of a draft Freedom of Information (FOI) Summary.

We have completed our review and have the following comments. Your FOI Summary has been revised and reformatted according to the Program Policy and Procedures Manual Guide 1243.5761 – Freedom of Information Summary for a New Animal Drug Application. The target animal safety and effectiveness sections of the FOI Summary are complete. A copy of the draft FOI Summary is included.

Future correspondence regarding this submission to the file for your INAD exemption should reference the date of this letter and our file number, INAD 004000 G 0096, and be addressed to the Document Control Unit, HFV-199. Please include only one request per submission, clearly stating the request in the first paragraph of the submission.

If you have any questions or comments regarding this correspondence, please telephone Dr. Susan Storey, Aquaculture Drugs Team at 301-827-7581.

Sincerely yours,

Joan C. Gotthardt, D.V.M.
Director, Division of Therapeutic
Drugs for Food Animals
Office of New Animal Drug Evaluation
Center for Veterinary Medicine

Enclosure

Date of Approval: _____

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA xxx-xxx

(proprietary and established product name)

“For the control of mortality in freshwater-reared salmonids caused by bacterial gill disease.”

Sponsored by:

(Sponsor with US address)

1. GENERAL INFORMATION

- a. File Number: NADA xxx-xxx
- b. Sponsor: (Company Name)
- c. Drug Labeler Code: xxxxxx
- d. Established Name: Chloramine-T
- e. Proprietary Name: (Product name)
- f. How Supplied: 25 kg plastic container
- g. How Dispensed: Over the counter
- h. Amount of Active Ingredient: 99.0-100%
- i. Route of Administration: Flow-through or static bath
- j. Species/Class: Salmonids
- k. Recommended Dosage: 12-20 mg/L for 60 minutes for 3 consecutive days or 3 treatments on alternate days
- l. Pharmacological Category: Sanitizing agent
- m. Indications: For the control of mortality in freshwater-reared salmonids caused by bacterial gill disease.

2. *EFFECTIVENESS:*

a. *Substantial Evidence*

1) **Study Number 4000-1-004**

Study Title: "Efficacy of Chloramine-T to Control Mortality Caused by Bacterial Gill Disease (BGD) in Fingerling Rainbow Trout"

Study Director: James D. Bowker

Study Location: Hotchkiss National Fish Hatchery
807 – 3150 Lane
Hotchkiss, Colorado 81419

General Design of the Study:

- a. Purpose: To evaluate the effectiveness of chloramine-T as a bath at a concentration of 12 mg/L for 60 minutes every other day for three treatments for the control of mortality associated with bacterial gill disease caused by flavobacters in rainbow trout.
- b. Animals: Approximately 1000 rainbow trout fingerlings
- c. Test article: Chloramine-T, Akzo Nobel Chemical, Inc.
lot number: 029905530037
- d. Study Design: The fish were randomly transferred into each of 6 test tanks. Untreated control and chloramine-T treatment groups were tested in triplicate. Before treatment, 5 fish from each tank were evaluated for the presence of BGD. Sixty minute chloramine-T treatments of 12 mg/L were administered as a static bath on Days 1, 3, and 5. The study duration was 19 days. Chloramine-T concentrations in the treated tanks were confirmed during treatments. Mortalities were counted twice daily. Fish were examined (body surface, fins, gills and internal organs) and kidney inocula were cultured for the presence of systemic bacteria. Stained gill imprint slides were examined. Stained gill squash slides were examined from 5 fish prior to the first treatment, on Day 5 following the last treatment and on Day 19.
- e. Parameters measured: Mortality and water quality parameters

Statistical Analysis: Mortality rates were analyzed using generalized linear models (GENMOD procedure), using a binomial error distribution and a logit link function. Treatment was included as a fixed effect and an overdispersion parameter was included.

Results: Mortality results are included in the following table.

Table 1. Percent cumulative mortality from Day 1 through 19.

Chloramine-T Concentration	Cumulative Mortality	Percent Cumulative Mortality	LSMean (GENMOD)
0 mg/L	773	25.8	-1.0581
12 mg/L	171	5.7	-2.8060
		p-value	<.0001

Conclusion: Chloramine-T administered at a concentration of 12 mg/L for 60-minutes every other day for 3 treatments was effective in the control of mortality associated with bacterial gill disease caused by flavobacters in rainbow trout.

2) Study Number 4000-1-003

Study Title: "Efficacy of Chloramine-T to Control Mortality in Apache Trout (*Oncorhynchus apache*) Caused by Bacterial Gill Disease Associated with Flavobacters"

Study Director: James D. Bowker

Study Location: Alchesay-Williams Creek National Fish Hatchery
Whiteriver, Arizona 85941

General Design:

- a. Purpose: To evaluate the effectiveness of chloramine-T as a bath at a concentration of 12 mg/L administered for 60 minutes every other day for three treatments for the control of mortality associated with bacterial gill disease caused by flavobacters in apache trout.
- b. Animals: Approximately 2340 apache trout fingerlings
- c. Test article: Chloramine-T, Akzo Chemical, Inc.
lot number: 0299408580654
- d. Study Design: The fish were randomly transferred into each of 6 test tanks. Untreated control and chloramine-T treatment groups were tested in triplicate. Sixty minute chloramine-T treatments of 12 mg/L were administered as a static bath on Days 1, 3, and 5. The study duration was 19 days. Chloramine-T concentrations were confirmed during treatments. Mortalities were counted twice daily. Before treatment and at the end of the study, 5-6 fish from each tank were evaluated for the presence of BGD. Fish were examined (body surface, fins, gills and internal organs) and kidney inocula were cultured. Stained gill squash slides were examined from 5 fish before treatment and after the third treatment.
- e. Parameters Measured: Mortality and water quality parameters

Statistical Analysis: Mortality rates were analyzed using generalized linear models (GENMOD procedure), using a binomial error distribution and a logit link function. Treatment was included as a fixed effect and an overdispersion parameter was included.

Results: Mortality results are included in the following table.

Table 2. Percent cumulative mortality from Day 1 through 19.

Chloramine-T Concentration	Cumulative Mortality	Percent Cumulative Mortality	LSMean (GENMOD)
0 mg/L	6397	98.1	3.9194
12 mg/L	2508	38.9	-0.4512
		p-value	<.0001

Conclusion: Chloramine-T administered at a concentration of 12 mg/L for 60-minutes every other day for 3 treatments was effective in the control of mortality associated with bacterial gill disease caused by flavobacters in apache trout.

3) Study Number 4000-1-002

Title: "Efficacy of Chloramine-T to Control Mortality Caused by Bacterial Gill Disease Associated with Flavobacters in Fall Chum Salmon (*Oncorhynchus keta*)"

Study Director: James D. Bowker

Study Location: Quilcene National Fish Hatchery
281 Fish Hatchery Road
Quilcene, Washington 98376

General Design of the Study:

- a. Purpose: To evaluate the effectiveness of chloramine-T as a bath at a concentration of 12 mg/L (12 ppm) for 60 minutes every other day for 3 treatments for the control of mortality associated with bacterial gill disease caused by flavobacters in fall chum salmon.
- b. Animals: Approximately 13,419 to 19,248 fall chum salmon
- c. Test article: Chloramine-T, Akzo Chemical, Inc.
lot number: 0299302520118
- d. Study Design: The fish were randomly transferred into each of 6 test tanks. Untreated control and chloramine-T treatment groups were tested in triplicate. Before treatment, 5 fish from each tank were evaluated for the presence of BGD. Sixty minute chloramine-T treatments of 12 mg/L were administered as a static bath on Days 1, 3, and 5. The study duration was 22 days. Chloramine-T concentrations were confirmed during

treatments. Mortalities were counted twice daily. Fish were examined (body surface, fins, gills and internal organs) and kidney inocula were cultured. Stained gill squash slides were examined from 5 fish before treatment and on Days 6, 11, and 22.

e. Parameters Measured: Mortality and water quality parameters

Statistical Analysis: Mortality rates were analyzed using generalized linear models (GENMOD procedure), using a binomial error distribution and a logit link function. Treatment was included as a fixed effect and an overdispersion parameter was included.

Results: Mortality results are included in the following table.

Table 3. Percent cumulative mortality from Day 1 through 19.

Chloramine-T Concentration	Cumulative Mortality	Percent Cumulative Mortality	LSMean (GENMOD)
0 mg/L	48067	99.6	5.6213
12 mg/L	3907	8.1	-2.4285
		p-value	<.0001

Conclusion: Chloramine-T administered at a concentration of 12 mg/L for 60-minutes every other day for 3 treatments was effective in the control of mortality associated with bacterial gill disease caused by flavobacters in fall chum salmon.

b. Administration Method Justification

The above studies were done with chloramine-T administered as a static bath. Under standard hatchery conditions, administering treatment in a static bath is not always preferred because of potential degradation of water quality conditions during treatment. The following study was designed to demonstrate that a target dose of chloramine-T can be achieved and maintained during flow-through treatment.

Title: “Analytical Verification of Chloramine-T to Confirm Target Dosage in a Bath Solution Administered Using a Flow-Through Treatment Method”

Study Director: James D. Bowker

Study Location: US Fish and Wildlife Service
Bozeman Fish Technology Center
4050 Bridger Canyon Road
Bozeman, MT 59715

General Design of the Study:

a. Purpose: To determine if concentrations of chloramine-T measured in water samples taken from various locations within a raceway at various times during

a one-hour treatment are within 25% of the target dose of 12 mg/L.

- b. Animals: None
- c. Test article: Chloramine-T
- d. Study Design: Two 58 ft X 6 ft X 3.7 ft outdoor raceways were used. The water-volume of each raceway was approximately 580 ft³. Each raceway was tested twice for a total of four trials. One raceway was tested each day for four days. With the water flow off, chloramine-T was added and manually mixed to establish an initial concentration of 12 mg/L. The amount of chloramine-T used was calculated using the following equation from Piper et al. (1982).

$$\text{Chloramine-T (g)} = \text{target dose (mg/L)} \times \text{water volume (gal)} \times 0.00378$$

Water flow was resumed at a predetermined flow rate. A chloramine-T solution was metered into the raceway inflow water. The amount of chloramine-T used was calculated using the following equation from Piper et al. (1982).

$$\text{Chloramine-T (g)} = \text{target dose (mg/L)} \times \text{water flow rate (gal/min)} \times \text{treatment duration (min)} \times 0.00378$$

Water samples were collected at 0, 30 and 60 minutes during the treatment period using a central aligned square grid systematic sampling scheme. Samples were collected from the raceway at the head-end, middle and tail-end; the surface, middle and bottom; and along each side and the midline.

- e. Parameters Measured: Chloramine-T concentration

Statistical Analysis: The null hypothesis tested was:

$$H_0: \mu_{\text{mean ChlorT conc. at } t=0, 30 \text{ and } 60 \text{ min}} = 12 \text{ mg/L chloramine-T } (\pm 25\%).$$

A one-sided, one-sample t-test was used to determine whether:

- (1) $H_0: \mu_{\text{mean ChlorT conc. at } t=0, 30 \text{ and } 60 \text{ min}} < 9 \text{ mg/L chloramine-T}$; and
- (2) $H_0: \mu_{\text{mean ChlorT conc. at } t=0, 30 \text{ and } 60 \text{ min}} > 15 \text{ mg/L chloramine-T}$.

The overall mean chloramine-T concentration for each time period was calculated using the chloramine-T concentrations from all measured samples. Mean chloramine-T concentrations for each strata were calculated using chloramine-T concentrations from all samples measured from that strata.

Results: The mean overall chloramine-T concentration from the four trials was 10.8 mg/L. The mean concentrations of chloramine-T for all studies and in all strata sampled were within 75-125% of the target concentration of 12 mg/L. The mean chloramine-T concentrations at 0, 30, and 60 minutes were 11.7, 10.5 and 10.2 mg/L, respectively. The overall mean chloramine-T concentration for all

trials, mean concentration for each individual trial, and overall mean chloramine-T concentrations of samples collected for all four dosing trials at 0, 30 and 60 minutes differed significantly ($P=0.000$) from the lower and upper limits (i.e., 9 and 15 mg/L) of the chloramine-T target dose.

The highest individual mean chloramine-T concentration was at the head-end of the raceway at 0 minutes, and the lowest individual mean chloramine-T concentration was at the head-end of the raceway at 60 minutes. Mean chloramine-T concentrations measured at 0 minutes were consistently higher than mean chloramine-T concentrations measured at 30 or 60 minutes. The mean chloramine-T concentrations from all four trials at the surface, middle and bottom of the raceway were 10.7, 11.0 and 10.7 mg/L, respectively. The mean chloramine-T concentrations from all four trials at the right-hand side, midline and left-hand side of the raceway were 10.7, 10.9 and 10.8 mg/L, respectively.

Conclusion: The target dose of chloramine-T can be accurately administered for a 60-minute treatment duration by initially adding chloramine-T to static water to obtain the target concentration followed by metered administration in a flow-through system.

3. **TARGET ANIMAL SAFETY:**

A. **Target Animal Safety Studies**

Title: "The Safety of Chloramine-T to Various Life Stages of Rainbow Trout (*Oncorhynchus mykiss*)"

Study Director: James D. Bowker, MS

Study Location: US Fish and Wildlife Service
Bozeman Fish Technology Center
4050 Bridger Canyon Road
Bozeman, MT 59715

General Design of the Study:

- a. Purpose: To demonstrate the safety of chloramine-T (CLT) administered as a bath to fry, fingerling and juvenile life-stages of rainbow trout, *Oncorhynchus mykiss*.
- b. Animals: Fry, fingerling and juvenile rainbow trout
- c. Test article: Chloramine-T.
- d. Study Design: The life stage, number of fish, chloramine-T concentrations and water temperature during studies are included in the following table.

Table 4-Life stage, number of fish, chloramine-T concentrations and water temperature during a series of safety studies.

Study Number	Life Stage	Chloramine-T Concentration (mg/L)	Number of Fish (*)	Water Temp. (°C)
1	Fry	0, 20, 60, 100	1200 (100)	8
2	Fry	0, 20, 60, 100	1200 (100)	14
3	Juvenile	0, 20, 60, 100	480 (40)	8
4	Juvenile	0, 20, 60, 100	360 (30)	14
5	Fingerling	0, 20, 40, 60	600 (50)	8
6	Fingerling	0, 20, 30, 40, 50, 60	900 (50)	14
8	Juvenile	0, 50, 60, 70, 80, 100	270 (15)	14
10	Juvenile	0, 20, 40, 60, 80, 100	270 (15)	14

*fish per tank

The same protocol was used for the eight studies. Chloramine-T was administered in static baths in multiples of a 20 mg/L concentration. Three treatments, three hours per treatment, were administered every other day with one exception. During Study Number 10, treatments were administered on three consecutive days. Mortality observations were made every 30 minutes during treatments. Approximately 1-2 hours into each of the treatments, water samples were collected for analysis of chloramine-T concentration.

- e. Parameters Measured: Mortality, chloramine-T concentrations and water quality parameters

GLP Compliant: Yes

Statistical Analysis: The cumulative mortality rates for both time periods in each study (24 hours and 14 days post-treatment) were analyzed using generalized linear models (GENMOD procedure in SAS). The model included the fixed effect of treatment and binomial error distributions with logit link functions. The experimental unit was the tank. Treatment comparisons were made between the active treatment groups and the control group for those treatment groups with mortalities recorded.

Results: Mortality results for each study are included in the following tables.

Table 5-Mortality results during a target animal safety study evaluating chloramine-T treatment of rainbow trout fry (Study No. 1).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	1	0.3
20 (1X)	0	0	0	0
60 (3X)	0	0	0	0
100 (5X)	5	1.7	8	2.7

Table 6-Mortality results during a target animal safety study evaluating chloramine-T treatment of rainbow trout fry (Study No. 2).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	7	2.3
20 (1X)	0	0	0	0
60 (3X)	0	0	1	0.3
100 (5X)	7	2.3	10	3.3

Table 7-Mortality results during a target animal safety study evaluating chloramine-T treatment of juvenile rainbow trout (Study No. 3).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	0	0
20 (1X)	0	0	5	4.2
60 (3X)	15	12.6	19	16.2
100 (5X)	121	100	121	100

Table 8-Mortality results during a target animal safety study evaluating chloramine-T treatment of juvenile rainbow trout (Study No. 4).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	0	0
20 (1X)	0	0	0	0
60 (3X)	21	23.3	21	23.3
100 (5X)	90	100	100	100

Table 9-Mortality results during a target animal safety study evaluating chloramine-T treatment of rainbow trout fingerlings (Study No. 5).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	1	0.7	4	2.7
20 (1X)	0	0	1	0.7
40 (2X)	0	0	0	0
60 (3X)	0	0	0	0

Table 10-Mortality results during a target animal safety study evaluating chloramine-T treatment of fingerling rainbow trout (Study No. 6).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	0	0
20 (1X)	0	0	0	0
30 (1.5X)	0	0	4	2.7
40 (2X)	0	0	1	0.7
50 (2.5X)	0	0	0	0
60 (3X)	0	0	0	0

Table 11-Mortality results during a target animal safety study evaluating chloramine-T treatment of juvenile rainbow trout (Study No. 8).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	1	2.2	2	4.4
50 (2.5X)	1	2.2	1	2.2
60 (3X)	2	4.4	4	8.9
70 (3.5X)	6	13.3	6	13.3
80 (4X)	17	37.8	17	37.8
100 (5X)	44	97.8	44	97.8

Table 12-Mortality results during a target animal safety study evaluating chloramine-T treatment of juvenile rainbow trout (Study No. 10).

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	0	0
20 (1X)	0	0	0	0
40 (2X)	0	0	0	0
60 (3X)	0	0	0	0
80 (4X)	30	33.3	31	34.4
100 (5X)	80	88.8	81	90.0

No differences were seen in the mortality rates of any life-stage of fish when comparing treatments at 8°C and 14°C. In all the studies with significant mortality, the greatest mortality occurred during and after the first treatment, with the signs of toxicity or mortality starting 2-2.5 hours into the 3-hour treatment. Toxicity was observed in the fry and fingerling stages at similar dose levels. Greater mortality was seen during some of the studies involving the juvenile life-stage.

Conclusions: These studies provide data to support the safety of chloramine-T administered to rainbow trout as a 60-minute bath for 3 consecutive days or 3 treatments on alternate days at a concentration of 20 mg/L.

B. Safety Study

Title: "The Safety of Chloramine-T Use on Lake Trout, *Salvelinus namaycush*"

Study Director: James D. Bowker, MS

Study Location: US Fish and Wildlife Service
Bozeman Fish Technology Center
4050 Bridger Canyon Road
Bozeman, MT 59715

General Design of the Study:

- a. Purpose: To demonstrate that the proposed maximum effective therapeutic dosage of chloramine-T (20 mg/L for 1 h) is safe to lake trout.
- b. Animals: 240 (20/tank) lake trout fingerlings
- c. Test article/controls: Chloramine-T
- d. Study Design: Chloramine-T was administered in static baths in multiples of a 20 mg/L dose. Three treatments were administered daily for 3 hours each. Each dose was tested in duplicate. Approximately 2 hours into the first treatment water samples were collected for analysis of chloramine-T concentration. Mortality observations were made every 30 minutes during each 3-hour treatment.
- e. Parameters Measured: Mortality and chloramine-T concentrations.

GLP Compliant: No.

Results: Mortality results are included in the following table.

Table 13- Mortality results during a target animal safety study evaluating chloramine-T treatment of lake trout fingerlings at ~12°C.

Chloramine-T Concentration (mg/L)	Cumulative Mortality			
	24 Hours Post-Treatment		14 Days Post-Treatment	
	Number	Percent	Number	Percent
0 (0X)	0	0	0	0
50 (2.5X)	0	0	0	0
100 (5X)	0	0	1	2.9
150 (7.5X)	3	8.8	3	8.8
200 (10X)	27	79.4	27	79.4
300 (15X)	34	100.0	34	100.0

Conclusions: These studies provide data to support the safety of chloramine-T administered to lake trout as a 60-minute bath for 3 consecutive days at a concentration of 20 mg/L.

C. Safety Study Evaluating Histopathologic Data

Title: “The Safety of Chloramine-T to Various Life Stages of Rainbow Trout, *Oncorhynchus mykiss*”

Study Director: James D. Bowker, MS

Study Location: US Fish and Wildlife Service
Bozeman Fish Technology Center
4050 Bridger Canyon Road
Bozeman, MT 59715

General Design of the Study:

- a. Purpose: To describe and evaluate the histological effects of six exposure concentrations of chloramine-T (0, 20, 40, 60, 80 and 100 mg/L) on three external (gill, skin and eye) and two internal (kidney and liver) tissues of juvenile rainbow trout.
- b. Animals: 540 (30/tank) rainbow trout fingerlings
- c. Test article/controls: Chloramine-T
- d. Study Design: Chloramine-T was administered in static baths at doses of 0, 20, 40, 60, 80 and 100 mg/L. Each dose was tested in triplicate. Three treatments were administered every other day for 3 hours each. Approximately 1 hour into each of the 3 hour treatments, water samples were collected for analysis of chloramine-T concentration. Mortality and behavior observations were made every 30 minutes during each 3-hour treatment. A maximum of five moribund fish per tank were collected for gross examination and tissues collection on Days 8 and 10. “Healthy-appearing” fish were collected for histologic sampling on Days 12, 19 and 26. Five fish per tank were collected for examination and tissue collection on Day 12 and 2 fish per

tank were collected on Days 19 and 26. For each histologic criterion evaluated, the histologist ranked the observed changes as 1=none, 2=mild, 3=moderate and 4=severe. The following histologic criteria were evaluated.

Gill	Scattered fusion of gill lamellae	Epithelial necrosis		
	Aneurysms in gill capillaries	Basal hyperplasia of gill epithelium		
	Necrotic RBCs in gill capillaries	Hypertrophy of gill epithelium		
	Epithelial separation from basement membrane			
Kidney	Tubule necrosis	Hydropic degeneration		
	Hyaline droplet degeneration	Tubule swelling		
	Erythrophagia	Hematopoietic hyperplasia		
Eye	Epithelial thickness	Degeneration	Edema	
Liver	Diffuse necrosis	Focal necrosis	Nuclear vacuolation	Cellular vacuolation
Skin	Mucus cell number	Mucus production	Necrosis	Degeneration

The histologist considered moderate and severe changes pathologic or abnormal and provided a report describing his findings.

- e. Parameters Measured: Mortality, histopathology criteria, behavior, chloramine-T concentration, and water quality parameters.

GLP Compliant: Yes.

Results: The mortality level in each of the dose groups during this study was similar to the mortality levels seen in the series of studies with rainbow trout and in the safety study done with lake trout. The gill and red blood cells (RBCs) in the gill capillaries appear to be the target tissue for acute toxicity associated with chloramine-T treatments. Moderate and severe necrotic RBCs in the capillaries, fusion of lamellae, epithelial separation from the basement membrane, epithelial basal hyperplasia, epithelial necrosis and epithelial hypertrophy were present in an increased proportion of the 40 mg/L and 50 mg/L dose group fish sampled during the treatment period and just after the third treatment. Moribund fish represented the majority of the fish sampled from the 40 mg/L and 50 mg/L dose groups. A few fish from the 30 mg/L dose group sampled during the treatment period and just after the third treatment had moderate and severe epithelial separation from the basement membrane and epithelial hypertrophy. Gill pathologies were seen with less frequency or less severe pathologies were seen in the fish sampled 1-2 weeks post-treatment compared to the healthy fish sampled immediately after the last treatment. Gill lesions in healthy appearing fish may resolve 1-2 weeks after treatment.

Conclusions: A good margin of safety exists since similar pathology was not seen in the 1X, 2X or 3X dose groups. Chloramine-T is safe to freshwater-reared

salmonids when administered as a 60 minute bath up to a concentration of 20 mg/L on 3 consecutive days or three treatments on alternate days.

4. HUMAN SAFETY:

5. AGENCY CONCLUSIONS:

6. ATTACHMENTS:

(facsimile labeling)