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Observations on the Efficacy of Chloramine-T Treatment to Control Mortality in a Variety of Salmonids

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Abstract.—Results and observations from 120 chloramine-T treatment trials to control mortality in a variety of salmonids caused by bacterial gill disease and columnaris are provided to aid fish culturists in determining more effective treatment regimes. When chloramine-T was used at 6, 10, or 15 mg/L, regardless of treatment frequency, efficacy in control of mortality was observed in 56%, 65%, and 61% of the trials, respectively. When chloramine-T was administered one, two, or three times, regardless of treatment concentration, efficacy was observed in 38%, 62%, and 88% of the trials, respectively.

Chloramine-T is an effective therapeutant for salmonids with bacterial gill disease (BGD; From 1980; Bullock et al. 1991). Bacterial gill disease can pose a serious threat to fish survival in intensive culture. Although death is generally from a massive infection of the gills, stressors associated with intense fish culture may predispose fish to infection. *Flavobacterium branchiophilum* is the bacteria that causes most outbreaks of BGD (Wakabayashi et al. 1989; Ferguson et al. 1991); however, other gram-negative bacteria have also been implicated. Moreover, inflamed gills associated with BGD are susceptible to secondary infections by opportunistic fungi. Integrated fish health management practices, including good diets and water quality, usually prevent the occurrence of these diseases. However, numerous factors, such as overcrowding, overfeeding, and increases in toxic metabolic waste (Lasee 1995; MacPhee et al. 1995) can lead to severe disease outbreaks requiring prompt treatment to prevent loss of fish.

Salmonids have been shown to be relatively tolerant of chloramine-T. Bills et al. (1988) established that the 1-h LC50 value (the concentration lethal to 50% of test animals over 1 h) for chloramine-T in rainbow trout *Onchorhynchus mykiss* was greater than 60 mg/L, except in soft acidic waters (pH 6.5) where the 1-h LC50 was 55.8 mg/L. Bullock et al. (1991) recommended a bath treatment of 8.5 mg chloramine-T/L for 1 h as an effective treatment for BGD in cultured salmonids. They also stated that a second or third treatment may be required in an advanced outbreak or if the fish are stressed. Best results have been obtained when treatment was initiated in the early stages of an outbreak.

Observations by staff at the National Fish Health Laboratory, Leetown, West Virginia, and anecdotal observations by hatchery managers throughout the United States indicate that chloramine-T also effectively controls external columnaris. They consider the use of 8.5 mg chloramine-T/L for 1 h in a flow-through or flush system adequate to control the external phase of the disease.

Chloramine-T has been used throughout the aquaculture industry, including the U.S. Fish and Wildlife Service (USFWS), to control mortality caused by BGD or external columnaris in a large number of intensively cultured fish species. Currently, all use of chloramine-T must be conducted under authorization of a compassionate Investigational New Animal Drug (INAD) exemption. The fish culture objective of treatments under INAD exemption has been to minimize the impacts of disease on fish health, fish quality, and survival in order to fully meet fishery management objectives. As directed by INAD exemption guidelines, ancillary data has been collected during the course of treatment, and results from these trials may benefit fish culturists by providing evidence of more efficacious treatment regimes. In addition, the Food and Drug Administration Center for Veterinary Medicine has stated that as a result of the data provided here, as well as data from other ancillary chloramine-T treatment trials, there was no need to conduct chloramine-T dose–titration studies. Instead, efforts to generate pivotal data to satisfy the efficacy component of a New Animal Drug Application (NADA) can be focused on field-based clinical efficacy trials. The purpose of this paper is to provide observations from ancillary field trials that could be used to determine the most appropriate treatment regime for controlling BGD and external columnaris in a variety of cultured salmonids.

Between 6 January 1995 and 3 June 1996, nine national fish hatcheries participated in developing

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TABLE 1.—Species, numbers, and size-groups of salmonids treated with chloramine-T during this evaluation.

Species	Number treated	Percent of fish in size-group: <5.1 cm	5.1–15.25 cm	>15.25 cm
Rainbow trout	2,675,800	37	57	6
Apache trout	186,400	29	71	
Bull trout	65,000			100
Cutthroat trout	37,000		100	
Chum salmon	2,194,000	94	6	
Coho salmon	197,000	100		
Kokanee	4,055,600	34	36	30
Total	9,392,800	50	35	15

ancillary clinical field trial data for chloramine-T flow-through or static-bath treatments on salmonids under USFWS INAD exemption number 4000. These facilities, located in Kalispell, Montana; Jones Hole, Utah; Hotchkiss, Colorado; Riverdale, North Dakota; Norfork, Arkansas; Neosho, Missouri; Whiteriver, Arizona; Quinault, Washington; and Quilcene, Washington, represent a wide range of fish culture environments. Ancillary data are defined as data produced by studies without negative controls or true replicates. Results based on ancillary data are not statistically defensible.

Treatment trials were conducted on seven species of salmonids and involved approximately 9.4 million fish. Species included rainbow trout, cutthroat trout *Onchorhynchus clarki*, Apache trout *O. apache*, bull trout *Salvelinus confluentus*, kokanee (lacustrine stocks of sockeye salmon *O. nerka*), chum salmon *O. keta*, and coho salmon *O. kisutch*. Treated fish ranged in age from fry to adult. Fish size categories were defined as less than 5.1 cm (2 in), between 5.1 and 15.25 cm (2–6 in) and more than 15.25 cm (>6 in). Approximately 50% of the fish were less than 5.1 cm, 35% were between 5.1 and 15.25 cm, and 15% were greater than 15.25 cm (Table 1).

Concentrations and dosing intervals tested during these trials were either 6, 10, or 15 mg chloramine-T/L applied on one to three consecutive or alternate days. Chloramine-T for all trials was supplied by Akzo Chemical, Inc. (Chicago, Illinois). The chemical was dissolved in water and applied as a bath solution for 1 h and then flushed from the fish-holding container, or it was metered for 1 h at a flow adequate to achieve the desired treatment concentration in a flowing system.

Overall, 120 treatment trials were conducted; approximately 16% of the trials used 6 mg chloramine-T/L, 51% used 10 mg/L, and 33% used 15 mg/L. The drug was administered one, two, or three times, regardless of concentration, in 26%, 49%, and 25% of the trials, respectively. The most commonly used treatment regime was 10 mg/L, administered two times.

The study design called for chloramine-T treatment to begin when disease signs were first evident, while mortality increased, and when the causative agent was being identified during a pretreatment pathological examination. However, this was not the case in many of the treatment trials reported here. Although a definitive diagnosis of BGD or columnaris was always recommended, occasionally treatment was initiated following a presumptive diagnosis only. A presumptive diagnosis was limited to observation of fish behavior and other disease signs, such as fish appearing lethargic, swimming near the water surface, etc. (Lasee 1995). Mortality was often the only response variable used to determine treatment efficacy. Although pretreatment data was supposed to be collected for at least 10 d and posttreatment data for at least 14 d, this was not always done. At times, mortality data was collected during the treatment and posttreatment periods only.

Because there were no controls or true replicates and because data could not be analyzed statistically, treatment efficacy was characterized by a set of subjective criteria. Treatments were considered effective if mortality was at least 30% lower after treatment than before or during treatment. In trials in which only posttreatment mortality was collected, the average daily mortality during the first half of the posttreatment period was compared with the average daily mortality during the second half of the posttreatment period. Mortality during the second half of the posttreatment period had to be at least 30% lower than during the first half of the posttreatment period to be considered efficacious. If mortality did not decrease by at least 30%, the treatments were considered ineffective. Trials were considered inconclusive if there was no substantial mortality before or after treatment, when fish were moved to other rearing units before sufficient mortality data could be collected, or when another disease was diagnosed requiring concomitant treatment therapy.

Efficacy, regardless of fish species treated, was observed for nearly all three treatment concentrations and at all three treatment frequencies (Table 2). Overall, treatment appeared effective in 56% of the trials at 6 mg chloramine-T/L, in 65% of trials at 10 mg/L, and in 61% of trials at 15 mg/L. With regards to treatment frequency, treatment ap-

TABLE 2.—Effectiveness of chloramine-T at three concentrations and three treatment frequencies to control mortality caused by bacterial gill disease and external flexibacteriosis in salmonids at nine national fish hatcheries.

	Treatment concentration							
	6 mg/L		10 mg/L		15 mg/L		Overall	
Frequency	Number of trials	Percent effective	Number of trials	Percent effective	Number of trials	Percent effective	Number of trials	Percent effective
1 treatment	13	46	4	0	7	43	24	38
2 treatments	1	100	33	63	16	56	50	62
3 treatments	2	100	15	87	8	88	25	88
All treatments	16	56	52	65	31	61	99	63

peared effective in 38% of trials in which the drug was administered once, in 62% of trials in which it was administered twice, and in 88% of trials in which it was administered three times.

Keeping in mind the limited data available (particularly at 6 mg chloramine-T/L) the data suggest that the frequency of treatment may have been as much, if not more, of a factor than concentration in controlling mortality caused by BGD or columnaris. There was no substantial difference in degree of efficacy between different treatment concentrations, although 10 and 15 mg chloramine-T/L resulted in apparent effectiveness more often than 6 mg/L. However, as indicated above, there seemed to be a substantial improvement in efficacy with increased treatment frequency. Based on these observations, the highest degree of efficacy may be achieved with three treatments of 10 or 15 mg chloramine-T/L. Although these observations are a simplified view of treatment efficacy and do not consider fish species, fish size, culture methods, environmental conditions, or timeliness of diagnosis and treatment, they may provide general guidelines and a starting point for controlled, replicated clinical field efficacy studies.

Results by species reflect apparent efficacy for nearly all species, regardless of treatment regime (Table 3). Of the 120 treatment trials, 57% appeared effective, 32% ineffective, and 12% inconclusive. For the 66 treatment trials with trout, 65% appeared effective, 29% ineffective, and 6% inconclusive. For the 54 treatment trials that involved salmon, 46% appeared effective, 35% ineffective, and 19% inconclusive.

TABLE 3.—Efficacy results of chloramine-T treatment by species.

Species	Effective trials	Ineffective trials	Inconclusive trials	Total
Rainbow trout	36	15	4	55
Apache trout	6	4	0	10
Cutthroat trout	1	0	0	1
All trout	43 (65%)	19 (29%)	4 (6%)	66
Kokanee	11	8	7	26
Coho salmon	0	0	3	3
Chum salmon	14	11	0	25
All salmon	25 (46%)	19 (35%)	10 (19%)	54
All salmonids	68 (57%)	38 (32%)	14 (12%)	120

Treatment of fish between 5.1 and 15.25 cm had the highest incidence of efficacy. Approximately 87% of the trials that involved trout of this size appeared efficacious, compared with 63% for larger fish and 31% for smaller fish. Similarly, 83% of the trials that involved salmon between 5.1 and 15.25 cm appeared efficacious, compared with 50% for larger fish and 55% for smaller fish.

Bacterial gill disease is often environmentally induced, and conditions associated with intensive fish culture may be a precursor to an infectious disease outbreak (Post 1987). Unfortunately, data collected during these studies do not adequately address the effects of culture methods and environmental factors on infectious disease outbreaks nor how or if they affect treatment efficacy. Other factors that may also influence treatment efficacy include timeliness of disease diagnosis and promptness of treatment. We noted repeatedly that results would probably have improved had treatment been initiated before the disease progressed. The U.S. Fish and Wildlife Service facilities that are near Fish Health Units or that conduct their own fish health exams usually treat diseases before they become severe, increasing the likelihood of effective treatment.

In spite of the factors mentioned above, these efforts reveal some positive results. In particular, additional insight appears to have been gained on the relationship between treatment concentration, treatment frequency, and trial efficacy. However, it must be noted, these data are supportive; pivotal clinical field efficacy data are necessary before any definitive conclusions can be drawn with regard to specific treatment regimes and efficacy.

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