

**SLICE® (emamectin benzoate) Clinical Field Trials -
INAD 11-370**

**Year 2010 Annual Summary Report on the Use of SLICE®
(emamectin benzoate) in Clinical Field Efficacy Trials**

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Summary

SLICE®(emamectin benzoate) has been used effectively in the U. S. under compassionate INAD Exemption #11-370 to control mortality in a variety of fish species caused by ectoparasites. In calendar year 2010 (CY10), the efficacy of SLICE® (emamectin benzoate) was evaluated in 14 ectoparasite trials involving approximately 0.9 million fish to control mortality in a variety of fish species caused by ectoparasites. Trials were conducted at a total of five fish culture facilities, including one state hatchery and four private hatcheries. The compassionate study protocol under which treatments were administered allowed the investigator to use SLICE® daily for 7 consecutive days at a dosage of 50 ug/kg/day. Overall, results of trials conducted in CY10 indicated that treatments appeared efficacious in 100% of the trials.

Introduction

External parasites (ectoparasites) form one of the largest groups of pathogenic organisms of cultured aquatic species (Post 1987). Affected species include finfish

(freshwater and marine) and invertebrates. Environmental conditions such as temperature change, poor water quality, and high organic loading due to intensive fertilization and feeding levels increase the incidence and spread of many external parasites. Stress (i.e., seining, handling, sorting, grading, vaccinating, anesthesia, crowding, and transport) is also a major contributor to most parasitic outbreaks in fish (Lasee 1995). Additionally, tissue damage induced by external parasites increases susceptibility to secondary bacterial and/or fungal infections (Lasee, 1995).

The organisms responsible for major parasitic infections on fish are, for the most part, protozoan and metazoan. These parasites are highly opportunistic and have tremendous reproductive capabilities. Under normal conditions (e.g., in wildstock populations) these organisms cause little pathology. However, under intensive culture where fish densities are typically high, many of these organisms can cause serious disease problems.

If parasitic infections are left untreated, they can cause substantial economic losses to commercial aquaculture, and severely impact the restoration, recovery, and preservation of depleted stocks of fish cultured by Federal and State agencies. The extent of losses of fish from parasites depends upon the severity of the primary cause of infection. Morbidity can vary from less than 10% to total loss of the population (Post 1987). Historically, immersion treatments (static and flush) using a variety of compounds have been used to control mortality caused by parasite infestations. A

number of these compounds have been found, both experimentally and under production settings, to be relatively effective.

SLICE[®] is an in-feed treatment that was developed specifically for the control of sea lice infestations in farmed salmon and trout. Control of sea lice (including *Lepeophtheirus salmonis*, *Caligus elongatus*, *C. rogercressyi*, and *C. teres*) on farmed fish is essential as lice feeding activity may result in mortalities, as well as susceptibility to a variety of other pathogens. SLICE[®] has been extensively tested in trials to evaluate environmental safety, efficacy, and tolerance in Atlantic salmon, *Salmo salar*, rainbow trout, *Oncorhynchus mykiss*, and brown trout, *Salmo trutta*, in the marine environment (Stone et al., 1999; Stone et al., 2000a; Stone et al., 2000b; Stone et al., 2000c; Stone et al., 2002; Roy et al., 2000; and Armstrong et al., 2000). Currently, SLICE[®] is approved for the control of sea lice in salmonid species in the UK, Europe, Norway, and Chile.

Purpose of Report

The purpose of this report is to summarize the results of CY10 supplemental SLICE[®] field efficacy data. We anticipate that CY10 data will be used to establish a SLICE[®] database for the purpose of developing an appropriate label claim for the legal use of this new animal drug in aquaculture.

Facilities, Materials, Treatment Procedures

1. Facilities

A total of 14 field efficacy trials were conducted at five fish culture facilities, including one state hatchery and four private hatcheries. Treatments were used to control mortality caused by ectoparasites in various fish species. Water temperature during treatments at the various testing facilities ranged from 52.0 - 85.2 °F, with a mean treatment temperature of 61.4°F.

2. Chemical material

The SLICE® premix used in CY10 trials consisted of 0.2% emamectin benzoate in an inert carrier, consisting of GM-free cornstarch, maltodextrin, antioxidant, and solvent. The premix has been formulated specifically for incorporation of emamectin benzoate onto fish feeds. All SLICE® used was supplied by Schering-Plough Animal Health, 1095 Morris Avenue, Union, NJ. SLICE® medicated feed was prepared either by top-coating SLICE® onto commercial fish feed at the testing site by the Investigator, Monitor, or their designee, or prepared by commercial fish feed manufacturers.

3. Drug dosages and duration

As described in the Study Protocol for INAD #11-370, Investigators were allowed to use SLICE® daily for 7 consecutive days at a dosage of 50 ug/kg/day. No deviations to this treatment regimen occurred during CY10.

Fish Species Treated and Fish Ectoparasites Involved in CY10 Trials

1. Species and size of fish treated

Two fish species, including one species of salmonids and one non-salmonid species were treated with SLICE® during CY10. Treated fish ranged in length from 7.0 - 45.0 in. and the mean length of all treated fish was 13.5 in. Fish species treated included:

Salmonids:

rainbow trout *Oncorhynchus mykiss*

Non-salmonids:

Atlantic sturgeon *Acipenser oxyrinchus*

2. Ectoparasite treated

Test fish were treated with SLICE® to control mortality caused by ectoparasites of the genera *Argulus* and *Salmincola*.

Data Collected

1. Pathologist's report

Fish health pathology reports provide essential information with respect to parasite confirmation and general fish health. No pathology reports were submitted with the CY10 trials.

2. Treatment response and drug accountability data

Drug receipt reports, drug use reports, diagnosis, treatment, and mortality reports (including adverse effects/toxicity observations), and fish disposition reports were prepared by study investigators. Such reports were routed through the study monitor for review, and then sent to the AADAP Office for review, data analysis and report writing, entering data into a database, and archiving in permanent files.

Discussion of Study Results

- 1. General observations on the efficacy of SLICE[®] for the control of ectoparasites in a variety of fish species** (Note: Table 1 provides a summary of all trials in which treatment appeared efficacious; Table 2 provides summary data for all trials; and Table 3 provides a brief description of all trials conducted during CY10 under INAD #11-370).

A. Efficacy of SLICE[®] at 50 ug/kg/day

Atlantic sturgeon and rainbow trout were treated with SLICE[®] at 50 ug/kg of fish biomass for 7 consecutive days in 14 trials (Table 1). SLICE[®] treatments appeared to be effective in all trials.

2. Observed Toxicity

No toxicity or adverse effects relating to SLICE[®] treatment were reported in any of the trials.

3. Observed Withdrawal Period

All withdrawal times were either met or exceeded.

Current Study Protocol for SLICE[®] (emamectin benzoate) INAD #11-370

Please see the attached current study protocol for SLICE[®] (emamectin benzoate) INAD #11-370. No changes have occurred to this study protocol.

Facility Sign-up List

Please see “Table 4. Facilities and Names of Investigators” for facilities that signed-up to participate in the SLICE[®] (emamectin benzoate) during CY10. Facilities not listed in Appendix III-a of the current SLICE[®] (emamectin benzoate) INAD #11-370 during CY10 study protocol have been highlighted.

The food-use authorization was not granted until May 21, 2010, so several facilities initially expressed interest in participating under the SLICE[®] INAD at the start of CY10. However, once the authorization was received some of these facilities decided not to participate. All facilities that conducted trials during CY10 were compliant with their reporting requirements to the NPDES authority; and

have been approved by CVM's environmental team to participate under the SLICE® INAD. A copy of their NPDES Authority has been attached to this report.

Correspondence sent to SLICE® (emamectin benzoate) INAD #11-370 Participants

Please see the attached correspondences that were sent to all SLICE® participants after the AADAP Office received their sign-up form for CY10; and once the food-use authorization was received.

Number of Treated Fish under Treatment Use Authorization

Total number of fish treated during CY10 was 870,069. The total number of treated fish to count against the current treatment use authorization dated May 21, 2010 is 870,069.

Summary of Study Results

SLICE® was used at a dosage of 50 ug/kg of fish biomass for 7 consecutive days in 14 trials. Atlantic sturgeon and rainbow trout were the only fish species treated and trials involved approximately 0.9 million fish. Treated fish ranged in size from 7.0 - 45.0 in. Water temperature during treatment ranged from 52.0 - 85.2°F, with a mean treatment temperature of 61.4°F. Overall, results showed that treatment appeared to be effective in 100% of the trials. There was no evidence of toxicity or adverse effects related to SLICE® treatment reported in any of the trials. Data from the CY10 trials indicate that the SLICE® treatment regimen recommended in INAD Protocol #11-370 is

safe and effective to control mortality in a variety of fish species caused by ectoparasites. As a result of the lack of quality criteria, such as dose verification, use of controls, replicates, and randomization, it is understood that these data will be considered as ancillary data, and that pivotal efficacy studies are needed to definitively demonstrate SLICE® efficacy for the treatment of ectoparasites. However, the ancillary data described above should provide useful, corroborative data to help support a label claim for the use of SLICE® to control mortality associated with ectoparasites in a variety of fish species. Although it is anticipated that the majority of future efficacy data collected under INAD #11-370 will also be ancillary data, efforts will be directed towards the continued generation of high quality data.

References

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Table 1. Summary of Year 2010 SLICE® Efficacy Results - Efficacious Studies

Hatchery	Number of efficacious trials	Fish Species	Fish Size (in.)	Number of Fish	Ectoparasite	Dose (ug/kg)	Number of treatment days	Temp. (°F)
Chalk Point Aquaculture Facility	2	ASN	35.0 - 45.0	228	Argulus	50	7	76.4 - 85.2
Crystal River SFH	1	RBT	7.00	3,000	Salmincola	50	7	52.0
Idaho Springs	1	RBT	8.00	77,400	Salmincola	50	7	59.0
Magic Springs Hatchery	8	RBT	8.0 - 10.9	789,232	Salmincola	50	7	59.0
Snake River Fish Hatchery	2	RBT	13.4 - 14.3	209	Salmincola	50	7	56.6 - 57.9

Table 2. Summary Data Regarding Year 2010 SLICE® Efficacy Studies

Total Number of Fish Treated:	870,069
Number of fish treated in efficacious trials	870,069
Total Number of Studies:	14
Efficacious trials	14
Treatment Regimens and Frequency Used:	
50 ug/kg; 7 days	14 trials
Treatment Water Temperature (°F):	
Temperature Range	52.0 - 85.2
Mean Temperature	61.4
Size of Treated Fish (in.):	
Size Range	7.0 - 45.0
Mean Length	13.5
Species Treated:	
<u>Salmonids:</u>	
rainbow trout <i>Oncorhynchus mykiss</i>	
<u>Non-salmonids:</u>	
Atlantic sturgeon <i>Acipenser oxyrinchus</i>	
