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

Year 2011 Annual Summary Report on the Use of SLICE® (emamectin benzoate) in Clinical Field Efficacy Trials

Prepared by:

Bonnie Johnson, Biologist
U. S. Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Bozeman, Montana

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 2011 (CY11), the efficacy of SLICE® (emamectin benzoate) was evaluated in 35 ectoparasite trials involving approximately 3.4 million fish to control mortality in a variety of fish species caused by ectoparasites. Trials were conducted at a total of six fish culture facilities, including one U.S. Fish and Wildlife Service National Fish Hatchery (NFH), 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 CY11 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 CY11 supplemental SLICE® field efficacy data. Similar data have been submitted by the Service in previous years. We anticipate that CY11 data will be used to enhance the existing SLICE® database established from previous years, and will be considered in the “body of evidence” for the purpose of developing an appropriate label claim for the use of SLICE® in aquaculture.

Facilities, Materials, Treatment Procedures

1. Facilities

A total of 35 field efficacy trials were conducted at six fish culture facilities, including one U.S. Fish and Wildlife Service NFH, 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 40.0 - 83.1 °F, with a mean treatment temperature of 57.4°F.

2. Chemical material

The SLICE® premix used in CY11 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 Merck Animal Health, 556 Morris Avenue, Summit, 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.

Note: there was one deviation to this treatment regimen when fish were fed for 10 days instead of the required 7 days. The investigator had wanted to use up all of the medicated feed they had on hand. Both the investigator and monitor were contacted and made aware that this deviation can not occur for any future studies. The treated fish were broodstock and will never be used for human consumption.

Fish Species Treated and Fish Ectoparasites Involved in CY11 Trials

1. Species and size of fish treated

Four fish species, including three species of salmonids and one non-salmonid species were treated with SLICE® during CY11. Treated fish ranged in length from 7.9 - 43.9 in. and the mean length of all treated fish was 11.0 in. Fish species treated included:

Salmonids:

brown trout *Salmo trutta*

rainbow trout *Oncorhynchus mykiss*

spring chinook salmon *Oncorhynchus tshawytscha*

Non-salmonids:

Atlantic sturgeon *Acipenser oxyrhinchus*

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. A pathology report was submitted with 11% of the CY11 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 CY11 under INAD #11-370).

A. Efficacy of SLICE® at 50 ug/kg/day

Atlantic sturgeon, brown trout, rainbow trout, and spring chinook salmon were treated with SLICE® at 50 ug/kg of fish biomass for 7 - 10 consecutive days in 35 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

No changes have occurred to the current study protocol for SLICE® (emamectin benzoate) INAD #11-370.

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 CY11. All facilities that conducted trials during CY11 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 CY11.

Number of Treated Fish under Treatment Use Authorization

Total number of fish treated during CY11 was 3,396,978. The total number of treated fish to count against the current treatment use authorization dated May 21, 2010 is 4,267,047.

Summary of Study Results

SLICE® was used at a dosage of 50 ug/kg of fish biomass for 7 - 10 consecutive days in 35 trials. Atlantic sturgeon, brown trout, rainbow trout and spring chinook salmon were the only fish species treated and trials involved approximately 3.4 million fish. Treated fish ranged in size from 7.9 - 43.9 in. Water temperature during treatment

ranged from 40.0 - 83.1°F, with a mean treatment temperature of 57.4°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 CY11 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 2011 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	1	ASN	43.90	44	Argulus	50	7	83.1
Idaho Springs	5	RBT	8.0 - 9.0	307,604	Salmincola	50	7	59.0
Magic Springs Hatchery	16	RBT	8.0 - 11.0	2,082,238	Salmincola	50	7	59.0
Pristine Springs/Blue Lakes	9	RBT	7.9 - 8.9	964,240	Salmincola	50	7	59.0
Mt. Shasta Hatchery	1	BNT	24.00	5,000	Salmincola	50	7	40.0
	2	RBT	24.00	37,600	Salmincola	50	7 - 10	40.0 - 42.0
Little White Salmon NFH	1	SCS	21.00	252	Salmincola	50	7	42.7

Table 2. Summary Data Regarding Year 2011 SLICE® Efficacy Studies

Total Number of Fish Treated:	**3,396,978**
Number of fish treated in efficacious trials	3,396,978
Total Number of Studies:	**35**
Efficacious trials	35

Treatment Regimens and Frequency Used:

50 ug/kg; 7 days	34 trials
50 ug/kg; 10 days	1 trial

Treatment Water Temperature (°F):

Temperature Range	40.0 - 83.1
Mean Temperature	57.4

Size of Treated Fish (in.):

Size Range	7.9 - 43.9
Mean Length	11.0

Species Treated:

Salmonids:
brown trout *Salmo trutta*
rainbow trout *Oncorhynchus mykiss*
spring chinook salmon *Oncorhynchus tshawytscha*

Non-salmonids:
Atlantic sturgeon *Acipenser oxyrhinchus*