Common Carp Pituitary Clinical Field Trials - INAD 8391

Year 2014 Annual Summary Report on the Use of
Common Carp Pituitary in Field Efficacy Trials

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Summary

Spawning aids such as common carp pituitary (CCP), luteinizing hormone-releasing hormone analogue, and human chorionic gonadotropin are routinely used in fisheries programs to induce gamete maturation in fish to enhance fish propagation programs. The U.S. Food and Drug Administration has authorized the use of CCP under the Compassionate Investigational New Animal Drug (INAD) Exemption #8391 for the purpose of gathering efficacy data to support a new animal drug approval for CCP. In calendar year 2014 (CY14), 10 INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Trials involved 7,820 treated fish and were conducted at nine different fish culture facilities, including two U.S. Fish and Wildlife Service facilities, four state hatcheries, and three private hatcheries. Efficacy was determined by whether or not treated fish (1) produced or yielded eggs or milt, or (2) produced or yielded more eggs or milt than untreated fish. Overall, results of

trials conducted in CY14 indicated that treatments appeared efficacious in approximately 90% of the trials and characterized as inconclusive in 10% of the trials.

Introduction

The use of hormones to induce spawning in fish is critical to the success of many federal, state, private, and tribal fisheries programs. A wide variety of programs, including several that involve the restoration of threatened/endangered species are dependent upon hormone treatment to complete final gamete maturation and ensure successful spawning.

The time of spawning is by its own nature a stressful period for all fish species. The handling required during the artificial spawning of fish complicates an already delicate situation. In order to maintain the health of both wild and domestic brood fish, it is beneficial to minimize overall fish handling. Successful hormone treatment can reduce handling requirements to a single hormone administration event followed by actual gamete collection, thereby greatly reducing overall fish handling.

Studies have shown that final gamete maturation in fish can be induced by the administration of a variety of hormones (Donaldson and Hunter 1983; Goetz 1983). The first reported studies investigating the hormonal control of reproduction in fish utilized intraperitoneal injection of freshly dissected pituitary glands (Houssay, 1931; von Ihering, 1937). The use of CCP was first reported in the United States by Hasler et al.,

(1939, 1940). These and many other early studies investigating the use of fish pituitaries to induce gamete maturation in a variety of fish species were thoroughly reviewed by Pickford and Atz (1957) in their comprehensive treatise on the fish pituitary gland.

The efficacy of common carp pituitary (CCP) to induce ovulation and spermiation in fish is well documented (Chaudhuri, 1976), CCP has been shown to induce gamete maturation in a wide variety of species, including certain threatened and endangered species. Common carp pituitary, which has been shown to be particularly effective when used in cool and warm water species, has had a significant, positive impact on federal, state, private, and tribal programs nationwide.

Purpose

The purpose of this report is to summarize the results of CY14 supplemental CCP field efficacy trials. Furthermore, it is expected that these data will be used to enhance the existing CCP database that has been established from previous years trials for the purpose of supporting a new animal drug approval for the use of CCP in aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

A total of 10 trials were conducted at nine fish culture facilities during CY14, including two U.S. Fish and Wildlife Service facilities, four state hatcheries, and three private hatcheries. Water temperature during treatments at the various testing facilities ranged from 50.0 - 80.0 °F. Overall mean treatment temperature from all trials was 65.3 °F.

2. CCP used in trials

All CCP used in CY14 trials was supplied either by Progressive Companies, Inc, Spirit Lake, IA; or by Argent Chemical Company, Redmond, WA.

3. Drug dosages

As described in the current authorization, Investigators were allowed to use CCP at doses ranging up to 25 mg CCP/kg body weight (bw). During this reporting period, the drug doses used ranged from 1 to 25 mg CCP/kg bw. CCP was administered as either a single injection or as a series of two injections.

Fish Species and Gender Treated

1. Species of fish treated

The following six fish species were treated with CCP during the reporting period:

Non-salmonids

Arkansas river shiner (*Notropis girardi*)

channel catfish (*Ictalurus punctatus*)

lake sturgeon (*Acipenser fulvescens*)

muskellunge (*Esox masquinongy*)

plains minnow (*Hybognathus placitus*)

suckermouth minnow (*Phenacobius mirabilis*)

2. Gender of fish treated

A total of 7,526 females and 294 males were injected with CCP during the reporting period. Typically, females are treated with spawning hormones to shorten the egg maturation period or synchronize ovulation. Males are treated to ensure that sufficient milt is available for egg fertilization.

Data Collected

1. Primary response variable (Maturation)

The primary response variable for evaluating the effect of CCP on fish was the percentage of ripe fish following treatment. These percentages reflected the number of female fish that ovulated and the number of male fish that reached active spermiation.

2. Egg development and milt evaluation

Secondary response variables for females included the relative number of eggs that reached the eyed stage and the number hatched. Secondary response variables for males included the volume of milt (ml) available from individual fish and an evaluation of milt motility (percent motile spermatozoa).

Discussion of Study Results

1. Summary results on the efficacy of CCP to induce gamete maturation (Note:

Tables 1 - 2 provides a summary of all efficacy trials; and Table 3 lists the number of treatment trials, number of fish and species treated, and treatment regimens used during CY14 under INAD #8391).

A. Efficacy of CCP on male fish treated between 1 and 25 mg/kg bw (1 injection)

Male fish were treated in five of the 10 trials and injected 1 time with CCP at a dosage between 1 and 25 mg/kg bw (Table 1) to induce gamete maturation. Fish species treated included Arkansas river shiner, lake sturgeon, muskellunge, plains minnow, and suckermouth minnow; control fish were used in one of the male trials involving muskellunge. Following treatment, there was 85.7% - 100% spermiation among all treated fish; as compared to 100% spermiation in the control fish.

B. Efficacy of CCP on female fish treated between 1 and 25 mg/kg bw (1 - 2 injections)

Female fish were treated in all 10 trials and injected 1 - 2 times with CCP at a dosage between 1 and 25 mg/kg bw (Table 2) to induce gamete maturation. Fish species treated included Arkansas river shiner, channel catfish, lake sturgeon, muskellunge, plains minnow, and suckermouth minnow; control fish were used in one trial involving muskellunge. Following treatment, there was 10.5 - 100% ovulation among all treated fish; as compared to no ovulation in the control fish.

Overall, treatments appeared efficacious in nine trials involving 7,612 fish; and was characterized as inconclusive in one trial involving 208 fish.

2. Observed Toxicity

No toxicity or adverse effects relating to CCP treatment were reported in any of the trials.

3. Observed Withdrawal Period

No withdrawal time is needed for fish treated with CCP under the Food-Use Authorizations dated June 19, 2012 and September 10, 2014.

Current Study Protocol for CCP INAD #8391

No changes have occurred to the current study protocol for CCP INAD #8391.

Facility Sign-up List

Please see "Table 4. Facilities and Names of Investigators" for facilities that signed-up to participate in the CCP INAD #8391 during CY14. The following facilities had CCP on hand; however, no studies were conducted:

1. E.W. Shell Fisheries Center

Correspondence sent to CCP Participants

Please see the attached correspondence that was sent to all CCP participants after the AADAP Office received their sign-up form for CY14.

Number of Treated Fish under Treatment Use Authorization

Total number of treated fish during CY14 was 7,820. The total number of treated fish to count against the treatment use authorization dated June 19, 2012 is 30,000 (including 12,765 fish carried over from the previous authorization). The total number of treated fish to count against the treatment use authorization dated September 10, 2014 is 3,215 (carried over from the previous authorization).

Summary of Study Results

The efficacy of CCP was evaluated in 10 trials involving six different fish species treated at doses ranging from 1 to 25 mg/kg bw. Treatment was administered as either a single injection or as a series of 2 injections. Control fish were used in two trials. A total of 7,820 adult fish were treated (7,526 females and 294 males). Water temperature during treatment ranged from 50.0 to 80.0°F. Overall, results showed that CCP treatment appeared efficacious in 90% of the and characterized as inconclusive in 10% of the trials. Investigators reported no evidence of toxicity or adverse effects related to CCP treatment in any of the trials. Because of the lack of pivotal field efficacy trials, it is understood that data summarized in this report can only be considered as ancillary data. None-the-less, the ancillary data described above should provide useful corroborative data to support a new animal drug approval for CCP. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #8391. In future trials conducted under INAD #8391, efforts will be directed towards the continued generation of high quality data.

References

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Table 1. Summary of CY14 CCP Male Efficacy Results - Injection						Males			
						Treated		Control	
Facility	**Efficacy**	**Number of Trials**	**Species**	**Dose (mg/kg)**	**Spawning Interval (hr)**	**Number Treated**	**% Spermiate**	**Number Controls**	**% Spermiate**
Tishomingo NFH	efficacious	1	Arkansas River Shiner	1.0	24	7	100	0	-
USFWS-NYFO	efficacious	1	Lake Sturgeon	1.0	24	7	85.7	0	-
Table Rock SFH	efficacious	1	Muskellunge	2.2	96	1	100	9	100
Native Aquatic Species Restoration Facility	efficacious	1	Plains Minnow	25.0	24	172	100	0	-
Native Aquatic Species Restoration Facility	Inconclusive (overall study - not able to break out male and female success)	1	Suckermouth Minnow	25.0	24	107	100	0	-

Table 2. Summary of CY14 CCP Female Efficacy Results - Injection						Females			
						Treated		Control	
Facility	**Efficacy**	**Number of Trials**	**Species**	**Dose (mg/kg)**	**Spawning Interval (hr)**	**Number Treated**	**% Ovulate**	**Number Controls**	**% Ovulate**
Tishomingo NFH	efficacious	1	Arkansas River Shiner	1.0	24	6	33.3	0	-
PHL Seining	efficacious	1	Channel Catfish	8	48	4,330	78.2	0	-
Tackett Fish Farm	efficacious	1	Channel Catfish	10.0	120	276	39.9	0	-
Wright Fish Farm	efficacious	1	Channel Catfish	10.0	24	2,555	75.0	0	-
USFWS-NYFO	efficacious	1	Lake Sturgeon	5.0	24	2	100	0	-
Hackettstown SFH	efficacious	1	Muskellunge	6.6	48	21	57.1	3	0
Spirit Lake SFH	efficacious	1	Muskellunge	6.5	72	9	100	0	-
Table Rock SFH	efficacious	1	Muskellunge	6.6	96	15	46.7	0	-
Native Aquatic Species Restoration Facility	efficacious	1	Plains Minnow	25.0	24	211	51.8 - 57.8 (ave 54.5)	0	-
Native Aquatic Species Restoration Facility	Inconclusive	1	Suckermouth Minnow	25.0	24	101	10.5 - 52.4 (ave 36.6)	0	-

Table 3. Description of number of trials conducted, species and number of fish treated, and treatment regimens used in CY14 under INAD #8391

Total Number of Trials Conducted:	10
Number of Efficacious Trials:	9
Number of Inconclusive Trials:	1
Total Number of Fish Treated:	7,820
Number of fish treated in efficacious trials	7,612
Number of fish treated in inconclusive trials	208
Treatment Regimes Used:	
1 - 10 mg/kg body weight (1 - 2 injections)	8 trials
25 mg/kg body weight (1 injection)	2 trials
Treatment Water Temperature (^{o}F):	50.0 - 80.0
Size of Treated Fish:	Adult
Species Treated:	
Non-salmonids	
Arkansas river shiner (*Notropis girardi*)	
channel catfish (*Ictalurus punctatus*)	
lake sturgeon (*Acipenser fulvescens*)	
muskellunge (*Esox masquinongy*)	
plains minnow (*Hybognathus placitus*)	
suckermouth minnow (*Phenacobius mirabilis*)	