Common Carp Pituitary Clinical Field Trials - INAD 8391

Year 2011 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 2011 (CY11), 19 INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Trials involved 12,563 treated fish and were conducted at nine different fish hatcheries, including one U.S. Fish and Wildlife Service fish hatchery, four state hatcheries, and four 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 CY11 indicated that treatments appeared efficacious in approximately 79% of the trials while 21% of the trials were ineffective.

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 CY11 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 19 trials were conducted at nine fish culture facilities during CY11, including one U.S. Fish and Wildlife Service fish hatchery, four state hatcheries, and four private hatcheries. Water temperature during treatments at the various testing facilities ranged from 52.0 - 80.0 °F. Overall mean treatment temperature from all trials was 68.6 °F.

2. CCP used in trials

All CCP used in CY11 trials was supplied either by Stoller Fisheries, 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 intraperitoneal (IP) injection, or as a series of two IP injections.

Fish Species and Gender Treated

1. Species of fish treated

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

Non-salmonids

channel catfish (*Ictalurus punctatus*)

common carp (*Cyprinus carpio*)

grass carp (*Ctenopharyngodon idella*)

muskellunge (*Esox masquinongy*)

plains minnow (*Hybognathus placitus*)

Rio Grande chub (*Gila pandora*)

suckermouth minnow (*Phenacobius mirabilis*)

Non-salmonid Marine

Atlantic sturgeon (*Acipenser oxyrhynchus*)

2. Gender of fish treated

A total of 11,989 females and 574 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; Table 3 lists the number of treatment trials, number of fish and species treated, and treatment regimens used; and Table 4 describes all trials conducted during CY11 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 six trials and injected 1 times with CCP at a dosage between 1 and 25 mg/kg bw (Table 1) to induce gamete maturation. Fish species treated included Atlantic sturgeon, common carp, grass carp, muskellunge, plains minnow, and suckermouth minnow; no control fish were used in any of the male trials. Following treatment, there was 0 - 100% spermiation among all treated fish. Overall, treatments appeared efficacious in four trials involving 546 fish and were ineffective in two trials involving 28 fish.

B. Efficacy of CCP on female fish treated between 4 and 25 mg/kg bw (1 - 2 injections)

Female fish were treated in 13 trials and injected 1 - 2 times with CCP at a dosage between 4 and 25 mg/kg bw (Table 2) to induce gamete maturation. Fish species treated included Atlantic sturgeon, channel catfish, common carp, grass carp, muskellunge, plains minnow, Rio Grande chub, and suckermouth minnow; one of the muskellunge trials included non-treated control groups. Following treatment, there was 0 - 100% ovulation among all treated fish; as compared to no ovulation in the control fish. Overall, treatments appeared efficacious in 11 trials involving 11,973 fish, and ineffective in five trials involving 16 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 Authorization dated June 19, 2012.

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 5. Facilities and Names of Investigators” for facilities that signed-up to participate in the CCP INAD #8391 during CY11. The following facilities had CCP on hand; however, no studies were conducted:

1. George Washington Carver Farm
2. Manning SFH
3. Tishomingo NFH
4. Gavins Point NFH

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 CY11.

Number of Treated Fish under Treatment Use Authorization

Total number of treated fish during CY11 was 12,563. The total number of treated fish to count against the treatment use authorization dated October 8, 2009 (valid through April 20, 2011) is 11,861. The total number of treated fish to count against the treatment use authorization dated April 21, 2011 (valid through December 6,2011) is 12,469.

Summary of Study Results

The efficacy of CCP was evaluated in 19 trials involving eight different fish species treated at doses ranging from 1 to 25 mg/kg bw. Treatment was administered as either a single IP injection or as a series of 2 IP injections. Control fish were used in one trial. A total of 12,563 adult fish were treated (11,989 females and 574 males). Water temperature during treatment ranged from 52.0 to 80.0°F. Overall, results showed that CCP treatment appeared efficacious in 79% of the trials while 21% of the trials were ineffective. 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 CY11 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**
Bears Bluff NFH	ineffective	1	ASN	1	-	4	0	0	na
E.W. Shell Fisheries Center	effective	1	CAP	2	24	6	100	0	na
E.W. Shell Fisheries Center	effective	1	GRC	2	22	3	100	0	na
Table Rock SFH	effective	1	MUE	2.2	5 - 6 days	11	100	0	na
Native Aquatic Species Restoration Facility	effective	1	PLM	25	24	526	?	0	na
Native Aquatic Species Restoration Facility	ineffective	1	SMM	25	24	24	0	0	na

Table 2. Summary of CY11 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
Bears Bluff NFH	ineffective	1	ASN	4	-	1	0	0	na
E.W. Shell Fisheries Center	effective	1	CAP	4	25	9	62	0	na
Baxter Land Co.	effective	1	CCF	10	24 - 26	769	68 - 100 (ave. 87)	0	na
America's Catch Catfish Farm	effective	1	CCF	10	40 - 48	6,470	12 - 80 (ave 40)	0	na
PHL Hatchery	effective	1	CCF	10	24	1455	30.1	0	na
E.W. Shell Fisheries Center	effective	1	CCF	10	24	30	45.4-100 (ave 70)	0	na
NeedMore Fisheries	effective	[1]	CCF	10	29 - 35	2599	31 - 98 (ave 71)	0	na
E.W. Shell Fisheries Center	effective	1	GRC	4	21	5	40	0	na
Hackettstown SFH	effective	1	MUE	6.6	3 - 9 days	21	100	2	0
Table Rock SFH	effective	1	MUE	6.6	5 - 6 days	3	100	0	na
Native Aquatic Species Restoration Facility	effective	1	PLM	25	24	582	?	0	na
Native Aquatic Species Restoration Facility	effective	1	RGC	25	24	30	57	0	na

Table 2. Summary of CY11 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
Native Aquatic Species Restoration Facility	ineffective	1	SMM	25	24	15	0	0	na

Table 3. Description of number of trials conducted, species and number of fish treated, and treatment regimens used in CY11 under INAD #8391

Total Number of Trials Conducted:	19
Number of Efficacious Trials:	15
Number of Ineffective Trials:	4
Total Number of Fish Treated:	12,563
Number of fish treated in efficacious trials	12,519
Number of fish treated in ineffective trials	44
Treatment Regimes Used:	
1 - 10 mg/kg body weight (1 - 2 injections)	14 trials
25 mg/kg body weight (1 injection)	5 trials
Treatment Water Temperature (^{o}F):	52.0 - 80.0
Size of Treated Fish:	Adult

Species Treated:

Non-salmonids
channel catfish (*Ictalurus punctatus*)
common carp (*Cyprinus carpio*)
grass carp (*Ctenopharyngodon idella*)
muskellunge (*Esox masquinongy*)
plains minnow (*Hybognathus placitus*)
Rio Grande chub (*Gila pandora*)
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Non-salmonid Marine
Atlantic sturgeon (*Acipenser oxyrhynchus*)