

Common Carp Pituitary Clinical Field Trials - INAD 8391

Year 2002 Annual Summary Report on the Use of Common Carp Pituitary in Field Efficacy Trials

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Summary

Spawning aids such as luteinizing hormone-releasing hormone analogue, human chorionic gonadotropin, and common carp pituitary (CCP) 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. During calendar year (CY) 2002, several INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Fifty-two such trials involving 2,309 treated fish were conducted at two U.S. Fish and Wildlife Service fish hatcheries, two state hatcheries, and one private hatchery. 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 more. Overall results of trials

conducted in CY 2002 indicated that approximately 92% of the trials appeared efficacious, 4% appeared ineffective, and 4% were characterized as inconclusive.

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. In many cases, especially with respect to captured wildstock species, final gamete maturation will not occur without hormone treatment.

Final gamete maturation in fish can be induced by the administration of a variety of hormones. Common carp pituitary (CCP) has been shown to induce gamete maturation in a number of fish 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 CY 2002 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 trials conducted in previous years for the purpose of supporting a new animal drug approval for the use of CCP in aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

Five fish culture facilities used CCP during CY 2002, including two U.S. Fish and Wildlife Service fish hatcheries, two state fish hatcheries, and one private fish hatchery .

2. CCP used in trials

All CCP used in CY 2002 trials was supplied by Stoller Fisheries, Spirit Lake IA.

3. Drug dosages

As described in the Study Protocol, Investigators were allowed to use CCP at dosages ranging from 4 to 10 mg CCP/kg body weight (bw). The drug dosages used in CY 2002 trials ranged from 1 to 10 mg CCP/kg bw and were used to induce gamete maturation in females and males. 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 five fish species were treated with CCP during CY 2002.

bonytail chub *Gila elegans*

channel catfish *Ictalurus punctatus*

muskellunge *Esox masquinongy*

Rio Grande silvery minnow *Hybognathus amarus*

shortnose sturgeon *Acipenser brevirostrum*

2. Gender of fish treated

A total of 2,273 females and 36 males were injected with CCP during CY 2002.

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. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. However, only one pathology report was submitted during CY 2002 trials.

2. Primary response variables

The primary response variables for evaluating the effect of CCP were the relative number of fish that ovulated or reach active spermiation. With respect to the treatment of females, in some cases, percent hatch and percent eyed eggs was also determined.

3. Spawning interval

The period of time between the final CCP treatment and when treated fish were evaluated for gamete maturation was documented.

Discussion of Study Results

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

Summary of CY 2002 CCP efficacy results are listed in Table 1; Table 2 describes the number of trials conducted, species and number of fish treated, and treatment

regimens used during CY 2002 CCP efficacy trials; and Table 3 describes all federal, state, and private individual CCP trials conducted in CY 2002.)

A. Efficacy at 1.0 mg/kg bw

Three trials were conducted in which male shortnose sturgeon were injected with CCP at a dosage of 1.0 mg/kg bw (Table 1). Percent spermiation was 75%; no control fish were used. Treatment appeared efficacious.

B. Efficacy at 2.2 mg/kg bw

One trial was conducted in which male muskellunge were injected with CCP at a dosage of 2.2 mg/kg bw (Table 1). Percent spermiation was 100%; no control fish were used. Treatment appeared efficacious.

C. Efficacy at 4.0 mg/kg bw

Five trials were conducted in which female shortnose sturgeon, and female and male bonytail chub were injected twice with CCP at a dosage of 4.0 mg/kg bw (Table 1). Percent ovulation in treated females were 50 - 75%, and percent spermiation in treated males were 100%; no control fish were used. Treatment appeared efficacious in all trials.

D. Efficacy at 5.0 mg/kg bw

Two trials were conducted in which female and male Rio Grande silvery minnows were injected twice with CCP at a dosage of 5.0 mg/kg bw (Table 1). Percent ovulation in treated females was 100%, and percent spermiation in treated males was 100%; no control fish were used. Both treatments appeared efficacious.

E. Efficacy at 6.6 mg/kg bw

Five trials were conducted in which female muskellunge were injected with CCP at a dosage of 6.6 mg/kg bw (Table 1). One trial involved the use of a non-treated control group. Percent ovulation of treated fish ranged between 0 - 100%. The control fish did not ovulate. Three treatments appeared efficacious, one trial appeared ineffective, and one trial was characterized as inconclusive.

F. Efficacy at 6.6 mg/kg bw

One trial was conducted in which female muskellunge were injected twice with CCP at a dosage of 6.6 mg/kg bw (Table 1). Percent ovulation in treated fish was 50%; no control fish were used. Treatment was characterized as inconclusive.

G. Efficacy at 10.0 mg/kg bw

Thirty-five trials were conducted in which female channel catfish were injected twice with CCP at a dosage of 10.0 mg/kg bw (Table 1). Percent ovulation in groups of test fish ranged from 7 - 98%; no control fish were used. Treatment appeared efficacious in 34 trials, and ineffective in 1 trial.

2. Observed Toxicity

No toxicity or adverse effects relating to CCP treatment were reported.

Summary of Study Results

The efficacy of CCP was tested in 52 trials involving bonytail chub, Rio Grande silvery minnow, muskellunge, shortnose sturgeon, and channel catfish treated at dosages ranging from 1 to 10 mg/kg bw. Treatment was administered as either a single IP injection, or as a series of two IP injections. Of the 52 trials conducted, one utilized non-treated control groups. A total of 2,309 adult fish were treated. Water temperature during treatment ranged from 52.0 to 82.4°F. Overall results indicated that CCP treatments appeared efficacious in 92% of the trials, ineffective in 4% of the trials, and inconclusive in 4% of the trials. Investigators reported no evidence of toxicity or adverse effects related to CCP treatment. Due to lack of criteria such as use of control fish, dose verification, randomization, and blinding, it is understood that these data will 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. Furthermore, it is anticipated that additional ancillary efficacy data will continue to be collected in future years under INAD #8391, and in such trials, efforts will be directed towards the continued generation of high quality data.

Table 1. Summary of CY 2002 CCP Efficacy Results							Females				Males			
							Treated		Control		Treated		Control	
Apparent Efficacy	Number of Trials	Facility	Species	Treatment Method	Dose (mg/kg)	Spawning Interval (hr)	Number Treated	% Ovulate	Number Controls	% Ovulate	Number Treated	% Spermiate	Number Controls	% Spermiate
Efficacious	2	Mora NFH & TC	Bonytail Chub	Injection	4.0	72	8	50	0	na	4	100	0	na
Efficacious	34	Harvest Select Farms	Channel Catfish	Injection	10.0	26	2,223	26 - 98	0	na	0	na	0	na
Ineffective	1	Harvest Select Farms	Channel Catfish	Injection	10.0	26	14	7	0	na	0	na	0	na
Efficacious	2	Hackettstown SFH	Musky	Injection	6.6	8 - 10 days	7	67 - 100	1	0	0	na	0	na
Ineffective	1	Hackettstown SFH	Musky	Injection	6.6	10 days	1	0	0	na	0	na	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	2.2	4 - 10 days	0	na	0	na	8	100	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	6.6	3 - 5 days	3	67	0	na	0	na	0	na
Inconclusive	2	Table Rock SFH	Musky	Injection	6.6	1 - 4 days	3	50 - 100	0	na	0	na	0	na
Efficacious	2	Mora NFH & TC	Rio Grande Silvery Minnow	Injection	5.0	1 - 3 days	4	100	0	na	12	100	0	na
Efficacious	3	Bears Bluff NFH	Shortnose Sturgeon	Injection	1.0	48	0	na	0	na	12	75	0	na
Efficacious	3	Bears Bluff NFH	Shortnose Sturgeon	Injection	4.0	24	10	67 - 75	0	na	0	na	0	na

Table 2. Number of Ccp Trial Conducted, Fish Treated, Treatment Regimens Used, and Fish Species Treated During Cy 2002 Efficacy Trials

Total Number of Trials Conducted:	52
<u>Number of Efficacious Trials:</u>	48
<u>Number of Ineffective Trials:</u>	2
<u>Number of Inconclusive Trials:</u>	2
Total Number of Fish Treated:	2,309
Treatment Regimes Used:	
<u>1.0 mg/kg body weight (one injection)</u>	3 trials
<u>2.2 mg/kg body weight (one injection)</u>	1 trial
<u>4.0 mg/kg body weight (two injections)</u>	5 trials
<u>5.0 mg/kg body weight (two injections)</u>	2 trials
<u>6.6 mg/kg body weight (one injection)</u>	5 trials
<u>6.6 mg/kg body weight (two injections)</u>	1 trial
<u>10.0 mg/kg body weight (two injections)</u>	35 trials
Treatment Water Temperature (°C):	52.0 - 82.4
Size of Treated Fish:	Adult
Species Treated:	bonytail chub <i>Gila elegans</i> channel catfish <i>Ictalurus punctatus</i> muskellunge <i>Esox masquinongy</i> Rio Grande silvery minnow <i>Hybognathus amarus</i> shortnose sturgeon <i>Acipenser brevirostrum</i>
