

## **Common Carp Pituitary Clinical Field Trials - INAD 8391**

### Year 2003 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) 2003, several INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Sixty-three such trials that involved 2,994 treated fish were conducted at five different fish hatcheries, including 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. Overall results of trials conducted in CY 2003 indicated that approximately 95% of the trials appeared efficacious while 5% 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 03 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**

Five fish culture facilities used CCP during CY 03, including two U.S. Fish and Wildlife Service fish hatcheries, two state fish hatcheries, and one private fish hatchery. Water temperature during treatments at the various testing facilities ranged from 42.0 - 82.4 °F. Overall mean treatment temperature from all trials was 75.7 °F.

### **2. CCP used in trials**

All CCP used in CY 03 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 these 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 four fish species were treated with CCP during CY 03:

channel catfish *Ictalurus punctatus*

muskellunge *Esox masquinongy*

northern pike *Esox lucius*

shortnose sturgeon *Acipenser brevirostrum*

### **2. Gender of fish treated**

A total of 2,957 females and 37 males were injected with CCP during CY 03.

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**

Although fish health pathology reports provide essential information with respect to disease confirmation and general fish health, no pathology report were submitted during CY 03 trials.

## **2. Primary response variables**

The primary response variables for evaluating the effect of CCP were (1) the relative number of female fish that ovulated, or (2) the number of male fish that reached 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 03 CCP efficacy results are listed in Table 1; Table 2 describes the number of trials conducted, fish species and number of fish treated, and treatment regimens used; and Table 3 describes individual CCP trials conducted at all federal, state, and private hatcheries under this INAD)

#### **A. Efficacy at 1.0 mg/kg bw**

Four 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 in treated males ranged from 62.5 to 100%; no control fish were used. All treatments 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 67%; no control fish were used. This treatment appeared efficacious.

#### **C. Efficacy at 4.0 mg/kg bw**

Four trials were conducted in which female shortnose sturgeon were injected twice with CCP at a dosage of 4.0 mg/kg bw (Table 1). Percent ovulation in treated females ranged from 50 to 100%; no control fish were used. Treatment appeared efficacious in three of the four trials, whereas results from one trial were characterized as inconclusive.

#### **D. 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). Four trials involved the use of a non-treated control group. Percent ovulation in treated females used in these trials ranged from 75 to 100%. The control fish did not ovulate. Percent ovulation in treated fish in which no controls were used was 60%. All treatments appeared efficacious.

### **E. Efficacy at 8.0 mg/kg bw**

Five trials were conducted in which female catfish were injected with CCP at a dosage of 8.0 mg/kg bw (Table 1). Percent ovulation in treated females ranged from 38 to 84%. All treatments appeared efficacious.

### **F. Efficacy at 10.0 mg/kg bw**

Forty-three trials were conducted in which female channel catfish were injected with CCP at a dosage of 10.0 mg/kg bw (Table 1). Percent ovulation in treated channel catfish ranged from 22 to 99%. One trial was conducted in which female northern pike were injected with CCP at a dosage of 10.0 mg/kg bw (Table 1). Percent ovulation in treated northern pike was 32%. Overall, treatment appeared efficacious in 42 of the 44 trials, whereas two trials were characterized as inconclusive.

## **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 63 trials involving muskellunge, northern pike, shortnose sturgeon, and channel catfish treated at dosages ranging from 1.0 to 10.0 mg/kg bw. Treatment was administered as either a single IP injection, or as a series of two IP injections. Of the 63 trials conducted, three utilized non-treated control groups.

A total of 2,994 adult fish were treated. Water temperature during treatment ranged from 42.0 to 82.4°F. CCP treatment appeared efficacious in 95% of the trials and inconclusive in 5% of the trials. Investigators reported no evidence of toxicity or adverse effects related to CCP treatment. Because of the lack of adherence associated with 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.

Table 1. Summary of CY 2003 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	5	Harvest Select Farms	Channel Catfish	Injection	8.0	24	322	79 - 100	0	na	0	na	0	na
Efficacious	41	Harvest Select Farms	Channel Catfish	Injection	10.0	26	2,438	45 - 99	0	na	0	na	0	na
Inconclusive	2	Harvest Select Farms	Channel Catfish	Injection	10.0	26	141	22 - 35	0	na	0	na	0	na
Efficacious	4	Hackettstown SFH	Musky	Injection	6.6	Up to 10 days	16	75 - 100	4	0	0	na	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	2.2	5 days	0	na	0	na	6	67	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	6.6	5 days	5	60	0	na	0	na	0	na
Efficacious	1	Genoa NFH	Northern Pike	Injection	10.0	2 - 4 days	25	32	0	na	0	na	0	na
Efficacious	4	Bears Bluff NFH	Shortnose Sturgeon	Injection	1.0	48	0	na	0	na	31	62.5 - 100	0	na
Efficacious	3	Bears Bluff NFH	Shortnose Sturgeon	Injection	4.0	24	9	50 - 100	0	na	0	na	0	na
Inconclusive	1	Bears Bluff NFH	Shortnose Sturgeon	Injection	4.0	24	1	100	0	na	0	na	0	na

**Table 2. Description of number of trials conducted, species and number of fish treated, and treatment regimens used in CY2003 under INAD #8391**

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<b>Total Number of Trials Conducted:</b>	63
<u>Number of Efficacious Trials:</u>	60
<u>Number of Inconclusive Trials:</u>	3
<b>Total Number of Fish Treated:</b>	2,994
<b>Treatment Regimes Used:</b>	
<u>1.0 mg/kg body weight (one injection)</u>	4 trials
<u>2.2 mg/kg body weight (one injection)</u>	1 trial
<u>4.0 mg/kg body weight (two injections)</u>	4 trials
<u>6.6 mg/kg body weight (one injection)</u>	5 trials
<u>8.0 mg/kg body weight (one injection)</u>	5 trial
<u>10.0 mg/kg body weight (one injection)</u>	44 trials
<b>Treatment Water Temperature (°F):</b>	42.0 - 82.4
<b>Size of Treated Fish:</b>	Adult
<b>Species Treated:</b>	channel catfish <i>Ictalurus punctatus</i>
	muskellunge <i>Esox masquinongy</i>
	northern pike <i>Esox lucius</i>
	shortnose sturgeon <i>Acipenser brevirostrum</i>

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