

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

## Year 2005 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. During calendar year 2005 (CY05), several INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Fourteen such trials that involved 2,802 treated fish were conducted at seven different fish hatcheries, including three 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 during

this period indicated that approximately 93% of the trials appeared efficacious, while 7% of the trials 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 various spawning hormones. Common carp pituitary (CCP) is one such hormone, and 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 CY05 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 14 trials were conducted at seven fish culture facilities during CY05, including three state fish hatcheries and four private fish hatcheries. Water temperature during treatments at the various testing facilities ranged from 52.0 - 84.0 °F. Overall mean treatment temperature from all trials was 64.8 °F.

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

All CCP used in CY05 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 doses ranging from 4 to 10 mg CCP/kg body weight (bw). During this reporting period, the drug doses used ranged from 2.0 to 10 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 four fish species were treated with CCP during the reporting period:

channel catfish *Ictalurus punctatus*

common carp *Cyprinus carpio*

grass carp *Ctenopharyngodon idella*

muskellunge *Esox masquinongy*

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

A total of 2,787 females and 15 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. Pathologists Reports**

Although fish health pathology reports provide essential information with respect to disease confirmation and general fish health, no pathology report were submitted for trials conducted in CY05.

### **2. Primary response variables**

The primary response variables for evaluating the effect of CCP were (1) the relative number of female fish that ovulated following treatment, or (2) the number of male fish that reached active spermiation following treatment. With respect to the treatment of females, in some cases, percent hatch and percent eyed eggs were also determined.

### **3. Spawning interval**

The spawning interval is the period of time between the final CCP treatment and when treated fish were evaluated for gamete maturation. Where appropriate, the spawning interval was documented.

## **Discussion of Study Results**

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

Summary of CY05 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 state and private hatcheries under this INAD)

#### **A. Efficacy at 2.0 - 2.2 mg/kg bw**

Two trials were conducted in which male muskellunge and grass carp were injected with CCP at a dose of 2.0 - 2.2 mg/kg bw (Table 1).

Following treatment, there was 71 - 100% spermiation among all treated fish; no control fish were used. Overall, treatment appeared efficacious in both trials.

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

Two trials were conducted in which female common carp and grass carp were injected with CCP at a dose of 4.0 mg/kg bw (Table 1). Following treatment, there was 54 - 100% ovulation among all treated fish; no control fish were used. Overall, treatment appeared efficacious in both trials.

### **C. Efficacy at 6.6 mg/kg bw**

Five trials were conducted in which female muskellunge were injected with CCP at a dose of 6.6 mg/kg bw (Table 1). Two trials involved the use of a non-treated control group. Following treatment, there was 78 - 100% ovulation among treated females. The control fish did not ovulate. In the trials in which controls were not used, the relative level of ovulation ranged from 69 - 100%. Overall, treatment appeared efficacious in all trials.

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

Five trials were conducted in which female channel catfish were injected with CCP at a dose of 10.0 mg/kg bw (Table 1). Following treatment, there was 30.8 - 82% ovulation among treated fish; no control fish were used. Overall, treatment appeared efficacious in four of the five trials. In one trial, results were characterized as inconclusive.

## **2. Observed Toxicity**

No toxicity or adverse effects relating to CCP treatment were reported in 13 of the 14 trials. However, the Investigator noted in one trial that 14 channel catfish died after the study. It was suspected that mortality was caused by a bacterial infection.

## **Summary of Study Results**

The efficacy of CCP was evaluated in 14 trials involving muskellunge, common carp, grass carp, and channel catfish treated at doses ranging from 2.0 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 14 trials conducted, two utilized non-treated control groups. A total of 2,802 adult fish were treated (2,787 females and 15 males). Water temperature during treatment ranged from 52.0 to 84.0°F. Overall, results showed that CCP treatment appeared efficacious in 93% of the trials, and inconclusive in the remaining 7% of the trials. Investigators reported no evidence of toxicity or adverse effects related to CCP treatment in any trial. 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.

Table 1. Summary of CY05 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	1	Baxter Land Co.	Channel Catfish	Injection	10.0	47 - 50 hr	639	34.6 - 60	0	na	0	na	0	na
Efficacious	1	Eagle Aquaculture Inc.	Channel Catfish	Injection	10.0	36 - 40 hr	88	30.8 - 34.7	0	na	0	na	0	na
Efficacious	1	Harvest Select Farms	Channel Catfish	Injection	10.0	42 - 54 hr	164	40 - 76	0	na	0	na	0	na
Inconclusive	1	Harvest Select Farms	Channel Catfish	Injection	10.0	42 - 50 hr	43	41.8	0	na	0	na	0	na
Efficacious	1	Jubilee Farms	Channel Catfish	Injection	10.0	42.5 - 48.5 hr	1790	31 - 82	0	na	0	na	0	na
Efficacious	1	North Auburn Fisheries Research Unit	Common Carp	Injection	4.0	24 hr	21	100	0	na	0	na	0	na
Efficacious	1	North Auburn Fisheries Research Unit	Grass Carp	Injection	2.0	24 hr	0	na	0	na	7	71	0	na
Efficacious	1	North Auburn Fisheries Research Unit	Grass Carp	Injection	4.0	24 hr	13	54	0	na	0	na	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	2.2	3 - 11 days	0	na	0	na	8	100	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	6.6	3 - 11 days	13	69	0	na	0	na	0	na
Efficacious	4	Hackettstown SFH	Musky	Injection	6.6	48 - 96 hr	16	78 - 100	2	0	0	na	0	na

**Table 2. Description of number of trials conducted, species and number of fish treated, and treatment regimens used in CY05 under INAD #8391**

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<b>Total Number of Trials Conducted:</b>	14
<u>Number of Efficacious Trials:</u>	13
<u>Number of Inconclusive Trials:</u>	1
<b>Total Number of Fish Treated:</b>	2,802
<b>Treatment Regimes Used:</b>	
<u>2.0 mg/kg body weight (two injections)</u>	1 trial
<u>2.2 mg/kg body weight (one injection)</u>	1 trial
<u>4.0 mg/kg body weight (two injections)</u>	2 trials
<u>6.6 mg/kg body weight (one injection)</u>	5 trials
<u>10.0 mg/kg body weight (two injections)</u>	5 trials
<b>Treatment Water Temperature (°F):</b>	52.0 - 84.0
<b>Size of Treated Fish:</b>	Adult
<b>Species Treated:</b>	channel catfish <i>Ictalurus punctatus</i>
	common carp <i>Cyprinus carpio</i>
	grass carp <i>Ctenopharyngodon idella</i>
	muskellunge <i>Esox masquinongy</i>

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