AQUACULTURE DRUGS: 17*α*-METHYLTESTOSTERONE TARGET ANIMAL SAFETY STUDY[1]

Project ***Termination Report*** for the Period
December 15, 2004 to August 31, 2008

NCRAC FUNDING: $50,000 (December 15, 2004 to December 31, 2007)

PARTICIPANT:

Anita M. Kelly	Southern Illinois University-Carbondale	Illinois
Industry Advisory Council Liaison:		
Rosalie A. Schnick	National Aquaculture NADA Coordinator	Wisconsin
Extension Liaison:		
Joseph E. Morris	Iowa State University	Iowa

REASON FOR TERMINATION

Anita Kelly is no longer at Southern Illinois University-Carbondale (SIUC) and other University personnel did not want to take over as the Principal Investigator on the grant.

PROJECT OBJECTIVES

(1) Interact with the Center for Veterinary Medicine (CVM) to determine the study design and protocol.

(2) Submit the study protocol to CVM and gain acceptance from CVM for the study protocol.

(3) Conduct a target animal safety study using 17α-methyltestosterone (MT) on tilapia according to CVM guidelines for a target animal safety study in feed under good laboratory practices (GLP).

(4) Write the final study report and submit to CVM through the MT Investigational New Animal Drug (INAD) Coordinator at Auburn University.

(5) Provide progress reports to the North Central Regional Aquaculture Center (NCRAC).

(6) Gain acceptance from CVM for the target animal safety study on MT in tilapia.

[1]NCRAC has funded seven Aquaculture Drugs projects. A termination report for the first project is contained in the 1997-98 Annual Progress Report; a termination report for the second project is contained in the 1996-97 Annual Progress Report, a termination report for the third project is contained in the 2001-02 Annual Progress Report, a termination report for the fourth project is contained in the 2006-07 Annual Progress Report, and a termination report for the seventh project is contained elsewhere in this report. A fifth project, which provided $60,000 for a portion of the funds required to purchase sufficient radiolabeled AQUI-S7 for use in a total residue depletion study in rainbow trout, is also reported on under the progress report for the National Coordinator for Aquaculture New Animal Drug Applications (NADAs) elsewhere in this report. This termination report is for the sixth Aquaculture Drugs project which was undertaken by Anita M. Kelly. It was a 2-year project that began December 15, 2004.

PRINCIPAL ACCOMPLISHMENTS

OBJECTIVE 1

The Principal Investigator for this project worked closely with CVM and the U.S. Fish

and Wildlife Service Aquatic Animal Drug Approval Partnership program (USFWS AADAP) which holds the INAD under which this research is being conducted to design and develop an acceptable protocol.

OBJECTIVE 2

The first protocol was submitted on August 8, 2005 to the USFWS AADAP which holds the INAD and must submit all protocols to CVM. They submitted the protocol on August 30, 2005. On December 7, 2005 CVM responded to the protocol submission, to AADAP, and found the protocol unacceptable. The AADAP forwarded the comments to Kelly on January 12, 2006. This correspondence included CVM's detailed explanation with a list of items they wanted corrected. CVM's concerns to the protocol were addressed and the protocol rewritten and sent to AADAP for review and comment. A revised protocol was sent to AADAP on May 2, 2006 and to CVM on May 16, 2006. The revised protocol was reviewed by CVM and the reply sent to AADAP on August 14, 2006. CVM found this protocol unacceptable and the AADAP forwarded the concerns of CVM to Kelly on August 18, 2006. The protocol was revised to address the new concerns of CVM. This revised protocol was accepted by CVM in February 2007.

OBJECTIVES 3-6

The target animal safety study was completed through the necropsy of the fish. Pathology has not been conducted on the fish used in this study. During the study, the laboratory was audited by the Food and Drug Administration (FDA) for GLP compliance. During the audit, the inspectors felt that too many fish were "missing" from the tanks. Cannibalism had been noted when apparent. The fish were netted from the tanks weekly, counted by two individuals, and the lengths of 10 random

individuals were measured and recorded. In addition to the missing fish, the FDA audit noted several other noncompliant items including feed discrepancies and lack of an official assignment of a Study Director in the absence of the assigned Study Director.

During the course of the study, the Study Director was in communication with CVM regarding the problems with GLP inspection. It was decided on August 17, 2007 that CVM could not accept the study as conducted due to numerous noncompliant items.

IMPACTS

The ability of culturists to produce fish that exhibit uniform growth while expending little to no energy toward reproduction will increase the profits and production from a facility. Currently, determination of the gender of tilapia by visual inspection is relatively difficult until the fish have attained sexual maturity. Sex reversal of fish prior to sexual differentiation in most cases enables the production of monosex populations. Under an existing INAD, tilapia are being sex reversed to create all male populations using MT. However, in order for this hormone to be approved by the FDA, a target animal safety study must be conducted and approved by CVM.

RECOMMENDED FOLLOW-UP ACTIVITIES

A new MT target animal safety study is to be conducted by personnel at the Harry K. Dupree Stuttgart National Aquaculture Center (SNARC). Kelly will be in contact with the researchers at SNARC to identify areas that were deemed problems in the GLP inspection. This collaborative effort should increase the probability of obtaining approval for the target animal safety study.

SUPPORT

NCRAC provided $50,000 to SIUC which was the entire amount of funding allocated for this project.

PUBLICATIONS, MANUSCRIPTS, OR PAPERS PRESENTED

See the Appendix for a cumulative output for all NCRAC-funded Aquaculture Drugs activities.