



The Aquatic Animal Drug Approval Partnership Program

“Working with our partners to conserve, protect and enhance the Nation’s fishery resources by coordinating activities to obtain U.S. Food and Drug Administration approval for drugs, chemicals and therapeutants needed in aquaculture”



Volume 2-1

AADAP NEWSLETTER

October 2005

WHAT’S SHAKIN’

NEWS FLASH !!!!

CVM Approves Florfenicol for ESC: We have all been waiting a long time for this, and it’s finally a reality!!! FDA’s Center for Veterinary Medicine announced on Tuesday, 25 October 2005, that they had approved the NADA submitted by Schering-Plough Animal Health (SPA) for Aquaflor® (florfenicol). SPA’s NADA (#141-246) is an antimicrobial Type-A Medicated Article and, at this time, is limited for the control of mortality due to enteric septicemia of catfish. For more details visit CVM’s website (<http://www.fda.gov/cvm/catfishapp.htm>).

There are a tremendous number of folks out there deserving of credit for making this happen, and they will be recognized. However, at the moment, suffice to say that none of this would have come about if it had not been for SPA’s dedication and commitment to the aquaculture industry – we salute you !!

NEWS FLASH !!!!

Newsletter via snail-mail: Starting with our next edition of the AADAP Newsletter (Volume 2-2, January 2006), we will provide a paper copy ONLY to those individuals that specifically request their name be placed on the paper-copy mail-list. We are sorry for any inconvenience that this may cause, but the time and expense to print and mail paper copies has become too high. To have your name placed on the paper-copy mail-list, contact us at <http://www.fws.gov/fisheries/aadap/contact.html>, and merely type “paper copy” in the subject line.

The 2006 INAD Sign-up Forms are available: Once again it is that time of year for renewal of your facility’s INADs for calendar year 2006. Please send in the completed sign-up sheets to the Bozeman INAD/AADAP Office by 31 December 2005. Invoices will then be mailed out by the end of January. Also, if you have not already done so, please send in all Form 2’s (Drug Inventory Form) and Form 3’s (Results Report Form) for each of the INADs that were used at your facilities for INAD Year 2005. All 2006 sign-up forms are available for downloading on our website at: (<http://www.fws.gov/fisheries/aadap/signup.htm>).

Quarterly INAD Investigator/Monitor Award: A tip-of-the-hat and a pat-on-the-back to Robert Piper of Bozeman, Montana and Joseph Hinton of the Makah Fisheries Tribal Hatchery, Washington. “Piper,” Bozeman Fish Technology Center Director emeritus, has played a key role, as the Study Monitor for all Montana Department of Fish, Wildlife and Parks facilities participating in the INAD process. Joe, as a study-site investigator, consistently provides, to AADAP, study results of the highest quality.

Drug Approval Coordination Workshop: The 11th Annual Drug Approval Coordination Workshop (formerly known as the INAD Workshop) was held this past August 2nd & 3rd in

Bozeman, Montana, and by all accounts it was a great success. This year’s Workshop rewrote the record book, with approximately 80 participants in attendance. As in the past, there was broad representation from pharmaceutical companies, academia, state and federal resource/research agencies, private aquaculture companies and federal regulatory agencies. Good fun was had by all at the Workshop BBQ (a small collage of pictures from the BBQ can be found on our website at (http://www.fws.gov/fisheries/aadap/inad_workshop_presentations.html)).

In an effort to make as much of the information exchanged at the Workshop available to as many interested parties as possible, most of the presentations from the Workshop have been made available on our website at the aforementioned address.

JSA Biologics Focus Group meeting: The Federal Joint Subcommittee on Aquaculture’s Working Group on Quality Assurance in Aquaculture Production (JSA-QAAP) recently sponsored a special meeting on biologics. The meeting was held in Bozeman, Montana on 1 August 2005, in conjunction with this year’s Drug Approval Coordination Workshop. The meeting was attended by over 20 scientists and government regulators. A few of the presentations from the meeting are likewise available on our website at the previously noted address. Incidentally, several presentations given at the Drug Approval Coordination Workshop are of particular relevance to the topic of biologics. Dr. Melisse Schilling’s presentation (Tuesday, August 2nd at 10:45 am) provided an overview of the biologics registration process. Dr. David Scarfe’s presentation (Wednesday, August 3rd at 1:45 pm) provided a synopsis of the Biologics Focus Group meeting from two days previous. Two other presentations at the Drug Approval Coordination Workshop (Wednesday, August 3rd at 1:45 pm) also focused on biologics and are available for viewing.

Requested SLICE® INAD not authorized: CVM recently responded to AADAP’s earlier request for a SLICE® (emamectin benzoate) INAD to be used as a freshwater ectoparasiticide. CVM responded by not authorizing the INAD, citing insufficient information regarding the environmental safety of effluents. AADAP is working with Schering Plough Animal Health to generate the necessary information/data to resolve these issues.

Aquaflor® (florfenicol) update:

NADA approved for ESC: see above.

Request for “Technical Section Complete” letter:

Following acceptance of an AADAP study to demonstrate the efficacy of florfenicol to control mortality in chinook salmon caused by furunculosis, AADAP requested that CVM consider all pivotal studies complete to support the following claim: “use of florfenicol-medicated feed administered at a dosage of 10 mg active drug per kg of fish per day administered for 10 consecutive days to control mortality in all freshwater-reared salmonids caused by

furunculosis." If CVM accepts this request, then the first amended label claim (i.e., for salmonids) should include language allowing the use of Aquaflor® to control mortalities in all freshwater reared salmonids, caused by bacterial coldwater disease (for which all required studies had been previously submitted and accepted) and furunculosis.

Chloramine-T update:

New source of chloramine-T: Axcentive SARL/International Specialty Chemicals, Inc. remains as one of the two sources of the investigational drug; however, the Axcentive SARL authorized distributor has changed to Mr. Larry Holzman (email lbh@ischem.com, phone 914-333-0606, FAX 914-333-0333). For further details on chloramine-T sources refer to AADAP website (<http://www.fws.gov/fisheries/aadap/chloramine.htm>).

17- α methyltestosterone update:

Pivotal Study Protocol submitted: An AADAP pivotal research protocol entitled "The Efficacy of 17- α Methyltestosterone Medicated Feed to Induce Gender Manipulation in Tilapia to Produce Populations Comprising \leq 20% Reproductively Capable Females" was submitted to CVM in May 2005. Following CVM review, changes were made to reach protocol concurrence. The revised protocol is now entitled "The Efficacy of 17- α Methyltestosterone Medicated Feed to Produce Predominately Male Populations of Tilapia." We hope to begin field efficacy trials under this revised protocol in the next few months.

AQUI-S® update:

Target Animal Safety – An AADAP TAS study was conducted in March 2005 on small fingerling rainbow trout to evaluate whether 40 mg/L (the highest proposed efficacious dose to sedate salmonids to the handleable stage) meets CVM's target animal safety criteria. Mortality and pathology associated with exposure to AQUI-S® were the two primary response variables measured. Histological evaluation to select tissues has been completed, and the data are currently being analyzed. Our goal is to complete the Final Study Report by the end of the calendar year. At that time, we will begin making preparations to evaluate the safety of AQUI-S® to representative cool- and warmwater fishes.

Efficacy Studies - AQUI-S® efficacy studies were recently completed on fingerling and juvenile Kokanee salmon and fingerling June suckers; Final Study Reports were submitted to CVM in September 2005.

In addition, a study was completed and report submitted to CVM that compared the efficacy of AQUI-S® on individually sedated and group-sedated fingerling walleye. Results from this study (1) showed that there was no significant difference between times to sedate fish to handleable when sedated either individually or in groups, and (2) were consistent with results from similar studies conducted on rainbow trout and channel catfish. Details of this study can be found in the second article of our Feature Articles Section of this newsletter. Many thanks to Montana Fish, Wildlife and Parks, Fish Breeders of Idaho, and the USFWS Bozeman Fish Tech Center for providing test fish.

Data to support a claim for all freshwater fish - Based on discussions with CVM, we believe that a sufficient number of studies have been completed to demonstrate the following efficacy claim: "AQUI-S® as an anesthetic to sedate all freshwater fish to the handleable stage of

anesthesia." Such a request was made to CVM, and we are awaiting their reply.

SE-MARK® (calcein) update:

Feed studies conducted: A USGS-funded Science Support Project (SSP) recently began at Bozeman Fish Technology Center (BFTC) to evaluate the effectiveness of calcein-medicated feed in marking calcified tissue of shovelnose sturgeon and Snake River cutthroat trout (two of six species being tested under the SSP project). Studies with the other species are scheduled to begin soon at the Lamar Fish Technology Center (LFTC) and the Appalachian Research Lab (NARL). Test fish will receive a standard dose of calcein mixed with feed in either an encapsulated or straight pre-mix form for one of several durations (5, 10, or 15 d). Marks resulting from administration of medicated feed will be compared with marks made when calcein is administered in the water as a static bath.

Pilot Studies Conducted: Preliminary results conducted at BFTC showed that shovelnose sturgeon readily ate calcein-medicated feed when calcein was incorporated in either the encapsulated form or as straight premix. The fins, scutes and other bony tissues "lit up like Times Square" when



Calcein marks on shovelnose sturgeon after 15 days of calcein-medicated feed

viewed with a SE-MARK® Detector in fish consuming the calcein medicated feed for 10-15 days. Preliminary studies with rainbow trout and Snake River cutthroats indicated that these species found certain levels of non-encapsulated calcein to be

unpalatable. Related pilot work at LFTC indicated that there may be a threshold level of non-encapsulated calcein below which some freshwater *Oncorhynchus* spp. find calcein palatable. Special thanks to Dale Honeyfield, NARL; Jerre Mohler and Tom Kehler, LFTC; and Greg Kindschi, BFTC.

Work under the INAD: If you are interested in mass-marking larval fish via immersion to produce a non-lethally detectable mark, SE-MARK® (calcein) may provide you with a useful management tool. For more information, please contact AADAP or Western Chemical, Inc. (phone 800-283-5292).

FEATURE ARTICLES

COMPARISON OF THE EFFICACY OF HYDROGEN PEROXIDE AND FORMALIN TO CONTROL FUNGUS ON LAKE TROUT EGGS

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Introduction

Aquatic fungi (Saprolegniales) are ubiquitous in natural water supplies of fish hatcheries and can cause serious disease

