U.S. Fish & Wildlife Service

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"

AADAP Aquatic Animal Drug Approval Partnership Program

Volume 3-3

AADAP NEWSLETTER

October 2007

WHAT'S SHAKIN'

NEWS FLASH ! NEWS FLASH ! NEWS FLASH !

Schering-Plough Animal Health does it again !!! A huge "Congratulations" is in order to the SPAH aquaculture team (and all the other private, public and academic entities that helped with data generation) for adding another claim to their Aquaflor® medicated feed label. Aquaflor® is now also approved (as of 6 November 2007) for use in all freshwater-reared salmonids to control mortality caused by furunculosis. Click the following links to view CVM's Announcment or SPAH's News Release.

New generic copy of formalin approved by CVM: B.L. Mitchell, Inc. (Leland, Mississippi) recently (13 August 2007) received formal FDA approval for their formalin product, Formacide-B® (a generic copy of Parasite-S®). It is approved as a water bath for the control of certain external parasites of finfish and shrimp, and for the control of fungi on finfish eggs. For additional information, see the 13 August 2007 Federal Register Notice.

Happy Halloween from the AADAP Staff!!

14th Annual Aquaculture Drug Approval Coordination Workshop (2008): Back by popular demand next year's Workshop will be held once again in Bozeman, Montana, USA. Like that of previous Workshops, the Workshop will take place on the Tuesday and Wednesday (29-30 July 2008) immediately before Bozeman's Sweet Pea Festival (1-3 August 2008). Be sure, as the time gets closer, to check AADAP's webpage for details.

Another great Aquaculture Drug Approval Coordination Workshop (2007) concludes: Each year they just seem to get better and better, and this year was no exception. Officially 72 fish-folks registered and were in attendance. Special thanks goes out to all that attended and made the workshop the success it was. Extra special appreciation is expressed to representatives or senior management of FDA's Center for Veterinary Medicine, US Geological Survey, US Fish & Wildlife Service and the Association of Fish and Wildlife Agencies for attending and providing keynote addresses. See below for more information on the Workshop.

THANK YOU, THANK YOU, THANK YOU !! This year's Workshop would not have been possible if it were not for the generous assistance of the chemical and pharmaceutical companies attending. Our hats go off to Axcentive SARL, Frontier Scientific Inc., Intervet Inc., Novartis Animal Health, Schering-Plough Animal Health and Western Chemical Inc.

13th Annual Aquaculture Drug Approval Coordination Workshop presentations NOW online: Especially for those not able to attend this year's Workshop, all formal presentations are now on AADAP's website. Click here to view.

U.S. Fish & Wildlife Service's Assistant Director for Fisheries and Habitat Conservation (ADFHC) retiring: Dr. Mamie Parker, the ADFHC recently announced her retirement from the USFWS. Ma Parker, as she likes to be called, will be leaving on 3 November 2007 after almost 30 years with the Service. Ma Parker has been a strong supporter of AADAP and the "consortium" of aquatic animal drug approval partners to which AADAP belongs. As the Assistant Director of the Program, of which AADAP is a part, she has been in a position to make a real difference in AADAP's role within the consortium. *Thank you Mamie; we, at AADAP, wish you the very best in your new adventures.*

Upper Midwest Environmental Sciences Center Lead Scientist to Retire: One of the key researchers in the aquaculture drug approval arena, Dr. William Gingerich, has announced his retirement.

Dr. Gingerich has headed-up the Aquaculture Drug Research and Development Program for more than a decade. His team has made substantial contributions to the approvals or pending approvals of several aquaculture drugs, including Aqui-S®, Halamid® (chloramine-T), Aquaflor® (florfenicol), formalin, 35% Perox-Aid® (hydrogen peroxide), and oxytetracycline. Dr. Gingerich was recently (11 June 2007) awarded the Food and Drug Administration Commissioner's Special Citation. The prestigious award recognizes Dr. Gingerich "For exceptional leadership, outstanding coordination of resources, and sustained efforts in the development of data for the approval of new animal drugs for aquaculture." Please refer to the USGS's Corner for more details on Bill's career and retirement. *Thank you Bill for all your hard work and dedication; we wish you the very best in the next chapter of your life.*

Mississippi State University researcher recognized: Dr. Patricia S. Gaunt, Associate Professor in Aquatic Animal Health at Mississippi State University College of Veterinary Medicine recently (27 September 2007) received the 2007 Pfizer Award for Research Excellence. This is a peer-selection award recognizing Dr. Gaunt for her research contributions in the area of veterinary medicine. Dr. Gaunt has been responsible for substantial work leading to the recently approved finfish claims for florfenicol. *Congratulations Pat and thanks so much for your critical contributions to aquatic animal drug approval work.*

Hydrogen peroxide INAD requested: AADAP recently resubmitted to CVM a request to establish an INAD for 35% PEROX-AID®. The submission included a protocol for testing 35% PEROX-AID® on a variety of freshwater and marine ectoparasites. At present, AADAP has been assigned an INAD number, but authorization to conduct studies is pending CVM's review. Stay tuned.

Sometime's it's all about the networking: Mike Barnes, hatchery biologist at McNenny State Fish Hatchery (South Dakota Game, Fish, and Parks), and outgoing AFS-Fish Culture Section President, attended the 13th Annual Aquaculture Drug Approval Coordination Workshop held in Bozeman, MT. Although Mike was a first time attendee, he jumped right in with both feet and invited AADAP to their hatchery in Spearfish, South Dakota to talk about the possibility of conducting much-needed field efficacy studies in his neck of the woods. As it has become abundantly clear that the only way to achieve broad drug approval label claims for all freshwater finfish is to work with as many partners as possible, we are thankful to Mike and the folks with the SDGF&P for providing us this opportunity. As always, stay tuned to see what happens next.

Upcoming INAD/NADA Workshop in Mississippi: At the 13th Annual Drug Approval Coordination Workshop this past August there was discussion regarding the need/benefit of providing aquaculturists in the southeast corner of the U.S. with an up-to-date overview of the aquatic species drug approval process. This discussion was initiated, in part, because this geographical segment of the aquaculture industry has been somewhat left out of mainstream drug approval efforts. As a result of this discussion, the AADAP program has agreed to coordinate a 1-day INAD/NADA Workshop that is tentatively scheduled for 6 February 2008 in Greenville, Mississippi. The Workshop will be held in conjunction with the Catfish Farmers of America Fish Farming Trade Show. As more detailed information regarding the Workshop becomes available, it will be posted on the AADAP website.

A "Statistical" Thank You: Pivotal efficacy studies conducted in support of aquaculture drug approvals are usually organized according to the five classic steps of controlled experiments: hypothesis, design, procedures, data analysis, and interpretation of observed results. Ideally, the biological, logistical, and statistical components of a controlled experiment "work together" to produce a valid hypothesis test. If not, researchers risk "not testing" the hypothesis of interest or otherwise misinterpreting the observed results.

For AADAP, "statistics" is oftentimes the most challenging component of pivotal efficacy studies. Hence, in the spirit of teamwork, we've begun working more closely with the U.S. Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and the U.S. Geological Survey's (USGS) Upper Midwest Environmental Sciences Center (UMESC; La Crosse, WI) when designing or analyzing pivotal efficacy studies.

Specifically, we thank Dr. Todd Blessinger (Mathematical Statistician, FDA/CVM), Dave Petullo (Mathematical Statistician, FDA/CVM), and Mark Gaikowski (Research Physiologist, USGS/UMESC) for their help with the analyses of data generated in several recent studies. Dr. Blessinger guided us through the analysis of a "multisite" study conducted with 17α-methyltestosterone and tilapia at SeaPac of Idaho (Buhl, ID) and Simaron Freshwater Fish (Hempstead, TX). Mr. Gaikowski, with input from Mr. Petullo and Dr. Blessinger, helped us to analyze mortality data from three studies conducted with either chloramine-T or hydrogen peroxide and largemouth bass at Richloam Fish Hatchery (Webster, FL). By employing experimental designs and data analysis methods acceptable to FDA/CVM, we hope to facilitate their reviews of our final study reports.

National Aquaculture Drug Research Forum activities: A meeting of the NADRF was held in conjunction with the 13th Annual Aquaculture Drug

Approval Coordination Workshop, and the meeting turned into one of the most productive meetings held to date. Some of the highlights included: 1) fruitful discussion relative to requirements necessary to satisfy the analytical method transfer study component of the human food safety package, 2) the establishment of a continuing education program to be held in conjunction with the Drug Approval Coordination Workshop, 3) CVM informing the group that submissions to CVM will soon be done electronically (within the next 3 yrs), and 4) the development of a rigorous peer-review process for NADRF products. For more information on this meeting, click here or see the "Notes from 2 August 2007" meeting on the AADAP website (click on Meeting Notes on the NADRF drop-down menu).

Follow-up discussions to the aforementioned items have been positive; we've received indication that fewer method transfer studies may be sufficient to satisfy this data requirement, and that individuals within CVM are "on-board" to help us launch the continuing education program. The next meeting of the NADRF will be held in conjunction with Aquaculture America 2008, which is scheduled for 9-12 February 2007 in Lake Buena Vista, Florida. The meeting will be held at the end of the Therapeutic Drug Research Special Session and all are invited to attend. For more information, contact Jim Bowker at 406-994-9910 or Mark Gaikowski at 608-781-6284.

Aquaflor® (florfenicol) updates:

Effectiveness Technical Section for Strep in tilapia: AADAP recently submitted a request to CVM that the Effectiveness Technical Section be considered complete for the following claim "Use Aquaflor® at a concentration of 10 mg florfenicol per kg fish body weight per day for 10 consecutive days to control mortality in hybrid striped bass caused by *Streptococcus iniae*." If CVM's Aquaculture Team concurs that the Technical Section is complete (and we anticipate that they will), then an approval for this claim may become a reality in the near future.

***Streptococcus iniae* optimal dosage model being developed:** Dr. Vaughn Ostland (Director of Pathology, Kent SeaTech Corp, Mecca, CA) and Jim Bowker (AADAP) are working on a Western Regional Aquaculture Center-funded project to evaluate whether the standard dosage for florfenicol (i.e., dose currently approved for other species/pathogen claims, which is 10 mg per kg fish body weight per day for 10 days) is the most effective treatment regimen for controlling mortality in hybrid striped bass caused by *Streptococcus iniae*. A disease challenge model has been developed that will allow these researchers to test various concentrations (10, 15 and 20 mg florfenicol per kg fish body weight) for various durations (10, 15 and 20 days) in a lab setting. The most cost-effective treatment regimen identified in the lab trials will be confirmed in field trials using test fish naturally infected with *S. iniae*. The first lab trial to evaluate the effectiveness of different concentrations of florfenicol for this claim will begin within the next month.

Paper on effectiveness against *Streptococcus iniae* published: Ahmed Darwish of USDA's Stuttgart National Aquaculture Research Center recently published (in the *Journal of Aquatic Animal Health*, Volume 19(1):1-7) a relevant article on florfenicol use in hybrid striped bass. Below is an expanded abstract. Our thanks to the author.

Laboratory Efficacy of Florfenicol against *Streptococcus iniae* Infection in Sunshine Bass

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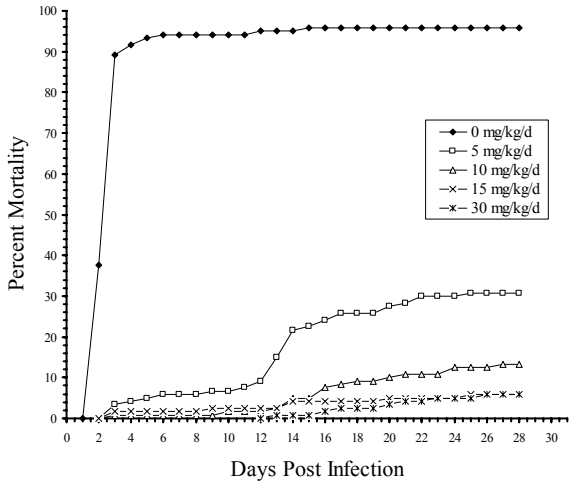
An experimental feeding trial was performed to evaluate the efficacy of florfenicol (FFC) in controlling *Streptococcus iniae* infection in sunshine bass (female white bass *Morone chrysops* X male striped bass *M. saxatilis*). Five dosage levels of FFC in medicated feed were administered daily: 0, 5, 10, 15, and 30 mg of active ingredient per kg of fish body weight. Treatment was started within 22-24 hours post-challenge by waterborne exposure to virulent *S. iniae.* The FFC medication was continued for 10 consecutive days, followed by a 25-day post-treatment observation period. At the conclusion of the experiment, FFC treatment significantly increased the survival (see Figure 1 below) of *S. iniae*-challenged sunshine bass from 4.2% in the non-medicated (positive control) group to 69.2% in the 5-mg/kg dosage group, 86.7% in the 10-mg/kg group, and 94.2% in the 15 and 30 mg per kg groups. Survival was significantly higher in the 15 and 30 mg per kg treatment groups than in the 5 mg per kg treatment group; differences among the 10 mg per kg and higher dosage groups were not significant. Survival curve analysis using a log-rank test indicated no significant difference between curves for the 10 and 15 mg per kg groups but a significant difference between curves for the 5 and 10 mg per kg groups. At the end of the experiment, no carriers were detected in any challenged group receiving an FFC-medicated diet, but the bacterium was recovered from the non-medicated challenged survivors of the infection. The results of the experiment suggest that the optimum therapeutic daily dose of FFC is between 10 and 15 mg per kg body weight for 10 days.

Figure 1: Cumulative mortality of sunshine bass infected by immersion exposure to *S. iniae* and fed 0, 5, 10, 15 and 30 mg (florfenicol) per Kg body weight per day for 10 days. Each treatment had 120 fish equally divided among six aquaria.



AQUI-S® updates:

Request for TAS "Technical Section Complete letter": AADAP recently submitted a request to CVM that the Target Animal Safety Technical Section for the use of AQUI-S® on all freshwater salmonids be considered complete. Based on the efficacy and safety data generated to date, AADAP proposed that the draft label language for this product will allow the user to sedate freshwater salmonids using 20-40 mg per L AQUI-S® for management and handling purposes. CVM's response is pending.

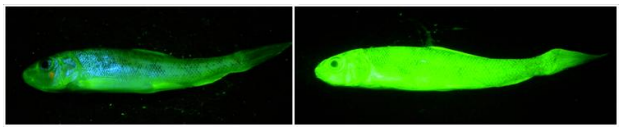
Reminder: status of the U.S. Fish & Wildlife Service's AQUI-S® INAD #10-541: Isoeugenol (the active ingredient in AQUI-S®) has been under evaluation by the National Toxicology Program (NTP), a Federal interagency program whose mission is to evaluate chemical agents for potential public health risks. Recently, the NTP was forced to delay (until February 2008) the review of their nearly completed two-year toxicology studies on isoeugenol because of higher priorities. Although the study data have not been fully analyzed, an independent preliminary assessment of the data does not eliminate the possibility that isoeugenol residues in treated fish could pose a human health risk.

Because we need to be absolutely certain that there are no human food safety issues that would preclude the use or approval of AQUI-S®, effective 2 May 2007 the U.S. Fish & Wildlife Service temporarily suspended all field activities under its Investigational New Animal Drug exemption (INAD #10-541) until the NTP review is complete. Although the decision to take such measures was not an easy one to make, it was the most prudent course of action. We look forward to reinstating all AQUI-S® INAD field activities in February 2008.

We appreciate your patience and understanding, and we remain committed to obtaining approval for a zero-withdrawal fish anesthetic for field operations. If you have any questions or comments, please do not hesitate to contact Dr. Dave Erdahl (email: dave_erdahl@fws.gov; phone: 406-994-9904).

Calcein (SE-MARK®) updates:

Even more pilot immersion marking studies completed: AADAP's continuing quest to establish the breadth (species- and life-stage-wise) of SE-MARK®'s effectiveness and safety recently resulted in testing on June sucker fingerlings (1-2" in length). Two separate study sets were conducted. The first was an effort to duplicate a previously reported use of SE-MARK® (conducted by another investigator at the low dose - long duration option under the INAD) that resulted in exceptionally high mortalities. The AADAP-conducted "duplicate" trial did not result in any mortality, and visible marks were produced, albeit not very bright. The second trial was a 1X & 10X "quick and clean" safety study. This study produced extremely bright marks (see below photos; 1X on the left, 10X on the right), even in the



1X dose. Unfortunately, it appears that June sucker juveniles are inordinately sensitive (compared to other species) to SE-MARK®; resulting in excess of 50% mortalities at the 10X dose. The 1X dose resulted in no mortality. Especially in light of these particular preliminary study results, AADAP will continue to test other species and life-stages, as they become available, for their "markability" and tolerance.

Paper to be published on the removal of SE-MARK® from discharge water: Jerre Mohler, USFWS's Northeast Fishery Center (Lamar, Pennsylvania) and Kelly Bradley, Lock Haven University (Lock Haven, Pennsylvania) have submitted for publication an article describing a procedure to remove calcein from hatchery discharge water. They kindly provided an expanded abstract for your information. Our thanks to the authors.

Removal of SE-MARK® calcein in wastewater produced from batch-marking fish[3]

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3. This work has been submitted as a manuscript to the *North American Journal of Fisheries Management* for publication.

The fluorochrome dye known as calcein (SE-MARK®) is currently the subject of numerous studies, under INAD #10-987, to investigate its efficacy in creating a lasting fluorescent mark on bony tissues of fish. Although waste marking solution may be stored on station in a secure leak-proof container, the INAD states that no discharge of calcein marking solution is permitted and it must ultimately be shipped to a waste handling company in Tacoma, Washington for disposal. This disposal requirement makes SE-MARK® impractical to use for marking fish where large volumes of water (hundreds of liters) are needed (e.g., for otolith marking of American shad and other Alosids). Finding a safe and effective technique for on-site removal of SE-MARK® from waste marking solutions may facilitate expanded use of this marking technique and provide a good alternative to the high cost and impracticality of shipping waste solutions for disposal. We performed laboratory tests at the Northeast Fishery Center, Lamar, Pennsylvania with three media: 1) limestone sand/screenings, 2) calcium carbonate, and 3) activated carbon to determine their effectiveness for removing SE-MARK® from waste fish-marking solutions.

Upon initial screening tests of the three media, only activated carbon was found to be efficient at removing the dye from solution. We tested the adsorption capacity of the activated carbon in laboratory tests and used the results to remove calcein from waste SE-MARK® solution in both packed column and batch treatments. Evaluation of the packed column showed that approximately 3.0 grams of carbon effectively removed the calcein from each liter of waste fish-marking solution at a concentration of 125 mg per L, while evaluation of a batch treatment showed that 5 grams of carbon was effective at removing the calcein from each liter of solution in a 250 mg per L concentration. Final concentrations of SE-MARK® after each type treatment were 1.0 mg per L or less. We conclude that activated carbon treatment provides a practical means of eliminating the calcein dye from waste fish-marking solutions. This treatment technique could eventually facilitate expanded use of SE-MARK® by fisheries managers as a tool which can be used alone or in conjunction with oxytetracycline to produce unique banding patterns on fish otoliths.

Copper sulfate update:

Paper to be published on effectiveness of copper sulfate and potassium permanganate against costia: Drew Mitchell and his colleagues at USDA's Stuttgart National Aquaculture Research Center had the opportunity to conduct a study this past summer (2007) testing the effectiveness of $CuSO_4$ and $KMnO_4$ against costia. Drew has kindly offered a brief summary of their study, which will be submitted soon for formal publication. Our thanks to the authors.

Comparing the Effectiveness of Two Applications of Copper Sulfate and Potassium Permanganate against Ichthyobodosis (Costiosis) on Sunshine Bass in Tanks

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The biflagellated single-cell parasite *Ichthyobodo nectator*, more commonly known as *Costia*, can cause significant losses among fish populations, particularly those cultured in tanks. It is often associated with young fish that have been crowded, underfed, and held in waters with low flow, but its occurrence is not limited to these conditions. A number of treatments including acetic acid, formalin, salt, potassium permanganate ($KMnO_4$), and copper sulfate ($CuSO_4$) have been used for more than 30 years, but most of the evidence for the effectiveness of these treatments is anecdotal.

Our study evaluated the effectiveness of $KMnO_4$ and $CuSO_4$ against a natural *I. nectator* infestation on sunshine bass (female white bass *Morone chrysops* X male striped bass *M. saxatilis*) reared in tanks. Twenty-three fish (3.1 g average) from the infested group were randomly placed in each of 12 tanks supplied with aeration and 10 L of flow-through water (about 200 mL per minute). Within an hour of stocking the fish, 4-hour static treatments of 3 mg per L $KMnO_4$ (2.5 mg per L above the determined $KMnO_4$ demand) and 2 mg per L $CuSO_4$ (the waters had an alkalinity of about 200 mg per L) were randomly applied to 4 tanks each. Four tanks remained as positive controls (PC). The same treatments were re-applied 2 days later to their respective tanks. Mortalities were recorded daily and survival percentages were determined at 2- and 5-days post-treatment (all mention of post-treatment refers to after the second treatment); based on 23 and 18 total fish per tank, respectively (lower fish number in second sampling was due to 5 fish per tank sampling loss for parasite evaluation taken after the survival determination 2-day post-treatment).

Ichthyobodo nectator infestations in the fish were evaluated prior to treatment (9 fish from initial infested group), on Day 2 (5 fish per tank), Day 5 (3 fish per tank) and Day 12 (3 fish per tank) post-treatment by a method we term the "60:60 Method". The method involved the microscopic examination of wet-mount preparations of both gill tissue and skin scrapings.

When the targeted wet mount tissue was in focus, a 60-second timer was started; observed parasites were counted for 60 seconds or until 60 were found, whichever came first. An infestation rating value (IRV) was assigned: 0 = no *Costia* found, 1 = 1 to 19 found, 2 = 20 to 59 found, and 3 = 60 or more found. Each fish was given two values, one for the gill tissue and another for scraped tissues. An average of these two values was assigned to each fish.

The total alkalinity and total hardness of the water used in the study was 206.6 and 95.0 mg per L, respectively. The maximum total ammonia nitrogen was 0.09 mg per L and the dissolved oxygen was ≥ 5.8 mg per L. The water temperature during the study ranged from 24.8° to 25.3°C.

Statistical Analysis - A one-way analysis of variance compared the mean parasite infestation values on 2-days and 5-days post-treatment using MINITAB and the differences among treatment means was determined using Tukey's Procedure. The survival percentages were arcsine transformed and subjected to one-way analysis of variance using MINITAB and the differences among treatment means was determined using Tukey's Procedure. Treatment effects were considered significant at $P < 0.05$.

At 2-days post-treatment, the survival in the $CuSO_4$ (90.2%) and $KMnO_4$ (92.4%) treatments was significantly higher than the PC (17.4%). At 5-days post-treatment, $CuSO_4$, $KMnO_4$, and PC treatments had significantly different average survivals; these were 87.5%, 37.5%, and 0%, respectively. By 12-days post-treatment, six (6) more $KMnO_4$ treated fish had died while only one (1) $CuSO_4$ treated fish died. No further mortalities were noted through 19-day post-treatment.

The average pre-treatment *I. nectator* IRV, as determined by the 60:60 Method, was 2.6. The 2-day post-treatment average IRV for $CuSO_4$, $KMnO_4$, and PC treatments was 0, 2.1, and 2.97, respectively (all were significantly different). The 5-day post-treatment average IRV for $CuSO_4$ and $KMnO_4$ was significantly different at 0.1 and 2.2, respectively. The 12-day post-treatment average IRV for $CuSO_4$ and $KMnO_4$ was significantly different at 0.17 and 0.67, respectively.

By 2-days post-treatment, $KMnO_4$ significantly curtailed the initial mortality and reduced the parasite loads. However, fish mortalities increased dramatically over the next 3 days and parasites loads remained constant. The 4-hour static treatment of $CuSO_4$ at 2 mg per L applied twice at a 2-day interval was effective in significantly lowering the parasite load (almost eliminating *I. nectator*) and maintaining the highest fish survival throughout the course of the study (19-days post-treatment).

Halamid® (chloramine-T) updates:

Largemouth bass efficacy study completed: Michael Matthews and his Richloam State Hatchery (Florida Bass Conservation Center) colleagues completed a pivotal efficacy study on largemouth bass diagnosed with external columnaris. A Final Study Report describing study results was submitted by AADAP to CVM on 25 September 2007 for review. Results from the study demonstrated that 20 mg per L chloramine-T administered as a static bath for 60 minutes on three alternate days was effective in controlling mortality caused by external columnaris in largemouth bass. We hope to hear back from CVM by early next year that the study has been accepted as pivotal.

A second study to substantiate the effectiveness of chloramine-T for the above-mentioned claim was completed by Michael and his colleagues. The data have been analyzed and the Final Study Report is being developed. Results from the two studies conducted on largemouth bass should complete the effectiveness technical section for this claim for this fish species.

Revised protocol accepted: The revised chloramine-T effectiveness research protocol entitled "A Research Protocol to Determine the Effectiveness of Chloramine-T to Control Mortality Due to Bacterial Gill Disease or External Columnaris" received CVM concurrence on 26 July 2007. We've got two words for that….Yee! Ha!

Oxytetracycline (OTC) updates:

Human Food Safety Technical Section: On 2 July 2007, Phibro Animal Health (PAH) submitted a letter to CVM, requesting that CVM consider the Human Food Safety Technical Section for their medicated feed product to be complete. They anticipate a response from CVM around the first of the year (2008).

Medicated Feed Label submitted: On 23 July 2007, PAH submitted a revised label for their OTC medicated feed. The label contained 1) a claim for coldwater disease in all freshwater-reared salmonids, 2) a claim for systemic columnaris in all *Oncorhynchus mykiss* (not just steelhead trout), and 3) the old skeletal marking claim (which was not on the original label). Additionally, the revised label now does not have a temperature restriction. Label-review is pending; we'll keep you apprised of any new information.

***Oncorhynchus mykiss* argument accepted by CVM:** In a letter dated 25 July 2007, CVM announced their agreement with a "white paper" submitted by AADAP proposing that efficacy and/or TAS studies conducted on either steelhead or rainbow trout be considered sufficient to satisfy data requirements for all *O. mykiss*. CVM acknowledged that effectiveness data accepted for freshwater-reared steelhead has

"significant inferential value" for other strains/subspecies of *O. mykiss*, and hence, has expanded the label claim for OTC medicated feed to "control mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared *O. mykiss*." CVM considers this label claim to represent all strains/subspecies of *O. mykiss* which include rainbow trout, steelhead trout, redband trout, and redband steelhead trout.

17α-methyltestosterone (17MT) updates:

Efficacy Studies: Since the last Newsletter (Vol. 3-2), there has been considerable progress with respect to completing the data requirements to demonstrate the effectiveness of 17MT to produce predominantly male populations of tilapia. In the past 3 months, 1) CVM accepted (see acceptance letter) the first 17MT efficacy study AADAP conducted on hybrid tilapia at SeaPac of Idaho (Buhl ID), 2) Final Study Reports were completed and submitted to CVM for (a) an effectiveness study conducted on Nile tilapia at Simaron Freshwater Fish (Hempstead TX), and (b) a second effectiveness study conducted on hybrid tilapia at SeaPac of Idaho, 3) a Final Study Report was submitted in which we combined the data from all three studies conducted and tested for a "site-times-treatment interaction" effect, and 4) an Effectiveness Technical Section complete letter was submitted to CVM for the following claim: "Administer feed medicated with 60 mg 17MT per kg feed to larval tilapia at a rate of 15% fish body weight per day for 28 days to produce predominantly male populations of fish." At this point, we're in the wait-and-see mode and hoping that CVM considers the technical section complete. As usual, stay tuned.

Intersex Fish: As mentioned in the last Newsletter (Vol. 3-2), AADAP has spent considerable time trying to resolve the issue associated with intersex fish (i.e., those fish with gonads containing both testicular and ovarian tissue). In virtually all cases, gonads of intersex fish predominately comprise normally maturing testicular tissue and scattered immature or atretic oocytes. As per CVM's suggestion, we consulted with an expert in this field (Dr. Jeff Malison, Aquaculture Program Director, University of Wisconsin – Madison). Dr. Malison provided us with an "Expert Position" paper that will be used to support our claim that such intersex fish possess male growth characteristics, and hence, treatment was efficacious. Many thanks to Dr. Malison for developing this position paper.

Environmental Assessment (EA) mini-meeting: A short meeting to discuss the next steps in the EA process took place on Monday, 30 July 2007 at the Bozeman Fish Technology Center. In attendance were Eric Silberhorn (CVM), Chuck Eirkson (CVM; via phone), Don Prater (CVM), Terry Barry (UW-Madison), Mark Gaikowski (USGS-UMESC), Ron Phelps (Auburn University), Jim Bowker (AADAP), Dave Erdahl (AADAP) and Tom Bell (AADAP). Several topics directly related to the pending EA were discussed, particularly those pertaining to toxicological endpoints and mitigation of discharge.

17MT research conducted at the University of Wisconsin-Madison: The 17MT Water Method final report and the 17MT Water Study Report were submitted to CVM (via UMESC) in September. As previously reported in the AADAP Newsletter (Vol. 3-2, page 5), the 17MT Feed Method was approved by the CVM. The MT Feed Final Report will be submitted to the CVM (via Rangen, Inc.) this month (October). *Information provided by Dr. Terry Barry; University of Wisconsin – Madison.*

35% PEROX-AID® (hydrogen peroxide) updates:

Research Protocol submitted to CVM: AADAP submitted the hydrogen peroxide effectiveness research protocol entitled "A Research Protocol to Determine the Effectiveness of Hydrogen Peroxide to Control Mortality Due to Bacterial Gill Disease or External Columnaris" to CVM for review on 27 September 2006. We hope to hear back from CVM (with protocol concurrence) by the end of December.

FINS & TAILS, BITS & BOBBERS

2008 INAD Sign-up Forms are now available: Once again it is that time of year for renewal of your facility's INAD's for Calendar Year 2008. Please send in the completed sign-up forms to the Bozeman INAD/AADAP Office by 31 December 2007. Invoices will be mailed out the end of January. All 2008 sign-up forms are available on the AADAP website at: http://www.fws.gov/fisheries/aadap/signup.htm.

End of the Year INAD Forms due: If you have not already done so, please send in all Form 2's (Chemical Use Logs) and Form 3's (Results Report Form) for each of the INAD's that were used at your facilities for INAD Year 2007. For the 17α-Methyltestosterone Medicated Feed participants, Form 6 (Year End Efficacy Report) will also need to be submitted.

Several INAD study protocols have received re-authorization: Updated Study Protocols, Forms, and slaughter authorizations are now available for INAD's 9332, 10-697 and 9033; while re-authorization is also expected for INAD's 9321, 10-969 and 11-236. New INAD notebooks will be sent out by the end of January 2008 to participants that sign up for these INAD's. Please note that if you need the updated information sooner, the Study Protocols and Forms will be available on our website as they are received.

Recommended Storage of 17α-Methyltestosterone Medicated Feed: In order to maintain the stability of 17α-Methyltestosterone (17MT) in medicated feed, you must store the medicated feed in the proper environment. It is recommended that you store any 17MT-medicated feed at temperatures of 4°C or lower. This is especially important if you plan to use the

medicated feed over a long period of time (i.e., several months). If you are planning to use the medicated feed over a short period of time (i.e., one month or less) you may be able to successfully store the feed at ambient room temperature. However, keep in mind that storing the feed at this higher temperature may likely reduce its potency. As reported in the last Newsletter (Vol. 3-2, page 5), storage of 17MT-medicated feed at room temperature can reduce the amount of 17MT by as much as 15% per month. Better yet, if you have the room and would like your 17MT-medicated feed to maintain its maximum potency, store your medicated feed in a freezer!

FEATURE ARTICLE

Use of Aquaflor® (florfenicol, 50%) under INAD 10-697: Calculation of the Amount of Aquaflor® to Add to Fish Feed

Daniel Carty, Jim Bowker, Molly Bowman, and Dave Erdahl

U.S. Fish and Wildlife Service,
Aquatic Animal Drug Approval Partnership Program
4050 Bridger Canyon Road,
Bozeman, Montana 59715, USA

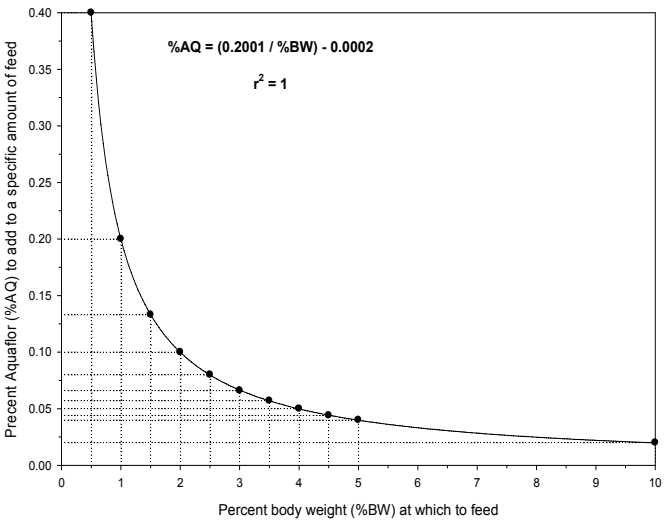
Aquaflor® Type A medicated article (hereafter referred to as Aquaflor®, a registered trademark of Schering-Plough Animal Health Corporation, Summit, NJ) is 50% active florfenicol, a broad-spectrum antibiotic with both bacteriostatic and bactericidal properties. Florfenicol is active against a variety of Gram-positive and Gram-negative bacteria.

In 2005, the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) approved Aquaflor® for use to control mortality in catfish due to enteric septicemia associated with *Edwardsiella ictaluri* (New Animal Drug Application [NADA] 141-246). In 2007, NADA 141-246 was amended to include use of Aquaflor® to control mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilum*. Also in 2007, FDA/CVM conditionally approved Aquaflor®-CA1 for use to control mortality in catfish due to columnaris disease associated with *Flavobacterium columnare* (NADA 141-259) Under NADAs 141-246 and 141-259, Aquaflor® and Aquaflor® CA1 can only be used with a Veterinary Feed Directive (VFD), must be purchased from a feed mill licensed to manufacture VFD medicated feeds, and are administered at 10 mg florfenicol per kg fish per day for 10 consecutive days.

Schering-Plough Animal Health Corporation is sponsoring additional Aquaflor® efficacy research to expand the product's label claims. Much of this work is conducted under Investigational New Animal Drug (INAD) exemption Florfenicol INAD 10-697, which is administered by the U.S. Fish and Wildlife Service's (FWS) Aquatic Animal Drug Approval Partnership (AADAP) program. The FWS INAD allows Aquaflor® to be used on a variety of fish species in a variety of experimental and production settings to generate efficacy data needed to support FDA/CVM approval of the following indications: (1) control of mortality in freshwater-reared salmonids due to furunculosis; (2) control of mortality in freshwater-reared salmonids due to systemic columnaris disease; and (3) control of mortality in hybrid striped bass due to Streptococcus iniae. For all three indications, the dose is 10 mg florfenicol per kg fish per day for 10 consecutive days.

Under INAD 10-697, Aquaflor®-medicated feed can be purchased directly from a licensed feed mill or Aquaflor® may be obtained and top dressed onto feed by hatchery personnel. The intended feeding rate must be taken into account when ordering or preparing Aquaflor®-medicated feed to ensure that the dose administered is 10 mg florfenicol per kg fish per day. For this dose, AADAP has developed a reference table for easily determining the amount (g) of Aquaflor® to add to a 20-kg or 50-lb bag of feed when fish are fed at 0.5 – 5.0% body weight (% BW) in 0.5% increments or are fed at 10% BW (Table 1).

Figure 1. Relation between percent body weight (%BW) and percent Aquaflor® (%AQ) to add to fish feed to achieve a dose of 10 mg florfenicol per kg fish per day.



However, it is not obvious how to calculate the amount of Aquaflor® to add to feed for %BWs not listed in Table 1.

In this article, we describe the mathematical relation between %BW and percent Aquaflor® (%AQ) to add to feed and explain how to calculate the amount of Aquaflor® to add to a specific amount of feed to achieve a dose of 10 mg florfenicol per kg fish per day when fish are fed at any %BW between 0.5 and 10% (as follows):

For a dose of 10 mg florfenicol per kg fish per day, the relation between %BW and %AQ is described by the equation (Figure 1),

$$\%AQ = [(0.2001 \div \%BW) - 0.0002]$$

Consequently, determining the amount (g) of Aquaflor® to add to a specific amount (g) of feed is a simple, three-step process:

(1) Enter %BW into the equation, and calculate %AQ (e.g., If fish will be fed at 1.5% BW, the %AQ to add to feed = [(0.2001 ÷ 1.5) - 0.0002] = 0.133%);

(2) Convert %AQ to a decimal fraction (e.g., 0.133% ÷ 100 = 0.00133); and

(3) Multiply the result by the amount (g) of treated feed to prepare (e.g., [0.00133 x 20,000 g feed] = 26.60 g Aquaflor® premix should be added to 20,000 g feed).

Table 1. To determine amount of Aquaflor® to add to either a 50-lb (22,680 g) or 20-kg (20,000 g) bag of fish feed, find the percent body weight (%BW) at which fish will be fed, go to the fourth or fifth row of the table, and read the amount (g) of Aquaflor® to add[a].

		Amount (g) of Aquaflor® to add to a bag of feed	
%BW to feed	%AQ to add	50 lb bag	20 kg bag
0.5	0.400	90.72	80.00
1.0	0.200	45.36	40.00
1.5	0.133	30.16	26.60
2.0	0.100	22.68	20.00
2.5	0.080	18.14	16.00
3.0	0.066	14.97	13.20
3.5	0.057	12.93	11.40
4.0	0.050	11.34	10.00
4.5	0.044	9.98	8.80
5.0	0.040	9.07	8.00
10.0	0.020	4.54	4.00

Footnote: **a.** Amount (g) of Aquaflor® to add to a specific amount (g) of feed = [(amount (g) of feed to be treated) x (percent Aquaflor® to add ÷ 100)].

USGS's CORNER

Congratulations Bill! The staff of the Upper Midwest Environmental Sciences Center is both happy and sad to inform our friends, partners, collaborators and supporters that Dr. William "Bill" Gingerich has announced his plans to retire after over 30 years of active research to support and enhance our Nation's natural resources. Always the thorough planner, his retirement plans have been in the works for the past couple of years and due to a fortunate series of events for Bill and his wife Sherryl, they will both be able to transition to retirement in January 2008. Bill started his federal career as a draftee in the U.S. Army in 1968 where he served as a lab technician in a hospital clinical diagnostic laboratory. After his time in "green", Bill completed his graduate work at California State University-Humboldt (M.S. 1972) and Oregon State University (Ph.D. 1977). After a stint as an assistant research professor at OSU, Bill rejoined government service in 1978 when he was selected to lead the Physiology Branch at the National Fisheries Research Center in La Crosse, WI. Though his career includes many notable achievements, the one with undoubtedly the greatest impact on our Nation's resources has been the leadership he provided from the inception of the Federal-State Aquaculture Drug Approval Project Partnership through the projects ultimate goal, the approval of new aquaculture drugs. Though Bill's daily leadership and guidance will be missed, Bill will remain active in graduate education as an adjunct faculty of the University of Wisconsin-La Crosse. He's also got a long list of interests and hobbies that will finally get his full attention. Please join all of us at UMESC in offering our warmest wishes and heartfelt thanks to Bill for his service and the best of luck as he transitions to a new career, one in which he (Sherryl) gets to set his schedule! Thanks and good luck Bill!!!

Thanks for your support! UMESC recently completed a 5-Year Center Review, mandated for all USGS Science Centers. The staff of the Fisheries Management Chemical and Aquaculture Drug Team would like to offer our sincere thanks to all of you for your support during this process. The comments you provided during our recent Partner Meeting, in the Partner Survey, and during the actual Center Review show the resolute support of our Partners to maintain UMESC's research capability and leadership to support aquaculture drug approvals. This research need was recognized by our Review Panel and by USGS leadership attending our Center Review. Your positive support of UMESC was directly reflected by the Review Panel recommending that UMESC maintain its core drug and chemical approval and registration capabilities and to expand it in new research areas. The comments from this Review Panel represent a course correction from our 2001 Center Review. We're extremely excited with the outcome of the present panel and feel that their recommendations will help chart our course into the future, one in which UMESC continues to provide the drug approval and chemical registration research and data to support the needs of the fisheries management community. UMESC greatly appreciates the efforts of all the panel members but would like to specifically recognize the contributions of Dr. Patricia Gaunt. Pat was resolute in ensuring the panel members understood the intricacies of the approval process and the research required. Combining your support with Pat's knowledge was a winning combination. Thanks again to all for your support! UMESC looks forward to a long and fruitful future of drug and chemical research to benefit our natural resource partners.

Chloramine-T environmental assessment accepted!!! UMESC received official notification (letter dated 12 October 2007) from CVM's Environmental Safety Team that the chloramine-T environmental assessment (EA) prepared by UMESC has been accepted by the Agency. In their acceptance letter, CVM indicated that the assessment was adequate to assure that chloramine-T use in aquaculture would not be expected to have a significant impact on the human environment provided that specific risk mitigation language are included on the chloramine-T animal drug label. Chloramine-T's EA was substantially different from the previous EA's UMESC

prepared for hydrogen peroxide and oxytetracycline-medicated feed. The chloramine-T EA is the first publicly prepared EA that includes underpinning proprietary data provided by the sponsor. The Axcentive data were critical to the development of this EA by UMESC and its ultimate acceptance by CVM and were recognized as such in CVM's notification to UMESC. CVM determined that the acute water quality benchmark (criterion) derived in the EA (0.13 mg per L) can be used by NPDES authorities to make informed decisions on discharge permits and the potential need for facility-specific effluent limits based on site-specific conditions (e.g., frequency of use, dilution in receiving water). Because the accepted EA discussed and relied heavily on proprietary data submitted independently by Axcentive and because labeling is needed to support risk mitigation, a technical section complete letter and a finding of no significant impact (FONSI) was not issued to UMESC by CVM. Rather, Axcentive (or another party given right of reference to Axcentive's data) will be able to refer to this public EA in order to complete the environmental safety technical section and have CVM issue a FONSI in support of a future chloramine-T approval. CVM's acceptance of the UMESC's chloramine-T EA represents one more significant step on the road to the ultimate broad approval of chloramine-T for use in aquaculture.

Oxytetracycline efficacy data accepted. UMESC was recently notified by CVM's Aquaculture Drug Team that data submitted on OTC-immersion therapy in channel catfish was accepted as supportive evidence of the effectiveness of OTC to control mortality associated with external columnaris. Three daily treatments of 10, 20, or 40 mg oxytetracycline-hydrochloride per L were administered as 60-min static bath immersions. The study was led by Jeff Rach and conducted at the Iowa Department of Natural Resources Rathbun Fish Hatchery with the excellent assistance of Alan Johnson. Nice job Jeff and Alan.

Environmental fate data submitted to support approval of 17α-methyltestosterone: UMESC staff working with Dr. Terrence Barry of University of Wisconsin-Madison submitted two studies to support the use of 17α-methyltestosterone in aquaculture. Studies submitted by UMESC to the environmental safety team at CVM include the fate study "Drug Approval Research on 17α-methyltestosterone: Transformation in Aquatic-Sediment Systems" and the analytical method validation study entitled "Drug approval research on 17α-methyltestosterone: Validation of MT water method for the determination of 17α-methyltestosterone in aquatic systems". The studies were submitted to CVM on 1 October 2007.

Mark Gaikowski, Fisheries Management Chemical and Aquaculture Drug Team, U.S. Geological Survey, Upper Midwest Environmental Sciences Center, La Crosse, Wisconsin.

MEETINGS, ETC.

Upcoming meetings

58th Annual Northwest Fish Culture Conference; 4-6 December 2007, Portland, Oregon, USA: This year's conference, hosted by the Oregon Department of Fish and Wildlife, will be held at the Doubletree Lloyd Center in Portland, Oregon. The conference theme is "Enhancing Fisheries – Creating Opportunities." Preliminary Program Topics include: Applied Aquaculture/Hatchery Operations; Applied Hatchery Research; Fish Health; Marine Culture and Tribal Co-Management. Important deadlines include: 5 November 2007 – abstract submission and 19 November 2007 - deadline for presentations to be included in the proceedings. For more information refer to the Conference webpage.

14th Annual Whirling Disease Symposium; 4-5 February 2008; Denver, Colorado, USA: The 2008 annual symposium, sponsored by the Whirling Disease Foundation (Bozeman, Montana, USA) is being held at the Grand Hyatt Regency (Denver, Colorado) on the 4th and 5th of February. Oral and poster presentations are solicited in the following topic areas for the contributed paper and expanded poster sessions: 1) oligochaete studies; 2) resistant trout research; 3) ecological/habitat studies; 4) distribution, dissemination and risk assessment; and 5) detection, management and control. Presentation/poster title submission due 1 December 2007, extended abstracts due 10 January 2008. For more information refer to the Foundation's "Call for Papers" announcement.

Aquaculture America 2008; 9-12 February 2008; Lake Buena Vista, Florida, USA: The 2008 conference will be held at Walt Disney World's Coronado Springs Resort. This year's conference is being held in conjunction with Marine Ornamentals '08. The deadline for submission of abstracts is 3 August 2007. For more information refer to the conference website.

Therapeutic Drug Research Special Session at Aquaculture America 2008; 10 February 2008, Lake Buena Vista, Florida, USA: Researchers from three federal agencies (U.S. Fish & Wildlife Service, U.S. Geological Survey and U.S. Department of Agriculture) involved in aquaculture drug research will once again co-moderate a special session on therapeutic aquaculture drug research. This is the 5th year of this special session established to allow scientists involved in this type of research to present their findings to their peers in the

academic and regulatory science community. This venue is typically well attended by CVM's Aquaculture Team members providing presenters with an opportunity for immediate informal feedback. If you plan on attending Aquaculture America 2008 next year, we hope that you will schedule the Therapeutic Drug Research session in your plans.

International Workshop on Koi Herpes Virus (CyHV-3); 17-18 February 2008; Caesarea, Israel: A 2-day meeting is being planned, during which there will be opportunities to discuss recent advances in our understanding of CyHV-3. The hope is that virologists, veterinarians and retailers, will contribute to this meeting. The workshop will take place in the resort city of Caesarea located on the Mediterranean shore close to the ancient city built by Herod. The hotel is near the aquaculture facilities of Israel. The event will give researchers interested in CyHV-3 and other amphibian herpes viruses an opportunity to hear about recent findings of pathogenesis, its evolutionary origin and classification, as well as virus spread, economic losses and available means to restrict and/or overcome them. The scientific program will also include structural and molecular biology, and virus evolution. All this is being provided in a mutual friendly atmosphere. Please contact Prof. M. Kotler at mkotler@cc.huji.ac.il if you are interested in receiving the second announcement.

33rd Eastern Fish Health Workshop; 31 March – 4 April 2008; Atlantic Beach, North Carolina, USA: This year's annual workshop is being held at the Oceanfront Sheraton Inn and Conference Center, and as always is being hosted by the U.S. Geological Survey's National Fish Health Research Laboratory (Kearneysville, West Virginia). Some important dates to remember: abstracts must be received by 1 February 2008, early registration must be postmarked before 1 February 2008; late registration received after 2 February 2008, hotel reservation must be made by 1 March 2008, and full presentations received by 15 March 2008. Special session titles include: 1) New Perspectives in Coral Disease; 2) A spoonful of Finquel helps the medicine go down: fish medicine and surgery; 3) Emergent diseases: betanodavirues, rickettsial-like/Francisella organisms; 4) Letting the catfish out of the bag: updates from the South; 5) What's abnormal in fish histology and histopathology; 6) Molluscs and their critters; 7) Crustacean health; and 8) The Aquatic Detective: unusual case studies. For more information, contact Dr. Rocco Cipriano at 304-724-4432 or via email at rcipriano@usgs.gov.

World Aquaculture 2008; 19-23 May 2008; Busan, Korea: The theme of next year's annual international World Aquaculture Society conference is "Aquaculture for Human Wellbeing-The Asian Perspective." It is being co-hosted by the Korean Aquaculture Society & KBMBX. The conference is being held at the Busan Exhibition and Conference Center, in Busan, South Korea. Scheduled sessions are too numerous to print here, but include Fish Health and Genetic, Functional Foods and Neutraceuticals, and Environmental and Health Management. The deadline for abstract submission is 1 November 2008, and can be done on-line. Please refer to the Conference Website for more information.

Seventh Symposium on Diseases in Asian Aquaculture; 22-26 June 2008; Taipei, Taiwan: The Fish Health Section (FHS) of the Asian Fisheries Society (AFS) is holding its Seventh Symposium on Diseases in Asian Aquaculture (DAA VII). It is being held in Taipei, Taiwan from the 22nd through the 26th of June 2008. The DAA Symposia are a series of triennial meetings of the world's leading scientists and students working in aquatic animal health, where all participants share their latest research findings, exchange ideas and establish new collaborations. To meet the current interest in disease control, DAA VII will also offer two "extra curricular" seminar/workshops on risk analysis and on recent advances on fish and shellfish immunology. More detailed information will be provided in the second official announcement. In the interim, a brochure and other Conference information can be found at: http://homepage.ntu.edu.tw/~daaseven/ or at: http://www.fhs-afs.org/.

ROZ's CORNER

On 18 July 2007, the National Coordinator for Aquaculture New Animal Drug Applications (NCANADA) gave an eight-hour presentation to the Canadian Veterinary Drugs Directorate (VDD) at its invitation. VDD is the Canadian equivalent of the U.S. Center for Veterinary Medicine (CVM). The VDD was interested in (1) the successful aquaculture drug approval processes in the USA, (2) our experience with various successful partnerships, and (3) insight into expediting the aquaculture drug approval processes in Canada.

On 28 September 2007, the North Central Regional Aquaculture Center sent out a "Call for Statements of Interest" to conduct efficacy studies on Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol) to control *Aeromonas* spp. in warmwater and coolwater fish species produced in the North Central region. Proposals are due Friday, November 2, 2007.

There were several highlights concerning aquaculture drug submissions, acceptances, and approvals this quarter:

- On 17 July 2007, an Abbreviated NADA (generic copy of Parasite-S®, sponsored by Western Chemical, Inc.) was granted by CVM for Formacide-B® (formalin) for control of certain external parasites on finfish and shrimp and for the control of certain fungi on finfish eggs. Formacide-B® is sponsored by B.L. Mitchell, Inc.
- On 23 July 2007, Axcentive SARL submitted to CVM a revised Guidance for Industry #159 document on the safety of residues in human food for all fish for Halamid® (chloramine-T) prepared by the NCANADA

with input from the Upper Midwest Environmental Sciences Center (UMESC). The revision was based on the agency's comments.

- On 28-29 August 2007, the NCANADA met with Kona Blue Aquatic Farms in Kona, Hawaii to discuss developing data to support a label claim for controlling certain external parasites with 35% PEROX-AID® (hydrogen peroxide) on the major fish species reared by Kona Blue, Kona Kampachi®.
- On 1 October 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17α-methyltestosterone that were conducted and developed by the University of Wisconsin-Madison.
- On 11 October 2007, UMESC received word that its final environmental assessment on Halamid® (chloramine-T) is acceptable to CVM.

The designation provision of the Minor Use and Minor Species Animal Health Act of 2004 (MUMS) gives sponsors seven years of marketing exclusivity. So far, the MUMS Office has granted 50 designations, 44 of those are to aquaculture drug sponsors who received extensive help from the NCANADA. The most recent MUMS designations are three for Pfizer Animal Health's Terramycin 343® (oxytetracycline hydrochloride) on 7 June 2007 and one for Aquatic Life Sciences, Inc.'s Ovaplant® (salmon gonadotropin releasing hormone analog) on 25 May 2007. There have been three NADA approvals of MUMS designations for Eka Chemicals, Inc.'s 35%PEROX-AID®, and two NADA approvals and one Conditional Approval of MUMS designations for Schering-Plough Animal Health's Aquaflor®.

Rosalie (Roz) Schnick, National Coordinator for Aquaculture New Animal Drug Applications, Michigan State University, La Crosse, Wisconsin.

CVM's NOTES

Reminder: Request Your Waiver for FY 2008 ADUFA Fees

If you are an INAD or NADA sponsor, have you requested your waiver from animal drug user fees for the 2008 fiscal year? This is your second and final reminder before the invoices go out in November. CVM sent sponsors a reminder letter earlier this year and many of you have responded, but for any of you who have not, the time is now!

The Animal Drug User Fee Act of 2003 (ADUFA) requires FDA to assess and collect user fees for certain applications, products, establishments, and sponsors. Fortunately, waivers can be granted for minor species indications - but you have to request them. While the application fee is a one-time payment, the other fees are annual and requests for waivers must be made annually for them. Let's take a closer look at the four different fees.

If you are an INAD sponsor, you are subject to the Animal Drug Sponsor Fee annually. You should set a reminder to yourself to submit a request for a waiver every September. INAD sponsors with inactive INAD's may wish to terminate their INAD's so that they do not need to keep submitting annual requests for waivers of the sponsor fee. However, if there are data in the INAD that may support a drug approval, getting a more active sponsor to take over the INAD is a way of relieving oneself of the obligation.

The three other ADUFA fees apply only to companies that are NADA sponsors. CVM encourages eligible sponsors to submit their request for a waiver of the Animal Drug Application and Supplement Fee within six months of, and at least 90 days before, an anticipated application. Note, though, that this waiver must be requested in the same fiscal year that the application is filed; our fiscal year runs from October 1 through September 30. Sponsors with approved drugs also have to pay annual fees for each approved product and each manufacturing site (Animal Drug Product Fee and Animal Drug Establishment Fee). If the product is only for minor species and the only animal drugs made at the manufacturing site are for minor species, the sponsor can request waivers from the product and establishment fees.

There are two Guidance for Industry documents, #170 and #173, that provide more detail on animal drug user fees and how to request fee waivers. These Guidance documents are on the CVM website at http://www.fda.gov/cvm/Guidance/published.htm [editor's note: Guidance Documents #170 and #173 also available at http://www.fws.gov/fisheries/aadap/guidancedocs.htm]. Roz Schnick, the National Coordinator for Aquaculture New Animal Drug Applications, has a template letter that numerous sponsors have used to request waivers from ADUFA fees. Should you need clarification or more information, contact CVM.

Dr. Jennifer Matysczak, Aquaculture Drugs Team, Office of New Animal Drug Evaluation, Center for Veterinary Medicine, Food and Drug Administration.