U.S. Fish & Wildlife Service

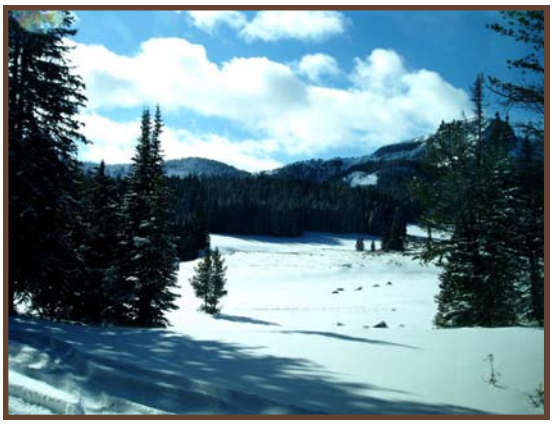
The Aquatic Animal Drug Approval Partnership Program

"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"

Volume 5-1

AADAP NEWSLETTER

February 2009



Winter in the Rockies - Gravelly Range of the Bighorn Mountains

TABLE OF CONTENTS

WHAT'S SHAKIN'

New AADAP-published "Aquaculture Drug Update" series: It's safe to assume we speak for all involved in the nitty-gritty world of aquaculture drug approvals in stating that quite a bit of excitement is generated following the infrequent announcements that a new drug has been approved for use in aquaculture or that a new claim has been added to an existing approval. This information has always been posted front and center on the AADAP website the same day it was announced by CVM, and in the very next issue of the AADAP newsletter. The information has been further disseminated by the efforts of the sponsor, CVM, the National Aquaculture New Animal Drug Application Coordinator, and groups like the USDA Cooperative States Research, Education and Extension Service's Joint Subcommittee on Aquaculture.

That's why we find it a little troubling that the "big news" does not appear to reach an important sector of our target audience, the end users. We consider end users those that, on occasion, actually use aquaculture drugs to help them hold, rear, or maintain healthy fish.

Consequently, AADAP staff initiated an effort by enlisting the help of partner organizations and asked them to assist us more broadly disseminate information via their list serves. Our strategy is to (1) identify information that we think is of critical importance (e.g., new or expanded approvals, recently regulatory changes, etc.) to end users, (2) develop brief "Aquaculture Drug Updates" that describe this information concisely in plain, simple language, and (3) in a timely manner, disseminate the information as broadly as possible.

For example, we recently sent out information about the revised Approved Drugs for Use in Aquaculture poster. With the help of our partners, we estimate that this information has now been sent out to over 5,000 individual computers. Although we acknowledge that some folks may have received this information from several sources, we are still delighted that this type of information is now being disseminated more broadly than ever before.

Our plan is to limit the information being disseminated in this manner to try to instill an understanding that each Aquaculture Drug Update contains important information that should have value to the end user.

All *Updates* will also be available (in several different text formats) on the following page on our website: http://www.fws.gov/fisheries/aadap/Aquaculture_Drug_Update.htm

New information on the 15th FWS Annual Aquaculture Drug Approval Coordination Workshop (2009) planned for Little Rock, Arkansas, USA: June 9th through 11th are the dates set for this year's Workshop. It will be held at the La Quinta Little Rock Downtown Conference Center. The meeting will be hosted by USDA—Agriculture Research Service's Stuttgart National Aquaculture Research Center, and will highlight regional aquaculture, including industry tours to a catfish hatchery, a baitfish farm and a hybrid striped

bass production facility. There will also be an opening mixer at a local brew-pub to get things started and allow everyone to become acquainted or reacquainted, as the case may be. Advanced information is now available, including a call for papers; registration forms; a draft agenda and schedule of activities; and hotel information. Click here to access the 2009 Workshop webpage.

Text provided by Dave Straus, Disease & Drug Approval Section, Harry K. Dupree – Stuttgart National Aquaculture Research Center, Agricultural Research Service, U.S. Dept. of Agriculture, Stuttgart, Arkansas, USA.

We are already making plans for the 16th FWS Annual (2010) Aquaculture Drug Approval Coordination Workshop to be held in Bozeman, Montana, USA: Although it may be a long way off, for those of you who like to plan ahead, the Workshop will be returning home to Bozeman, Montana in 2010. As has always been the case when it takes place in Bozeman, the Drug Approval Coordination Workshop will be scheduled for the last week in July or the first week in August, or more accurately, the week immediately before the Sweet Pea Festival weekend. So mark it on your 2010 calendar (if you have one) and just don't forget to check the AADAP website for news of upcoming workshops.

AADAPer's take a two-week "vacation" at FDA's Center for Veterinary Medicine or Dan and Niccole's Excellent Adventure: In January 2009, Niccole Lawson and Dan Carty completed a 2-week detail at the U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) in Rockville, Maryland, USA. Their detail was part of an informal AADAP-CVM employee-exchange program initiated a couple years ago by CVM's Dr. Don Prater (Acting Director, Division of Scientific Support) and AADAP's Branch Chief, Dr. Dave Erdahl. The goals of the detail were to (1) learn more about the overall structure and function of CVM, (2) "see" the new animal drug approval (NADA) and postapproval regulatory processes from CVM's perspective, and (3) explore ways in which AADAP could improve its aquatic animal drug-approval efficacy and target animal safety research. The detail was not taken lightly—Dan and Niccole were not only representing themselves but also representing AADAP and the U.S. Fish & Wildlife Service.

The AADAPer's were hosted by CVM's Acting Aquaculture Drugs Team Leader, Dr. Jennifer Matysczak, the other members of CVM's Aquaculture Team (Drs. Susan Storey, Stacey Gore, and Eric Anderson), and Dr. Todd Blessinger of CVM's Biostatistics Team. Before they arrived, Dr. Matysczak arranged for them to participate in an extensive series of interviews, discussions, and meetings—as well as a field trip to CVM's Office of Research (OR) in Laurel,

Niccole Lawson and Dan Carty at the Center for Veterinary Medicine's Office of Research Laboratories

Maryland, USA. In the end—and to their lasting benefit—these "activities" combined to produce a very intensive and rewarding experience.

Dan and Niccole had the privilege and pleasure of talking with CVM Director, Dr. Bernadette Dunham. Dr. Dunham's enthusiasm and obvious pride in CVM's mission, professional values, and people were evident throughout their conversation. Before meeting with Dr. Dunham, Dan had spent a day shadowing Dr. Steve Vaughn (Director, Office of New Animal Drug Evaluation (ONADE)), and Niccole had spent a day shadowing Dr. Beth Luddy (ONADE Deputy Director for Policy). While "shadowing," they learned much about CVM's administrative and organizational processes and its emphasis on functioning as a high-performance organization. They had also talked with Dr. Eric Dubbin (CVM's "executive coach"), who acquainted them with CVM's long-term efforts and programs to build and maintain a positive work culture for its employees.

Niccole and Dan met frequently with Dr. Matysczak and the Aquaculture Team and with a "subset" of the Biostatistics Team (Dr. Blessinger, Dr. Bob Abugov, and Dr. Eric Backlund). Primarily, they discussed aquaculture drug efficacy and target animal safety research, e.g., (1) writing, reviewing, and revising study protocols, final study reports (FSRs), and freedom of information summaries (FOIs); (2) designing experiments and statistically analyzing data; (3) timing of submissions and how different types of submissions are handled under the recently implemented End Review Amendment (ERA) process; (4) potential new uses of AADAP's Investigational New Animal Drug (INAD) database; (5) possible ways to "temperature-group" fish for new or expanded drug claims; and (6) how differences between regulatory- and academic-based science affect study hypotheses, designs, conduct, data analysis, and interpretation of observed results. They gleaned additional tips on target animal

safety research in a short training session given by Dr. "Chellie" Stull (Antimicrobial Drugs Team). Much thanks goes to Dr. Cindy Burnsteel (Director, Division of Therapeutic Drugs for Food Animals) and Dr. Anna Nevius (Team Leader, Biostatistics) for allowing Niccole and Dan to spend "so much time" with their teams.

Other highlights included orientation to or discussions of the following offices or topics:

1. Environmental Safety and Risk Assessment, with Dr. Prater and Environmental Safety Team members Dr. Eric Silberhorn and Mr. Charles Eirkson.
2. External Communications, with Dr. Carmen Stamper (Office of the Center Director). A big thank you to Dr. Stamper for being part of the AADAP-American Fisheries Society-CVM partnership that produced the current version of the Approved Drugs for Use in Aquaculture poster.
3. Office of Minor Use and Minor Species (including the NRSP-7 program and drug indexing), with Drs. Meg Oeller (Director) and Joan Gotthardt (Veterinary Medical Officer).
4. Manufacturing Practices, with Division of Manufacturing Technologies, Biotherapeutics Team members Mr. Mike Popek (Team Leader), and Drs. James Nitao and Heather Gennadios.
5. Internal Communications, a CVM working group led by Dr. Ann Stohlman (Canine and Feline Team).
6. Tour of the CVM Office of Research, with Dr. Renate Reimschuessel, Mr. Charlie Gieseker, and Mr. Eric Evans.
7. Generic Animal Drugs, with Team Leader Dr. Ken Harshman (a native of Montana!).
8. Post-Approval Compliance, with Ms. Frances Pell (Office of Surveillance and Compliance).
9. Human Food Safety and Tissue Residue Depletion, with Dr. Julia Oriani (Residue Chemistry Team).
10. Project Management, with Ms. Jennifer Love.

Finally, Niccole and Dan recognize Ms. Brandi Johnson, Executive Assistant to Dr. Steve Vaughn, for her friendliness and efficiency during our detail.

Overall, Niccole and Dan had an excellent adventure and were very impressed by CVM's professional values, organizational processes, positive work culture, and high-quality people. The employees of CVM are clearly dedicated to accomplishing FDA's overall mission: "To protect and promote the health of all Americans by ensuring the safety of foods, cosmetics, drugs, biologics, and medical devices."

Text provided by Dan Carty and Niccole Lawson, USFWS.

Update on the search for a new candidate "zero-withdrawal" (henceforth referred to as "immediate-release") anesthetic: Since the last update in the previous edition of the AADAP Newsletter (October 2008), substantive progress has been made. Although the Association of Fish and Wildlife Agencies' (AFWA) Drug Approval Working Group (DAWG) is still in the process of selecting one of two candidate drugs upon which to focus, the DAWG has moved closer to being able to make that decision.

Progress has been made on several different fronts, all but the last three of which the DAWG, through the AFWA, has provided the necessary seed money.

1. Coordinated by the USGS's Upper Midwest Environmental Sciences Center (UMESC), all the parties have been identified, the division of labor determined and progress has been made on establishing a postsedation catchability timeframe for each of the two candidate drugs (benzocaine and eugenol). Such criteria are essential to determine if either drug will potentially meet requirements for an "immediate release" claim for food fish. Final reports on this work should be available for submission to CVM by the fourth quarter of this year.
2. UMESC has begun the planning and background work to complete residue chemistry studies needed to address unresolved issues related to total residue depletion of eugenol, as well as developing the determinative/confirmatory methods for eugenol and benzocaine. Bench-top work is scheduled to begin in the fourth quarter of this year.
3. USFWS's Aquatic Animal Drug Approval Coordination Partnership (AADAP) program has solicited and received quotes from six private labs to conduct the genotoxicity battery of studies for benzocaine. A contract is planned to be let by 1 April 2009, and a final report will be ready for submission to CVM by 1 August 2009.
4. AADAP has obtained all available study reports and data sets generated by the U.S. National Institutes of Health - National Toxicology Program's study battery on eugenol. The data package was submitted on 2 February 2009 to CVM requesting it be reviewed with respect to its applicability and acceptability to fulfill the toxicological portion of the Human Food Safety Technical Section requirements for eugenol. CVM's review completion is expected within 6 months.
5. The U.S. National Oceanographic and Atmospheric Administration (NOAA) Portland, Oregon, USA; AADAP and the Nez Perce Tribe of Idaho organized and convened a workshop to

address the Pacific Northwest's (PNW) pressing need for an immediate release anesthetic/ sedative. Invited participants included representatives from numerous PNW Native American tribes, nearly all PNW state and federal agencies involved in salmon recovery and representatives from the DAWG and AADAP. The workshop focused on the pro's and con's of current sedation procedures being used, DAWG–related activities underway to obtain an "immediate release" sedative, and potential involvement of "user" organizations. A task force was formed to provide oversight of action items and to assist in identifying potential new funding sources.

6. A Norwegian pharmaceutical company ACD Pharmaceuticals AS, has begun to actively and aggressively pursue a U.S. NADA for their benzocaine product, Benzoak®, already approved in some European countries. Minor Use Minor Species (MUMS) designation is being sought for several claims.
7. Related to their Aquafrin® (a topical microbiocide) development program, Frontier Scientific, Inc., from Logan, Utah USA, likewise is actively pursuing MUMS designation for several benzocaine claims.
8. The New Zealand company AQUI-S New Zealand LTD, in January 2009, announced that its eugenol-based AQUI-S E® product, has received MUMS designation in the U.S. for eight separate claims. Consequently, they too are actively and aggressively pursuing a U.S. NADA. AQUI-S E® either has pending or currently has an aquaculture approval for use in several countries.

New AADAP "Drug Research Information Bulletin" (DRIB) published and now available: The most recent DRIB, *"Calculate Amount of Terramycin® 200 for Fish to Add to Fish Feed"* has just been published. This short-format documents provides step by step methods to calculate how much oxytetracycline premix to add to your feed to obtain the proper dose for your specific feeding rate. To download a copy, visit: http://www.fws.gov/fisheries/aadap/publications.htm

AADAP and the ERA (no, not that ERA!)

Ch-ch-ch-changes: In mid-September 2008, FDA/CVM implemented a new policy and new procedures for integrating an End-Review Amendment (yes, that ERA!) into the Investigational New Animal Drug (INAD) study protocol submissions review-and-revision process. The ERA was implemented under Animal Drug User Fee Amendments of 2008 and affects, among others, type "E" submissions, which are study protocols (without supporting data) submitted to CVM for review. Briefly, the ERA specifies roles, responsibilities, and timelines that CVM and sponsors must meet during a study protocol review and revision process. For details, please see CVM's Notes or access CVM's Policy and Procedures Index at http://www.fda.gov/cvm/FOI/ppindex.html and download Policy and Procedures Manual No. 1243.4070.

Give me just a little more time: The primary advantage of the ERA is that a submitted study protocol is reviewed, and potentially revised and concurred with (or not) "sooner" than in the past. If a sponsor receives protocol concurrence sooner, then a sponsor can initiate a study sooner. If a sponsor initiates a study sooner, then a sponsor can complete a study sooner. If a sponsor completes a study sooner, then a sponsor can…well, you get the idea. A secondary advantage of the ERA is that there are clear expectations and requirements placed on CVM and on sponsors; hence, miscommunications and misunderstandings are minimized.

The disadvantage of the ERA—from our view, anyway—is that there is little or no leeway in the timelines (i.e., deadlines) that must be met. Therefore, we sometimes need to forget about leaving work early or taking that extra day off to go trail-running, bicycling, fishing or whatever. Instead, after revising a protocol as requested and color-coding the revisions, we "hang about" the copy machine to ensure that the revised protocol (three copies) is printed correctly. After printing, we hastily collate, assemble, and package the revised protocol for shipping. Finally, we arrange to ship the revised protocol to CVM such that it is "clocked into" CVM Document Control by the pre-specified "deadline."

When the music's over: To date, we have submitted three study protocols to CVM under the ERA. Submitting, revising, and re-submitting the first protocol (Efficacy of Terramycin® 200 for Fish for the Skeletal Marking of Rainbow Trout, *Oncorhynchus mykiss*) was very much a learning experience. However, we met the re-submission deadline and received protocol concurrence. Submitting, revising, and re-submitting the other two protocols (The Safety of AQUAFLOR® to sunshine bass, female *Morone chrysops* × male *M. saxatilis*, and yellow perch, *Perca flavescens*, respectively) went relatively smoothly, and both protocols are currently under re-review by CVM. We are cautiously optimistic that CVM will concur with these two protocols. In the end, the ERA appears to be working well and appears to have improved the protocol review-and-revision process.

National Aquaculture Drug Research Forum meeting held at Aquaculture America 2009: The 8th meeting of the National Aquaculture Drug Research Forum (NADRF) was convened on Monday, 16 February 2009 in conjunction with the Aquaculture

America Conference held in Seattle, Washington, USA. The meeting was attended by an assortment of researchers, drug sponsors, the National NADA Coordinator, a representative from CVM's Aquaculture Team, and the Chairman of Association of Fish and Wildlife Agencies' Drug Approval Working Group.

Agenda topics included an (1) update of the parasite survey disseminated in June, 2008; (2) a presentation on the utility of SAS PROC GLIMMIX to analyze binomial data such as mortality, (3) status of an effort to more effectively utilize INAD data to reduce the number of pivotal field efficacy studies required to complete effectiveness technical sections, (4) involvement of NADRF members on Indexing Expert Panels, and (5) that the new home for the NADRF is now under the new (see below) AFS Fish Culture Section's Working Group on Aquaculture Chemicals (WGAC). For more information on the NADRF meeting, please see the meeting minutes (coming soon) on the AADAP website.

There was considerable discussion about the parasite survey and the findings that (1) at least one response was received from virtually every state, (2) most survey responses were provided by fish health specialists or fish culturists from public/not for profit production or research facilities, and (3) protozoans and monogeneans appear to be of greatest concern. Protozoans of greatest concern included Ich and *Ichthyobodo* spp., and to a lesser extent *Trichodina* spp. and *Chilodonella* spp. The monogeneans of greatest concern were *Gyrodactylus* spp. and *Dactylogyrus* spp. For more information about survey results, please contact Mark Gaikowkski at mgaikowski@usgs.gov.

Inaugural meeting of the American Fisheries Society's Working Group on Aquaculture Chemicals: The Working Group on Aquaculture Chemicals (WGAC), recently established as a working group of the American Fisheries Society Fish Culture Section (FCS) by Dr. Curry Woods (FCS President), held its inaugural meeting 15 February 2009 during Aquaculture America in Seattle, Washington, USA. The impetus to create the WGAC arose out of the Joint Subcommittee on Aquaculture's (JSA) recent decision to sunset the Working Group on Aquaculture Drugs Biologics and Pesticides (WGADBP). The JSA formally sunsetted the WGADBP on 23 October 2008 in response to concerns regarding compliance with the Federal Advisory Committee Act.

The initial intent of the WGAC is to provide a method through which interested organizations and individuals may work together to enhance overall aquatic animal health, particularly in the areas of drug, pesticide and biologic research, development, and judicious use. Additionally, the WGAC will strive to serve as a forum where industry, academia, non-governmental organizations, state natural resource agencies, etc. are provided an opportunity to come together with federal partners to interact and share ideas in a venue similar to what the JSA WGADBP was once able to provide.

The first meeting of the WGAC was attended by 19 individuals from several federal and state agencies, private aquaculture, non-governmental organizations and the animal health industry. The meeting initially focused on what the group hopes to accomplish, including defining its mission and objectives. Much of the first meeting was spent discussing organization and procedures, with emphasis on inclusion/representation of different organizations and federal partners. In addition to discussions on developing objectives and the conduct our WG business, Drs. Curry Woods and Jesse Trushenski (AFS-FCS President-Elect) emphasized the flexibility provided to the WGAC under the FCS – that ideas can be identified and small groups developed to rapidly respond as needed.

The meeting concluded with the identification of a small subgroup tasked to develop a mission statement over the next couple of months. The next WGAC meeting will be in Little Rock, Arkansas in June 2009 in conjunction with the FWS Aquaculture Drug Approval Coordination Workshop. The WG will also meet annually at Aquaculture America. Interested parties should participate in this meeting by bringing their list of "hot topics/issues" to the table (either in person, or by submitting them prior to the meeting to Mark Gaikowski, WGAC Chairman at mgaikowski@usgs.gov).

DRUG UPDATES:

General: Not too much to report this quarter. If you recall from the last AADAP Newsletter, we were pretty excited about the number of protocols and final study reports (FSRs) we had submitted during the previous quarter. Unfortunately, we're still waiting to hear back from CVM regarding each of the final study report submissions. As usual, we're keeping our fingers crossed that CVM will agree that results from the studies will support new or expanded aquaculture drug approvals.

Florfenicol (Aquaflor®) update:

Target Animal Safety Research Study Protocols: Two research study protocols that were submitted to CVM for review were returned to us via an End Review Amendment (ERA). The protocols were developed to describe procedures to evaluate the safety of Aquaflor® to yellow perch and sunshine bass. According to CVM guidelines, we had a short period of time to address the comments and send the protocol back to CVM for a final review. The amended protocols were due back on the primary reviewer's desk (after first making its way through CVM's Document Control Unit) within 10 calendar days of the ERA announcement. Dan Carty took the lead to address comments provided by the

Aquaculture Team and Biometric Team reviewers, and the amended protocols were submitted to CVM in early February. From the individual dates of receipt, CVM has 20 days to get back to us with what we hope will be good news….protocol concurrence!

Target Animal Safety – preliminary study on sunshine bass: The AADAP crew is assisting Dr. Dave Straus (USDA - Agriculture Research Service's Stuttgart National Aquaculture Research Center) and his staff, in conducting a preliminary target animal safety study on sunshine bass (to be ultimately followed by a pivotal study). Dave received the amended protocol, as described above, and has shared it with his research collaborators. The purpose of the preliminary study is to evaluate how well fish feed when administered feed top-coated with Aquaflor® at concentrations of 15, 45, and 75 mg florfenicol per kg fish body weight per day for 20 days. The AADAP crew provided Dr. Straus with medicated feeds for each of the treatment concentrations (including a control feed containing no florfenicol) and randomizations to allocate fish to tanks and assign one of the four treatment conditions to each of the 12 test tanks. The Stuttgart crew will collect all pertinent data to help assess the utility of the data collection forms. The preliminary study was initiated on 20 February and is scheduled to be completed on 11 March 2009.

Halamid® (chloramine-T) update:

Bluegill/external columnaris study: In the last newsletter, we reported that the FSR describing the results from a study evaluating the efficacy of chlorarmine-T to control mortality caused by external columnaris was submitted to CVM in July 2008. The study was conducted at the Richloam SFH in Florida. Briefly, mean percent cumulative mortality at the end of the 14-day posttreatment period in treated tanks (12.9%) was significantly lower (P = 0.0304) than that in control tanks (26.9%). Mortality results such as these typically mean that the study will be considered pivotal by CVM, and in January 2009 we were informed that in fact CVM had accepted the study as pivotal. More specifically, the study results supported the claim that chloramine-T when administered at a dose of 20 mg per liter for 60 min per day on three alternate days controls mortality due to external columnaris in bluegill.

Oxytetracycline (OTC) update:

Skeletal marking efficacy protocol concurrence: In the last AADAP Newsletter, we reported that a research study protocol to evaluate the effectiveness of OTC medicated feed to mark skeletal tissue of rainbow trout had been submitted to CVM for review. Not unexpectedly, CVM had several comments/ concerns that needed to be addressed (through the ERA process) for protocol concurrence. Dan Carty once again took the lead to address the comments. The amended protocol was submitted to CVM on 30 December 2008, and AADAP received protocol concurrence from CVM on 12 January 2009.

Efficacy study: Dan Carty (Study Director) and Miranda Dotson (Study Investigator) recently launched a study to demonstrate the effectiveness of OTC medicated feed to mark rainbow trout fingerling skeletal tissue when administered at a dose of 3.75 g OTC per 100 lbs fish per day for 10 days. The study started on 26 February and is scheduled to end 29 March (21 days posttreatment). Prior to the official study initiation, Ken Peters (USFWS; Bozeman Fish Health Center) assisted by performing fish health evaluations on fish from the reference population. Jim Peterson (ye old, and now retired, Montana Fish, Wildlife, and Parks Fish Health Coordinator) is scheduled to make the long trip from his digs in Great Falls, Montana to our haven in Bozeman the week of 30 March to evaluate vertebral marks. So far, the study is running smoothly…so stay tuned.

Certificates of Appreciation: At the most recent (18 February 2009) Aquaculture America conference in Seattle, Washington, USA, Mr. Paul Duquette

Roz Schnick receiving a Certificate of Appreciation from Paul Duquette, Phibro Animal Health, for her contributions to recent oxytetracycline label expansions. *(photo courtesy of Paul Duquette)*

(Phibro Animal Health), provided a beautiful "Certificate of Appreciation" plaque to numerous folks. The plaques were offered in recognition for the recipients' work to help Phibro gain the most recent label expansions to their OTC medicated feed product (Terramycin® 200 for Fish). For details on the complete label claims for OTC medicated feed, click here to view the current "Aquaculture Drug-Use Guidance" poster.

17α-Methyltestosterone update:

Effectiveness technical section complete: On 10 December 2008, AADAP received a letter from CVM's stating that the effectiveness technical section is considered complete for 17 α-methyltestosterone Type C medicated feed for tilapia fry for the production of predominantly (>80%) male populations of tilapia. For more information, see the CVM response letter and the attached Freedom of Information Summary posted on the AADAP website. We know we've said it before, but here it goes again….Yeeha!

17MT mini-session: Aquaculture America 2009 in Seattle, Washington, USA was the site of the most recent NADA coordination meeting of 17α-methyl-testosterone researchers and participants. Representatives from USGS, USFWS, USDA, CVM, the Western and North Central Regional Aquaculture Centers, the US tilapia industry, Rangen, Inc. (the pharmaceutical sponsor), the World Wildlife Fund, and the National Coordinator for Aquaculture New Animal Drug Applications were in attendance. Technical Section completion timelines were revised based on completed work and delayed work. Although there was general consensus that good progress is being made, some concern was expressed about the apparent inability to stay on schedule. The tilapia industry emphasized the importance of gaining the 17MT approval as quickly as possible.

FINS & TAILS, BITS & BOBBERS

AFS-AADAP "Aquaculture Drug-use Guidance" Poster current user-statistics and status: In January 2009 AADAP began distribution of 1000 copies of the second and revised printing of the "Approved Drugs for Use in Aquaculture" poster. As of the end of February more than **900 copies** of the AADAP/AFS poster had already been distributed. The second printing was made possible with CVM funding and with assistance of CVM's Communications Staff (a special thanks goes out to Dr. Carmen Stamper). Discussions are already underway with CVM to initiate a third printing. To obtain your free copy or copies, click here.

Provided below is a breakdown of the second edition distribution to date:

- 47 states
- 13 foreign countries (e.g., Scotland, Malaysia, Venezuela)
- 35% were requested by state employees
- 34% were requested by the private sector
- 13% were requested by federal/tribal employees
- 13% were requested by university or extension offices.

RELEVANT LITERATURE

The following is a list of journal publications with particular relevance to the broad topic of drug-use in aquaculture. This list comprises citations exclusively from 2008 and 2009. Please note that this list does not include those provided in previous issues of the AADAP Newsletter.

If you have come across literature that you believe would be of interest to the readership of the AADAP Newsletter, please forward the citation to Tom Bell (thomas_a_bell@fws.gov) and we will place it in the next edition.

The inclusion of a citation within the AADAP Newsletter does not imply: (1) recommendation of the technique to any particular situation, (2) concurrence with a treatment procedure/drug, (3) acceptance by the U.S. Food and Drug Administration's Center for Veterinary Medicine of the drug's safety or effectiveness, nor (4) in any way an endorsement of a product by the U.S. Fish & Wildlife Service.

Balasubramanian, G, et al. 2008. Studies on the immunomodulatory effect of extract of *Cyanodon dactylon* in shrimp *Penaeus monodon* and its efficacy to protect the shrimp from white spot syndrome virus (WSSV). *Fish & Shellfish Immunology* **25(6):820-828**.

Boyer, SE, et al. 2009. Effects of the fish anesthetic, clove oil (eugenol), on coral health and growth. *Journal of Experimental Marine Biology and Ecology* **369(1):53-57**.

Bravo, S, et al. 2008. Sensitivity assessment of *Caligus rogercresseyi* to emamectin benzoate in Chile. *Aquaculture* **282(1-4):7-12**.

Bueno, MJM, et al. 2009. Application of passive sampling devices for screening of micro-pollutants in marine aquaculture using LC-MS/MS. *Talanta* **77 (4):1518-1527**.

Cabrita, E, et al. 2009. Successful cryopreservation of sperm from sex-reversed dusky grouper *Epinephelus marginatus*. *Aquaculture* **287(1-2):152 -157**.

Clearwater, SJ, et al. 2008. Overview of potential piscicides and molluscicides for controlling aquatic pest species in New Zealand. *New Zealand Department of Conservation Research and Development Series* **283:5-72**.

Darwish, A, et al. 2008. *In Vitro* and *in vivo* evaluation of potassium permanganate treatment efficacy for the control of acute experimental infection *by*

Flavobacterium columnare in channel catfish. *North American Journal of Aquaculture* **70(3):314-322**.

de Amorim, MP, et al. 2009. Early development of the silver catfish *Rhamdia quelen* (Quoy & Gaimard, 1824) (Pisces: Heptapteridae) from the Sao Francisco River Basin, Brazil. *Aquaculture Research* **40(72-180)**.

Gaikowski, MP, et al. 2009. Histopathology of repeated, intermittent exposure of chloramine-T to walleye *Sander vitreum* and channel catfish *Ictalurus punctatus*. *Aquaculture* **287(1-2):28-34**.

Godoy, DT, et al. 2008. Patterns of resistance to florfenicol and bicyclomycin in Brazilian strains of motile aeromonads. *Aquaculture* **285(1-4):255-259**.

Green, BW, and Teichert-Coddington, DR. 2000. Human food safety and environmental assessment of the use of 17α-methyltestosterone to produce male tilapia in the United States. *Journal of the World Aquaculture Society* **31(3):337-357**. (Special listing because of relevance to current 17α-methyltestosterone approval work.)

Haggard, BE, and Bartsch, LD. 2009. Net changes in antibiotic concentrations downstream from an effluent discharge. *Journal of Environmental Quality* **38(1):343-352**.

Harikrishnan, R, and Balasundaram, C. 2009. *In vitro* and *in vivo* studies of the use of some medicinal herbals against the pathogen *Aeromonas hydrophila* in goldfish. *Journal of Aquatic Animal Health* **20 (3):165-176**.

Hemaprasanth, KP, et al. 2008. Efficacy of doramectin against natural and experimental infections of *Lernaea cyprinacea* in carps. *Veterinary Parasitology* **156(3-4):261-269**.

Hoegfors, E, et al. 2008. Immunization of rainbow trout, *Oncorhynchus mykiss* (Walbaum), with a low molecular mass fraction isolated from *Flavobacterium psychrophilum*. *Journal of Fish Diseases* **31(12):899-911**.

Iversen, M., et al. 2009. Potential benefit of clove oil sedation on animal welfare during salmon smolt, *Salmo salar* L., transport and transfer to sea. *Aquaculture Research* **40: 233-241**.

Kiessling, A, et al. 2009. Pharmacokinetics, plasma cortisol, and effectiveness of benzocaine, MS-222, and isoeugenol measured in individual dorsal aorta-cannulated Atlantic salmon *Salmo salar* following bath administration. *Aquaculture* **286(3-4):301-308**.

Krogh, KA, et al. 2008. Development of an analytical method to determine avermectins in water, sediments, and soils using liquid chromatography-tandem mass spectrometry. *Journal of Chromatography "A"* **1212(1-2):60-69**.

Krol, J, et al. 2009. The effects of commercial preparations containing two different GnRH analogues and dopamine antagonists on spermiation and sperm characteristics in the European smelt *Osmerus eperlanus* (L.). *Aquaculture* **286(3-4):328-331**.

Lai, H, et al. 2009. Effects of chloramphenicol, florfenicol, and thiamphenicol on growth of algae *Chlorella pyrenoidosa*, *Isochrysis galbana*, and *Tetraselmis chui*. *Ecotoxicology and Environmental Safety* **72(2):329-334**.

Lees, F, et al. 2008. Factors associated with changing efficacy of emamectin benzoate against infestations of *Lepeophtheirus salmonis* on Scottish salmon farms. *Journal of Fish Diseases* **31(12):947-951**.

Lin, BL, et al. 2009. The fragmented testis method: development and its advantages of a new quantitative evaluation technique for detection of testis-ova in male fish. *Ecotoxicology and Environmental Safety* **72(2):286-292**.

Ma, CW, et al. 2009. Removal of pathogenic bacteria and nitrogens by *Lactobacillus* spp. JK-8 and JK-11. *Aquaculture* **287(3-4):266-270**.

Mayor, DJ, et al. 2008. Acute toxicity of some treatments commonly used by the salmonid aquaculture industry to *Corophium volutator* and *Hediste diversicolor*: whole sediment bioassay tests. *Aquaculture* **285(1-4):102-108**.

Melian, JAH, et al. 2008. Degradation and detoxification of formalin wastewater with aerated biological filters and wetland reactors. *Process Biochemistry* **43(12):1432-1435**.

Mohler, JW, and Bradley, KM. 2008. Removal of calcein in wastewater produced from the batch marking of fish. *North American Journal of Fisheries Management* **28(4):1177-1181**.

Navarrete, P, et al. 2009. Oxytetracycline treatment reduces bacterial diversity of intestinal microbiota of Atlantic salmon. *Journal of Aquatic Animal Health* **20(3):177-183**.

Park, MO, et al. 2009. Efficacy and physiological responses of rock bream *Oplegnathus fasciatus* to anesthetization with clove oil. *Aquaculture* **287(3-4):427-430**.

Penston, MJ, et al. 2008. Reduced *Lepeophtheirus salmonis* larval abundance in a sea loch on the west coast of Scotland between 2002 and 2006. *Diseases of Aquatic Organisms* **81(2):109-117**.

Pieters, N, et al. 2008. Efficacy of in-feed probiotics against *Aeromonas bestiarum* and *Ichthyophthirius multifiliis* skin infections in rainbow trout (*Oncorhynchus mykiss*, Walbaum). *Journal of Applied Microbiology* **105(3):723-732**.

Ross, LG, and Ross, B. 2008. Anaesthetic and sedative techniques for aquatic animals, 3rd edition. Blackwell Publishing, Ames, Iowa.

Rowland, SJ, et al. 2008. Use of formalin and copper to control ichthyophthiriosis in the Australian freshwater fish silver perch (*Bidyanus bidyanus* Mitchell). *Aquaculture Research* **40:44-54**.

Sadigh Eteghad, S, et al. 2008. Comparative survey on anesthetizing effects of medicinal herbs *Valerian officinalis*, *Melissa officinalis*, *Papaver somniferum*, and *Papaver bracteatum* on gold fish *Carassius auratus*. *Iranian Scientific Fisheries Journal* **17(1):91-98**.

Skilbrei, OT, et al. 2008. A laboratory study to evaluate the use of emamectin benzoate in the control of sea lice in sea-ranched Atlantic salmon (*Salmo salar* L.). *Aquaculture* **285(1-4):2-7**.

Smith, P, et al. 2008. Reducing inter-operator variation in disc diffusion assays by the inclusion of internal controls in a standard susceptibility test protocol. *Aquaculture* **285(1-4):273-276**.

Straus, DL. 2008. Copper sulfate toxicity to channel catfish fry: yolk-sac versus swim-up fry. *North American Journal of Aquaculture* **70 (3):323-327**.

Tacon, AGJ, and Metian, M. 2008. Aquaculture feed and food safety. *Annals of the New York Academy of Sciences* **1140(1):50-59**.

Verner - Jeffreys, DW, et al. 2009. Development of bactericidal and virucidal testing standards for aquaculture disinfectants. *Aquaculture* **286 (3-4):190-197**.

Wang, HP, et al. 2008. Effects of estradiol-17 beta on survival, growth performance, sex reversal, and gonadal structure of bluegill sunfish *Lepomis macrochirus*. *Aquaculture* **285(1-4):216-223**.

Westcott, JD, et al. 2008. Optimization and field use of a bioassay to monitor sea lice *Lepeophtheirus salmonis* sensitivity to emamectin benzoate. *Diseases of Aquatic Organisms* **79(2):119-13**.

Wilkinson, RJ, et al. 2008. The effects of pre-harvest stress and harvest method on the stress response, rigor onset, muscle pH, and drip loss in barramundi *Lates calcarifer*. *Aquaculture* **282(1-4):26-32**.

Yao, H, et al. 2009. A high throughput chemiluminescence method for determination of chemical oxygen demand in waters. *Analytica Chimica Acta* **633(1):76-80**.

USGS's CORNER

Hydrogen peroxide: U.S. Geological Survey's Upper Midwest Environmental Sciences Center (UMESC) has submitted three pivotal efficacy study protocols to FDA-CVM for review. UMESC received notification that CVM concurred with the study design for the two protocols to evaluate the ability of 35% PEROX-AID® to control mortality caused by saprolegniosis on rainbow trout and walleye. Studies with rainbow trout will be initiated in March 2009 and in walleye shortly thereafter. Successful completion of these two studies should provide the data required to expand the 35% PEROX-AID® label to control mortality caused by saprolegniosis on all freshwater-reared finfish.

The third 35% PEROX-AID® protocol submitted by UMESC was a pivotal efficacy protocol to evaluate the efficacy of 35% PEROX-AID® to control *Gyrodactylus* spp. on coaster brook trout *Salvelinus fontinalis*. Though FDA-CVM did not concur with our design, we did not have sufficient time to submit a revised protocol before conducting the study. However, CVM review comments were incorporated into the study protocol before conducting the study. The study was completed at the U.S. Fish & Wildlife Service's Iron River National Fish Hatchery (IRNFH) in December 2008 and data summary is on-going. Preliminary review of the results indicated near complete removal of the ectoparasites from the brook trout. Unexpectedly, we observed a significant difference in the parasite infestation density between male and female trout. Many thanks are due the staff of the IRNFH for conducting an excellent field trial as well as to Eric Leis and Becky Lasee of the USFWS La Crosse Fish Health Center for their parasite enumeration and identification.

In addition to the pivotal efficacy studies for 35% PEROX-AID®, a supporting efficacy trial was conducted by the Illinois Department of Natural Resources' Jake Wolf State Fish Hatchery to evaluate hydrogen peroxide efficacy to control mortality caused by saprolegniosis in largemouth bass, *Micropterus salmoides*. The final report is pending submission to FDA-CVM for review. A supporting efficacy trial is in preparation at the Michigan Department of Natural Resources' Marquette State Fish Hatchery to control

Gyrodactylus spp. on brook trout. Treatments at the Marquette hatchery should be initiated in mid-February.

Chloramine-T: One of the outstanding pieces of work needed to support the approval of Halamid® (chloramine-T) is refinement of the analytical method to detect para-toluenesulfonamide (*p*-TSA) in fish tissue. The FDA-CVM considers *p*-TSA to be the marker residue of chloramine-T exposure to fish. UMESC was recently notified that the likely tolerance limit for *p*-TSA will be 20 parts per billion (ppb), substantially lower than the working tolerance limit of 1 part per million originally discussed for *p*-TSA. The original analytical method developed by UMESC had a limit of quantitation (LOQ) of ~34 ppb. Though FDA-CVM accepted (ca 2003) the marker residue depletion studies UMESC completed, FDA-CVM is now requiring a LOQ of <20 ppb. Studies are on-going at UMESC to refine the *p*-TSA tissue method to meet this new requirement.

UMESC also recently published the following manuscript describing the animal safety studies completed to evaluate the safety of chloramine-T to cool and warmwater fish: M.P. Gaikowski, C.L. Densmore, V.S. Blazer. 2009. Histopathology of repeated, intermittent exposure of chloramine-T to walleye (*Sander vitreum*) and channel catfish (*Ictalurus punctalus*) . *Aquaculture* **287:**28–34.

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

USDA's CORNER

The U.S. Department of Agriculture's Stuttgart National Aquaculture Research Center's (SNARC) crew has been busy with ongoing research and the following is an update on recent happenings.

Aquaculture America 2009: The Therapeutic Drug Research special session was a big hit again with 13 presentations and plenty of discussion followed by, the previously reported on, National Aquaculture Drug Research Forum meeting. The session was organized and moderated by Jim Bowker, Mark Gaikowski and Dave Straus. This was the 7th consecutive year we have held this session focusing on research activities involving aquaculture therapeutants.

Annual Drug Approval Coordination Workshop: Plans are firming up for the meeting scheduled for June 9th through 11th at the LaQuinta Little Rock Downtown Conference Center (Little Rock, Arkansas, USA); there will be additional meetings on June 8th and June 12th, so come enjoy a week in Arkansas! There will be the usual opening mixer at a local brew-pub. Also, as usual, the workshop will focus on priority therapeutants. The workshop will provide to us an opportunity to highlight regional aquaculture, and will include industry tours to a catfish hatchery, baitfish farm, ornamental fish farm and hybrid striped bass production facility. Hope y'all can make this meeting and experience some Southern Hospitality! Click here for more information.

Copper Sulfate - Label for Ich: SNARC has partnered with Phelps Dodge Refining Corporation (now Freeport-McMoRan) to draft a label for their Triangle Brand® Copper Sulfate product. FDA/CVM has concurred with the draft label we have prepared and the sponsor will begin the process of moving it through their channels to create a mock-label that they will formally submit to FDA/CVM.

Copper Sulfate - Human Food Safety technical section for Ich: A hazard characterization was submitted for the Human Food Safety technical section for Triangle Brand® Copper Sulfate. In a letter received in December 2008, the FDA concluded that the microbial food safety risks associated with the proposed use of copper sulfate in finfish was low. Based on this information, CVM's Division of Human Food Safety considers the Human Food Safety technical section complete for ALL finfish.

Copper Sulfate Effectiveness – Fungus on Channel Catfish Eggs: Final Study Reports for the laboratory dose-confirmation (conducted at 10 mg/L copper) and independent substantiation at a commercial hatchery are in process.

Copper Sulfate Target Animal Safety – Channel Catfish Eggs: A Final Study Report for the Target Animal Safety study is in review by our Quality Assurance group and their comments will be addressed prior to submission to FDA/CVM.

Potassium Permanganate - Effectiveness: Research is being conducted to develop a consistent method to induce columnaris disease first in channel catfish and then in hybrid striped bass.

Publications related to our drug approval work:

Straus, D.L. 2008. Copper Sulfate Toxicity to Channel Catfish Fry: Yolk Sac versus Swim-up Fry. *North American Journal of Aquaculture*. **70(3):**323-327.

Straus, D.L. 2008. Comparison of Copper Sulfate Concentrations to Control Ichthyophthiriasis in Fingerling Channel Catfish. Jour*nal of Applied Aquaculture,* **20 (4):**272-284.

Text provided by Dave Straus, Disease & Drug Approval Section, Harry K. Dupree – Stuttgart National Aquaculture Research Center, Agricultural Research Service, U.S. Dept. of Agriculture, Stuttgart, Arkansas, USA.

MEETINGS, ETC.

Upcoming meetings

Catfish Farmers of America Annual Convention; 5-7 March 2009; Natchez, Mississippi, USA: The 2009 annual meeting will be held at the Eola Hotel in Natchez. During the annual meeting, the 2009 Catfish Culture Research Symposium is being held. The Symposium is intended to be a forum for exchange of scientific and technical information among researchers, extension personnel, catfish farmers and graduate students of aquaculture. The organizers are encouraging contributions on results of specific research projects as well as reviews of recent advances in technology. Due to the current financial difficulties faced by the U.S. farm-raised catfish industry, preference will be given to those authors whose findings demonstrate a positive economic impact on commercial facilities. For more information on the Symposium contact Jimmy Avery (phone: 662-686-3273; email: javery@drec.msstate.edu; fax: 662-686-3320) For general details on the convention (email: catfishjournalth@bellsouth.net; phone: 601-206-1600; fax: 601-977-9632).

World Aquaculture 2009; 25-29 May 2009; Veracruz, México: The World Trade Center in Veracruz is the site for the 2009 International meeting of the World Aquaculture Society. The conference theme is "blue revolution to feed the world." The organizers "invite you to join them on a journey to the world of aquaculture science and technology, to explore the whole range of possibilities and make this new 'Blue Revolution' possible." The program focuses on eight major topic areas comprising nearly 60 sessions, including those on therapeutic drugs, aquaculture regulations and health and biosecurity. Online registration, deadlines, conference brochures and information accommodations and tours can be found on the conference website.

AQUAVET® I & II Courses; 17 May—13 June 2009 and 17-30 May 2009, respectively; Woods Hole, Massachusetts, USA: The detailed announcements for the 2009 AQUAVET® I and AQUAVET® II courses are now available. Both courses are designed for veterinary students and practicing veterinarians who have an interest in applying their veterinary training to aquatic animals. Enrollment is limited and applications are due no later than 15 January 2009. For more information visit their website by clicking here.

AFS-FHS and Western Fish Disease Workshop combined meeting; 8-10 June 2009; Park City, Utah, USA: The 2009 joint meeting of the Fish Health Section of AFS and the Western Fish Disease Conference will be held at the Prospector Square Lodge and Conference Center, Park City, Utah, USA. The conference will include a half day continuing education course "Applications of Bacterial Genomics to Fish Diagnostics" presented by Dr. Mark Lawrence, Mississippi State and 1½ to 2 days of scientific presentations. The continuing education course will be held Monday morning from 8 am to noon. The general meeting sessions will begin at 1 pm Monday, June 8th and will end either Tuesday afternoon or Wednesday at noon dependent on the number of abstracts received. Registration will include the Monday night social and Tuesday night banquet. Click here for additional information about the joint meeting.

Genomics in Aquaculture; 5-7 July 2009; Bodø, Norway: The 'Genomics in Aquaculture' symposium will review the state-of-the-art of genomics research in aquaculture, its industrial applications and future perspectives, thus contributing to bridge the gap between fundamental genomics research and the needs of the aquaculture industry. The symposium will have the participation of several invited experts in aquaculture genomics, as well as attendants from feed companies and government representatives. For more information, click here to access the conference website.

International Aquaculture Biosecurity Conference; 17-18 August 2009; Trondheim, Norway: The theme of the conference, to be held in conjunction with Aqua Nor 2009, is "Practical Approaches for the Prevention, Control, and Eradication of Disease." The goal of the conference is to provide expert opinions and tools for implementing practical, economic and effective biosecurity plans and programs. Planned topics include: economic impact of disease and biosecurity programs; components of ideal biosecurity plans and programs; international, regional and national strategies; identifying and prioritizing hazardous diseases and evaluating risks; determining and mitigating hazardous disease critical control points and risks; disease epidemiology, surveillance and monitoring; determining disease status and freedom; control and eradication contingency plans and programs; disease diagnostics, medical and farm record keeping; and implementing, auditing and certifying biosecurity programs. For more detailed information regarding accommodations, registration, etc. visit the conference website: http://www.iabconference.org.

Aqua Farming International Conference and Exhibition 2009; 16-19 September 2009; Vigo, Spain: The First Aqua Farming International Conference and Exhibition (AQA) will be held from the 16-19 September 2009 alongside the World Fishing Exhibition (WFE) in Vigo, Spain. Conference topics will be confirmed shortly and the exhibition will feature more than 3000 m^2 of new products and the latest innovations. Co-location with the World Fishing Exhibition, the World's largest commercial fishing exhibition, meanws that not only will AQA benefit from the WFE's extensive worldwide marketing program, but also from the same features, such as the Fisheries Ministers Conference, that make the WFE truly unique. For more information, click here to access the conference website.

XI Ecuadorian Aquaculture Conference & Aquaexpo - AQUA 2009; 12-15 October 2009; Guayaquil, Ecuador: AQUA 2009 constitutes the 11th edition of the Ecuadorian Aquaculture Conference & Aquaexpo, an event which has established itself as the leading aquaculture conference and trade show in Latin America. AQUA 2009 will include a Scientific Program with presentations by renowned international and national experts as well as a trade show where the leading companies in the industry will display their latest developments in aquaculture products and services. For more information contact Camila Parra (phone 5934-2-269494 or email at: cparra@cna-ecuador.com.

ROZ's CORNER

Progress on Chloramine-T (HALAMID® AQUA): Two initial label claims are close to completion (1) control of mortality due to bacterial gill disease on all freshwater-reared salmonids and (2) control of mortality due to external columnaris disease on walleye (and possibly an all warmwater-reared finfish label claim).

- On 6 November 2009, the National Coordinator for Aquaculture New Animal Drug Applications (NCANADA) met with the sponsor of HALAMID® AQUA, Axcentive SARL, in Chicago, Illinois USA to discuss the remaining data requirements for the above described approvals: (1) Response from the CVM on the Chemistry, Manufacturing, and Controls (CMC) Technical Section submission, (2) audit at manufacturing site, (3) determination of changes to the final labeling for acceptance by CVM, (4) an Environmental Safety (ES) Technical Section Complete Letter to CVM requesting the consideration that this section is complete, (5) resolution of issues associated with Guidance for Industry (GFI) #159, and (6) summary of data research for All Other Information Technical Section.
- On 14 November 2008, Axcentive SARL received a response to their submission of a full CMC Technical Section. The company is working on a response.
- In January 2009, Axcentive SARL submitted an ES Technical Section Complete Letter request to CVM in collaboration with Upper Midwest Environmental Sciences Center (UMESC) and the National Aquaculture NADA Coordinator.
- On 2 January 2009, CVM accepted the effectiveness study as pivotal from the Aquatic Animal Drug Approval Partnership Program (AADAP) for the control of mortality

in bluegill due to external columnaris disease.

- UMESC continues to conduct research to resolve the GFI #159 issues (i.e., improving the determinative method performance so the marker residue can be reliably quantitated to 20 ppb).

New Group called the Working Group on Aquaculture Chemicals (WGAC): The NCANADA attended the inaugural meeting, held at Aquaculture America 2009, of this new group. For detailed information on the meeting, refer to WGAC story on page 5.

Potential Potassium Permanganate (CAIROX®) Salmonid Label Claims: In December 2008, the NCANADA worked with Clear Springs Foods, AADAP, and Carus Chemical Company (sponsor of Cairox®) to determine what label claims can be supported for salmonids through cooperative efforts. The NCANADA also prepared a revised Minor Use and Minor Species Annual Report to reflect those aspects.

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

CVM's NOTES

The CVM End Review Amendment (ERA) process: As part of the Animal Drug User Fee Amendments of 2008 ("ADUFA II") legislation passed by Congress and signed into law last year by President Bush, CVM agreed to a number of performance goals (http://www.fda.gov/cvm/ADUFAIIreauthorization.htm). Among them is the new End Review Amendment (ERA) process which took effect 1 October 2008. The performance goals for the ERA process are outlined in the reauthorization letter. This process affects investigational new animal drug (INAD) data submissions, protocol submissions, non-administrative new animal drug applications (NADAs), and non-manufacturing supplemental animal drug applications. This process was created to enable CVM to work with a sponsor to address deficiencies at the end of the review process rather than sending an incomplete action or non-concurrence letter. It should improve efficiency by reducing the number of submission review cycles. Once CVM has completed a review of the submitted information, CVM may request an ERA if we determine that the submission of additional non-substantial data or information would likely complete the application or submission.

Three new Policy and Procedure (P&P) guides further explain the process. They can be found at the following weblinks:

- Investigational Animal Drug Protocol without Data submissions http://www.fda.gov/cvm/Policy_Procedures/1243_4070.pdf;
- Investigational Animal Drugs Study Submissions http://www.fda.gov/cvm/Policy_Procedures/1243_4075.pdf; and
- Non-administrative Animal Drug Applications and Non-manufacturing Supplemental Animal Drug Applications http://www.fda.gov/cvm/Policy_Procedures/1243_5730.pdf.

These documents include many critical dates. If an ERA is requested, an email will be sent to the sponsor requesting specific information or data and indicating when it needs to be received by CVM. If the information is not received by CVM by the specified date, then it will result in an incomplete submission. Please note that the "CVM received date" means received in and date stamped by the CVM Document Control Unit (DCU), and not delivered to the building mail room. Please allow sufficient time for mail room and DCU processing when sending submissions. To expedite the processing of an ERA, please reference the submission number identified in CVM's email, and address the submission to the DCU and not the CVM review division. Specific instructions for submitting an ERA are described in the P&Ps and must be followed in order for CVM to accept and review the ERA.

Another important reminder is to start including an email address of the official contact person in cover letters. Since the ERA process now incorporates emails as part of the official correspondence, CVM should have the correct email address of the sponsor. In addition, we recommend the inclusion of a "back-up" contact person's email should the primary contact be out of town when the ERA request or notification email is sent. This is especially important with ERAs associated with protocol submissions because a sponsor only has 10 calendar days to provide the requested information.

Although this process may be daunting in the beginning, we do expect it to streamline the review process and help drugs reach approval faster. Additional information can be found on CVM's website http://www.fda.gov/cvm.

Please feel free to contact us if you have any questions about the ERA process. We are happy to help you with this new process. Our contact information is:

Dr. Jennifer Matysczak
Acting Team Leader, Aquaculture Drugs Team
phone: 240-276-8338
email: jennifer.matysczak@fda.hhs.gov

Dr. Stacey Gore
Veterinary Medical Officer, Aquaculture Drugs Team
phone: 240-276-8283
email: stacey.gore@fda.hhs.gov

Text provided by Dr. Stacey Gore, Aquaculture Drugs Team, Office of New Animal Drug Evaluation, Center for Veterinary Medicine, Food and Drug Administration.