

**NATIONAL COORDINATOR FOR AQUACULTURE NEW
ANIMAL DRUG APPLICATIONS**

FOURTEENTH ANNUAL REPORT OF ACTIVITIES

May 15, 2008 to May 14, 2009

Submitted by

**Rosalie A. Schnick
National Aquaculture NADA Coordinator
Michigan State University
3039 Edgewater Lane
La Crosse, Wisconsin 54603-1088
Phone: (608) 781-2205
Fax: (608) 783-3507
E-mail: RozSchnick@centurytel.net
Web site: <http://aquanic.org/aquadrugs>**

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ACRONYMS AND ABBREVIATIONS USED

AADAP	Aquatic Animal Drug Approval Partnership Program
ADI	acceptable daily intake
AFS	American Fisheries Society
AFWA	Association of Fish and Wildlife Agencies (formerly was IAFWA; the AFWA Project refers to the Federal-State Aquaculture Drug Approval Partnership Project)
CCP	crude carp pituitary
CVM	Center for Veterinary Medicine
DAWG	Drug Approval Work Group, provides oversight to the former AFWA Project
EA	environmental assessment
EPA	U.S. Environmental Protection Agency
FDCA	Food, Drugs, and Cosmetic Act
FOI	Freedom of Information
FMCS	Fishery Management Chemicals Subcommittee
FWS	U.S. Fish and Wildlife Service
g	gram
GFI	Guidance for Industry document
HPLC	high performance liquid chromatography
INAD	Investigational New Animal Drug
kg	kilogram(s)
lb	pound(s)
LHRHa	luteinizing hormone-releasing hormone analog
mg	milligram(s)
MSCG	Multi-State Conservation Grant
MT	17 α -methyltestosterone
MUMS	Minor Use and Minor Species
NADA	New Animal Drug Application
NAI-TAP	National Aquaculture Industry Therapeutic Agent Program
NCRAC	North Central Regional Aquaculture Center
NCTR	National Center for Toxicological Research
NHP	necrotizing hepatopancreatitis
NRSP-7	National Research Support Project Number Seven (7)
NTP	National Toxicology Program
OTC	oxytetracycline
ppm, ppb	parts per million, parts per billion
p-TSA	para-toluenesulfonamide
®	registered name
RED	Reregistered Eligibility Decision
SIUC	Southern Illinois University at Carbondale
SNARC	Harry K. Dupree Stuttgart National Aquaculture Research Center
SOP	standard operating procedures
SPAH	Schering-Plough Animal Health
UID	University of Idaho
UMESC	Upper Midwest Environmental Sciences Center
USDA	U.S. Department of Agriculture
UW-M	University of Wisconsin-Madison
VDD	Veterinary Drugs Directorate

**FOURTEENTH ANNUAL SUMMARY OF ACTIVITY HIGHLIGHTS FOR THE NATIONAL
COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS
(NATIONAL AQUACULTURE NADA COORDINATOR)
(MAY 15, 2008 TO MAY 14, 2009)**

APPROVAL!!

- **SUPPLEMENTAL NADA APPROVAL: TERRAMYCIN® 200 FOR FISH (OXYTETRACYCLINE DIHYDRATE) FOR CONTROL OF MORTALITY IN (1) ALL FRESHWATER-REARED SALMONIDS DUE TO COLDWATER DISEASE AND (2) *ONCORHYNCHUS MYKISS* DUE TO COLUMNARIS DISEASE. THE LIMITATION ON TREATING SALMONIDS IN WATER TEMPERATURES BELOW 9°C WAS REMOVED. (APPROVED JULY 6, 2008).**

CHLORAMINE-T (HALAMID® AQUA)—EXTERNAL ANTIBACTERIAL

Three initial label claims close to completion: Control of mortality in: (1) freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium psychrophilum*, (2) all coolwater finfish due to external columnaris disease associated with *Flavobacterium columnare*, and (3) all warmwater finfish due to external columnaris disease

- On May 23, 2008, CVM accepted from Axcentive SARL the draft text of its labeling but requesting some minor revisions.
- On July 9, 2008, AADAP submitted efficacy data on the control of mortality in bluegill due to external columnaris disease.
- On July 11, 2008, AADAP resubmitted efficacy data on the control of mortality in largemouth bass due to external columnaris disease and requested an Effectiveness Technical Section Complete.
- On August 6, 2008, CVM offered two options to complete Human Food Safety (HFS) Technical Section: (1) provide human intestinal flora data or (2) improve the determinative method performance so the marker residue can be reliably quantitated to lower levels. If this is accomplished, then CVM would assign an 11- OR 13-day withdrawal time.
- On October 8, 2008, AADAP submitted an efficacy study for the control of mortality in largemouth bass caused by external columnaris disease.
- On October 8, 2008, AADAP submitted a request to consider the Effectiveness Technical Section complete for the following label claim, "Use chloramine-T administered in a flow-through or static water bath at a concentration of 20 mg/L for 60 min/d on three alternate or consecutive days to control mortality caused by external columnaris in all warmwater finfish."
- On November 6, 2009, the National Aquaculture NADA Coordinator met with the sponsor of HALAMID® AQUA, Axcentive SARL, in Chicago, IL to discuss the remaining data requirements for its approval: (1) Response from the Center for Veterinary Medicine (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 November 14, 2008, Axcentive SARL received a response to their submission of a full Chemistry, Manufacturing, and Controls (CMC) Technical Section. The company is working on a response.

- In January 2009, Axcentive SARL submitted an Environmental Safety (ES) Technical Section Complete Letter request in collaboration with Upper Midwest Environmental Sciences Center (UMESC) and the National Aquaculture NADA Coordinator.
- In response to the August 6, 2008 CVM response on Guidance for Industry #159 submitted by Axcentive SARL, UMESC is modifying the determinative analytical method for the chloramine-T marker residue para toluene sulfonamide (p-TSA) to reduce the method quantitation limit to <20 ppb. Following consultation with CVM to gain concurrence of the additional method processes, a method validation study will be initiated to determine how robust the additional method processes are when applied to other fish tissues (i.e., can a method quantitation limit of <20 ppb be attained in a variety of fish species). The method validation study is expected to be initiated in the summer of 2009 and completed by December 2009. Identification of additional method cleanup procedures required more time than originally estimated, thus delaying the estimated completion date of the method validation portion of the study. If CVM accepts the proposed modifications to the analytical method and agrees that the quantitation limit is 20 ppb then CVM could assign an 11-day or 13-day withdrawal time with a tolerance of 20 ppb.
- On January 2, 2009, CVM accepted the efficacy study submitted by AADAP for the control of mortality in bluegill caused by external columnaris disease as pivotal.
- On April 2, 2009, CVM accepted the efficacy study submitted by AADAP on October 8, 2008 for the control of mortality in largemouth bass caused by external columnaris disease as pivotal.
- On April 2, 2009, CVM requested from AADAP any additional raw data on chloramine-T from effectiveness studies conducted at the state of Florida's Richloam Fish Hatchery.
- On April 7, 2009, AADAP submitted a white paper titled, "Request to Consider the Chloramine-T Effectiveness Technical Section Complete for the Control of Mortality in All Freshwater-Reared Coolwater and Warmwater Finfish due to External Columnaris Disease Associated with *Flavobacterium columnare*."
- On April 13, 2009, AADAP submitted a letter to CVM requesting (1) the effectiveness technical section complete for all freshwater-reared warmwater finfish, and (2) to resolve any raw data issues on effectiveness stated in the letter from CVM dated April 2, 2009.
- On May 6, 2009, AADAP submitted an amendment to the chloramine-T white paper. The amendment summarized chloramine-T field efficacy trials conducted in 2000 – 2007 under the Pennsylvania Fish and Boat Commission compassionate INAD.

COPPER SULFATE (TRIANGLE BRAND COPPER SULFATE®)—EXTERNAL MICROBICIDE
One initial label claim close to completion: (1) control of mortality due to ichthyophthiriasis on channel catfish

- In December 2008, CVM accepted as complete the Human Food Safety Technical Section for all finfish.

ERYTHROMYCIN (AQUAMYCIN 100®)—ORAL ANTIBACTERIAL
One initial label claim close to completion: (1) control of mortality due to bacterial kidney disease in salmonids

- UMESC completed a 21-day daphnia study to complete requirements for the environmental assessment.

- Bimeda completed the stability batches for the Chemistry, Manufacturing, and Controls Technical Section.
- Bimeda submitted the SOP for HPLC methods for erythromycin to CVM's Office of Research to finalize the analytical methods.

FLORFENICOL (AQUAFLO[®])—ORAL ANTIBACTERIAL

Three supplemental label claims close to completion: Control of mortality in: (1) freshwater-reared salmonids due to systemic columnaris disease caused by *Flavobacterium columnare* (2) coolwater and warmwater finfish due to systemic columnaris disease caused by *Flavobacterium columnare* and (3) hybrid striped bass and tilapia due to *Streptococcus iniae*; Label claims for supplemental NADAs under development: Control of mortality in: (1) coolwater and warmwater fish due to *Aeromonas* sp. and (2) freshwater-reared salmonids due to bacterial kidney disease associated with *Renibacterium salmoninarum*

- On April 4, 2008, AADAP completed the Effectiveness Technical Section for control of mortality in hybrid striped bass due to *Streptococcus iniae* and forwarded the information to Intervet/Schering-Plough Animal Health.
- On September 17, 2008, AADAP submitted to CVM a Final Study Report on the use of AQUAFLO[®] for the control of systemic columnaris disease in largemouth bass. On February 3, 2009, CVM did not accept the efficacy study because there were issues with the homogeneity of the florfenicol-medicated feed and oxytetracycline contamination in the florfenicol-medicated feed.
- On December 9, 2008, AADAP submitted to CVM a Final Study Report on the use of AQUAFLO[®] for the control of systemic columnaris disease in rainbow trout.
- On December 9, 2008, AADAP submitted a request to consider the Effectiveness Technical Section complete for the following label claim: Use of AQUAFLO[®] to control mortality caused by systemic columnaris disease in all freshwater-reared salmonids when administered at a dose of 10 mg florfenicol/kg fish body weight/d for 10 consecutive days.
- From March 10 to April 9, 2009, AADAP and SNARC conducted the in-life phase of the Target Animal Safety study on sunshine bass at the SNARC testing facility. All raw data and tissue samples are now at the AADAP Program facility to be processed and analyzed.
- UMESC submitted in December 2008 the Final Study Report of a pivotal field effectiveness trial that evaluated the efficacy of AQUAFLO[®] to control the mortality caused by *Streptococcus iniae* in tilapia to Intervet, Inc. The study was fully funded by Intervet/Schering-Plough Animal Health (now called Intervet, Inc.) through its Cooperative Research and Development Agreement (CRADA) with UMESC.
- UMESC has initiated a marker residue depletion study to determine the decline of the marker residue of florfenicol (FFC), florfenicol amine (FFA), in the edible tissue (scaled, skin-on fillet) of market-weight tilapia (*Oreochromis* spp.) following feeding of Aquaflor-medicated feed at 20 mg/kg bodyweight/d for 10 d (1.33x proposed dose and 1x proposed duration) in a recirculating aquaculture system (RAS). The study will also determine FFC levels in waters removed from a RAS in which the system population is fed Aquaflor[®]-medicated feed at 20 mg/kg bodyweight/d for 10 d. The in-house phase of the study is expected to be completed in July 2009. The study was fully funded by Intervet, Inc. through its CRADA with UMESC.
- UMESC will initiate a target animal safety study to determine the safety of florfenicol to tilapia administered in medicated feed at 0, 1, 3, and 5x the proposed 15 mg/kg bodyweight/d dose. The in-house phase of the study is expected to be initiated in October 2009. The study will be fully funded by Intervet, Inc. through its CRADA with UMESC.

FORMALIN (FORMALIN-F®, PARASITE-S®, PARACIDE-F®, FORMACIDE-B®)—EXTERNAL MICROBICIDE**One supplemental label claim close to completion: (1) control of mortality due to saprolegniasis on all freshwater-reared fish**

- Pivotal efficacy study for control of mortality due to saprolegniasis on channel catfish conducted by CVM-OR (animal phase completed in January 2007; Final Study Report in Quality Assurance at CVM and is expected to be submitted within the next three months).

HYDROGEN PEROXIDE (35% PEROX-AID®)**Supplemental NADAs close to completion: Control of mortality in: (1) freshwater-reared finfish due to saprolegniasis and (2) all warmwater finfish (including channel catfish already approved) due to external columnaris disease associated with *Flavobacterium columnare*; Supplemental NADAs under development: Control of mortality in: (1) freshwater-reared finfish due to external parasites, (2) selected saltwater-reared finfish due to external parasites, and (3) freshwater-reared finfish (salmonids already approved) due to bacterial gill disease associated with *Flavobacterium branchiophilum***

- On February 26, 2009, AADAP submitted to CVM the Final Study Report for efficacy of hydrogen peroxide to control mortality caused by external columnaris disease in bluegill.
- On February 26, 2009, AADAP submitted a request to consider the Effectiveness Technical Section complete for the following claim, "Use 35% PEROX-AID® to control mortality in all freshwater-reared, warmwater finfish due to columnaris disease associated with *Flavobacterium columnare*."
- On May 5, 2009, CVM accepted the efficacy study submitted by AADAP on November 5, 2008 on largemouth bass as pivotal for external columnaris disease.
- UMESC obtained CVM concurrence pivotal efficacy study protocols for use of 35% PEROX-AID® for control of mortality caused by saprolegniasis on rainbow trout and walleye. CVM concurrence was obtained for both protocols.
- In May 2009, UMESC submitted a Final Study Report to CVM that summarized a supportive efficacy trial conducted at the Illinois Department Natural Resources Jake Wolf State Fish Hatchery to control mortality caused by saprolegniasis in largemouth bass.
- UMESC submitted a pivotal efficacy protocol of 35% PEROX-AID® for control of *Gyrodactylus* sp. on brook trout to CVM in October 2008. CVM did not concur with the design but UMESC incorporated their comments before conducting the study at the FWS Iron River NFH in December 2008. The data summary is on-going and the Final Study Report is expected to be submitted to CVM in June 2009.
- UMESC is preparing the Final Study Reports to document supportive efficacy trials conducted by Marquette State Fish Hatchery to control *Gyrodactylus* sp. on brook trout. The Final Study Reports are expected to be submitted to CVM in June 2009

17 α -METHYLTESTOSTERONE=MT (MASCULINIZING FEED FOR TILAPIA®)—GENDER MANIPULATION AID**One initial label claim in progress: (1) masculinization of female early life-stage tilapia**

- On June 13, 2008, NCRAC informed the National Aquaculture NADA Coordinator that the WRAC had agreed to help fund along with NCRAC the repeat of the target animal safety study in tilapia and the feed method transfer study.
- On September 30, 2008, the National Aquaculture NADA Coordinator completed the full proposal for

the repeat of the target animal safety study in tilapia and the feed method transfer study and submitted it to NCRAC and WRAC for review. The proposal was finalized on May 5, 2009.

OXYTETRACYCLINE DIHYDRATE (TERRAMYCIN® 200 FOR FISH)—ORAL ANTIBACTERIAL
Three supplemental label claims close to completion: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in all freshwater-reared salmonids; (3) skeletal marking in salmonids; one label claim in progress: (1) control of mortality in penaeid shrimp due to NHP

- On May 8, 2008, CVM accepted from Phibro Animal Health the Labeling Technical Section for Terramycin® 200 for Fish as being complete control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in all freshwater-reared salmonids. Phibro Animal Health will add the previously approved label claim (September 23, 1970) for marking skeletal tissue of Pacific salmon to this labeling (250 mg of oxytetracycline per kg of fish per day in fish feed); it was never on any previous labels. Additionally, the temperature restriction on treating salmonids below 9°C. is removed from the label as a result of UMESC data.
- On May 23, 2008, CVM accepted the Freedom of Information summary and the All Other Information Technical Sections for the first two label claims listed above.
- On June 2, 2008, Phibro Animal Health submitted the Administrative NADA for TERRAMYCIN® 200 FOR FISH for the following: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in freshwater-reared salmonids. Phibro Animal Health will add the previously approved label claim (23 September, 1970) for marking skeletal tissue of Pacific salmon to this labeling (250 mg of oxytetracycline per kg of fish per day in fish feed); it was never on any previous labels. Additionally, the temperature restriction on treating salmonids below 9°C. is removed from the label as a result of UMESC data. CVM has 60 days to review the NADA package.
- **Supplemental NADA approval: Terramycin® 200 for Fish** (oxytetracycline dihydrate) for control of mortality in (1) all freshwater-reared salmonids due to coldwater disease and (2) *Oncorhynchus mykiss* due to columnaris disease. The limitation on treating salmonids in water temperatures below 9°C was removed (Approved July 6, 2008).
- On November 4, 2008, AADAP submitted a protocol to CVM to evaluate the effectiveness of oxytetracycline dihydrate-medicated feed to mark skeletal tissue of rainbow trout; ERA request from CVM received by AADAP on December 22, 2008; amended protocol submitted to CVM on December 30, 2009; protocol accepted by CVM on January 2, 2009
- In February and March 2009, AADAP conducted the in-life phase of the oxytetracycline dihydrate-medicated feed skeletal marking study on rainbow trout. The Final Study Report is scheduled to be submitted by the end of August 2009.

POTASSIUM PERMANGANATE (CAIROX®)

Original NADA under development: Control of mortality in (1) hybrid striped bass and channel catfish due to external columnaris disease associated with *Flavobacterium columnare* in ponds with no outflows

- In December 2008, the National Aquaculture NADA Coordinator worked with Clear Springs Foods, AADAP, and Carus Chemical Company (sponsor of Cairox®) to determine what label claims for potassium permanganate can be supported for salmonids through cooperative efforts. She also prepared a revised Minor Use and Minor Species Annual Report to reflect those aspects.
- On April 2, 2009, the National Aquaculture NADA Coordinator sent to AADAP an analysis from the 2005 survey of AFWA Project supporters of the unmet label claim needs for potassium permanganate

along with the contact information. This document should help AFWA determine whether to proceed with any efforts for drug approval for potassium permanganate.

- On May 14, 2009, Clear Springs Foods submitted to CVM a “white paper” entitled “Potassium permanganate: What is it and how can we ensure it is safely used in US aquaculture”. This white paper was prepared to provide an overview summarizing the various aspects of aquaculture uses, some of the research conducted to date, and some of the challenges associated with NADA efforts so that the aquaculture industry can explore with CVM the options for approval if in fact it is considered a drug by CVM and not a pesticide or disinfecting agent.

SALMON GONADOTROPIN RELEASING HORMONE ANALOG AND DOMPERIDONE (OVAPRIM®)—SPAWNING AID.

Original NADA under development: One initial label claim in progress: (1) Spawning aid for ornamental and aquarium fish.

- On March 19, 2009, Western Chemical, Inc. (Ferndale, Washington) received Indexing for Salmon Gonadotropin Releasing Hormone analog and Domperidone (Ovaprim®) for use as a spawning aid in ornamental fish.

GENERAL

- **MUMS DESIGNATIONS.** The designation provision of the MUMS Act of 2004 gives sponsors seven years of marketing exclusivity. As of May 14, 2009, the MUMS Office has granted 64 designations, 55 of those are to aquaculture drug sponsors, many of whom have received extensive help from the National Aquaculture NADA Coordinator.
- **FORMATION OF A NEW GROUP.** Because of the potential concern that the Joint Subcommittee on Aquaculture Working Group on Aquaculture Drugs, Biologics, and Pesticides may be acting as a Federal Advisory Committee, an informal meeting was convened on February 9, 2008 to solicit input from non-federal stakeholders on future roles and direction. The new group was tentatively named the National Aquaculture Industry Therapeutic Agent Program (NAI-TAP) and was to be a coalition of aquaculture industry stakeholders and invited non-industry entities who would have addressed and supported the development, approval, availability, and optimal use of drug, biologic, nutritional, and other products that affect the health and production of aquatic animals. However, because of the lack of private aquaculture industry representation on the working group, it became the Working Group on Aquaculture Drugs, Chemicals, and Biologics under the American Fisheries Society Fish Culture Section.
- **14th ANNUAL DRUG APPROVAL COORDINATION WORKSHOP.** The 14th Annual Drug Approval Coordination Workshop was held in Bozeman, Montana on July 29-31, 2008. The topics included celebration of approval for Terramycin® 200 for Fish, approval status of all aquaculture drugs, and the dilemma concerning a sedative for aquaculture and fish management needs. On August 1, 2008, a meeting of the National Aquaculture Drug Research Forum and the organizational meeting of the National Aquaculture Industry Therapeutic Agent Program (now the Working Group on Aquaculture Drugs, Chemicals, and Biologics) occurred.
- **DAWG MEETINGS.** The DAWG met on September 8-9, 2008 and February 15, 2009 to discuss the approval status of the AFWA Project drugs and to formulate and implement plans to identify an alternative sedative to isoeugenol.
- **CANDIDATE IMMEDIATE RELEASE AND ZERO WITHDRAWAL SEDATIVES FOR AQUATIC FOOD ANIMALS.** The DAWG held a series of conference calls (June 17, October 10, and 23, 2008) to discuss where the DAWG will go from here to select a candidate sedative, to determine the data requirements, and how to address the data requirements. The candidate sedatives were narrowed to two by the DAWG: benzocaine and eugenol. CVM revealed that the NCTR study on benzocaine showed no acute toxic effects related to methemoglobinemia. The DAWG determined that the

remaining funds (\$202,577) from the Multi-State Conservation Grant on isoeugenol should be used as follows: (1) studies on immediate release (~\$22,577), (2) benzocaine: (a) genotoxicity battery, (b) residue chemistry studies and/or (c) develop determinative methods (~\$90,000), and (3) eugenol: (a) purchase radiolabeled eugenol, (b) residue chemistry studies and/or (c) develop determinative methods (~\$90,000).

- At the request of AADAP, the DAWG and potential sponsors met with CVM to determine the data requirements for prospective candidate sedatives: benzocaine, eugenol, and tricaine on August 20, 2008.
- On August 22, 2008, the National Aquaculture NADA Coordinator provided estimates of zero withdrawal sedative needs for the private aquaculture (finfish) industry to potential sponsors and the DAWG chair.
- On February 17, 2009, the U.S. National Oceanographic and Atmospheric Administration (NOAA) Portland, Oregon, 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 pros and cons 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.
- UMESC, in collaboration with Viterbo University, has initiated studies to determine the time required for fish to resume feeding behavior ("time to first feeding") following sedation by either benzocaine or eugenol. This study will provide the initial information needed to assess whether an "immediate release" claim for either benzocaine or eugenol will provide sufficient time between removals from the sedative bath to availability for human consumption to allow the tissue residues to deplete to a level safe for human consumption.
- The University of Wisconsin-La Crosse, in collaboration with UMESC, has initiated a literature review to evaluate the effects of (1) handling stress, (2) electrofishing, and (3) angling or other capture methods on feeding behavior of fish, especially with regards to the likelihood of striking a lure or other bait. The literature review will be combined with the laboratory study evaluating the time to first feeding following sedation to further the assessment of a proposed immediate release sedative.

Activities related to either candidate sedative are presented below:

Benzocaine

- During the week of February 2, 2009, ACD Pharmaceuticals AS (Ålesund, Norway) indicated that they are pursuing an approval under their INAD exemption for their benzocaine product, BENZOAK[®], for label claims to include sedation to handleable condition and sedation during transport for all freshwater finfish and saltwater-reared salmonids. ACD obtained MUMS designation for one label claim in June 2009).
- In June 2009, Frontier Scientific, Inc., (Logan, Utah) obtained MUMS designation for three label claims for its benzocaine product.
- In May 2009, AADAP tested BENZOAK[®] (ACD Pharmaceuticals, Norway) to identify parameters and use patterns for further study under the compassionate INAD protocol.

- **Eugenol**

- On January 12, 2009, AQUI-S New Zealand obtained MUMS designation for eight label claims for its eugenol product (AQUI-S® E).
- On February 2, 2009, AADAP submitted to CVM all available study reports and data on eugenol generated by the National Toxicology Program.
- In May 2009, AADAP tested AQUI-S® E to identify parameters and use patterns for further study under the compassionate INAD protocol.
- UMESC will initiate a study to develop the analytical methods to detect and quantify eugenol in the edible fillet of freshwater fish in the summer of 2009. The analytical method is a critical component of all human food safety studies including the total residue depletion study and must be completed before a total residue depletion study may be initiated. UMESC will conduct a total residue depletion study using radiolabeled eugenol once the analytical method has been developed and after identifying funding to purchase the radiolabeled eugenol and to dispose of the radioactive wastes generated during the study.

PUBLICATIONS, PRESENTATIONS, AND SPECIAL REPORTS

The National Coordinator for Aquaculture New Animal Drug Applications had one publication, presented nine papers, and wrote 30 special reports during this time period.

PROJECT OBJECTIVES

The overall goal of this project is for the National Coordinator for Aquaculture New Animal Drug Applications (National Aquaculture NADA Coordinator) to coordinate activities for investigational new animal drug exemptions (INADs) and new animal drug applications (NADAs) to expedite approval for the use of various drugs in aquaculture. Specific objectives related to that goal are to:

- Serve as an information conduit between INAD/NADA applicants and the U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM);
- Identify and encourage prospective INAD participants to become involved in specific investigational studies and NADA approval-related research;
- Seek the support and participation of pharmaceutical sponsors for INAD studies and NADAs and coordinate with INAD/NADA sponsors to achieve CVM approval more quickly;
- Guide prospective and current INAD holders on the format for INAD exemption requests and related submissions to CVM;
- Identify existing data and remaining data requirements for NADA approvals;
- Review, record, and provide information on the status of INADs and NADAs;
- Provide liaison and coordination among all the federal agencies involved in the INAD/NADA process; and
- Provide public education related to training and guidance in obtaining INAD exemptions and pursuing NADA approval.

PROGRESS AND PRINCIPAL ACCOMPLISHMENTS

The National Aquaculture NADA Coordinator provided many information transfers from May 15, 2008 to May 14, 2009 and worked to obtain INADs, NADAs, and approvals for a number of drugs that are considered to be of high priority for approval by the public and private aquaculture communities.

THERAPEUTANTS

AMOXICILLIN TRIHYDRATE USP POWDER—ORAL ANTIBACTERIAL

Early development stage; antimicrobial resistance issue needs to be addressed. Kent Sea Tech Corporation, the U.S. representative for the sponsor, GB Research, submitted a Research and Development Plan to CVM files.

Progress on amoxicillin (May 15, 2008 to May 14, 2009):

- Kent Sea Tech Corporation, the U.S. representative for the sponsor, GB Research has stopped its efforts to gain approval for amoxicillin. The company has ceased to produce fish.

CHLORAMINE-T (HALAMID® AQUA+)—EXTERNAL ANTIBACTERIAL

Was an AFWA Project drug with current oversight by the DAWG for AADAP and UMESC; Under development by the sponsor (Axcentive SARL); three initial label claims close to completion: Control of mortality in: (1) freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium psychrophilum*, (2) all coolwater finfish due to external columnaris disease associated with *Flavobacterium columnare*, and (3) all warmwater finfish due to external columnaris disease

Progress on chloramine-T (May 15, 2008 to May 14, 2009):

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- On November 6, 2009, the National Aquaculture NADA Coordinator met with the sponsor of HALAMID® AQUA, Axcentive SARL, in Chicago, IL to discuss the remaining data requirements for its approval: (1) Response from the Center for Veterinary Medicine (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 November 14, 2008, Axcentive SARL received a response to their submission of a full Chemistry, Manufacturing, and Controls (CMC) Technical Section. The company is working on a response.

- In January 2009, Axcentive SARL submitted an Environmental Safety (ES) Technical Section Complete Letter request in collaboration with Upper Midwest Environmental Sciences Center (UMESC) and the National Aquaculture NADA Coordinator.
- In response to the August 6, 2008 CVM response on Guidance for Industry #159 submitted by Axcentive SARL, UMESC is modifying the determinative analytical method for the chloramine-T marker residue para toluene sulfonamide (p-TSA) to reduce the method quantitation limit to <20 ppb. Following consultation with CVM to gain concurrence of the additional method processes, a method validation study will be initiated to determine how robust the additional method processes are when applied to other fish tissues (i.e., can a method quantitation limit of <20 ppb be attained in a variety of fish species). The method validation study is expected to be initiated in the summer of 2009 and completed by December 2009. Identification of additional method cleanup procedures required more time than originally estimated, thus delaying the estimated completion date of the method validation portion of the study. If CVM accepts the proposed modifications to the analytical method and agrees that the quantitation limit is 20 ppb then CVM could assign an 11-day or 13-day withdrawal time with a tolerance of 20 ppb.
- On January 2, 2009, CVM accepted the efficacy study submitted by AADAP for the control of mortality in bluegill caused by external columnaris disease as pivotal.
- On April 2, 2009, CVM accepted the efficacy study submitted by AADAP on October 8, 2008 for the control of mortality in largemouth bass caused by external columnaris disease as pivotal.
- On April 2, 2009, CVM requested from AADAP any additional raw data on chloramine-T from effectiveness studies conducted at the state of Florida's Richloam Fish Hatchery.
- On April 7, 2009, AADAP submitted a white paper titled, "Request to consider the chloramine-t effectiveness technical section complete for the control of mortality in all freshwater-reared coolwater and warmwater finfish due to external columnaris disease associated with *Flavobacterium columnare*."
- On April 13, 2009, AADAP submitted a letter to CVM requesting (1) the effectiveness technical section complete for the control of mortality in all freshwater-reared coolwater and warmwater finfish due to external columnaris disease, and (2) to resolve any raw data issues on effectiveness stated in the letter from CVM dated April 2, 2009.
- On May 6, 2009, AADAP submitted an amendment to the chloramine-T white paper. The amendment summarized chloramine-T field efficacy trials conducted in 2000 – 2007 under the Pennsylvania Fish and Boat Commission compassionate INAD.

Current status of technical sections on chloramine-T:

- *Product Chemistry*—The sponsor, Axcentive SARL (a 100% daughter company of PNP Holding bv, Bouc Bel Air, France) submitted a partial product chemistry technical section for HALAMID PHARMA GRADE® (now HALAMID® AQUA) to CVM on May 22, 2006 and a complete Chemistry, Manufacturing, and Controls Technical Section on May 16, 2008. CVM responded on November 14, 2008 and the sponsor is working on a response.
- *Environmental Safety*—CVM accepted from UMESC a dilution model to detect effluents from waterborne drugs at the outlet pipe (May 7, 2003). UMESC submitted an environmental summary to CVM into Public Master File Number 5637 (October 31, 2002); these data are available to any chloramine-T sponsors. UMESC also developed a proprietary EA that was submitted by Axcentive SARL on July 16, 2003 to CVM under INAD #8086 for HALAMID PHARMA GRADE®. CVM sent a review to the sponsor on September 17, 2004; UMESC revised the EA and submitted it to CVM on February 9, 2006. UMESC revised the EA based on CVM comments of August 28, 2006 and submitted it to CVM on April 13, 2007. The final EA was accepted October 12, 2007. In January 2009, Axcentive SARL submitted a request for a Technical Section complete letter.

- *Human Food Safety–Toxicology*—Axcentive SARL addressed this technical section on HALAMID® AQUA+. CVM declared that para-toluenesulfonamide (p-TSA) is not genotoxic based on proprietary data submitted by Axcentive SARL on (July 19, 2002). CVM accepted additional proprietary mammalian safety data on HALAMID® AQUA+ from Axcentive SARL; based on those data, CVM declared that the safe concentration (tolerance) of p-TSA in edible tissue of fish is 1 ppm (April 9, 2003).
- *Human Food Safety–Residue Chemistry*—CVM accepted as complete from UMESC (1) total residue depletion and metabolism of chloramine-T in rainbow trout; p-TSA was established as the major metabolite in fish and declared as a marker residue for chloramine-T in juvenile rainbow trout (July 20, 1995), (2) liquid chromatographic determination of p-TSA in edible tissue from three fish species (May 18, 1999), (3) marker residue depletion in rainbow trout, yellow perch, and hybrid striped bass (April 23, 2002), (4) regulatory method for p-TSA in edible tissue of rainbow trout, channel catfish, and walleye (April 24, 2003), (5) validation of the p-TSA determinative method in several species and species from several regions of the U.S. (April 24, 2003), and (6) confirmatory method for p-TSA in fish tissue to satisfy an all fish label claim (March 4, 2005). UMESC submitted a FOI summary on human food safety to CVM (April 23, 2002). CVM declared that the safe concentration of p-TSA in edible tissue of fish is 1 ppm (April 9, 2003).
- *Human Food Safety–Microbial Food Safety*—Axcentive SARL submitted GFI #152 and #159 on HALAMID® AQUA in November 2006 to CVM. CVM accepted GFI #152 on HALAMID® AQUA+ from Axcentive SARL (May 2007). The GFI #159 revision on HALAMID® AQUA was submitted by Axcentive on July 27, 2007 and it was provisionally accepted by CVM on December 10, 2007 with the provision that there be an 11-day withdrawal period.
- *Human Food Safety Technical Section*- On February 8, 2008, Axcentive SARL submitted to CVM the Human Food Safety Technical Section Complete Letter on HALAMID® AQUA+ based on data generated by UMESC and results of CVM review of GFI #159 in which CVM suggested an 11-day withdrawal period in lieu of additional studies. On August 6, 2008, CVM offered two options to complete Human Food Safety (HFS) Technical Section: (1) provide human intestinal flora data or (2) improve the determinative method performance so the marker residue can be reliably quantitated to lower levels. If this is accomplished, then CVM would assign an 11-day withdrawal time. UMESC is working on revisions of the analytical method for p-TSA to meet the changes.
- *Target Animal Safety*—CVM accepted as complete from (1) AADAP the target animal safety technical section on freshwater-reared salmonids (September 13, 2002) and (2) UMESC the target animal safety technical section on all coolwater and warmwater fish (March 11, 2004 and March 11, 2005).
- *Effectiveness*—CVM accepted from UMESC a simple colorimetric procedure for use in effectiveness studies for monitoring chloramine-T concentrations in treatment waters (July 27, 1997 and January 15, 2003). CVM accepted as supportive from UMESC data call-in on effectiveness studies for control of mortality due to bacterial gill disease on (1) tiger musky (November 29, 1999) and (2) salmonids (July 12, 2000). CVM accepted as pivotal from AADAP for control of mortality in largemouth bass (April 2, 2009) and bluegill (January 2, 2009) due to external columnaris disease. CVM accepted as complete from (1) AADAP the effectiveness technical section for control of mortality due to bacterial gill disease on all freshwater-reared salmonids (June 10, 2002), (2) AADAP the effectiveness technical section for controlling external columnaris disease on walleye (March 3, 2008), and (3) UMESC the effectiveness technical section for controlling external columnaris disease on walleye (January 30, 2004). AADAP submitted effectiveness studies for control of mortality in largemouth bass due to external columnaris disease (September 25, 2007).

COPPER SULFATE (TRIANGLE BRAND COPPER SULFATE®)—EXTERNAL MICROBICIDE

Was an AFWA Project drug with current oversight by the DAWG for SNARC; Under development by the sponsor (Phelps Dodge Sales Company); one initial label claim close to completion: (1) control of mortality due to ichthyophthiriasis on channel catfish.

Progress on copper sulfate (May 15, 2008 to May 14, 2009):

- In December 2008, CVM accepted as complete the Human Food Safety Technical Section for all finfish.

Current status of technical sections on copper sulfate:

- *Product Chemistry*—CVM accepted as complete from the sponsor, Phelps Dodge Refining Corporation (May 1999).
- *Environmental Safety*—The revised environmental safety technical section for use in earthen ponds with no outflows was reviewed by CVM in 2000 and CVM required an additional study. A study at SNARC addressing the use of copper sulfate in ponds was completed and was incorporated into a revised EA submitted to CVM in December 2006. CVM is requiring additional changes.
- *Human Food Safety-Toxicology*—CVM accepted as complete from the sponsor, Phelps Dodge Refining Corporation; FOI summary written by CVM on March 3, 2000.
- *Human Food Safety-Residue Chemistry*—CVM accepted as complete from SNARC the human food safety technical section; FOI written by CVM on March 3, 2000—no tolerances, regulatory methods, or withdrawal times are needed for finfish treated with copper sulfate.
- *Human Food Safety-Microbial Food Safety*—CVM is requiring a GFI #152 for an all freshwater-reared finfish acceptance for the human food safety technical section.
- *Human Food Safety Technical Section Completion*—CVM accepted Human Food Safety Technical Section Complete Letter for channel catfish (December 2007)
- *Target Animal Safety*—SNARC submitted literature on target animal safety studies and a target animal safety study on channel catfish with a histopathology component as requested by CVM. The channel catfish study was accepted by CVM May 25, 2005. CVM accepted the Target Animal Safety Technical Section as complete for channel catfish (April 2006).
- *Effectiveness*—CVM accepted as complete from SNARC the effectiveness technical section for control of ichthyophthiriasis on all fish (December 1998). SNARC is also conducting pivotal effectiveness studies to control fungi on catfish eggs.

DIQUAT DIBROMIDE—EXTERNAL MICROBICIDE)

No sponsor is available to complete the approval process at the present time.

1. AADAP has an INAD (#10-969) to generate data to help determine appropriate diquat treatment regimens for controlling mortality in a variety of cultured fishes diagnosed with bacterial gill disease or external columnaris disease. Syngenta Crop Protection, Inc. is the sole supplier of diquat to all Investigators.

ERYTHROMYCIN (AQUAMYCIN 100®)—ORAL ANTIBACTERIAL

One initial label claim close to completion: (1) control of mortality due to bacterial kidney disease in salmonids

Progress on erythromycin (May 15, 2008 to May 14, 2009):

- UMESC completed a 21-day daphnia study to complete requirements for the environmental assessment.
- Bimeda completed the stability batches for the Chemistry, Manufacturing, and Controls Technical Section.
- Bimeda submitted the SOP for HPLC methods for erythromycin to CVM's Office of Research to finalize the analytical methods.

Current status of technical sections on erythromycin:

- *Product Chemistry*—By agreement with Abbott Laboratories; analytical method in feed—in progress.
- *Environmental Safety*—CVM requested revisions to the EA (October 23, 2007). UID is working with UMESC and NRSP-7 to complete the revisions.
- *Human Food Safety-Toxicology*—By agreement with Abbott Laboratories; previously accepted.

- *Human Food Safety-Residue Chemistry*—accepted by CVM from UID marker residue depletion for salmonids; bridged official microbial inhibition assay with HPLC method for detection—submitted by UID.
- *Human Food Safety-Microbial Food Safety*—accepted by CVM from UID GFI #152 and #159 (January 11, 2007).
- *Human Food Safety Technical Section Completion*- A right to reference proprietary toxicological data is needed to complete the Human Food Safety Technical Section.-
- *Target Animal Safety*—Accepted by CVM from UID for salmonids.
- *Effectiveness*—Accepted by CVM from UID for bacterial kidney disease in salmonids.

FLORFENICOL (AQUAFLO[®])—ORAL ANTIBACTERIAL

The sponsor, SPAH, recently gained Aquaflor[®] original and supplemental approvals to control mortality due to: (1) enteric septicemia in catfish (October 24, 2005), (2) coldwater disease in freshwater-reared salmonids (March 19, 2007), and (3) furunculosis in freshwater-reared salmonids (October 26, 2007); and one conditional approval for the control of mortality in catfish due to columnaris disease (April 18, 2007); Was previously an AFWA Project drug and now completely under development by the sponsor with research efforts from UMESC, AADAP, and Mississippi State University; three supplemental label claims close to completion: Control of mortality in: (1) freshwater-reared salmonids due to systemic columnaris disease caused by *Flavobacterium columnare* (2) coolwater and warmwater finfish due to systemic columnaris disease caused by *Flavobacterium columnare* and (3) hybrid striped bass and tilapia due to *Streptococcus iniae*; Label claims for supplemental NADAs under development: Control of mortality in: (1) coolwater and warmwater fish due to *Aeromonas* sp. and (2) freshwater-reared salmonids due to bacterial kidney disease associated with *Renibacterium salmoninarum*.

Progress on florfenicol (May 15, 2008 to May 14, 2009):

- On April 4, 2008, AADAP completed the Effectiveness Technical Section for control of mortality in hybrid striped bass due to *Streptococcus iniae* and forwarded the information to Intervet/Schering-Plough Animal Health.
- On September 17, 2008, AADAP submitted to CVM a Final Study Report on the use of AQUAFLO[®] for the control of systemic columnaris disease in largemouth bass. On February 3, 2009, CVM did not accept the efficacy study because there were issues with the homogeneity of the florfenicol-medicated feed and oxytetracycline contamination in the florfenicol-medicated feed.
- On December 9, 2008, AADAP submitted to CVM a Final Study Report on the use of AQUAFLO[®] for the control of systemic columnaris disease in rainbow trout.
- On December 9, 2008, AADAP submitted a request to consider the Effectiveness Technical Section complete for the following label claim: Use of AQUAFLO[®] to control mortality caused by systemic columnaris disease in all freshwater-reared salmonids when administered at a dose of 10 mg florfenicol/kg fish body weight/d for 10 consecutive days.
- From March 10 to April 9, 2009, AADAP and SNARC conducted the in-life phase of the Target Animal Safety study on sunshine bass at the SNARC testing facility. All raw data and tissue samples are now at the AADAP Program facility to be processed and analyzed.
- UMESC submitted in December 2008 the Final Study Report of a pivotal field effectiveness trial that evaluated the efficacy of AQUAFLO[®] to control the mortality caused by *Streptococcus iniae* in tilapia to Intervet, Inc. The study was fully funded by Intervet/Schering-Plough Animal Health (now called Intervet, Inc.) through its Cooperative Research and Development Agreement (CRADA) with UMESC.
- UMESC has initiated a marker residue depletion study to determine the decline of the marker residue of florfenicol (FFC), florfenicol amine (FFA), in the edible tissue (scaled, skin-on fillet) of market-weight

tilapia (*Oreochromis* spp.) following feeding of Aquaflor-medicated feed at 20 mg/kg bodyweight/d for 10 d (1.33x proposed dose and 1x proposed duration) in a recirculating aquaculture system (RAS). The study will also determine FFC levels in waters removed from a RAS in which the system population is fed Aquaflor®-medicated feed at 20 mg/kg bodyweight/d for 10 d. The in-house phase of the study is expected to be completed in July 2009. The study was fully funded by Intervet, Inc. through its CRADA with UMESC.

- UMESC will initiate a target animal safety study to determine the safety of florfenicol to tilapia administered in medicated feed at 0, 1, 3, and 5x the proposed 15 mg/kg bodyweight/d dose. The in-house phase of the study is expected to be initiated in October 2009. The study will be fully funded by Intervet, Inc. through its CRADA with UMESC.

Current status of technical sections on florfenicol:

- *Product Chemistry*—Accepted from Schering-Plough Animal Health Corporation=SPAH.
- *Environmental Safety*—Accepted from SPAH for ponds and for flow-through systems.
- *Human Food Safety-Toxicology*—Accepted from SPAH.
- *Human Food Safety-Residue Chemistry*—human food safety package for catfish and all freshwater-reared salmonids—Accepted from SPAH; analytical method—Accepted from SPAH.
- *Human Food Safety-Microbial Food Safety*—accepted by CVM from SPAH.
- *Target Animal Safety*—Accepted from SPAH (conducted by UMESC) for channel catfish; Accepted from SPAH for salmonids.
- *Effectiveness*—Accepted from SPAH for enteric septicemia in catfish (conducted by Mississippi State University); Accepted from SPAH (conducted by AADAP) for coldwater disease in freshwater-reared salmonids, *Streptococcus iniae* in hybrid striped bass (December 9, 2004), and furunculosis in freshwater-reared salmonids; UMESC validated methods to analyze for florfenicol in finfish feeds to support effectiveness studies at AADAP and provided valuable information for the environmental assessment.

FORMALIN (FORMALIN-F®, PARASITE-S®, PARACIDE-F®, FORMACIDE-B®)—EXTERNAL MICROBICIDE

Supplemental NADAs approved on June 18, 1998 and November 25, 2002 and an abbreviated NADA on July 17, 2007 for control of certain fungi on the eggs of all finfish, certain external protozoa, and monogenetic trematodes on all finfish, and certain external protozoa on penaeid shrimp; Was an AFWA Project drug with current oversight by the DAWG for UMESC research; CVM's Office of Research is continuing to develop effectiveness data; under development by the sponsors (Natchez Animal Supply Company, Western Chemical Inc., Argent Chemical Laboratories, and B.L. Mitchell, Inc.); **One supplemental label claim close to completion: (1) control of mortality due to saprolegniasis on all freshwater-reared fish.**

Progress on formalin (May 15, 2008 to May 14, 2009):

- Pivotal efficacy study for control of mortality due to saprolegniasis on channel catfish conducted by CVM-OR (animal phase completed in January 2007; Final Study Report in Quality Assurance at CVM and is expected to be submitted within the next three months).

Current status of technical sections on formalin:

- *Product Chemistry*—Accepted by CVM.
- *Environmental Safety*—Accepted by CVM.
- *Human Food Safety-Toxicology*—Accepted by CVM
- *Human Food Safety-Residue Chemistry*—Accepted by CVM.
- *Target Animal Safety*—Accepted by CVM.
- *Effectiveness*—CVM informally accepted as supportive effectiveness data on formalin for control of saprolegniasis on salmonids from the U.S. Fish and Wildlife Service (FWS) and UMESC efforts. CVM

accepted from UMESC as supportive effectiveness studies for the control of saprolegniasis on channel catfish (November 16, 2004) and from CVM Office of Research as pivotal effectiveness studies for the control of saprolegniasis on rainbow trout (July 19, 2005).

HYDROGEN PEROXIDE (35% PEROX-AID®)—EXTERNAL MICROBICIDE

On January 11, 2007, the sponsor, Eka Chemicals, Inc. gained an original NADA approval of 35% PEROX-AID® for the control of mortality due to (1) saprolegniasis on all finfish eggs, (2) bacterial gill disease on all freshwater-reared salmonids, and (3) external columnaris disease on all coolwater fish and channel catfish with the research data generated by UMESC along with the environmental assessment. Low regulatory priority drug for use as a fungicide on fish and fish eggs was rescinded May 2, 2007; Was an AFWA Project drug with current oversight by the DAWG for UMESC and AADAP; Under development by the sponsor (Eka Chemicals Inc.); **Supplemental NADAs close to completion: Control of mortality in: (1) freshwater-reared finfish due to saprolegniasis and (2) all warmwater finfish (including channel catfish already approved) due to external columnaris disease associated with *Flavobacterium columnare*; Supplemental NADAs under development: Control of mortality in: (1) freshwater-reared finfish due to external parasites, (2) selected saltwater-reared finfish due to external parasites, and (3) freshwater-reared finfish (salmonids already approved) due to bacterial gill disease associated with *Flavobacterium branchiophilum*.**

Progress on hydrogen peroxide (May 15, 2008 to May 14, 2009):

- On February 26, 2009, AADAP submitted to CVM the Final Study Report for efficacy of hydrogen peroxide to control mortality caused by external columnaris disease in bluegill.
- On February 26, 2009, AADAP submitted a request to consider the Effectiveness Technical Section complete for the following claim, "Use 35% PEROX-AID® to control mortality in all freshwater-reared, warmwater finfish due to columnaris disease associated with *Flavobacterium columnare*."
- On May 5, 2009, CVM accepted the efficacy study submitted by AADAP on November 5, 2008 on largemouth bass as pivotal for external columnaris disease.
- UMESC obtained CVM concurrence pivotal efficacy study protocols for use of 35% PEROX-AID® for control of mortality caused by saprolegniasis on rainbow trout and walleye. CVM concurrence was obtained for both protocols.
- In May 2009, UMESC submitted a Final Study Report to CVM that summarized a supportive efficacy trial conducted at the Illinois Department Natural Resources Jake Wolf State Fish Hatchery to control mortality caused by saprolegniasis in largemouth bass.
- UMESC submitted a pivotal efficacy protocol of 35% PEROX-AID® for control of *Gyrodactylus* sp. on brook trout to CVM in October 2008. CVM did not concur with the design but UMESC incorporated their comments before conducting the study at the FWS Iron River NFH in December 2008. The data summary is on-going and the Final Study Report is expected to be submitted to CVM in June 2009.
- UMESC is preparing the Final Study Reports to document supportive efficacy trials conducted by Marquette State Fish Hatchery to control *Gyrodactylus* sp. on brook trout. The Final Study Reports are expected to be submitted to CVM in June 2009.

Current status of technical sections on hydrogen peroxide:

- *Product Chemistry*—Accepted from Eka Chemicals, Inc. (February 11, 2004).
- *Environmental Safety*—Accepted from UMESC with a Finding of No Significant Impact (June 22, 2006).
- *Human Food Safety-Toxicology*—Accepted from Eka Chemicals, Inc. (March 22, 2000).

- *Human Food Safety–Residue Chemistry*—Accepted from Eka Chemicals, Inc. with no tolerances, regulatory methods, or withdrawal times needed for finfish and their eggs treated with hydrogen peroxide.
- *Human Food Safety–Microbial Safety*—GFI #52 (now GFI #159) accepted from Eka Chemicals, Inc. (June 6, 2005); GFI #152 accepted from Eka Chemicals, Inc. (September 16, 2005).
- *Human Food Safety*—Accepted FOI summary for human food safety (September 16, 2005).
- *Target Animal Safety*—Accepted from UMESC for all finfish (October 4, 2001) and from UMESC for all finfish eggs (March 17, 2000, August 16, 2002, and November 26, 2003).
- *Effectiveness*—Accepted from UMESC for the control of mortality due to (1) saprolegniasis on all freshwater-reared finfish eggs (March 17, 2000, August 16, 2002, and February 10, 2004), (2) bacterial gill disease on all freshwater-reared salmonids (October 12, 2000), (3) external columnaris disease on all coldwater fish (November 15, 2002 and November 21, 2003), and (4) external columnaris disease on channel catfish (November 21, 2003). CVM accepted as pivotal effectiveness data from UMESC for the control of mortality due to saprolegniasis on catfish but requested additional supportive data before this technical section can be considered as complete (November 24, 2004). CVM accepted as supportive effectiveness data from UMESC for the treatment of external parasitic infestations on all salmonids (September 26, 2002).

OXYTETRACYCLINE DIHYDRATE (TERRAMYCIN® 200 FOR FISH)—ORAL ANTIBACTERIAL

Currently approved for control of certain systemic bacterial diseases in catfish, salmonids, and lobsters and as an oral marking agent in Pacific salmon; Supplemental NADA approval: Terramycin® 200 for Fish (oxytetracycline dihydrate) for control of mortality in (1) all freshwater-reared salmonids due to coldwater disease and (2) *Oncorhynchus mykiss* due to columnaris disease. The limitation on treating salmonids in water temperatures below 9°C was removed (Approved July 6, 2008); Was an AFWA Project drug with current oversight by the DAWG for UMESC and AADAP; Under development by the sponsor (Phibro Animal Health, formerly Pfizer, Inc.); **Three supplemental label claims close to completion: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in all freshwater-reared salmonids; (3) skeletal marking in salmonids; one label claim in progress: (1) control of mortality in penaeid shrimp due to NHP.**

Progress on oxytetracycline dihydrate (May 15, 2008 to May 14, 2009):

- On May 8, 2008, CVM accepted from Phibro Animal Health the Labeling Technical Section for Terramycin® 200 for Fish as being complete control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in all freshwater-reared salmonids. Phibro Animal Health will add the previously approved label claim (September 23, 1970) for marking skeletal tissue of Pacific salmon to this labeling (250 mg of oxytetracycline per kg of fish per day in fish feed); it was never on any previous labels. Additionally, the temperature restriction on treating salmonids below 9°C. is removed from the label as a result of UMESC data.
- On May 23, 2008, CVM accepted the Freedom of Information summary and the All Other Information Technical Sections for the first two label claims listed above.
- On June 2, 2008, Phibro Animal Health submitted the Administrative NADA for TERRAMYCIN® 200 FOR FISH for the following: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in freshwater-reared salmonids. Phibro Animal Health will add the previously approved label claim (23 September, 1970) for marking skeletal tissue of Pacific salmon to this labeling (250 mg of oxytetracycline per kg of fish per day in fish feed); it was never on any previous labels. Additionally, the temperature restriction on treating salmonids below 9°C. is removed from the label as a result of UMESC data. CVM has 60 days to review the NADA package.
- **Supplemental NADA approval: Terramycin® 200 for Fish** (oxytetracycline dihydrate) for control of mortality in (1) all freshwater-reared salmonids due to coldwater disease and (2) *Oncorhynchus mykiss* due to columnaris disease. The limitation on treating salmonids in water temperatures below 9°C was removed (Approved July 6, 2008).

- On November 4, 2008, AADAP submitted a protocol to CVM to evaluate the effectiveness of oxytetracycline dihydrate-medicated feed to mark skeletal tissue of rainbow trout; ERA request from CVM received by AADAP on December 22, 2008; amended protocol submitted to CVM on December 30, 2009; protocol accepted by CVM on January 2, 2009.
- In February and March 2009, AADAP conducted the in-life phase of the oxytetracycline dihydrate-medicated feed skeletal marking study on rainbow trout. The Final Study Report is scheduled to be submitted by the end of August 2009.

Current status of technical sections on oxytetracycline dihydrate:

- *Product Chemistry*—Previously accepted by CVM under original NADA from Pfizer, Inc. (now owned by Phibro Animal Health). The sponsor obtained acceptance for the change to dihydrate salt formulation (June 30, 2006).
- *Environmental Safety*—Previously accepted by CVM under original NADA from Pfizer, Inc. (now owned by Phibro Animal Health). FINFISH: CVM requested a new EA for any new label claims. UMESC submitted an EA written to meet current guidelines and requirements to CVM (October 15, 2004). UMESC submitted an EA on oxytetracycline to CVM on April 3, 2006 and a final EA on April 13, 2007. CVM accepted UMESC's EA February 21, 2008. PENAEID SHRIMP: University of Arizona—additional data needed to complete the EA as required on November 2, 2001.
- *Human Food Safety-Toxicology*—Previously accepted by CVM under original NADA from Pfizer, Inc. (now owned by Phibro Animal Health).
- *Human Food Safety-Microbial Food Safety*—FINFISH: Sponsor, AADAP, UMESC, and National Aquaculture NADA Coordinator—CVM accepted as complete from Phibro Animal Health GFI #159 for all finfish (September 20, 2006); from AADAP GFI #152 for all freshwater-reared salmonids (March 15, 2007). PENAEID SHRIMP: CVM accepted as complete from University of Arizona—GFI #159 (August 18, 2006).
- *Human Food Safety-Residue Chemistry*—FINFISH: Previously accepted by CVM for certain label claims under original NADA from Pfizer, Inc. for OTC for cold water species above 9°C and warm water species above 16°C. Recently, CVM accepted (1) residue chemistry studies submitted by UMESC for use of OTC below the label claim limit of 9°C which established a withdrawal time of three days for juvenile salmonids, (2) residue depletion studies submitted by UMESC for the use of OTC in juvenile cool water species with a zero withdrawal time, (3) an HPLC method developed by UMESC to detect OTC in feed and fish tissue, (4) a study completed by UMESC bridging the HPLC OTC detection method to the official microbial assay method, (5) extrapolated withdrawal times for salmonids (May 17, 2002), (6) liquid chromatographic determination of OTC in edible tissues of six species of fish (September 9, 2002), and (7) validation of an HPLC method in coho salmon and northern pike (September 9, 2002). UMESC petitioned CVM to shorten the withdrawal time for OTC in all freshwater fish species based on its residue depletion data and the new tolerance of 2 ppm. PENAEID SHRIMP: Accepted as complete from University of Arizona residue depletion study in penaeid shrimp (November 4, 1999).
- *Human Food Safety Technical Section Complete*—Phibro submitted request for Technical Section Complete Letter based on UMESC data (July 2, 2007) and it was accepted February 6, 2008.
- *Target Animal Safety*—FINFISH: Previously accepted by CVM for catfish, salmonids, and lobsters under original NADA from Pfizer, Inc. CVM accepted as complete from UMESC the target animal safety technical section for coolwater and scaled warmwater fish (December 19, 2003). PENAEID SHRIMP: University of Arizona submitted to CVM a target animal safety study in penaeid shrimp (August 2004); a new study needs to be completed.
- *Effectiveness*—FINFISH: Previously accepted by CVM under original NADA from Pfizer, Inc. for OTC use on catfish, salmonids, and lobsters to control certain systemic bacterial diseases. CVM accepted as complete from AADAP the effectiveness technical section for the use of OTC at 3.75 g/100 lb of fish for 10 days as effective in reducing mortality from (1) columnaris disease in steelhead trout (November 14, 2000) to all freshwater-reared *Oncorhynchus mykiss* (July 25, 2007) and (2) coldwater disease in freshwater-reared salmonids (November 23, 2001). The effectiveness technical section developed by UMESC from a data call-in was accepted as supporting data for control of (1)

Aeromonas sp. in coolwater species, and (2) systemic columnaris disease in salmonids (February 1, 2000). PENAEID SHRIMP: Accepted as complete from University of Arizona effectiveness data to control mortality due to NHP in penaeid shrimp (June 28, 2000).

OXYTETRACYCLINE HYDROCHLORIDE (TERRAMYCIN-343®)—EXTERNAL ANTIBACTERIAL

Was an AFWA Project drug with current oversight by the DAWG for UMESC; under development by the sponsor (Pfizer Animal Health); one label claim in progress: control of mortality in coolwater and warmwater finfish due to external columnaris disease.

Progress on oxytetracycline hydrochloride ((May 15, 2008 to May 14, 2009):

- No progress to report.

Current status of technical sections on immersion OTC:

- *Product Chemistry*—Accepted by CVM.
- *Environmental Safety*—Accepted by CVM for marking by immersion from NRSP-7.
- *Human Food Safety-Toxicology*—Accepted by CVM.
- *Human Food Safety-Residue Chemistry*—Accepted for all fish by CVM for marking by immersion from NRSP-7.
- *Target Animal Safety*—Accepted for all fish by CVM for marking by immersion from NRSP-7.
- *Effectiveness*—On April 8, 2003, CVM responded to an October 28, 2002 submission from UMESC on the effectiveness of OTC immersion treatment of bacterial diseases in and on coolwater fish. CVM commented that OTC immersion may be effective against bacterial diseases in a variety of species and the effectiveness data may support future pivotal data. On September 14, 2007, CVM accepted from UMESC effectiveness data on oxytetracycline hydrochloride as being supportive for control of mortality in channel catfish due to external columnaris disease.

PET FISH THERAPEUTANTS—VARIOUS DRUGS AND PESTICIDES

Major effort to resolve non-food fish issues for these drugs through MUMS legislation.

POTASSIUM PERMANGANATE (CAIROX®)—EXTERNAL MICROBICIDE

Was an AFWA Project drug with current oversight by the DAWG for SNARC: Under development by the sponsor (Carus Chemical Company); **Original NADA under development: Control of mortality in (1) hybrid striped bass and channel catfish due to external columnaris disease associated with *Flavobacterium columnare* in ponds with no outflows**

Progress on potassium permanganate (May 15, 2008 to May 14, 2009):

- In December 2008, the National Aquaculture NADA Coordinator worked with Clear Springs Foods, AADAP, and Carus Chemical Company (sponsor of Cairox®) to determine what label claims for potassium permanganate can be supported for salmonids through cooperative efforts. She also prepared a revised Minor Use and Minor Species Annual Report to reflect those aspects.
- On April 2, 2009, the National Aquaculture NADA Coordinator sent to AADAP an analysis from the 2005 survey of AFWA Project supporters of the unmet label claim needs for potassium permanganate along with the contact information. This document should help AFWA determine whether to proceed with any efforts for drug approval for potassium permanganate.
- On May 14, 2009, Clear Springs Foods submitted to CVM a “white paper” entitled “Potassium permanganate: What is it and how can we ensure it is safely used in US aquaculture”. This white paper was prepared to provide an overview summarizing the various aspects of aquaculture uses, some of the research conducted to date, and some of the challenges associated with NADA efforts so that the aquaculture industry can explore with CVM the options for approval if in fact it is considered a drug by CVM and not a pesticide or disinfecting agent.

Current status of technical sections on potassium permanganate:

- *Product Chemistry*—The sponsor, Carus Chemical Company, submitted product chemistry technical section for all fish to CVM on December 8, 1998; CVM asked for additional data; the sponsor provided additional data (March 2002) and CVM is asking for clarification (April 2002).
- *Environmental Safety*—The sponsor submitted a request for a categorical exclusion from an EA for all fish to CVM on February 23, 1998; CVM is requiring an EA. Efforts at Arkansas State University began in January 2002 on environmental fate and effects studies with funding from the MSCG Program. The studies were completed in November 2005.
- *Human Food Safety–Toxicology*—Accepted by CVM.
- *Human Food Safety–Residue Chemistry*—CVM accepted as complete from SNARC.
- *Target Animal Safety*—Planned on channel catfish.
- *Effectiveness*—SNARC completed pivotal effectiveness studies that demonstrate effectiveness to prevent ichthyophthiriasis on channel catfish and tilapia. SNARC completed controlled effectiveness studies for control of ichthyophthiriasis on channel catfish and tilapia. SNARC prepared an effectiveness protocol for conducting effectiveness studies on external columnaris disease in channel catfish.

PRAZIQUANTEL—TREMATODE AND CESTODE CONTROL

Some interest on the part of potential sponsor in a NADA approval in the U.S. but needs positive marketing information and a completed mammalian safety technical section if considered for food finfish; has approval in several countries.

PYCEZE®--EXTERNAL MICROBICIDE

Sponsor submitted an INAD/NADA letter of intent and summary of all major technical sections; met with CVM on development of data; no current progress.

ROMET® 30 AND ROMET® TC—ORAL ANTIBACTERIAL

Romet-30® has approvals for control of enteric septicemia in catfish and furunculosis in salmonids; no current progress for extensions and expansions; sponsor resolved palatability for Romet-TC® (new label name for Type B medicated feed; previously called Romet-B®).

Current status of technical sections on ROMET®:

- *Product Chemistry*—Accepted by CVM.
- *Environmental Safety*—Accepted by CVM.
- *Human Food Safety–Toxicology*—Accepted by CVM.
- *Human Food Safety–Residue Chemistry*—Accepted for catfish and salmonids by CVM.
- *Target Animal Safety*—Accepted for catfish and salmonids by CVM.
- *Effectiveness*—Accepted for control of enteric septicemia in catfish and furunculosis in salmonids by CVM; palatability problems resolved by sponsor.

SARAFLOXACIN—ORAL ANTIBACTERIAL

Previously, most of the NADA technical sections were submitted by Abbott Laboratories and accepted by CVM for control of enteric septicemia in catfish with sarafloxacin. However, the Centers for Disease Control and Prevention presented concerns about the use of all fluoroquinolones in animal health because of the perceived potential for developing pathogen resistance to drugs used in humans. It is doubtful that a new NADA on sarafloxacin or any fluoroquinolone will be allowed for aquaculture uses by CVM. Sarafloxacin was replaced by florfenicol as the oral antibacterial and model drug for crop grouping research in January 1998 by a unanimous vote of the AFWA Project stakeholders.

SEA LICE CONTROL—VARIOUS DRUGS AND PESTICIDES

Various drugs and pesticides (azamethiphos or Salmosan™, cypermethrin or Excis™) were previously pursued by the U.S. and Canada and none are currently active for approval. Uses of several drugs and

pesticides are being challenged on the East coast, particularly in Maine. An INAD for Slice™ (emamectin benzoate) was allowed by CVM as a result of great need for a control that could not be challenged to the extent that the others have been.

TRICHLORFON—EXTERNAL PARASITE CONTROL

Some interest on the part of potential sponsors in a NADA approval in the United States; has approvals in several countries. Several Special Local Need registrations were obtained in 1998 for control of predaceous insects.

ANESTHETICS AND SEDATIVES

- **CANDIDATE IMMEDIATE RELEASE AND ZERO WITHDRAWAL SEDATIVES FOR AQUATIC FOOD ANIMALS.** The DAWG held a series of conference calls (June 17, October 10, and 23, 2008) to discuss where the DAWG will go from here to select a candidate sedative, to determine the data requirements, and how to address the data requirements. The candidate sedatives were narrowed to two by the DAWG: benzocaine and eugenol. CVM revealed that the NCTR study on benzocaine showed no acute toxic effects related to methemoglobinemia. The DAWG determined that the remaining funds (\$202,577) from the Multi-State Conservation Grant on isoeugenol should be used as follows: (1) studies on immediate release (~\$22,577), (2) benzocaine: (a) genotoxicity battery, (b) residue chemistry studies and/or (c) develop determinative methods (~\$90,000), and (3) eugenol: (a) purchase radiolabeled eugenol, (b) residue chemistry studies and/or (c) develop determinative methods (~\$90,000).
 - At the request of AADAP, the DAWG and potential sponsors met with CVM to determine the data requirements for prospective candidate sedatives: benzocaine, eugenol, and tricaine on August 20, 2008.
 - On August 22, 2008, the National Aquaculture NADA Coordinator provided estimates of zero withdrawal sedative needs for the private aquaculture (finfish) industry to potential sponsors and the DAWG chair.
 - On February 17, 2009, the U.S. National Oceanographic and Atmospheric Administration (NOAA) Portland, Oregon, 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 pros and cons 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.
 - UMESC, in collaboration with Viterbo University, has initiated studies to determine the time required for fish to resume feeding behavior ("time to first feeding") following sedation by either benzocaine or eugenol. This study will provide the initial information needed to assess whether an "immediate release" claim for either benzocaine or eugenol will provide sufficient time between removals from the sedative bath to availability for human consumption to allow the tissue residues to deplete to a level safe for human consumption.
 - The University of Wisconsin-La Crosse, in collaboration with UMESC, has initiated a literature review to evaluate the effects of (1) handling stress, (2) electrofishing, and (3) angling or other capture methods on feeding behavior of fish, especially with regards to the likelihood of striking a lure or other bait. The literature review will be combined with the laboratory study evaluating the time to first feeding following sedation to further the assessment of a proposed immediate release sedative.

Activities related to either candidate sedative are presented below:**BENZOCAINE**

- During the week of February 2, 2009, ACD Pharmaceuticals AS (Ålesund, Norway) indicated that they are pursuing an approval under their INAD exemption for their benzocaine product, BENZOAK[®], for label claims to include sedation to handleable condition and sedation during transport for all freshwater finfish and saltwater-reared salmonids. ACD obtained MUMS designation for one label claim in June 2009).
- In June 2009, Frontier Scientific, Inc., (Logan, Utah) obtained MUMS designation for three label claims for its benzocaine product.
- In May 2009, AADAP tested BENZOAK[®] (ACD Pharmaceuticals, Norway) to identify parameters and use patterns for further study under the compassionate INAD protocol.

- **EUGENOL**

- On January 12, 2009, AQUI-S New Zealand obtained MUMS designation for eight label claims for its eugenol product (AQUI-S[®] E).
- On February 2, 2009, AADAP submitted to CVM all available study reports and data on eugenol generated by the National Toxicology Program.
- In May 2009, AADAP tested AQUI-S[®] E to identify parameters and use patterns for further study under the compassionate INAD protocol.
- UMESC will initiate a study to develop the analytical methods to detect and quantify eugenol in the edible fillet of freshwater fish in the summer of 2009. The analytical method is a critical component of all human food safety studies including the total residue depletion study and must be completed before a total residue depletion study may be initiated. UMESC will conduct a total residue depletion study using radiolabeled eugenol once the analytical method has been developed and after identifying funding to purchase the radiolabeled eugenol and to dispose of the radioactive wastes generated during the study.

ISOEUGENOL (AQUI-S[®])

[ALL ACTIVITIES ON ISOEUGENOL TERMINATED BY THE DAWG] Was an AFWA Project drug with oversight by the DAWG; was under development by the sponsor (AQUI-S New Zealand Ltd.); one label claim terminated: zero withdrawal anesthetic for sedation to (1) handleable condition in all freshwater finfish.

Progress on AQUI-S[®] (May 15, 2008 to May 14, 2009):

- The DAWG terminated any activities related to isoeugenol.

Current status of technical sections on AQUI-S[®] (**ALL ACTIVITIES TERMINATED**):

- *Product Chemistry*—The sponsor (AQUI-S New Zealand Ltd.) submitted studies on activity of AQUI-S[®] to CVM (October 2003).
- *Environmental Safety*—AQUI-S New Zealand Ltd. submitted a summary to CVM in the late 1990s and environmental biodegradation studies in freshwater and saltwater (November 24, 2003). The sponsor conducted a series of ecotoxicity and physico-chemical studies in 2004 to 2006.
- *Human Food Safety-Toxicology*—AQUI-S New Zealand Ltd. conducted a review of the mammalian safety literature to determine whether to continue with the original active ingredient in light of NTP studies to test for its potential carcinogenicity. A 90-day feeding study demonstrated no

carcinogenicity but NTP decided to proceed with a two-year study that was completed in Spring 2004; the final report was not available until April 2007. AQUI-S New Zealand Ltd. concluded that the active ingredient is safe and presented these conclusions to CVM on November 18, 1999 and decided to proceed with the drug approval in the U.S. for the original active ingredient based on their assessment of scientific data that the active ingredient is not a carcinogen. The sponsor submitted a series of NTP studies to CVM: Teratology study (November 1, 2004; accepted June 13, 2005) and continuous breeding study (November 26, 2004; accepted June 24, 2005). NTP 2-year carcinogenicity studies were reviewed in February 2008 and found to be clear evidence of carcinogenicity in male mouse livers causing all work to be terminated.

- *Human Food Safety-Residue Chemistry*—UMESC conducted a series of pilot studies to delineate the design of the total residue depletion study so that the exact amount of radiolabeled material needed for the study is known. UMESC submitted a pivotal total residue depletion study to CVM on March 14, 2006, received comments from CVM on August 23, 2006, and submitted a response on January 31, 2007.
- *Target Animal Safety*—Pivotal target animal safety studies on salmonids were started in March 2005 by AADAP. AQUI-S New Zealand Ltd. submitted to CVM target animal safety studies on Atlantic salmon completed in Canada (July 6, 2004) and CVM declared them as supportive (May 17, 2005); AADAP requested Technical Section complete for all freshwater salmonids (October 9, 2007).
- *Effectiveness*—AQUI-S New Zealand Ltd. submitted to CVM pivotal effectiveness studies on Atlantic salmon completed in Canada (July 6, 2004) and CVM declared them as supportive (May 17, 2005); Accepted from AADAP effectiveness for handleable for all freshwater-reared finfish (November 28, 2006).

METOMIDATE (AQUACALM®)

One label claim for use as a sedative during transport of ornamental (non-food) finfish underway in U.S.; currently, work on a label claim for food fish is being carried out in other countries; Aquatic Life Sciences, Inc. plans on doing further work on food fish.

TRICAINE METHANESULFONATE (FINQUEL®, TRICAINE-S®)

Has 21-day withdrawal time.

SPAWNING AND GENDER MANIPULATION AIDS

CRUDE CARP PITUITARY (CCP)

Interested parties proceeding toward NADA approval but sponsor, Stoller Fisheries, has decided not to pursue a response to CVM request for a revision of its product chemistry technical section.

Progress on CCP (May 15, 2008 to May 14, 2009):

1. No progress to report.

Current status of technical sections on CCP:

- *Product Chemistry*—The sponsor submitted the product chemistry technical section for CCP to CVM on September 21, 1999. The sponsor received a response on November 22, 1999 from CVM that asked for more information. The sponsor has decided not to pursue a response.
- *Environmental Safety*—Accepted by CVM.
- *Human Food Safety-Toxicology*—Accepted by CVM.
- *Human Food Safety-Residue Chemistry*—Accepted by CVM.
- *Target Animal Safety*—A literature review on target animal safety of CCP was completed, presented on August 5, 1998 in Bozeman, Montana, and submitted to CVM in summer 1999 by the Southeastern region of NRSP-7. On October 12, 2004, Southern Illinois University submitted the final report for the target animal safety study to NRSP-7 and this report was submitted to CVM.

- *Effectiveness*—Accepted as complete from NRSP-7 by CVM as a spawning aid in freshwater-reared female finfish (July 17, 2002). CVM has requested additional information.

HUMAN CHORIONIC GONADOTROPIN (CHORULON®)

Human chorionic gonadotropin was approved on September 7, 1999 by CVM as a spawning aid by intramuscular injection for all fish and requires a prescription under the direction of a veterinarian.

LUTEINIZING HORMONE-RELEASING HORMONE ANALOG (LHRHA)

Auburn University gained an INAD for LHRHa in spring 2003; early development stage.

17 α -METHYLTESTOSTERONE (MASCULINIZING FEED FOR TILAPIA®)—GENDER MANIPULATION AID

One initial label claim in progress: (1) masculinization of female early life-stage tilapia.

Progress on MT (May 15, 2008 to May 14, 2009):

- On June 13, 2008, NCRAC informed the National Aquaculture NADA Coordinator that the WRAC had agreed to help fund along with NCRAC the repeat of the target animal safety study in tilapia and the feed method transfer study.
- On September 30, 2008, the National Aquaculture NADA Coordinator completed the full proposal for the repeat of the target animal safety study in tilapia and the feed method transfer study and submitted it to NCRAC and WRAC for review. The proposal was finalized on May 5, 2009.

Current status of technical sections on MT:

- *Product Chemistry*—The sponsor, Rangen, Inc., submitted a product chemistry technical section on 17 α -methyltestosterone to CVM on November 8, 2000. CVM is requiring more information, stability studies, and an analytical method with greater recoveries. UW-M was selected as the contractor to complete these requirements and completed the laboratory phase of the studies in fall 2006. CVM accepted the analytical method to detect MT in feed (December 2, 2005). Rangen, Inc. submitted feed studies to CVM (April 8, 2008).
- *Environmental Safety*—Auburn University received a response from CVM on November 8, 1999 regarding the revised EA for MT that requested additional information, a biodegradation study, and a more sensitive method to detect MT in water. On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17 α -methyltestosterone that were conducted and developed by the UW-M. CVM accepted the water method and requested additional information on the environmental safety studies (March 31, 2008). Auburn University is in the process of writing the EA.
- *Human Food Safety-Toxicology*—Accepted by CVM.
- *Human Food Safety-Residue Chemistry*—Accepted by CVM.
- *Target Animal Safety*—Cornell University submitted to CVM an animal safety study on tilapia; CVM found a target animal safety study on percids by SIUC to be inadequate; literature review on other species completed and submitted by Auburn University. CVM recently determined that a target animal safety study on tilapia was needed and NCRAC has agreed to fund this study; SIUC was selected to perform the target animal safety study on tilapia. The study was rejected (August 17, 2007) and the study needs to be repeated.
- *Effectiveness*—Cornell University submitted to CVM a final report on the effectiveness of MT to tilapia; Auburn University is coordinating a compassionate INAD on tilapia and completed and submitted the final report to CVM in December 2003; AADAP requested a Technical Section complete for tilapia (November 5, 2007).

SALMON GONADOTROPIN RELEASING HORMONE ANALOG (OVAPLANT®)—SPAWNING AID

Aquatic Life Sciences, Inc. is in the early development stages with the University of Florida performing the efficacy studies. One label claim under investigation: For the induction of spawning in ornamental fish.

**SALMON GONADOTROPIN RELEASING HORMONE ANALOG AND DOMPERIDONE (OVAPRIM®)—
SPAWNING AID.**

Aquatic Life Sciences, Inc. is in the early development stages with the University of Florida performing the efficacy studies. One initial label claim in progress: (1) Spawning aid for ornamental and aquarium fish.

- On March 19, 2009, Western Chemical, Inc. (Ferndale, Washington) received Indexing for Salmon Gonadotropin Releasing Hormone analog and Domperidone (Ovaprim®) for use as a spawning aid in ornamental fish.

CHEMICAL MARKING AGENTS

CALCEIN (SE-MARK®)

Aquatic Life Sciences, Inc. is in the early development stages with AADAP as chemical marking aid.

**OXYTETRACYCLINE HYDROCHLORIDE (OXYMARINE®, OXYTETRACYCLINE HCL SOLUBLE
POWDER-343®, TERRAMYCIN 343®, TETROXY AQUATIC®)**

Marking aid by immersion approved for all fish with four NADA sponsors.

STRONTIUM CHLORIDE

Western Chemical Inc. is the sponsor; some work completed in Alaska; some effectiveness studies underway under Western NRSP-7.

PISCICIDES (ROTENONE AND ANTIMYCIN)

These products are used by hatcheries in resource agencies and private aquaculture facilities to help control diseases in cultured fish by removing undesirable fish in ponds and to help in the effective product of cultured fish.

- The National Aquaculture NADA Coordinator, as Chair of the AFS Task Force on Fishery Chemicals, and the Fish Management Chemicals Subcommittee (FMCS) attended a meeting on August 13, 2008 to resolve remaining issues regarding the labeling and the Rotenone SOP) Manual required by EPA to complete the reregistration of rotenone.
- On October 27-30, 2008, the FMCS met in Reno, Nevada to start drafting the Rotenone SOP Manual using FWS funding.
- The National Aquaculture NADA Coordinator completed Section 1.0 on December 28, 2008 and Section 1.2 to 1.4 on March 13, 2009 of the Rotenone SOP Manual.

PUBLIC INFORMATION AND MEETINGS

- **MUMS DESIGNATIONS.** The designation provision of the MUMS Act of 2004 gives sponsors seven years of marketing exclusivity. As of May 14, 2009, the MUMS Office has granted 64 designations, 55 of those are to aquaculture drug sponsors, many of whom have received extensive help from the National Aquaculture NADA Coordinator.
- **FORMATION OF A NEW GROUP.** Because of the potential concern that the Joint Subcommittee on Aquaculture Working Group on Aquaculture Drugs, Biologics, and Pesticides may be acting as a Federal Advisory Committee, an informal meeting was convened on February 9, 2008 to solicit input from non-federal stakeholders on future roles and direction. The new group was tentatively named the National Aquaculture Industry Therapeutic Agent Program (NAI-TAP) and was to be a coalition of aquaculture industry stakeholders and invited non-industry entities who would have addressed and

supported the development, approval, availability, and optimal use of drug, biologic, nutritional, and other products that affect the health and production of aquatic animals. However, because of the lack of private aquaculture industry representation on the working group, it became the Working Group on Aquaculture Drugs, Chemicals, and Biologics under the American Fisheries Society Fish Culture Section.

- **14th ANNUAL DRUG APPROVAL COORDINATION WORKSHOP.** The 14th Annual Drug Approval Coordination Workshop was held in Bozeman, Montana on July 29-31, 2008. The topics included celebration of approval for Terramycin® 200 for Fish, approval status of all aquaculture drugs, and resolution of the dilemma concerning a sedative for aquaculture and fish management needs. On August 1, 2008, a meeting of the National Aquaculture Drug Research Forum and the organizational meeting of the National Aquaculture Industry Therapeutic Agent Program occurred.
- **DAWG MEETING.** The DAWG met on September 8-9, 2008 to discuss the approval status of the AFWA Project drugs and to formulate plans to identify an alternative sedative.

PUBLICATIONS, MANUSCRIPTS, PAPERS PRESENTED, AND SPECIAL REPORTS

PUBLICATIONS

Schnick, R.A. 2008. News: Fisheries: Aquaculture drug approval for Terramycin® for Fish. Fisheries 33(7):317.

PAPERS PRESENTED

Schnick, R.A. 2008. Partnerships: The key to AFWA Project successes. 14th Annual Drug Approval Coordination Workshop, Bozeman, Montana, July 29-31, 2008.

Schnick, R.A. 2008. Zero withdrawal sedative dilemma and solutions. 14th Annual Drug Approval Coordination Workshop, Bozeman, Montana, July 29-31, 2008.

Schnick, R.A. 2008. Aquaculture drug approvals: Successes and challenges. US Trout Farmers Association Annual Meeting, Milwaukee, Wisconsin, September 19, 2008.

Schnick, R.A. 2008. It's been a wonderful life. Onalaska Rotary Club, Onalaska, Wisconsin, December 10, 2008.

Schnick, R.A. 2009. Aquaculture drug approvals: Successes and challenges. NRSP-7 Spring Meeting, Washington, DC, January 26, 2009.

Schnick, R.A. 2009. Introduction and brief overall progress toward aquaculture drug approvals, Part I. Aquaculture Drug Approval Successes, Aquaculture America 2009, Seattle, Washington, February 18, 2009.

Schnick, R.A. 2009. Overall progress toward aquaculture drug approvals, Part II. Aquaculture Drug Approval Successes, Aquaculture America 2009, Seattle, Washington, February 18, 2009.

Schnick, R.A. 2009. Update on product approvals for fish health. Striped Bass Growers Association, Aquaculture America 2009, Seattle, Washington, February 18, 2009.

Schnick, R.A. 2009. Aquaculture drugs—Status report. North Central Regional Aquaculture Center Board of Directors and 2009 Program Planning Meeting, Kansas City, Missouri, February 28, 2009.

SPECIAL REPORTS

- Schnick, R.A. 2008. Notes on the National Aquaculture Industry Therapeutic Agent Program (NAI-TAP) teleconference call of April 24, 2008. Submitted to NAI-TAP members, May 2, 2008. 3 pp.
- Schnick, R.A. 2008. National Aquaculture Industry Therapeutic Agent Program (NAI-TAP), Operating Guidelines. Submitted to NAI-TAP members, May 2, 2008. 3 pp.
- Schnick, R.A. 2008. Human food safety data requirements for candidate zero withdrawal sedatives and the respective costs associated with the studies (updated May 9, 2008). Submitted to DAWG, May 9, 2008. 1 pp.
- Schnick, R.A. 2008. Thirteenth annual report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2007 to May 14, 2008). Submitted to Ted Batterson, NCRAC for distribution. May 19, 2008. 33 pp.
- Schnick, R.A. 2008. Roz's Corner: AADAP newsletter contribution. Submitted to AADAP, June 25, 2008. 2 pp.
- Schnick, R.A. 2008. Human food safety status of candidate sedatives based on March 19, 2008 informal conference call with CVM's Division of Human Food Safety. Submitted to DAWG, July 2, 2008. 7 pp.
- Schnick, R.A. and B.J. Finlayson. 2008. Task Force on Fishery Chemicals annual report to the AFS Governing Board, August 2008. Submitted to the AFS Executive Director, July 21, 2008. 4 pp.
- Schnick, R.A. 2008. Second quarter 2008 quarterly report for Multistate Conservation Grant Number DC M-48-R-1 (AQUI-S®). Submitted to AFWA, July 22, 2008. 6 pp.
- Schnick, R.A. 2008. National Aquaculture Industry – Therapeutic Agent Program (NAI-TAP) Organizational Meeting. Submitted to NAI-TAP members. August 7, 2008. 2 pp.
- Schnick, R.A. 2008. Estimates of zero withdrawal sedative needs in the private aquaculture (finfish) industry (August 2008). Submitted to potential sponsors and DAWG members. August 22, 2008. 3 pp.
- Schnick, R.A. 2008. Approvals and final submissions projected for AFWA Project drugs (August 27, 2008). Submitted to DAWG members. August 27, 2008. 2 pp.
- Schnick, R.A. 2008. AFWA Project drugs: Remaining requirements and progress March 2008 to September 2008 (as of September 6, 2008). Submitted to DAWG members. September 6, 2008. 16 pp.
- Schnick, R.A. 2008. Drug approval research on 17 α -methyltestosterone. Submitted to North Central Regional Aquaculture Center and the Western Regional Aquaculture Center for peer review, September 30, 2008. 21 pp.
- Schnick, R.A. 2008. Roz's Corner: AADAP newsletter contribution. Submitted to AADAP, October 21, 2008. 4 pp.
- Schnick, R.A. 2008. Status of the National Coordinator for Aquaculture New Animal Drug Applications. Submitted to Ted Batterson, North Central Regional Aquaculture Center, October 21, 2008. 1 pp.
- Schnick, R.A. 2008. (DRAFT): Third quarter 2008 quarterly report for Multistate Conservation Grant Number DC M-48-R-1 (AQUI-S®). Submitted to Steve Sharon who prepared the final report, October 22, 2008. 5 pp.

- Schnick, R.A. 2008. North Central Regional Aquaculture Center annual report for National Coordinator for Aquaculture New Animal Drug Applications. Submitted to Ted Batterson, North Central Regional Aquaculture Center, October 31, 2008. 12 pp.
- Schnick, R.A. 2008. Highlights of Fourteenth Mid-Year Report for the National Coordinator for Aquaculture New Animal Drug Applications (National Aquaculture NADA Coordinator). Provided to potential funding sources, December 26, 2008. 5 pp.
- Schnick, R.A. 2008. Section 1.0, Rotenone SOP Manual. Submitted to Chair, Fish Management Chemicals Subcommittee, December 28, 2008. 5 pp.
- Schnick, R.A. and B.J. Finlayson. 2009. Task Force on Fishery Chemicals mid-year report to the AFS Governing Board, February 2009. Submitted to the AFS Executive Director, February 11, 2009. 4 pp.
- Schnick, R.A. 2009. Roz's Corner: AADAP newsletter contribution. Submitted to AADAP, February 12, 2009. 2 pp.
- Schnick, R.A. 2009. AFWA Project drugs: Remaining requirements and progress September 2008 to February 2009 (as of February 14, 2009). Submitted to DAWG Chair. February 14, 2009. 9 pp.
- Schnick, R.A. 2009. AFS Working Group on Aquaculture Chemicals Meeting, February 15, 2009 (notes). Submitted to Chair of Working Group on Aquaculture Chemicals, February 26, 2009. 5 pp.
- Schnick, R.A. 2009. Estimates of zero withdrawal sedative needs in the private aquaculture (finfish) industry (updated March 2009). Submitted to potential sponsors. March 12, 2009. 3 pp.
- Schnick, R.A. 2009. Section 1.2 to 1.4, Rotenone SOP Manual. Submitted to Chair, Fish Management Chemicals Subcommittee, March 13, 2009. 4 pp.
- Schnick, R.A. 2009. Potassium permanganate unmet label claim needs. Submitted to AADAP, April 2, 2009. 1 pp.
- Schnick, R.A. 2009. Original, supplemental, abbreviated and conditional aquaculture NADA approvals; Index of Legally Marketed Unapproved New Animal Drugs For Minor Species, from 1995 to April 2009 and anticipated either through 2010 or 2011+. Submitted to CVM, April 13, 2009. 5 pp.
- Schnick, R.A. 2009. Transition from the position of the National Coordinator for Aquaculture New Animal Drug Applications. Submitted to Ted Batterson, North Central Regional Aquaculture Center, April 24, 2009. 5 pp.
- Schnick, R.A. 2009. Drug approval research on 17 α -methyltestosterone (final). Submitted to North Central Regional Aquaculture Center and the Western Regional Aquaculture Center, May 5, 2009. 22 pp.