NATIONAL COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS (NADAs)

Facilitator: Ted R. Batterson

Funding Request: $25,000

Duration: 1 Year (May 15, 2008 - May 14, 2009)

Tasks:

1. Serve as an information conduit between Investigational New Animal Drug/New Animal Drug Applications (INAD/NADA) applicants and the U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM);

2. Identify and encourage prospective INAD participants to become involved in specific investigational studies and NADA approval-related research;

3. 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;

4. Guide prospective and current INAD holders on the format for INAD exemption requests and related submissions to CVM;

5. Identify existing data and remaining data requirements for NADA approvals;

6. Review, record, and provide information on the status of INADs and NADAs;

7. Provide liaison and coordination among all the federal agencies involved in the INAD/NADA process; and

8. Provide public education related to training and guidance in obtaining INAD exemptions and pursuing NADA approval.

Proposed Budget:

Institution	Facilitator	Tasks	Year 1	Total
Michigan State University	Ted R. Batterson	1-8	$25,000	$25,000
		Totals	**$25,000**	**$25,000**

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BACKGROUND AND JUSTIFICATION

The Joint Subcommittee on Aquaculture (JSA) recognized in the 1990s that investigation and approval of safe therapeutants for use by the aquaculture industry to help manage diseases was one of the highest priorities currently facing the industry. At that time, only a few approved compounds were available to the industry and further development of the aquaculture industry is severely constrained by a lack of approved drugs essential for treating over 50 known aquaculture diseases. The U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM) has afforded the aquaculture industry throughout the U.S. with a "window of opportunity" to seek approval of drugs to be used legally in their production practices. The need for additional drugs is great, but securing data necessary to satisfy the requirements of CVM for drug approval is time consuming, costly, and procedures are rigorous. The INAD/NADA process is the one method that allows the industry to provide CVM with data on efficacy and also aids producers in their production practices.

The JSA's Working Group on Quality Assurance in Aquaculture Production previously identified the need for a National Coordinator for Aquaculture INADs. This position was supported through Cooperative Agreement No. 92-COOP-1-8021 with funds from U.S. Department of Agriculture's Cooperative State Research, Education, and Extension Service (USDA/CSREES) beginning September 1, 1992. Dr. Robert Ringer, Professor Emeritus of Michigan State University, was hired on a part-time basis (0.14 FTE) to serve as the INAD Coordinator. Dr. Ringer continued as the INAD Coordinator for a second year, September 1, 1993 - August 31, 1994, working on a part-time basis (0.14 FTE). Funds to support his second year's activities were provided by CSREES and CVM through the Cooperative Agreement. The North Central Regional Aquaculture Center (NCRAC) also provided support for his activities.

During Dr. Ringer's second year, the JSA's Working Group on Quality Assurance in Aquaculture Production identified the need for a National Coordinator for Aquaculture NADAs to build upon those activities undertaken and developed by the National INAD Coordinator, continuing to develop a collaborative working relationship between the private aquacultural sector and various federal agencies, particularly the CVM, the U.S. Department of Interior's (USDI) Fish and Wildlife Service (USFWS), and the USDI's Geological Survey's (USGS) Biological Resources Discipline (formerly the National Biological Service). The National Coordinator serves as a conduit between an INAD/NADA applicant and CVM. The National Coordinator for Aquaculture NADAs helps to alleviate time demands on CVM staff, thus allowing more time to process a greater number of applications as well as increasing the breadth of research endeavors within the industry. The grouping of INAD applicants should help to alleviate redundancy, amalgamate efforts, and increase the amount of efficacy data, all of which should result in greater progress toward developing available, approved therapeutic and production drugs.

On May 15, 1995, Ms. Rosalie (Roz) Schnick, recently retired Registration Officer from the USGS National Biological Service's Upper Mississippi Science Center (now the Biological Resources Discipline's Upper Midwest Environmental Science Center = UMESC), was hired on a three-quarter time basis as the National Coordinator for Aquaculture NADAs. Funds to support her position came from 15 different public and private sector sources. Because of her performance and success as the National Coordinator for Aquaculture NADAs, additional monies became available and on May 15, 1996, her position was increased to a full-time basis through Year 6 (May 15, 2000 to May 14, 2001). Given carry-over of private funds from previous years and the amount of funds that were pledged for 2001-2002, Schnick's position was reduced to a three-quarter time level for Year 7: May 15, 2001 to May 14, 2002. For Year 8 (May 15, 2002 to May 14, 2003) carry-over and pledged funds allowed the position to return to full-time. For Year 9 (May 15, 2003 to May 14, 2004) carry-over and pledged funds required that the position be reduced to three-quarter time as of October 1, 2003. For Years 10-13 (May 15, 2004 to May 14, 2005, May 15, 2005 to May 14, 2006, May 15, 2006 to May 14, 2007, and May 15, 2007 to May 14, 2008) carry-over and pledged funds enabled the position to increase to 87.5% time. For Year 14 (May 15, 2008 to May 14, 2009) carry-over and pledged funds (see Table 1) will enable to position to continue at 87.5% time.

COORDINATION

The National Coordinator for Aquaculture NADAs has been based at Michigan State University under the aegis of NCRAC. The Coordinator has worked closely and collaboratively with the following: USDA/CSREES; Regional Aquaculture Center (RAC) Program; CVM; JSA's Working Group on Aquaculture Drugs, Biologics, and Pesticides (formerly known as the Working Group on Quality Assurance in Aquaculture Production); NRSP-7 (formerly IR-4) Minor Use Animal Drug Program; UMESC; USDA's Agricultural Research Service National Aquaculture Research Center at Stuttgart, Arkansas; other aquaculture industry representatives; pharmaceutical/chemical companies involved with aquaculture; Cooperative Extension Services, Sea Grant Marine Advisory Services and RAC Extension programs; other aquaculture coordinators, state, regional and national. An Advisory Committee has been formed to evaluate this position.

TASKS

Tasks for the National Coordinator are as follows.

1. Serve as an information conduit between Investigational New Animal Drug/New Animal Drug Applications (INAD/NADA) applicants and the U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM);

2. Identify and encourage prospective INAD participants to become involved in specific investigational studies and NADA approval-related research;

3. 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;

4. Guide prospective and current INAD holders on the format for INAD exemption requests and related submissions to CVM;

5. Identify existing data and remaining data requirements for NADA approvals;

6. Review, record, and provide information on the status of INADs and NADAs;

7. Provide liaison and coordination among all the federal agencies involved in the INAD/NADA process; and

8. Provide public education related to training and guidance in obtaining INAD exemptions and pursuing NADA approval.

FUNDS TO SUPPORT THE NATIONAL COORDINATOR

The funds to support the National Coordinator for Aquaculture NADA's position have come from a variety of public and private sources. During 2008-2009 a number of government agencies, private associations, and other organizations have pledged over $127,000 for the NADA Coordinator's position. Those sources of funds are presented in Table 1.

Table 1. Funds pledged for support of the National Coordinator for Aquaculture NADAs for 2008-2009.

Source	2008-09 Amount
CVM[1, 2]	$50,000
USDI/USGS[1, 2]	$5,000
North Central Regional Aquaculture Center	$25,000
Akzo Nobel/Eka Chemicals, Inc.	$7,500
Alabama Catfish Producers	$3,000
American Veterinary Medical Association	$10,000
AQUI-S® Ltd.	$6,000
Axcentive	$8,500
Fish Culture Section of AFS	$500
Fish Health Section of AFS	$1,000
Florida Tropical Fish Farms Association, Inc.	$1,500
Idaho Aquaculture Association	$200
Kent SeaTech Corporation	$500
National Aquaculture Association	$2,000
Phibro Animal Health Corporation	$2,000
Schering-Plough Animal Health Corporation	$5,000
Striped Bass and Hybrid Producers Association	$2,000
Syndel Lab., Ltd./Aquatic Life Sciences	$5,000
U.S. Trout Farmers Association	$2,000
Western Chemical, Inc.	$2,500
TOTAL	$139,200

[1]Funds to be provided through Cooperative Agreement between CSREES and Michigan State University

[2]The amount that will be received less USDA's 10% administrative fee for an interagency transfer

The Board of Directors of NCRAC, based on input from the Center's Industry Advisory Council, indicated at various Annual Program Planning Meetings (2003 through 2008) that funds should be made available for activities that would lead to aquaculture drug approvals. The top priority drugs as identified by NCRAC were 17α-Methyltestosterone (MT) and AQUI-S®. These drugs had been identified in various NCRAC white papers (e.g., Tilapia, Salmonids) as being critical for the aquaculture industry in the 12-state North Central Region. Therefore, not only did the NCRAC Board approve funds for projects on both of those drugs, they also approved funds to support the National Coordinator for Aquaculture NADAs for coordinating and supervising the research efforts on those drug projects as well as for gaining approval of other drugs critical to the industry.

WORK PLANNED

The National NADA Coordinator will continue to coordinate efforts to obtain approvals for high priority aquaculture drugs through interactions with the JSA's Working Group on Aquaculture Drugs, Biologics and Pesticides, and all the various potential sponsors.

BUDGET

The budget that has been established for the fourteenth 12-month period (May 15, 2008 - May 14, 2009) for the National Coordinator for Aquaculture NADAs are presented in Table 2 below.

Table 2. Proposed fourteenth year budget for the National Coordinator for Aquaculture NADAs: May 15, 2008 - May 14, 2009.

Salary (0.875 FTE)	$83,659
Fringe Benefits	$25,090
Total Salary and Fringe Benefits	$108,749
Nonexpendable Equipment	$0
Materials and Supplies	$5,000
Travel	$8,000
TOTAL COSTS	$121,749

This request is for $25,000 for the partial support of the costs for the National Coordinator for Aquaculture NADAs during her fourteenth year. Completed CSREES-2004 budget forms for each of those years are presented on the next two pages. On page 8 is an explanation for the various components of the proposed budget. Along with the pledges from public and private sources as indicated in Table 1, this request, and carryover of funds from previous years there are sufficient funds available for the above budget.

OMB Approved 0524-0039
Expires 03/31/2004

BUDGET

ORGANIZATION AND ADDRESS
North Central Regional Aquaculture Center
Michigan State University
East Lansing, MI 48824-1222

PROJECT DIRECTOR(S)
Ted R. Batterson

USDA AWARD NO. Year 1: Tasks 1-8

	CSREES FUNDED WORK MONTHS			Duration Proposed Months: 12 **Funds Requested by Proposer**	Duration Proposed Months: ____ **Funds Approved by CSREES** (If different)	Non-Federal Proposed Cost-Sharing/ Matching Funds (If required)	Non-federal Cost-Sharing/ Matching Funds Approved by CSREES (If Different)
A. Salaries and Wages	Calendar	Academic	Summer				
1. No. of Senior Personnel							
a. ___ (Co)-PD(s)	2.5			$17,108			
2. No. of Other Personnel (Non-Faculty)							
a. ___ Research Associates-Postdoctorates . . .							
b. ___ Other Professionals							
c. ___ Paraprofessionals							
d. ___ Graduate Students							
e. ___ Prebaccalaureate Students							
f. ___ Secretarial-Clerical							
g. ___ Technical, Shop and Other							
Total Salaries and Wages →				$17,108	$0	$0	$0
B. Fringe Benefits (If charged as Direct Costs)				$5,423			
C. Total Salaries, Wages, and Fringe Benefits (A plus B) →				$22,531	0	$0	$0
D. Nonexpendable Equipment (Attach supporting data. List items and dollar amounts for each item.)							
E. Materials and Supplies				$ 469			
F. Travel				$2,000			
G. Publication Costs/Page Charges							
H. Computer (ADPE) Costs							
I. Student Assistance/Support (Scholarships/fellowships, stipends/tuition, cost of education, etc. Attach list of items and dollar amounts for each item.)							
J. All Other Direct Costs (In budget narrative, list items and dollar amounts and provide supporting data for each item.)							
K. Total Direct Costs (C through I) →				$25,000	0	$0	$0
L. F&A/Indirect Costs. (If applicable, specify rate(s) and base(s) for on/off campus activity. Where both are involved, identify itemized costs in on/off campus bases.)							
M. Total Direct and F&A/Indirect Costs (J plus K) →				$25,000	0	$0	$0
N. Other →							

O. Total Amount of This Request ..... →	$25,000	0	$0	$0

P. Carryover -- (If Applicable) . . . . . **Federal Funds: $** **Non-Federal funds: $** **Total $**

Q. Cost Sharing/Matching (Breakdown of total amounts shown in line O)		
Cash (both Applicant and Third Party) ..... →		
Non-Cash Contributions (both Applicant and Third Party) ..... →		

NAME AND TITLE (Type or print)	**SIGNATURE** (required for revised budget only)	**DATE**
Project Director		
Authorized Organizational Representative		
Signature (for optional use)		

According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0524-0039. The time required to complete this information collection is estimated to average 1.00 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing the reviewing the collection of information.

Form CSREES-2004 (12/2000)

BUDGET EXPLANATION FOR MICHIGAN STATE UNIVERSITY

A. Salaries and Wages. This amount would provide 2.5 months of salary for the National Coordinator for Aquaculture NADAs at 0.875 FTE.

B. Fringe Benefits. The fringe benefit loading rate for FY 2008-09 is 31.7%.

E. Materials and Supplies. General office supplies including, paper, pens, toner, envelopes, file folders, etc.

F. Travel. Partial support for transportation, lodging, and meal expenses for two meetings with drug sponsors at locations to be determined.

SUMMARY OF ACCOMPLISHMENTS

The National Coordinator's annual report for her 13th year highlighting her accomplishments is contained in an Appendix to this proposal which follows.

NATIONAL COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS

THIRTEENTH ANNUAL REPORT OF ACTIVITIES

May 15, 2007 to May 14, 2008

Submitted by

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May 19, 2008

APPENDIX

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	17α-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
NHP	necrotizing hepatopancreatitus
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

THIRTEENTH ANNUAL SUMMARY OF ACTIVITY HIGHLIGHTS FOR THE NATIONAL COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS (NATIONAL AQUACULTURE NADA COORDINATOR) (May 15, 2007 to May 14, 2008)

MAY 15, 2007 TO MAY 14, 2008 APPROVALS!!

1. **ABBREVIATED NADA APPROVAL: FORMACIDE-B®** (FORMALIN) FOR CONTROL OF CERTAIN EXTERNAL PARASITES ON FINFISH AND SHRIMP AND FOR THE CONTROL OF CERTAIN FUNGI ON FINFISH EGGS (Approved July 17, 2007)
2. **SUPPLEMENTAL NADA APPROVAL: AQUAFLOR®** (FLORFENICOL) FOR CONTROL OF FURCUNCULOSIS ON FRESHWATER-REARED SALMONIDS (Approved October 26, 2007)

CHLORAMINE-T (HALAMID® AQUA+)—EXTERNAL ANTIBACTERIAL
Two initial label claims close to completion: (1) control of mortality due to (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye and possibly largemouth bass

1. On July 23, 2007, Axcentive SARL submitted to CVM a revised Guidance for Industry (GFI) document #159 on the safety of residues in human food for all fish for HALAMID® AQUA+ (chloramine-T).
2. On August 14, 2007, AADAP submitted pivotal effectiveness studies conducted by Rathbun Fish Culture Research Facility (Moravia, Iowa) on chloramine-T to CVM for control of mortality in walleye due to external columnaris disease.
3. On September 25 and November 21, 2007, AADAP submitted pivotal effectiveness studies conducted by Richloam Fish Hatchery (Florida) on chloramine-T to CVM for control of mortality in largemouth bass due to external columnaris disease.
4. On October 12, 2007, CVM accepted the EA on HALAMID® AQUA+ developed by UMESC.
5. On December 10, 2007, CVM accepted the GFI #159 on HALAMID® AQUA+ from Axcentive SARL if the sponsor accepts a withdrawal time of 11 days.
6. On February 8, 2008, Axcentive SARL submitted the Human Food Safety Technical Section Complete Letter on HALAMID® AQUA+ based on data generated by UMESC.
7. On February 13, 2008, Axcentive SARL submitted text for the Labeling on HALAMID® AQUA+ for the following: control of mortality due to (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye.
8. On March 3, 2008, CVM accepted from AADAP the Effectiveness Technical Section on chloramine-T as being complete for control of mortality in walleye due to external columnaris disease.
9. On May 19, 2008, Axcentive SARL submitted the complete Chemistry, Manufacturing, and Controls Technical Section on HALAMID® AQUA+ to CVM.

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

1. In June 2007, CVM commented on the copper sulfate final EA for earthen pond systems from SNARC and required additional revisions.
2. In December 2007, CVM accepted copper sulfate Human Food Safety Technical Section Complete Letter for channel catfish.
3. In January 2008, the sponsor, Phelps Dodge Sales Company, received comments from CVM on the draft Labeling and required revisions for TRIANGLE BRAND COPPER SULFATE®.

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

1. On January 11, 2007, CVM accepted as complete the GFI document #159 on the safety of erythromycin residues in human food for all freshwater-reared salmonids from the University of Idaho. A right to reference proprietary toxicological data is needed to complete the Human Food Safety Technical Section.
2. On October 23, 2007, CVM responded to the erythromycin EA submission from NRSP-7 by indicating that it needs significant revision.

FLORFENICOL (AQUAFLOR®)—ORAL ANTIBACTERIAL
Several label claims under development

1 On April 19, 2007, CVM accepted from AADAP as complete the Effectiveness Technical Section on AQUAFLOR® for control of mortality in freshwater-reared salmonids due to furunculosis.

2. On October 4, 2007, AADAP requested that CVM consider the Effectiveness Technical Section on AQUAFLOR® to be complete for control of mortality in hybrid striped bass due to *Streptococcus iniae*.
3. ON OCTOBER 26, 2007, CVM APPROVED AQUAFLOR® FOR A SUPPLEMENTAL APPROVAL FOR CONTROL OF MORTALITY IN FRESHWATER-REARED SALMONIDS DUE TO FURUNCULOSIS. AQUAFLOR® IS SPONSORED BY SCHERING-PLOUGH ANIMAL HEALTH.
4. On February 23, 2008, NCRAC announced that UMESC had received a contract to develop effectiveness data for the control of mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).
5. Because it is difficult to get feed mills to supply small amounts of AQUAFLOR®, the Wyoming Game and Fish Department established it own feed distributorship which allows the state agency to receive AQUAFLOR® medicated feed directly from the mill and then deliver it to the fish culture facilities under order of a veterinarian for a Veterinary Feed Directive.

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

1. ON JULY 17, 2007, AN ABBREVIATED NADA (GENERIC COPY OF PARASITE-S®, SPONSORED BY WESTERN CHEMICAL, INC.) WAS GRANTED BY CVM FOR FORMACIDE-B® (FORMALIN) FOR CONTROL OF CERTAIN EXTERNAL PARASITES ON FINFISH AND SHRIMP AND FOR THE CONTROL OF CERTAIN FUNGI ON FINFISH EGGS. FORMACIDE-B® IS SPONSORED BY B.L. MITCHELL, INC.
2. On December 19, 2007, CVM granted Minor Use and Minor Species (MUMS) designation to Western Chemical Inc. for their formalin product, PARASITE-S®, for the following label claim: For the control of mortality in freshwater-reared finfish due to saprolegniasis associated with fungi in the family Saprolegniaceae.

HYDROGEN PEROXIDE (35% PEROX-AID®)—EXTERNAL MICROBICIDE
One label claim in progress: Control of mortality in (1) all warmwater fish due to saprolegniasis and (2) all warmwater fish due to external columnaris disease

1. On April 20, 2007, Eka Chemicals, Inc. submitted a Special Supplement on minor changes to the labeling for 35% PEROX-AID® to be in compliance with the Department of Transportation requirements for shipments of hazardous material.
2. On October 15, 2007, CVM accepted the special supplement for minor changes in the 35% PEROX-AID® labeling.
3. On October 31, 2007, Eka Chemicals, Inc. submitted a Periodic Drug Experience Report—Six-Month Reporting (21 CFR 514.80) for Original NADA # 142-255 for 35% PEROX-AID®.
4. On November 7, 2007, AADAP submitted to CVM effectiveness studies on 35% PEROX-AID® conducted by Richloam Fish Hatchery (Florida) for the control of mortality in largemouth bass due to external columnaris disease.

ISOEUGENOL (AQUI-S®)—ANESTHETIC
[ALL ACTIVITIES ON HOLD] One initial label claim was in progress: (1) zero withdrawal anesthetic for sedation to handleable condition of all freshwater fish

1. The DAWG suspended funding for AQUI-S® following the initial NTP release in April 2007 that isoeugenol might be a carcinogen in male mouse livers. This action was taken by the DAWG and a Multi-State Conservation Grant (MSCG) from AFWA was suspended pending the final report on the results on February 28, 2008. AADAP and UMESC followed suite and suspended activities.
2. In spring 2007, AQUI-S New Zealand, LTD. submitted the Gibbs method used to detect isoeugenol in effectiveness and target animal safety studies to CVM.
3. On October 9, 2007, AADAP requested that CVM consider the Target Animal Safety Technical Section on isoeugenol to be complete for freshwater salmonids.
4. On January 15, 2008, CVM accepted the Gibbs Method to detect isoeugenol in water with conditions.
5. On February 28, 2008, the NTP peer review panel confirmed that there is clear evidence of isoeugenol carcinogenicity in male mouse livers and thus triggered the Delaney Clause, a 1958 amendment to the Food, Drugs, and Cosmetic Act (FDCA). This fact makes it very difficult if not impossible to gain a zero withdrawal period for isoeugenol.
6. In a March 19, 2008 conference call between UMESC, National Aquaculture NADA Coordinator, and CVM's Division of Human Food Safety, four potential candidates (benzocaine, eugenol, metomidate, and tricaine methanesulfonate) would require the development of at least some mammalian safety and residue chemistry studies to support a potential approval.
7. The DAWG met on March 26-28, 2008 to discuss the available options for, and limitations to, an isoeugenol approval and to formulate plans to identify an alternative sedative.

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

1. On July 27, 2007, CVM provided comments to 17α-methyltestosterone effectiveness studies on tilapia submitted by AADAP that more data are needed.
2. On July 30, 2007, interested parties met in Bozeman, Montana to discuss environmental safety issues on 17α-methyltestosterone and to determine a course of action.

3. On August 17, 2007, CVM indicated it could not accept the 17α-methyltestosterone target animal safety study on tilapia conducted at SIUC and that the study needed to be repeated.
4. On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17α-methyltestosterone that were conducted and developed by the University of Wisconsin-Madison (UW-M).
5. On November 5, 2007, AADAP submitted data and requested that CVM consider the Effectiveness Technical Section to be complete for the use of 17α-methyltestosterone to produce predominantly male populations of tilapia.
6. In December 2007, AADAP worked with the American Tilapia Association through a survey to develop baseline information relative to hatchery discharge in support of an EA for 17α-methyltestosterone.
7. On February 10, 2008, interested parties met in Orlando, Florida to discuss the remaining data requirements for the approval of 17α-methyltestosterone for tilapia, find solutions, and develop schedules for completion.
8. On February 23, 2008, the National Aquaculture NADA Coordinator requested $50,000 from NCRAC to fund a repeat of the target animal safety study on tilapia and a feed method transfer study on 17α-methyltestosterone. The NCRAC Board approved up to that amount to fund those two studies, but hoped that another RAC or some other entity would partially or fully fund those studies.
9. On March 31, 2008, CVM accepted the 17α-methyltestosterone method validation study in water but not the validation in sediment as developed by UW-M.
10. On March 31, 2008, CVM requested additional information from UW-M concerning the study report on the transformation of 17α-methyltestosterone in aquatic-sediment systems.
11. On April 8, 2008, Rangen, Inc. submitted to CVM the data on stability, homogeneity, and segregation of 17α-methyltestosterone feed based on studies by UW-M.
12. On April 21, 2008, NCRAC requested assistance from the Western Regional Aquaculture Center to help fund the repeat target animal safety study on tilapia and a feed method transfer study on 17α-methyltestosterone.

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

1. On July 2, 2007, Phibro Animal Health submitted to CVM a request for a Terramycin® 200 for Fish Human Food Safety Complete Letter for that Technical Section.
2. On July 23, 2007, Phibro Animal Health submitted to CVM a Labeling Technical Section on Terramycin® 200 for Fish to add the three new label claims and request the removal of the warning statement concerning use below 9 degrees C.
3. On July 25, 2007, CVM accepted the justification from AADAP for accepting the effectiveness studies on oxytetracycline dihydrate for freshwater-reared steelhead trout to be sufficient to satisfy the effectiveness requirements for all freshwater-reared *Oncorhynchus mykiss*.
4. On August 7, 2007, UMESC submitted additional information to CVM in the final amended EA on oxytetracycline dihydrate that CVM had requested in April 2007.
5. In December 2007, CVM requested a pivotal efficacy study from AADAP to complete the marking label claim for oxytetracycline dihydrate. This request was in response to an ADDAP request for an effectiveness complete letter for marking data submitted by AADAP.

6. On February 6, 2008, CVM accepted the Human Food Safety Technical Section for Terramycin® 200 for Fish from Phibro Animal Health as being complete for all freshwater-reared finfish based on data generated by UMESC.
7. On February 14, 2008, Phibro Animal Health submitted an All Other Information Technical Section for Terramycin® 200 for Fish to complete the final technical section submission for an Administrative NADA submission for the following: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in freshwater-reared salmonids**.**
8. On February 21, 2008, CVM accepted the Environmental Safety Technical Section for oxytetracycline dihydrate as being complete for all freshwater-reared finfish based on data generated by UMESC.
9. On February 23, 2008, NCRAC announced that UMESC had received a contract to develop effectiveness data for the control of mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).
10. 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.

OXYTETRACYCLINE HYDROCHLORIDE (TERRAMYCIN-343®)—EXTERNAL ANTIBACTERIAL
One label claim in progress: control of mortality in coolwater and warmwater finfish due to external columnaris disease

1. On June 7, 2007, CVM granted MUMS designations to Pfizer Animal Health, sponsor of Terramycin-343®, for the following label claims: For the control of mortality in freshwater-reared finfish fry and fingerlings due to (1) external columnaris disease associated with *Flavobacterium columnare*, (2) bacterial gill disease associated with *Flavobacterium branchiophilum*, and (3) systemic columnaris disease associated with *Flavobacterium columnare*.
2. 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.

SALMON GONADOTROPIN RELEASING HORMONE ANALOG (OVAPLANT®)—SPAWNING AID
One label claim under investigation: For the induction of spawning in ornamental fish

1. On July 25, 2007, CVM granted MUMS designation to Aquatic Life Sciences, Inc., the sponsor of Ovaprim®, for the induction of spawning in ornamental fish.

TRICAINE METHANESULFONATE (TRICAINE-S®)—ANETHETIC. One label claim under investigation: For the euthanasia of finfish not intended for food.

1. On January 4, 2008, CVM granted MUMS designation to Western Chemical Inc., the sponsor of Tricaine-S®, for the euthanasia of finfish not intended for food.

GENERAL

1. **CANADIAN VETERINARY DRUGS DIRECTORATE SEMINAR.** On July 18, 2007, the National Aquaculture NADA Coordinator gave an eight-hour seminar to the Veterinary Drugs Directorate (VDD) at its invitation. VDD is the Canadian equivalent of the U.S. Center for Veterinary Medicine (CVM). The VDD was interested in (1) the successful aquaculture drug approval processes in the U.S., (2) our

experience with various successful partnerships, and (3) insight into expediting the aquaculture drug approval processes in Canada.

2. **CVM SEMINAR.** On December 5, 2007, the National Aquaculture NADA Coordinator gave a two-hour seminar to CVM on the status and background of the aquaculture drug approvals, the roles, responsibilities, and accomplishments of the National Aquaculture NADA Coordinator, and coordination needs after her retirement.
3. **PRODUCER SESSION.** National Aquaculture NADA Coordinator convened a producer session at Aquaculture America 2008 on February 12, 2008.
4. **MUMS DESIGNATIONS.** The designation provision of the MUMS Act of 2004 gives sponsors seven years of marketing exclusivity. As of May 15, 2008, the MUMS Office has granted 53 designations, 46 of those are to aquaculture drug sponsors, many of whom have received extensive help from the National Aquaculture NADA Coordinator.
5. **MUMS INDEXING:** The final regulation for Indexing (i.e., legal marketing of unapproved drugs) was published December 6, 2007. This provision should allow companies to provide legally marketed drugs to our non-food fish industries (e.g., bait fish, ornamental fish). Companies began to submit requests on February 19, 2008.
6. **13th ANNUAL DRUG APPROVAL COORDINATION WORKSHOP.** The 13th Annual Drug Approval Coordination Workshop was co-hosted by AADAP and SNARC in Bozeman, Montana on July 31 to August 1, 2007. The topics included celebrations of approvals for 35% PEROX-AID® and AQUAFLOR® and approval status of all aquaculture drugs. On August 2, 2007, the National Aquaculture Drug Research Forum met and UMESC held a Partner Meeting.
7. **FORMATION OF A NEW INDUSTRY-DRIVEN 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 is tentatively named the National Aquaculture Industry Therapeutic Agent Program (NAI-TAP) and is a coalition of aquaculture industry stakeholders and invited non-industry entities who address and support the development, approval, availability, and optimal use of drug, biologic, nutritional, and other products that affect the health and production of aquatic animals.
8. **CANDIDATE ZERO WITHDRAWAL SEDATIVES FOR AQUATIC FOOD ANIMALS.** The National Aquaculture NADA Coordinator began working in February 2008 with CVM, AFWA's DAWG, any potential sponsors, involved researchers, and potential users to determine a course of action for a replacement candidate for a zero withdrawal sedative based on the peer review finding that the NTP study results for the male mouse carcinogenicity study on isoeugenol still stand, i.e., that there is clear evidence of carcinogenicity. The DAWG has also played a major role in these efforts (see details below).
9. **DAWG MEETINGS.** The DAWG met on September 17, 2007 and March 26-28, 2008 to discuss the approval status of the AFWA Project drugs and on March 26-28, 2008 to discuss available options for, and limitations to, an isoeugenol approval and to formulate plans to identify an alternative sedative.
10. **WEBSITE.** The National Aquaculture NADA Coordinator requested help from AquaNic to change her website address to http://aquanic.org/aquadrugs because USDA could no longer be involved because of the Federal Advisory Committee Act.

PUBLICATIONS, PRESENTATIONS, AND SPECIAL REPORTS

1. The National Coordinator for Aquaculture New Animal Drug Applications had two publications, presented 16 papers, and wrote 51 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, 2007 to May 14, 2008 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, 2007 to May 14, 2008):

1. No progress to report.

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); two initial label claims close to completion: (1) control of mortality due to (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye and possibly largemouth bass

Progress on chloramine-T (May 15, 2007 to May 14, 2008):

1. On July 23, 2007, Axcentive SARL submitted to CVM a revised GFI document #159 on the safety of residues in human food for all fish for HALAMID® AQUA+ (chloramine-T) prepared by the National Aquaculture NADA Coordinator with input from UMESC. The revision was based on the agency's comments.
2. On August 14, 2007, AADAP submitted pivotal effectiveness studies on HALAMID® AQUA+ (chloramine-T) conducted by the Iowa Department of Natural Resources Rathbun Fish Culture Research Station to CVM for control of mortality in walleye due to external columnaris disease.
3. On September 25 and November 21, 2007, AADAP submitted to CVM pivotal effectiveness studies on HALAMID® AQUA+ for control of mortality in largemouth bass due to external columnaris disease. These studies were conducted by Richloam Fish Hatchery (Florida Bass Conservation Center).
4. On October 12, 2007, CVM accepted the EA on HALAMID® AQUA+ developed by UMESC.
5. On December 10, 2007, CVM accepted the GFI #159 on HALAMID® AQUA+ from Axcentive SARL if the sponsor accepts a withdrawal time of 11 days in lieu of additional studies.
6. 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 a letter drafted by the National Aquaculture NADA Coordinator. Axcentive SARL accepted the concept of an 11-day withdrawal period in lieu of additional studies.
7. On February 13, 2008, Axcentive SARL submitted to CVM text for the Labeling on HALAMID® AQUA+ for the following: control of mortality due to (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye. The National Aquaculture NADA Coordinator helped develop the draft text for the Labeling.
8. On March 3, 2008, CVM accepted from AADAP the Effectiveness Technical Section on chloramine-T as being complete for control of mortality in walleye due to external columnaris disease (10-20 ppm for 60 minutes once daily on alternative or consecutive days for three treatments). This treatment is in addition to the accepted UMESC data that supports once daily on alternate days.
9. On May 12, 2008, the National Aquaculture NADA Coordinator wrote a draft MUMS report for HALAMID® AQUA+ and sent it to the sponsor of HALAMID® AQUA+, Axcentive SARL.
10. On May 19, 2008, Axcentive SARL submitted the complete Chemistry, Manufacturing, and Controls Technical Section on HALAMID® AQUA+ to CVM. The National Aquaculture NADA Coordinator helped develop the draft covering letter.

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. The sponsor submitted the complete Chemistry, Manufacturing, and Controls Technical Section on May 16, 2008.
- *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.
- *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 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.
- *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 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, 2007 to May 14, 2008):

1. In June 2007, CVM commented on the copper sulfate final EA for earthen pond systems from SNARC and required additional revisions.

1. In December 2007, CVM accepted Human Food Safety Technical Section Complete Letter for channel catfish on TRIANGLE BRAND COPPER SULFATE® from Phelps Dodge Sales Company. The technical section acceptance was based on SNARC data.

2. In January 2008, Phelps Dodge Sales Company received comments from CVM on the draft Labeling and required revisions for TRIANGLE BRAND COPPER SULFATE®. SNARC helped the sponsor with the labeling text.

3. In February 2008, the National Aquaculture NADA Coordinator provided a template to SNARC for the hazard characterization for GFI #152 so that the Human Food Safety Technical Section Complete Letter on TRIANGLE BRAND COPPER SULFATE® received in December 2007 could be expanded from channel catfish to all freshwater-reared 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 is requiring 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 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, 2007 to May 14, 2008)

1. On January 11, 2007, CVM accepted as complete the GFI document #159 on the safety of erythromycin residues in human food for all freshwater-reared salmonids from the University of Idaho (UID). A right to reference proprietary toxicological data is needed to complete the Human Food Safety Technical Section.
2. On October 23, 2007, CVM responded to the erythromycin EA submission from NRSP-7 by indicating that it needs significant revision. The National Aquaculture NADA Coordinator worked with the sponsor, Bimeda, Inc. and the University of Idaho on how to approach revising the EA based on comments from CVM received in October 2007.
3. On December 6, 2007, the National Aquaculture NADA Coordinator attended a meeting to discuss the progress on the AQUAMYCIN® Chemistry, Manufacturing, and Controls Technical Section at CVM with Bimeda, Inc. and the principal investigator from the University of Idaho.

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).
- *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.
- *Target Animal Safety*—Accepted by CVM from UID for salmonids.
- *Effectiveness*—Accepted by CVM from UID for bacterial kidney disease in salmonids.

FLORFENICOL (AQUAFLOR®)—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; several label claims under development.

Progress on florfenicol (May 15, 2007 to May 14, 2008):

1. On April 19, 2007, CVM accepted from AADAP as complete the Effectiveness Technical Section on AQUAFLOR® for control of mortality in freshwater-reared salmonids due to furunculosis.
2. On September 24, 2007, the National Aquaculture NADA Coordinator completed the Call for Statements of Interest for “Effectiveness research leading to approvals for controlling mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).” This document was sent out by NCRAC to solicit proposals for research from facilities throughout the United States.
3. On October 4, 2007, AADAP requested that CVM consider the effectiveness Technical section on AQUAFLOR® to be complete for control of mortality in hybrid striped bass due to *Streptococcus iniae*.
4. ON OCTOBER 26, 2007, CVM APPROVED AQUAFLOR® FOR A SUPPLEMENTAL APPROVAL FOR CONTROL OF MORTALITY IN FRESHWATER-REARED SALMONIDS DUE TO FURUNCULOSIS.
5. On February 23, 2008, NCRAC announced that UMESC had received a contract to develop effectiveness data for the control of mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).
6. Because it is difficult to get feed mills to supply small amounts of AQUAFLOR®, the Wyoming Game and Fish Department established it own feed distributorship which allows the state agency to receive AQUAFLOR® medicated feed directly from the mill and then deliver it to the fish culture facilities under order of a veterinarian for a Veterinary Feed Directive.

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 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, 2007 to May 14, 2008):

1. ON JULY 17, 2007, AN ABBREVIATED NADA (GENERIC COPY OF PARASITE-S®, SPONSORED BY WESTERN CHEMICAL, INC.) WAS GRANTED BY CVM FOR FORMACIDE-B® (FORMALIN) FOR CONTROL OF CERTAIN EXTERNAL PARASITES ON FINFISH AND SHRIMP AND FOR THE CONTROL OF CERTAIN FUNGI ON FINFISH EGGS. FORMACIDE-B® IS SPONSORED BY B.L. MITCHELL, INC.
2. The CVM Office of Research conducted formalin pivotal effectiveness studies on formalin for the control of mortality due to saprolegniasis on channel catfish and is in the process of writing up the final study report for submission to CVM.

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.); two additional label claims close to completion: control of mortality in (1) all finfish due to saprolegniasis and (2) warmwater finfish due to external columnaris disease.

Progress on hydrogen peroxide (May 15, 2007 to May 14, 2008):

1. On April 20, 2007, Eka Chemicals, Inc. submitted a Special Supplement on minor changes to the labeling for 35% PEROX-AID® to be in compliance with the Department of Transportation requirements for shipments of hazardous material.
2. On August 28-29, 2007, the National Aquaculture NADA Coordinator met with a private fish farm in Hawaii to discuss developing data to support a label claim for controlling certain external parasites with 35% PEROX-AID® (hydrogen peroxide) on a major fish species.
3. On October 15, 2007, CVM accepted the special supplement for minor changes in the 35% PEROX-AID® labeling.
4. On October 31, 2007, Eka Chemicals, Inc. submitted a Periodic Drug Experience Report—Six-Month Reporting (21 CFR 514.80) for Original NADA #142-255 for 35% PEROX-AID®. The National Aquaculture NADA Coordinator helped Eka Chemicals, Inc. on preparing the report.
5. On November 7, 2007, AADAP submitted to CVM effectiveness studies on 35% PEROX-AID® conducted by the Richloam State Fish Hatchery for the control of mortality in largemouth bass due to external columnaris disease.
6. The National Aquaculture NADA Coordinator worked on a funding proposal on 35% PEROX-AID® for external parasite label claims that was submitted in December 2007 but not funded.
7. The National Aquaculture NADA Coordinator worked with the sponsor, Eka Chemicals, Inc., on preparing the annual report for the activities on 35% PEROX-AID® associated with the MUMS designation submitted in February 2008.

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; 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 all 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, 2007 to May 14, 2008):

1. On July 2, 2007, Phibro Animal Health submitted to CVM a request for a TERRAMYCIN® 200 FOR FISH Human Food Safety Complete Letter for that Technical Section based on data generated by UMESC.
2. On July 23, 2007, Phibro Animal Health submitted to CVM a TERRAMYCIN® 200 FOR FISH Labeling Technical Section to add the three new label claims and request the removal of the warning statement concerning use below 9 degrees C.
3. On July 25, 2007, CVM accepted the justification from AADAP for accepting the effectiveness studies on TERRAMYCIN® 200 FOR FISH on freshwater-reared steelhead trout to be sufficient to satisfy the effectiveness requirements for all freshwater-reared *Oncorhynchus mykiss*.
4. On August 7, 2007, UMESC submitted additional information to CVM in the final amended EA on oxytetracycline dihydrate that CVM had requested in April 2007.
5. On September 24, 2007, the National Aquaculture NADA Coordinator completed the Call for Statements of Interest for “Effectiveness research leading to approvals for controlling mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).” This document was sent out by NCRAC to solicit proposals for research from facilities throughout the United States.
6. In December 2007, CVM requested a pivotal efficacy study from AADAP to complete the marking label claim for TERRAMYCIN® 200 FOR FISH for all freshwater-reared salmonids. This request was in response to an AADAP request for an effectiveness complete letter for marking data submitted by AADAP; thus, this marking claim will not be on the next label claim.
7. On February 6, 2008, CVM accepted the TERRAMYCIN® 200 FOR FISH Human Food Safety Technical Section as being complete for all freshwater-reared finfish based on data generated by UMESC.
8. On February 14, 2008, Phibro Animal Health submitted an All Other Information Technical Section for TERRAMYCIN® 200 FOR FISH to complete the final technical section submission for an Administrative NADA submission for the following: control of mortality due to (1) columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) coldwater disease in all freshwater-reared salmonids. The National Aquaculture NADA Coordinator provided a template for this technical section.
9. On February 21, 2008, CVM accepted the Environmental Safety Technical Section for TERRAMYCIN® 200 FOR FISH as being complete for all freshwater-reared finfish based on an environmental assessment written by UMESC.
10. On February 23, 2008, NCRAC announced that UMESC had received a contract to develop effectiveness data for the control of mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol).
11. On May 8, 2008, CVM accepted the TERRAMYCIN® 200 FOR FISH Labeling Technical Section 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.

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, 2007 to May 14, 2008):

1. On June 7, 2007, CVM granted MUMS designations to Pfizer Animal Health, sponsor of Terramycin-343®, for the following label claims: For the control of mortality in freshwater-reared finfish fry and fingerlings due to (1) external columnaris disease associated with *Flavobacterium columnare*, (2) bacterial gill disease associated with *Flavobacterium branchiophilum*, and (3) systemic columnaris disease associated with *Flavobacterium columnare*.
2. 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.

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); one label claim in progress: control of mortality in channel catfish due to external columnaris disease.

Progress on potassium permanganate (May 15, 2007 to May 14, 2008):

1. The National Aquaculture NADA Coordinator met in February 2008 with the sponsor, Carus Chemical Company, to discuss the development of the revision for the Cairox® Chemistry, Manufacturing, and Controls Technical Section and completion of the other sponsor related technical sections.

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®).

Progress on Romet® (May 15, 2007 to May 14, 2008):

1. No progress to report.

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

BENZOCAINE

Major effort by AFWA Project for NADA approval terminated because of decision by AFWA Project stakeholders to select AQUI-S® as the candidate anesthetic in the U.S. public aquaculture sector. Benzocaine may be a potential candidate sedative again because of the issues with isoeugenol.

EUGENOL (CLOVE OIL)

Oil of cloves (eugenol) is considered Generally Recognized as Safe when used as a direct food additive (21CFR184.1257); however, to use eugenol as an anesthetic on fish, it must be approved by CVM for that purpose. A sponsor is required to proceed toward approval. CVM provided guidance on the use of clove oil in GFI #150: Status of Clove Oil and Eugenol for Anesthesia of Fish (updated April 24, 2007). Eugenol may be a potential candidate sedative because of the issues with isoeugenol.

ISOEUGENOL (AQUI-S®)

[ALL ACTIVITIES ON HOLD] Was an AFWA Project drug with current oversight by the DAWG for UMESC, and AADAP: Under development by the sponsor (AQUI-S New Zealand Ltd.); one label claim suspended: zero withdrawal anesthetic for sedation to (1) handleable condition in all freshwater finfish.

Progress on AQUI-S® (May 15, 2007 to May 14, 2008):

1. The DAWG suspended funding for AQUI-S® following the initial NTP release in April 2007 that isoeugenol might be a carcinogen in male mouse livers. This action was taken by the DAWG and a MSCG from AFWA was suspended pending the final report on February 28, 2008. AADAP and UMESC followed suite and suspended activities.
2. In spring 2007, AQUI-S New Zealand, LTD. submitted the Gibbs method used to detect isoeugenol in effectiveness and target animal safety studies to CVM.
3. Status of the total residue depletion study on AQUI-S® that was conducted by UMESC: UMESC completed the laboratory portion of the total residue depletion study on rainbow trout in the spring 2005. UMESC submitted the final report to CVM on March 14, 2006. On January 31, 2007, UMESC submitted a response to CVM's August 23, 2006 comments on the total residue depletion studies and a letter requesting the selection of the marker residue. The response was not definitive because of some concern of the radiochemical purity (95%) of the isoeugenol. CVM indicated that the agency cannot determine the significance of using test material with low radiochemical purity until the safe concentration for isoeugenol is calculated. CVM's recommendation is intended to ensure that the reported total radioactivity in tissues is an accurate measurement of total residues. The total residue concentration is then related to the safe concentration determined by the acceptable daily intake (ADI). An ADI daily intake has not been assigned for isoeugenol because the toxicological requirements for isoeugenol have not been completed. This issue will not be resolved until NTP has its meeting on isoeugenol toxicology studies in February 2008 and one more toxicology study is completed by the sponsor.

   If the safe concentration for isoeugenol is much lower than the reported total residues at the time point of concern (in this case 0-h for a zero hour withdrawal anesthetic), the issue of low radiochemical purity may be insignificant. If the safe concentration for isoeugenol is much higher than the reported total residues at the time point of concern, the low radiochemical purity of the test material may have to be addressed.
4. On October 9, 2007, AADAP requested that CVM consider the Target Animal Safety Technical Section on AQUI-S® to be complete for freshwater salmonids.
5. On January 15, 2008, CVM accepted the Gibbs Method to detect isoeugenol in water with conditions.
6. The National Aquaculture NADA Coordinator worked with the sponsor, AQUI-S New Zealand LTD, on preparing for the February 28, 2008 meeting on the results of the NTP peer review on the isoeugenol mouse and rat studies.

7. On February 28, 2008, the NTP peer review panel confirmed that there is clear evidence of isoeugenol carcinogenicity in male mouse livers; there was no or equivocal evidence of carcinogenicity for the female mouse and male and female rat. Finding clear evidence of carcinogenicity in the male mouse triggered the Delaney Clause, a 1958 amendment to the FDCA. The clause states that "the Secretary of the Food and Drug Administration shall not approve for use in food any chemical additive found to induce cancer in man, or, after tests, found to induce cancer in animals". CVM recently stated that it was “very, very unlikely” that a zero withdrawal period could be gained for isoeugenol based on the NTP interpretation of the results of the male mouse study and the application of the Delaney Clause to the FDCA.
8. In a March 19, 2008 conference call between UMESC, National Aquaculture NADA Coordinator, and CVM’s Division of Human Food Safety, four potential candidates (benzocaine, eugenol, metomidate, and tricaine methanesulfonate) would require the development of at least some mammalian safety and residue chemistry studies to support a potential approval.
9. On March 26-28, 2008, the DAWG met to discuss the available options for, and limitations to, an isoeugenol approval and to formulate plans to identify an alternative sedative. The DAWG presented information on the status of isoeugenol and the potential to develop other candidate sedatives to the AFWA MSCG committee so the MSGC committee could determine the disposition of the MSGC funds initially allocated to develop residue chemistry and animal safety data to support the approval of AQUI-S® as a zero-withdrawal anesthetic. The MSCG committee directed the DAWG to identify a new candidate sedative to which the remaining MSGC funds (~$190,000) could be allocated and report back to the MSGC committee on the selection by June 2, 2008. If a candidate sedative is not identified, the MSCG funds would revert to the AFWA general fund and AFWA efforts to develop a zero-withdrawal sedative would stop.
10. The DAWG members are in the process of gathering information on the use patterns and data requirements for candidate sedatives and working with potential sponsors to determine their interest in supporting a U.S. approval of their sedative.
11. A statement will be released to summarize the results of the DAWG actions to identify an alternate sedative to AQUI-S® in June 2008. The DAWG looks forward to the opportunity of continuing its collaborative research efforts soon with a focus on obtaining approval for a zero-withdrawal fish sedative for field operations.

Current status of technical sections on AQUI-S® **(ALL ACTIVITIES ON HOLD)**:

- *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 suspended.
- *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.

1. On January 4, 2008, CVM granted MUMS designation to Western Chemical Inc., the sponsor of Tricaine-S®, for the euthanasia of finfish not intended for food.

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, 2007 to May 14, 2008):

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.

LHRHA + 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.

17α-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, 2007 to May 14, 2008):

1. On July 27, 2007, CVM provided comments to 17α-methyltestosterone effectiveness studies on tilapia submitted by AADAP that more data are needed.
2. On July 30, 2007, interested parties met in Bozeman, Montana to discuss environmental safety issues on 17α-methyltestosterone and to determine a course of action.
3. On August 17, 2007, CVM indicated it could not accept the 17α-methyltestosterone target animal safety study on tilapia conducted at SIUC and that the study needed to be repeated.
4. On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17α-methyltestosterone that were conducted and developed by UW-M. The National Aquaculture NADA Coordinator worked with UW-M on preparing the analytical method in water and the biodegradation studies for submission.
5. On November 5, 2007, AADAP submitted data and requested that CVM consider the Effectiveness Technical Section to be complete for the use of 17α-methyltestosterone to produce predominantly male populations of tilapia.
6. In December 2007, AADAP worked with the American Tilapia Association through a survey to develop baseline information relative to hatchery discharge in support of an EA for 17α-methyltestosterone.
7. On February 10, 2008, interested parties, including the National Aquaculture NADA Coordinator met in Orlando, FL to discuss the remaining data requirements for the approval of 17α-methyltestosterone for tilapia, find solutions, and develop schedules for completion.
8. On February 18, 2008, the National Aquaculture NADA Coordinator provided to Rangen, Inc. a draft letter to request exemption from the Application of the Controlled Substances Act for 17α-methyltestosterone when used as a gender manipulation aid for tilapia in medicated feed. This letter will be submitted by the sponsor to the Drug Enforcement Administration.
9. On February 23, 2008, the National Aquaculture NADA Coordinator requested $50,000 from NCRAC to fund a repeat of the target animal safety study on tilapia and a feed method transfer study on 17α-methyltestosterone. The NCRAC Board approved up to that amount to fund those two studies, but hoped that another RAC or some other entity would partially or fully fund those studies.
10. The National Aquaculture NADA Coordinator worked in February 2008 with SNARC on the status of the target animal safety study in tilapia and on the funding needs for histopathology consumables, feed analysis, and quality assurance for the repeat target animal safety study in tilapia that will be funded mainly with their base funds.
11. The National Aquaculture NADA Coordinator worked in February 2008 with CVM, Rangen, Inc., UW-M, and UMESC on the design of the feed method transfer study.
12. On March 31, 2008, CVM accepted the 17α-methyltestosterone method validation study in water but not the validation in sediment as developed by UW-M.
13. On March 31, 2008, CVM requested additional information from UW-M concerning the study report on the transformation of 17α-methyltestosterone in aquatic-sediment systems.
14. On April 8, 2008, Rangen, Inc. submitted to CVM the data on stability, homogeneity, and segregation of 17α-methyltestosterone feed based on studies by UW-M. The National Aquaculture NADA

Coordinator provided a covering letter and worked with the sponsor, Rangen, Inc., from November 2007 to February 2008 on preparing the submission of the feed studies conducted by the University of Wisconsin-Madison.

15. On April 21, 2008, NCRAC requested assistance from the Western Regional Aquaculture Center to help fund the repeat target animal safety study on tilapia and a feed method transfer study on 17α-methyltestosterone.
16. On May 14, 2008, the National Aquaculture NADA Coordinator wrote a draft MUMS annual report and covering letter for 17α-methyltestosterone and sent it to the sponsor of MASCULINIZING FEED FOR TILAPIA®, Rangen, Inc.

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 17α-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).
- *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

1. On July 25, 2007, CVM granted MUMS designation to Syndel Laboratories, LTD, a company under Aquatic Life Sciences, Inc., the sponsor of Ovaplant®, for the induction of spawning in ornamental fish.
2. Aquatic Life Sciences, Inc., the sponsor, is focused on developing target animal safety and effectiveness protocols on Ovaplant®. Supportive studies have been completed. In the U.S. and in other countries.

CHEMICAL MARKING AGENTS

CALCEIN (SE-MARK®)
Aquatic Life Sciences, Inc. is in the early development stages with AADAP as chemical marking aid.

1. Aquatic Life Sciences, Inc. and AADAP are building the data for the target animal safety and effectiveness for calcein. The sponsor is also working on a human food safety component.

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.

1. Fish Management Chemicals Training Course. The FMCS in conjunction with Utah State University at Logan gave a week-long, AFS-approved training course in May 2007 for Planning and Executing Successful Rotenone and Antimycin Projects to 24 participants from several state, federal and Canadian fish and wildlife agencies. The next course is anticipated for May 2008 at the same location. To date, the course instructors have trained over 100 biologists from the U.S., England, Canada, Scotland, Norway and South Africa.
2. The National Aquaculture NADA Coordinator, as Chair of the AFS Task Force on Fishery Chemicals, and the FMCS attended a meeting in June 2007 with the registrants and EPA to discuss the requirements for label changes and mitigation measures for rotenone.
3. After EPA issued the Reregistration Eligibility Decision (RED) authorizing the reregistration of rotenone, FMCS provided written comments on proposed risk mitigation measures and labeling changes in a July 3, 2007 letter to EPA. The Rotenone Task Force and many state and federal fish and wildlife agencies followed suit by providing similar comments to EPA. Significant concerns include enforceability and content of operation manuals versus labels, need for additional safety gear, allowable treatment rates and sites, chemical neutralization and restrictive application procedures. EPA has informed FMCS and the registrants that they will be addressing these concerns in writing by the end of February 2008. FMCS anticipates drafting a Standard Operations Procedures (SOP) manual for rotenone using FWS funding in 2008.
4. FMCS provided written comments to the antimycin RED on proposed risk mitigation measures and labeling changes in a July 27, 2007 letter to EPA. Many state and federal fish and wildlife agencies followed suit by providing similar comments to EPA. Concerns were similar to those for rotenone. FMCS does not know the status of the reregistration and there may be supply issues from the registrant.
5. The FMCS coordinated a day-long symposium on global piscicide use issues during the September 2007 Annual AFS National Meeting in San Francisco, California. The symposium examined how government directives, regulations and permitting requirements, piscicide applicator training, public understanding of native fish recovery, and concerns about human and environmental safety are reflected in policies governing the use of piscicides in restoration projects. The symposium heard talks from a variety of state agencies including New York, California, Nevada, Montana and Oregon, federal agencies including the U.S. Forest Service and FWS, foreign countries including Norway, Spain, and South Africa and non-government organizations including The Nature Conservancy. A facilitated panel discussion that followed focused on issues that need to be addressed in piscicide projects that result in efficacy while protecting humans and the environment. The symposium provided a better understanding of how to integrate these issues into policies, guidelines, and projects and in the development a long-term strategy for the use of chemicals in fish management. The panel concluded that the piscicide training offered by AFS was a good forum articulating and dispensing the constantly evolving strategy within the U.S. and around the world.

6. On May 7, 2008, EPA provided a response to the comments on the rotenone RED from the registrants, FMCS, state fish management agencies, interested groups, members of the public, and the user community. FMCS and the registrants plan on meeting with EPA to discuss the remaining issues and then start on the SOP manual.

PUBLIC INFORMATION AND MEETINGS

1. **CANADIAN VETERINARY DRUGS DIRECTORATE SEMINAR**. On July 18, 2007, the National Aquaculture NADA Coordinator gave an eight-hour seminar to the Veterinary Drugs Directorate (VDD) at its invitation. VDD is the Canadian equivalent of CVM. The VDD was interested in (1) the successful aquaculture drug approval processes in the U.S., (2) our experience with various successful partnerships, and (3) insight into expediting the aquaculture drug approval processes in Canada.
2. **CVM SEMINAR.** On December 5, 2007, the National Aquaculture NADA Coordinator gave a two-hour seminar to CVM on the status and background of the aquaculture drug approvals, the roles, responsibilities, and accomplishments of the National Aquaculture NADA Coordinator, and coordination needs after her retirement.
3. **PRODUCER SESSION.** National Aquaculture NADA Coordinator convened a producer session at Aquaculture America 2008 on February 12, 2008. The session covered the overall progress toward aquaculture drug approvals and included status of approvals for oxytetracycline dihydrate (TERRAMYCIN® 200 FOR FISH), hydrogen peroxide (35% PEROX-AID®), potassium permanganate (CAIROX®), and the drugs under development by Aquatic Life Sciences, Inc. CVM provided an update on its aquaculture drug approval activities. Researchers from AADAP, SNARC, and UMESC provided updates on their research activities toward aquaculture drug approvals.
4. **MUMS DESIGNATIONS.** The designation provision of the Minor Use and Minor Species Animal Health Act of 2004 (MUMS) gives sponsors seven years of marketing exclusivity. So far, the MUMS Office has granted 53 designations, 46 of those are to aquaculture drug sponsors who received extensive help from the National Aquaculture NADA Coordinator. Recent MUMS designations include (1) one for Aquatic Life Sciences, Inc.'s Ovaplant® (salmon gonadotropin releasing hormone analog) on May 25, 2007, (2) three for Pfizer Animal Health's Terramycin 343® (oxytetracycline hydrochloride) on June 7, 2007, (3) one for Western Chemical Inc.'s PARASITE-S®, and (4) one for Western Chemical Inc.'s TRICAINE-S®. There have been an original NADA approval of three MUMS designations for Eka Chemicals, Inc.'s 35%PEROX-AID® and two supplemental NADA approvals and one Conditional Approval of three MUMS designations for SPAH's Aquaflor®.
5. **MUMS INDEXING:** The final regulation for Indexing (i.e., legal marketing of unapproved drugs) was published December 6, 2007. This provision should allow companies to provide legally marketed drugs to our non-food fish industries (e.g., bait fish, ornamental fish). Companies began to submit requests on February 19, 2008. Dr. Joan Gotthardt, formerly the Director of the Division of Therapeutic Drugs for Food Animals, will be in charge of implementing these regulations.
6. **13th ANNUAL DRUG APPROVAL COORDINATION WORKSHOP.** The 13th Annual Drug Approval Coordination Workshop was co-hosted by AADAP and SNARC in Bozeman, Montana on July 31 to August 1, 2007. The topics covered included (1) overviews of CVM activities and regulatory discussions, (2) celebrations of approvals for 35% PEROX-AID® and AQUAFLOR®, (3) approval status of original AFWA Project drugs including the historical background of this partnership by the National Aquaculture NADA Coordinator, and (4) approval status of non-AFWA Project drugs. On August 2, 2007, the National Aquaculture Drug Research Forum met and UMESC held a Partner Meeting.
7. **FORMATION OF A NEW INDUSTRY-BASED 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 is

tentatively named the National Aquaculture Industry Therapeutic Agent Program (NAI-TAP) and is a coalition of aquaculture industry stakeholders and invited non-industry entities who address and support the development, approval, availability, and optimal use of drug, biologic, nutritional, and other products that affect the health and production of aquatic animals. The National Aquaculture NADA Coordinator (1) participated in the initial meeting of NAI-TAP, (2) developed draft operating guidelines for the group, (3) participated in a April 24, 2008 teleconference call of NAI-TAP members, (4) was selected as Chair of NAI-TAP on April 24, 2008, (5) wrote up the notes to the teleconference and (6) sent out the notes and revised operating guidance for review on May 2, 2008. The first organizational meeting of NAI-TAP will be to set its mission and objectives and discuss how to continue similar functions and activities of the Working Group on Aquaculture Drugs, Biologics and Pesticides. This meeting will be convened at the end of the 14th Annual Drug Approval Coordination Workshop in Bozeman, Montana on August 1, 2008 from 1 to 5 PM.

8. **CANDIDATE ZERO WITHDRAWAL SEDATIVES FOR AQUATIC FOOD ANIMALS.** The National Aquaculture NADA Coordinator began working in February 2008 with CVM, AFWA's DAWG, any potential sponsors, involved researchers, and user groups to determine whether there was a chance for AQUI-S® approval and chart a course of action for a replacement candidate for a zero withdrawal sedative based on the peer review finding that the NTP study results for the male mouse carcinogenicity study on isoeugenol still stand, i.e., that there is clear evidence of carcinogenicity. The National Aquaculture NADA Coordinator did the following:

   - Prepared tables on February 29, 2008 that illustrate the preliminary status of all the major technical sections for potential candidate zero withdrawal sedatives for food fish (eugenol, benzocaine, tricaine methanesulfonate, and metomidate) and submitted them to the DAWG members;
   - Discussed the isoeugenol status with the sponsor, AQUI-S New Zealand LTD;
   - Was involved in the March 19, 2008 teleconference with CVM and UMESC to determine the mammalian safety and residue chemistry requirements for the candidate sedatives and what option the user community had for achieving a zero withdrawal time for isoeugenol given its status under the Delaney Clause;
   - Wrote a status report on human food safety data requirements for isoeugenol, eugenol, benzocaine, tricaine methanesulfonate, and metomidate based on the March 19, 2008 informal teleconference with CVM'S Division of Human Food Safety and major input from UMESC;
   - Contacted several potential sponsors concerning the possibility of developing a sedative for a practical zero withdrawal time for food finfish applications;
   - Contacted a private laboratory that conducts mammalian safety studies to determine what each mammalian safety study would cost to meet the mammalian safety data requirements of each candidate sedative; provided that information in a report to the DAWG;
   - Discussed with CVM how the mammalian safety data requirements could be reduced or met for each candidate sedative; discussed the impact that reports of methemoglobinemia attributed to applications of benzocaine would have on the approvability of benzocaine as a zero withdrawal sedative for aquaculture;
   - Asked CVM to identify any mammalian safety studies conducted elsewhere for the minor use permit for benzocaine in Australia and approval of eugenol in Japan;
   - Wrote a statement with UMESC entitled "Status of approval for a zero withdrawal sedative for aquaculture and fishery management use" for potential distribution.
   - Provided the dilemma faced with the status of isoeugenol because of the Delaney Clause and the possible solutions to identifying a viable candidate sedative at a presentation to the DAWG at its March 26, 2008 meeting;
   - Provided insight to what would be required for the private sector to gain approval for a zero withdrawal sedative for harvest and transport at the USDA ARS/CSREES Aquaculture Stakeholder Workshop in Kansas City, Missouri on April 15-16, 2008.

9. **BACKGROUND ON THE DAWG AND ITS MEETINGS.** In 1994, FWS, USGS, and AFWA, on behalf of 38 participating states, developed a 5-year cooperative initiative to fund and carry out research

directed both toward gaining approval of eight high priority aquaculture drugs (seven therapeutics and one anesthetic). The initiative was formally named the Federal-State Aquaculture Drug Approval Partnership Project, but has been referred to as the AFWA Project (Project). At the start of the Project, AFWA was unaware of the time requirement and reality of drug approval process and added three additional years of funding from participating state to be finalized by 2002.

a. The Fisheries and Water Resources Policy Committee of AFWA sponsored the Project and formed the DAWG as an oversight body to maintain direction and decision making for the Project drugs. The DAWG now includes three AFWA state agency representatives (Wyoming, Arkansas, and Iowa) covering coldwater, warmwater and coolwater aquaculture as well as representatives from USGS's UMESC, AADAP, SNARC, CVM, and the National Aquaculture NADA Coordinator. All participants are voting members excluding CVM and the National Aquaculture NADA Coordinator. Although annual Project funding terminated in 2002, AFWA and the DAWG participants agreed to maintain the working group to maintain a concerted effort and oversight for approvals of the eight drugs. The DAWG meets biannually at the annual AFWA meeting in September and the North American Wildlife and Natural Resources Conference in March to review the progress of each technical group and set direction.

b. The DAWG met in September 2007 in Louisville, Kentucky and in March 2008 in Phoenix, Arizona to focus is on the approval and continued labeling of seven drugs (chloramine-T, hydrogen peroxide, oxytetracycline dihydrate, oxytetracycline hydrochloride, florfenicol, formalin, and copper sulfate) and a sedative/anesthetic to replace AQUI-S®, following NTP's finding that isoeugenol has "clear evidence" of carcinogenicity.

c. Prior to these two meetings, a very specific action item of the DAWG was suspension of funding for AQUI-S® when following the initial NTP release in April 2007. This action was taken by the DAWG and a MSCG from AFWA was suspended pending the final report in February 2008. AADAP and USGS followed suite and suspended activities. Also, although funding is not presently provided from AFWA beyond the grant, the DAWG and AFWA are fully engaged in the continued coordination and oversight for the AFWA Project drug approval.

d. Additional items of discussion at the September 2007 and the March 2008 DAWG meetings were: (1) efficacy table for waterborne drugs, (2) Hydrogen peroxide fact sheet, (3) remaining data requirements for the AFWA Project drugs, and (4) design of parasite studies and survey of needs.

10. **WEBSITE.** The National Aquaculture NADA Coordinator requested help from AquaNic to change her website address to http://aquanic.org/aquadrugs because USDA could no longer be involved because of the Federal Advisory Committee Act.

National Aquaculture NADA Coordinator Position Funding Needs

The National Aquaculture NADA Coordinator position stayed at 35 hours per week to maintain adequate funding. Contributions totaled $132,580 for Year 13 (May 15, 2007 to May 14, 2008).

PUBLICATIONS, MANUSCRIPTS, PAPERS PRESENTED, AND SPECIAL REPORTS

PUBLICATIONS

Schnick, R.A. 2007. News: Fisheries: Aquaflor® approved for furunculosis in salmonids. Fisheries 32(12):578.

AFS Task Force on Fishery Chemicals, Fish Management Chemicals Subcommittee. 2007. News: Fisheries: Update on piscicides rotenone and antimycin. Fisheries 32(11):526.

PAPERS PRESENTED

Schnick, R.A. 2007. Progress towards aquaculture drug approvals. 144th AVMA Annual Convention, Washington, DC, July 14-18, 2007.

Schnick, R.A. 2007. Possibilities for expediting Canadian aquaculture drug approval processes. Veterinary Drugs Directorate, Ottawa, Ontario, Canada, July 18, 2007.

Schnick, R.A. 2007. Historical background to this fabulous partnership. 13th Annual Drug Approval Coordination Workshop, Bozeman, Montana, July 31-August 1, 2007.

Schnick, R.A. 2007. The future of this fabulous partnership. 13th Annual Drug Approval Coordination Workshop, Bozeman, Montana, July 31-August 1, 2007.

Schnick, R.A. 2007. The AFWA Project: NADA approvals, label claims under development for initial and/or expanded NADA approvals, and status of technical section completions. 13th Annual Drug Approval Coordination Workshop, Bozeman, Montana, July 31-August 1, 2007.

Schnick, R.A. 2007. Progress on new aquaculture drug approvals for disease management. Disease Management Strategies for the Aquatic Environment: Alternatives & Innovations. AFS Annual Meeting, San Francisco, California, September 5, 2007.

Schnick, R.A. 2007. Emerging issues from the reregistration process for piscicides. Global issues and policies affecting ecosystem restoration projects using Rotenone and Antimycin. AFS Annual Meeting, San Francisco, California, September 6, 2007.

Schnick, R.A. 2007. Strategic review of UMESC's Fish Management and Drug Research Program. La Crosse, Wisconsin, September 13, 2007.

Schnick, R.A. 2007. Update discussion of AFWA Project Drugs. Drug Approval Working Group. AFWA Annual Meeting, Louisville, Kentucky, September 17-18, 2007.

Schnick, R.A. 2007. Major efforts and accomplishments: National Coordinator for Aquaculture New Animal Drug Applications. Center for Veterinary Medicine, Rockville, Maryland, December 5, 2007.

Schnick, R.A. 2007. Efforts to gain aquaculture drug approvals. Center for Veterinary Medicine, Rockville, Maryland, December 5, 2007.

Schnick, R.A. 2008. Update on product approvals for fish health. Striped Bass Growers Association Industry Forum, Aquaculture America 2008, Orlando, Florida, February 10, 2008.

Schnick, R.A. 2008. Overall progress toward aquaculture drug approvals. Aquaculture Drug Approval Successes, Aquaculture America 2008, Orlando, Florida, February 12, 2008.

Schnick, R.A. 2008. Status report on aquaculture drug approvals. North Central Regional Aquaculture Center Annual Program Planning Meeting, Indianapolis, Indiana, February 22-24, 2008.

Schnick, R.A. 2008. Isoeugenol (AQUI-S®) and sedative issue. Drug Approval Working Group, 73rd North American Wildlife and Natural Resources Conference, Phoenix, Arizona, March 26-28, 2008.

Schnick, R.A. 2008. Update discussion on AFWA Project drugs. Drug Approval Working Group,73rd North American Wildlife and Natural Resources Conference, Phoenix, Arizona, March 26-28, 2008.

SPECIAL REPORTS

Schnick, R.A. 2007. Statement on isoeugenol (AQUI-S®). Submitted to AFWA and other interested entities, May 16, 2007. 1 pp.

Schnick, R.A. 2007. Matrices updated: Chloramine-T, copper sulfate, erythromycin, florfenicol, formalin, hydrogen peroxide, isoeugenol, 17α-methyltestosterone, oxytetracycline dihydrate, and oxytetracycline hydrochloride. Submitted to National Aquaculture NADA Coordinator website and AADAP, May 20, 2007. Various paginations.

Schnick, R.A. 2007. Statement of continued support for the major participants In the Federal-State Aquaculture Drug Approval Partnership Project. Submitted to DAWG, June 4, 2007. 1 pp.

Schnick, R.A. 2007. Twelfth annual report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2006 to May 14, 2007). Submitted to Ted Batterson, NCRAC for distribution. June 14, 2007. 25 pp.

Schnick, R.A. 2007. Roz's corner: AADAP newsletter contribution. Submitted to AADAP. June 21, 2007. 1 pp.

Finlayson, B.J. and R.A. Schnick. 2007. Response to Reregistration Eligibility Decision (RED) for Rotenone (EPA 738-R-07-005, dated March 31, 2007). Submitted to EPA and state Fish Chiefs,July 3, 2007. 13 pp.

Schnick, R.A. 2007. Letter to Bimeda, Inc. on Aquamycin® approval. Submitted to Gavin Tierney, Bimeda, July 2, 2007. 2 pp.

Schnick, R.A. 2007. Response to CVM's February 27, 2007 letter on the assessment of the effect of residues (i.e., marker residue, *para*-toluenesulfonamide=*p*-TSA) of chloramine-T (HALAMID® PHARMA GRADE) on the human intestinal bacteria. Submitted to Axcentive SARL for forwarding to CVM, July 12, 2007. 5 pp.

Schnick, R.A. 2007. Second quarter 2007 quarterly report for Multistate Conservation Grant Number DC M-48-R-1 (AQUI-S®). Submitted to AFWA. July 26, 2007. 5 pp.

Finlayson, B.J. and R.A. Schnick. 2007. Response to Reregistration Eligibility Decision (RED) for Antimycin A (EPA 738-R-07-007, dated May 16, 2007). Submitted to EPA and state Fish Chiefs, July 27, 2007. 8 pp.

Schnick, R.A. and B.J. Finlayson. 2007. Task Force on Fishery Chemicals Annual Report to the AFS Governing Board, September 2007. Submitted to the AFS Executive Director, August 5, 2007. 4 pp.

Schnick, R.A. 2007. Task Force on Fishery Chemicals Financial Report to the AFS Governing Board, September 2007. Submitted to the AFS Executive Director, August 5, 2007. 1 pp.

Schnick, R.A. 2007. Notes on UMESC Partnership Meeting. Submitted to UMESC, August 5, 2007. 2 pp.

Schnick, R.A. 2007. AFWA Project Drugs: Remaining requirements and progress March 2007 to September 2007 (as of September 15, 2007). Submitted to DAWG, September 16, 2007. 4 pp.

Schnick, R.A. 2007. Call for Statements of Interest for "Effectiveness research leading to approvals for controlling mortality in coolwater and warmwater finfish due to aeromonad infections with Terramycin 200 for Fish® (oxytetracycline dihydrate) and Aquaflor® (florfenicol)." This document was sent out by NCRAC to solicit proposals for research from facilities throughout the United States, September 24, 2007. 3 pp.

Schnick, R.A. 2007. Template for "Records and reports concerning experience with approved new animal drugs (21 CFR 514.80)". Submitted to Eka Chemicals, Inc., September 25, 2007. 5 pp.

Schnick, R.A. 2007. Activity highlights for the National Coordinator for Aquaculture New Animal Drug Applications (January to September 2007). Submitted to the AVMA, September 26, 2007. 3 pp.

Schnick, R.A. 2007. BAP Catfish Farm Standards, Standard 11—Food Safety: Drug and Chemical Management. Sent to Global Aquaculture Alliance, September 28, 2007. 2 pp.

Schnick, R.A. and B.J. Finlayson. 2007. Request for EPA Response to Registrants' Response to Reregistration Eligibility Decision (RED) for Rotenone (EPA 738-R-07-005, dated March 31, 2007). Submitted to Rotenone Registrants for forwarding to EPA, September 30, 2007. 2 pp.

Schnick, R.A. 2007. Product development meeting regarding Investigational New Animal Drug (INAD) exemptions: 11-665, 11-666, 11-667, and 11-668. Submitted to Kent SeaTech Corporation, October 1, 2007. 2 pp.

Schnick, R.A. 2007. Third Quarter 2007 Quarterly Report for Multistate Conservation Grant Number DC M-48-R-1 (AQUI-S®). Submitted to AFWA, October 24, 2007. 5 pp.

Schnick, R.A. 2007. Roz's Corner: AADAP newsletter contribution. Submitted to AADAP, October 24, 2007. 1 pp.

Schnick, R.A. 2007. 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 26, 2007. 11 pp.

Schnick, R.A. 2007. Table: 2005 figures for salmonid production. Submitted to potential sponsor, October 30, 2007. 1 pp.

Schnick, R.A. 2007. Letter supporting funding for the NRSP-7 Program. Submitted to NASAC, November 1, 2007. 1 pp.

Schnick, R.A. 2007. Thirteenth mid-year report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2007 to November 9, 2007). Submitted to Ted Batterson, NCRAC for distribution, November 9, 2007. 21 pp.

Schnick, R.A. 2007. Matrices revised and reformatted in PDF: chloramine-T, copper sulfate, erythromycin, florfenicol, formalin, hydrogen peroxide, isoeugenol, 17 α-methyltestosterone, oxytetracycline dihydrate, oxytetracycline hydrochloride, and potassium permanganate. Submitted to National Aquaculture NADA Coordinator Website, AADAP, CVM, UMESC, SNARC, UID, NRSP-7, NCRAC, and MS State University, November 16, 2007. Various paginations.

Schnick, R.A. 2007. NADA approvals—1997-2007. Submitted to CVM, November 20, 2007. 1 pp.

Schnick, R.A. 2007. NADA approvals achieved and anticipated for all aquaculture drugs—1967-2010+. Submitted to CVM, December 2, 2007. 1 pp.

Schnick, R.A. 2007. Chloramine-T label. Submitted to sponsor, December 6, 2007. 5 pp.

Schnick, R.A. 2007. News release: major aquaculture drug approval for AQUAFLOR®. Submitted to news outlets, December 13, 2007. 1 pp.

Schnick, R.A. 2007. 2007 Highlights for the activities of the National Coordinator for Aquaculture New Animal Drug Applications. Submitted to contributors to the position, December 28, 2007. 2 pp.

Schnick, R.A. 2008. Fourth quarter 2007 quarterly report for Multistate Conservation Grant Number DC M-48-R-1 (AQUI-S®). Submitted to AFWA, January 4, 2008. 5 pp.

Schnick, R.A. 2008. Template: Technical section submission on (trade name) related to Guidance for Industry #152: "Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern". Submitted to SNARC, February 7, 2008. 5 pp.

Schnick, R.A. and B.J. Finlayson. 2008. Task Force on Fishery Chemicals mid-year report to the AFS Governing Board, February 2008. Submitted to the AFS Executive Director, February 16, 2008. 3 pp.

Schnick, R.A. 2008. [Draft] Exemption from the application of the Controlled Substances Act for 17α-methyltestosterone when used as a gender manipulation aid for tilapia in medicated feed. Submitted to sponsor, February 18, 2008. 2 pp.

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Schnick, R.A. 2008. Status of potential approval for aquatic food animal sedatives with a zero withdrawal time other than isoeugenol. Submitted to DAWG, February 29, 2008. 2 pp.

Schnick, R.A. 2008. Repeat of the 17α-methyltestosterone target animal safety study in tilapia. Submitted to NCRAC, March 3, 2008. 1 pp.

Schnick, R.A. 2008. 17 α-methyltestosterone feed method transfer study. Submitted to NCRAC, March 3, 2008. 2 pp.

Schnick, R.A. 2008. Table: Status of effectiveness studies for waterborne AFWA Project Drugs. Submitted to the DAWG, March 24, 2008; revised April 27, 2008. 2 pp.

Schnick, R.A. and M.P. Gaikowski. 2008. [Draft] AFWA Fact Sheet #1: 35% PEROX-AID® (hydrogen peroxide). Submitted to the DAWG, March 28, 2008. 3 pp.

Schnick, R.A. 2008. Anticipated Federal FY 2008 and 2009 funding needs: National Coordinator for Aquaculture New Animal Drug Applications. Submitted to the DAWG Chair, March 18, 2008. 6 pp.

Schnick, R.A. 2008. Human food safety status of candidate sedatives based on March 19, 2008 informal teleconference with CVM'S Division of Human Food Safety. Submitted to the DAWG, March 26, 2008. 7 pp.

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Schnick, R.A. 2008. March 2007-March 2008: Highlights for the activities of the National Coordinator for Aquaculture New Animal Drug Applications. Submitted to NCRAC, April 4, 2008. 3 pp.

Schnick, R.A. and M.P. Gaikowski. 2008. Status of approval for a zero withdrawal sedative for aquaculture and fishery management use. Submitted to the DAWG, April 11, 2008. 2 pp.

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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.