NATIONAL COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS (NADAs)

Facilitator: Ted R. Batterson

Funding Request: $40,000

Duration: 2 Years (September 1, 2006 - August 31, 2008)

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	Year 2	Total
Michigan State University	Ted R. Batterson	1-8	$20,000	$20,000	$40,000
		Totals	**$20,000**	**$20,000**	**$40,000**

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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 and 11 (May 15, 2004 to May 14, 2005 and May 15, 2005 to May 14, 2006) carry-over and pledged funds enabled the position to increase to 87.5% time. For Year 12 (May 15, 2006 to May 14, 2007) carry-over and pledged funds (see Table 1) will enable to position to continue at 87.5% time. It is anticipated that the same will be true for Year 13 (May 15, 2007 to May 14, 2008).

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 2006-2007 a number of government agencies, private associations, and other organizations have pledged over $134,000 for the NADA Coordinator's position. Those sources of funds are presented in Table 1. Similar pledges are expected for 2007-2008.

Table 1. Funds pledged for support of the National Coordinator for Aquaculture NADAs for 2006-2007.

Source	2006-07
	Amount
CVM[1, 2]	$50,000
U.S. Geological Survey[1, 2]	$5,000
U.S. Fish and Wildlife Service[1, 2]	$5,000
International Association of Fish and Wildlife Agencies (IAFWA) Activities Toward the Approval of AQUI-S	$10,000
North Central Regional Aquaculture Center	$20,000
American Veterinary Medical Association	$10,000
AFS - Fish Health Section	$1,000
AFS - Fish Culture Section	$500
Alabama Catfish Producers	$1,500
Akzo Nobel/Eka Chemicals, Inc.	$3,500
AQUI-S®	$7,500
Axcentive	$7,500
Catfish Farmers of America	$500
Catfish Farmers of Mississippi	$1,000
National Aquaculture Association	$3,000
Schering-Plough	$5,000
Striped Bass and Hybrid Producers Association	$2,000
U.S. Trout Farmers Association	$1,000
	$134,000

[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 2006) 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 twelfth and thirteenth 12-month periods (May 15, 2006 - May 14, 2007 and May 15, 2007 - May 14, 2008, respectively) for the National Coordinator for Aquaculture NADAs are presented in Table 2 below.

Table 2. Proposed twelfth and thirteenth year budgets for the National Coordinator for Aquaculture NADAs: May 15, 2006 - May 14, 2007 and May 15, 2007 - May 14, 2008.

	Year 12	Year 13
Salary (0.875 FTE)	$78,982	$80,971
Fringe Benefits	$26,096	$25,130
Total Salary and Fringe Benefits	$105,078	$106,100
Nonexpendable Equipment	$0	$0
Materials and Supplies	$5,000	$5,000
Travel	$10,000	$10,000
TOTAL COSTS	$120,078	$121,100

This request is for $40,000 for the partial support of the costs for the National Coordinator for Aquaculture NADAs during her twelfth and thirteenth years (Years 1 and 2 of this project, respectively) at $20,000 per year. Completed CSREES-2004 budget forms for each of those years are presented on the next two pages. On page 9 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.

UNITED STATES DEPARTMENT OF AGRICULTURE
COOPERATIVE STATE RESEARCH, EDUCATION, AND EXTENSION SERVICE

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

USDA AWARD NO. Year 1: Tasks 1-8

PROJECT DIRECTOR(S)
Ted R. Batterson

	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)							
b. _1_ Senior Associates	2.25			$14,577			
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 →				$14,577	$0	$0	$0
B. Fringe Benefits (If charged as Direct Costs)				$4,621			
C. Total Salaries, Wages, and Fringe Benefits (A plus B) →				$19,198	0	$0	$0
D. Nonexpendable Equipment (Attach supporting data. List items and dollar amounts for each item.)							
E. Materials and Supplies							
F. Travel							
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.)				$802			
K. Total Direct Costs (C through I) →				$20,000	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) →				$20,000	0	$0	$0
N. Other →							
O. Total Amount of This Request →				$20,000	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)		

Form CSREES-2004 (12/2000)

UNITED STATES DEPARTMENT OF AGRICULTURE
COOPERATIVE STATE RESEARCH, EDUCATION, AND EXTENSION SERVICE

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

USDA AWARD NO. Year 2: Tasks 1-8

PROJECT DIRECTOR(S)
Ted R. Batterson

	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 1. No. of Senior Personnel	Calendar	Academic	Summer				
a. ___ (Co)-PD(s)							
b. 1 Senior Associates	2.25			$14,942			
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 →				$14,942	$0	$0	$0
B. Fringe Benefits (If charged as Direct Costs)				$4,692			
C. Total Salaries, Wages, and Fringe Benefits (A plus B) →				$19,634	0	$0	$0
D. Nonexpendable Equipment (Attach supporting data. List items and dollar amounts for each item.)							
E. Materials and Supplies							
F. Travel							
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.)				$366			
K. Total Direct Costs (C through I) →				$20,000	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) →				$20,000	0	$0	$0
N. Other →							
O. Total Amount of This Request →				$20,000	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)		

Form CSREES-2004 (12/2000)

BUDGET EXPLANATION FOR MICHIGAN STATE UNIVERSITY

A. Salaries and Wages. Year 1: This amount would provide 2.25 months of salary for the National Coordinator for Aquaculture NADAs at 0.875 FTE; Year 2: This amount would provide 2.25 months of salary for the National Coordinator for Aquaculture NADAs at 0.875 FTE.

B. Fringe Benefits. Year 1: The fringe benefit loading rate for FY 2006-07 is 31.7%; Year 2: The fringe benefit rate for FY 2007-08 is 31.4%.

I. All Other Direct Costs. Year 1: Telephone ($650), fax ($52), and postage ($100) for conducting activities associated with the National Coordinator for Aquaculture NADAs; Year 2: Telephone ($275), fax ($49), and postage ($42).

SUMMARY OF ACCOMPLISHMENTS TO DATE

A cumulative Progress Report for the National Coordinator's activities since 1992 is contained in an Appendix to this proposal which follows.

PROGRESS REPORT FOR THE NATIONAL COORDINATOR FOR AQUACULTURE NADAs

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:

(1) Serve as an information conduit between 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.

PROGRESS AND PRINCIPAL ACCOMPLISHMENTS

PROGRESS AND PRINCIPAL ACCOMPLISHMENTS

The National Aquaculture NADA Coordinator provided many information transfers from May 15, 2005 to November 9, 2005 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 (oral antibacterial)—Status: 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.

Chloramine-T (external antibacterial)—Status: Was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (Axcentive SARL, formerly Axcentive bv Akzo Nobel Chemicals, Inc.), UMESC, and AADAPP; two label claims close to completion: control of mortality due to (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye.

Progress on chloramine-T (May 15, 2005 to November 9, 2005):

- On July 6, 2005, the sponsor submitted a product chemistry package for their chloramine-T product (Halamid®). CVM responded that it needed more information.

- On August 1, 2005, the National Aquaculture NADA Coordinator, the sponsor (Axcentive SARL), and UMESC met with CVM to discuss the remaining requirements for the sponsor's proprietary EA on chloramine-T and developed a strategy to meet the requirements.
- On October 5, 2005, the National Aquaculture NADA Coordinator, UMESC, and AADAPP met with CVM to discuss the data requirements for microbial food safety. The sponsor was invited but was not able to attend. The National Aquaculture NADA Coordinator will prepare the documents.

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) is committed to developing the product chemistry technical section and submitting it to CVM into INAD #8086.
- *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 environmental assessment that was submitted by Axcentive SARL on July 16, 2003 to CVM under INAD #8086. CVM sent a review to the sponsor on September 17, 2004 that is being reviewed for a response.
- *Human Food Safety–Toxicology*—Axcentive SARL addressed this technical section. CVM declared that p-TSA is not genotoxic based on proprietary data submitted by Axcentive SARL (July 19, 2002). CVM accepted additional proprietary mammalian safety data from Axcentive SARL; based on those data, CVM declared that the safe concentration 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 US (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).
- *Target Animal Safety*—CVM accepted as complete from (1) the Aquatic Animal Drug Approval Partnership Program (AADAPP) 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, March 11, 2005).
- *Efficacy*—CVM accepted from UMESC a simple colorimetric procedure for use in efficacy 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 efficacy 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) AADAPP the efficacy technical section for control of mortality due to bacterial gill disease on all freshwater-reared salmonids (June 10, 2002) and (2) UMESC the efficacy technical section for controlling external columnaris disease on walleye (January 30, 2004).

Copper Sulfate (external microbicide)—Status: Was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (Phelps Dodge Sales Company) and SNARC; one label claim close to completion: control of mortality due to ichthyophthiriasis on channel catfish in earthen ponds with no outflows.

Progress on copper sulfate (May 15, 2005 to November 9, 2005): No progress to report.

Current status of technical sections on copper sulfate:

- *Product Chemistry*—CVM accepted as complete from the sponsor, Phelps Dodge Refining Corporation.

- *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 addressed the use of copper sulfate in ponds was completed and will be incorporated into a revised EA and submitted to CVM.
- *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.
- *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. Channel catfish study in ponds accepted by CVM May 25, 2005. CVM needs the Freedom of Information (FOI) Summary for the literature and catfish study for this Technical Section to be complete for channel catfish.
- *Efficacy*—CVM accepted as complete from SNARC the efficacy technical section for control of ichthyophthiriasis on all fish. SNARC also conducted pivotal efficacy studies to control fungi on catfish eggs.

Diquat Dibromide (external microbicide)—Status: No sponsor is available to complete the approval process at the present time.

Erythromycin (oral antibacterial)—Status: Most technical sections submitted by University of Idaho; sponsor (Bimeda Inc.) needs to submit product chemistry; University of Idaho needs to submit hazard in the environment (to complete the Environmental Safety Technical Section); one label claim close to completion: control of mortality due to bacterial kidney disease in salmonids when the EA is written and accepted.

- The University of Idaho received preliminary confirmation that the risk assessment for microbial food safety has been accepted.

Florfenicol (oral antibacterial)—Status: The sponsor, Schering-Plough Animal Health, gained florfenicol (AQUAFLOR®) approval in the United States on October 24, 2005 to control mortality due enteric septicemia in catfish; was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor, UMESC, and AADAPP; three other label claims close to completion: control of mortality due to (1) coldwater disease in freshwater-reared salmonids, (2) furunculosis in freshwater-reared salmonids, and (3) systemic columnaris disease in freshwater-reared salmonids and catfish.

Progress on florfenicol (May 15, 2005 to November 9, 2005):

MAJOR APPROVAL: FLORFENICOL APPROVED FOR CONTROL OF MORTALITY DUE TO ENTERIC SEPTICEMIA IN CATFISH ON OCTOBER 24, 2005!!

- On November 1, 2005, the National Aquaculture NADA Coordinator issued a news release on the florfenicol approval.

Current status of technical sections on florfenicol:

- *Product Chemistry*—accepted by CVM from sponsor.
- *Environmental Safety*—accepted by CVM from sponsor for ponds and for flow-through systems.
- *Human Food Safety–Toxicology*—accepted by CVM from sponsor.
- *Human Food Safety–Residue Chemistry*—human food safety package for catfish and all freshwater-reared salmonids—accepted by CVM from sponsor; analytical method—accepted by CVM from sponsor.
- *Human Food Safety–Microbial Food Safety*—accepted by CVM from sponsor.
- *Target Animal Safety*—CVM accepted as complete from sponsor (and conducted by UMESC) the target animal safety technical section on channel catfish; salmonids—accepted by CVM from sponsor.

- *Efficacy*—accepted by CVM from sponsor enteric septicemia in catfish, and from AADAPP coldwater disease in salmonids and *Streptococcus iniae* in hybrid striped bass (December 9, 2004); UMESC validated methods to analyze for florfenicol in finfish feeds to support efficacy studies at AADAPP; AADAPP submitted efficacy studies to CVM on systemic columnaris disease and furunculosis in salmonids.

Formalin (external microbicide)—Status: 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 a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsors (Natchez Animal Supply Company, Western Chemical Inc. and Argent Chemical Laboratories), UMESC, and CVM's Office of Research; one additional label claim close to completion: control of mortality due to saprolegniasis on all freshwater-reared finfish.

Progress on formalin (May 15, 2005 to November 9, 2005):

- On July 19, 2005, CVM accepted as pivotal efficacy studies for the control of saprolegniasis on rainbow trout conducted by CVM Office of Research.

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.
- *Efficacy*—CVM informally accepted as supportive efficacy data for control of saprolegniasis on salmonids from FWS and UMESC efforts. CVM accepted from UMESC as supportive efficacy studies for the control of saprolegniasis on channel catfish (November 16, 2004) and from CVM Office of Research as pivotal efficacy studies for the control of saprolegniasis on rainbow trout (July 19, 2005).

Hydrogen peroxide (external microbicide)—Status: Currently considered as a low regulatory priority drug for use as a fungicide on fish and fish eggs but CVM has encouraged the development of a NADA; was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (Eka Chemicals Inc.) and UMESC; four label claims close to completion: control of mortality due to (1) saprolegniasis on all finfish eggs, (2) bacterial gill disease on all freshwater-reared salmonids, (3) external columnaris disease on all coolwater fish and channel catfish, and (4) saprolegniasis on all finfish.

Progress on hydrogen peroxide (May 15, 2005 to November 9, 2005):

- On September 16, 2005, CVM accepted the Microbial Food Safety submission for Guidance Document #152 and noted that the Human Food Safety Technical Section is now considered complete. CVM provided an FOI summary for human food safety that will be inserted into the Administrative NADA.

- On November 8, 2005, UMESC submitted to CVM the final revised environmental assessment for hydrogen peroxide for use in freshwater culture systems.

- On November 9, 2005, the sponsor, Eka Chemicals, Inc., met with the National Aquaculture NADA Coordinator to discuss the final arrangements for an Administrative NADA on PEROX-AID® (hydrogen peroxide) for the first three broad label claims listed above.

Current status of technical sections on hydrogen peroxide:

- *Product Chemistry*—Accepted by CVM (February 11, 2004).
- *Environmental Safety*—A model was developed by UMESC to estimate discharged environmental concentrations based on UMESC hatchery survey and a point source dilution model from the U.S.

Geological Survey. UMESC wrote an environmental assessment (EA) to support an all fish label claim and submitted it to CVM on March 14, 2000 and the final review by CVM was completed on June 24, 2002 when it was provisionally accepted. CVM required a 21-day chronic toxicity study on daphnia (study completed and summary submitted to CVM February 16, 2005 and final revision of the environmental assessment was submitted to CVM November 8, 2005.

- *Human Food Safety–Toxicology*—Accepted by CVM. The FOI summary was written by CVM on March 22, 2000.
- *Human Food Safety–Residue Chemistry*—Accepted by CVM. The initial FOI summary was written by CVM on March 22, 2000—no tolerances, regulatory methods, or withdrawal times are needed for finfish and their eggs treated with hydrogen peroxide.
- *Human Food Safety–Microbial Safety*—Guidance document #52 accepted by CVM (June 6, 2005); Guidance Document #152 accepted by CVM (September 16, 2005).
- *Human Food Safety*—The Human Food Safety Technical Section is now considered complete. CVM provided an FOI summary for human food safety that will be inserted into the Administrative NADA (September 16, 2005).
- *Target Animal Safety*—CVM accepted as complete from UMESC the target animal safety technical section on all finfish (October 4, 2001) and the target animal safety technical section for all finfish eggs (March 17, 2000, August 16, 2002, and November 26, 2003).
- *Efficacy*—CVM accepted as complete from UMESC the efficacy technical sections 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 efficacy 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 efficacy data from UMESC for the treatment of external parasitic infestations on all salmonids (September 26, 2002).

Oxytetracycline (OTC, oral antibacterial)—Status: Currently approved for control of certain systemic bacterial diseases in catfish, salmonids, and lobsters and as an oral marking agent in Pacific salmon; was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (Phibro Animal Health, formerly Pfizer, Inc.), UMESC, and AADAPP; two label claims close to completion: control of mortality due to (1) systemic columnaris disease in steelhead trout and (2) systemic coldwater disease in all freshwater-reared salmonids.

Progress on oral oxytetracycline (May 15, 2005 to November 9, 2005):

- On September 21, 2005, Phibro Animal Health submitted to CVM the product chemistry package to change from the OTC quaternary salt formulation to the dihydrate salt formulation.

- On October 5, 2005, the National Aquaculture NADA Coordinator, UMESC, AADAPP, University of Arizona, and Phibro met with CVM to discuss the data requirements for microbial food safety for oral OTC. All entities will be involved in developing the documents needed for approval.

- On December 9, 2005, the National Aquaculture NADA Coordinator developed strategic plans to address the microbiological toxicology of residues and microbial food safety data requirements for changes to the oral OTC NADAs.

Current status of technical sections on oral oxytetracycline:

- *Product Chemistry*—Previously accepted by CVM under original NADA from Pfizer, Inc. (now owned by Phibro Animal Health). The sponsor is working on changing the formulation.
- *Environmental Safety*—Previously accepted by CVM under original NADA from Pfizer, Inc. (now owned by Phibro Animal Health). FINFISH: CVM is requiring 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 is preparing under contract with the University of Wisconsin-Madison a model to describe the fate of oxytetracycline released into the environment from aquaculture facilities.

Validation of the estimated model concentrations will be conducted at an aquaculture facility and the results will be submitted as an amendment to the environmental assessment report. PENAEID SHRIMP: University of Arizona—additional data needed to complete the environmental assessment 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 and National Aquaculture NADA Coordinator—in progress. PENAEID SHRIMP: University of Arizona—in progress.
- *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. UMESC submitted a letter package addressing the antimicrobial resistance issues with human food safety; CVM replied that a microbial food safety assessment is required. Efforts by the National Aquaculture NADA Coordinator and the sponsor are underway to address this issue. PENAEID SHRIMP: Accepted as complete from University of Arizona residue depletion study in penaeid shrimp (November 4, 1999).
- *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).
- *Efficacy*—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 AADAPP the efficacy technical section the use of OTC at 3.75 g/100 lb of fish for 10 days as effective in reducing mortality from (1) systemic columnaris disease in steelhead trout and (2) systemic coldwater disease in fingerling coho salmon. The efficacy 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. PENAEID SHRIMP: Accepted as complete from University of Arizona efficacy data to control mortality due to necrotizing hepatopancreatitus in penaeid shrimp (June 28, 2000).

Oxytetracycline (OTC, immersion antibacterial)—Status: No current sponsor for antibacterial use; one label claim close to completion: control of mortality due to external columnaris disease on coolwater and warmwater finfish.

Progress on immersion OTC (May 15, 2005 to November 9, 2005):

- On June 13, 2005, CVM approved the supplemental NADA for Pfizer, Inc.'s oxytetracycline product (TERRAMYCIN-343®) as an otolith marking aid for all fish fry and fingerlings.

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.

- *Efficacy*—On April 8, 2003, CVM responded to an October 28, 2002 submission from UMESC on the efficacy 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 efficacy data may support future pivotal data. Pivotal efficacy studies underway by UMESC on coolwater and warmwater fish for control of (1) bacterial gill disease, (2) external columnaris disease, and (3) systemic columnaris disease.

Pet Fish Therapeutants (various drugs and pesticides)—Status: Major effort to resolve non-food fish issues for these drugs through Minor Use Minor Species legislation.

Potassium Permanganate (external microbicide)—Status: Was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (Carus Chemical Company) and SNARC; one label claim in progress: control of ichthyophthiriasis on channel catfish in earthen ponds with no outflows

Progress on potassium permanganate (May 15, 2005 to November 9, 2005): No progress to report.

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 environmental assessment for all fish to CVM on February 23, 1998; CVM is requiring an environmental assessment. Efforts at Arkansas State University began in January 2002 on environmental fate and effects studies with funding from the Multi-State Conservation Grant Program. The studies are scheduled to be completed in December 2004.
- *Human Food Safety–Toxicology*—Accepted by CVM.
- *Human Food Safety–Residue Chemistry*—CVM accepted as complete from SNARC the human food safety technical section.
- *Target Animal Safety*—SNARC completed a target animal safety study on channel catfish.
- *Efficacy*—SNARC completed pivotal efficacy studies that demonstrate efficacy to prevent Ichthyophthirius on channel catfish and tilapia. SNARC completed controlled efficacy studies for control of Ichthyophthirius on channel catfish and tilapia. A pivotal efficacy study is planned when seasonal water temperatures are optimal for control of Ichthyophthirius on channel catfish. SNARC is also conducting efficacy studies on external columnaris disease in channel catfish.

Praziquantel (trematode and cestode control)—Status: Some interest on the part of potential sponsor in a NADA approval in the United States but needs positive marketing information; has approval in several countries.

Pyceze® (external microbicide)—Status: Sponsor submitted an INAD/NADA letter of intent and summary of all major technical sections; met with CVM on development of data; early development stage.

Romet® (oral antibacterial)—Status: Romet-30® has approvals for control of enteric septicemia in catfish and furunculosis in salmonids; early development stage 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, 2005 to November 9, 2005): 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.

- *Efficacy*—Accepted for control of enteric septicemia in catfish and furunculosis in salmonids by CVM; palatability problems resolved by sponsor.

Sarafloxacin (oral antibacterial)—Status: 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 (CDC) 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 IAFWA Project stakeholders.

Sea Lice Control (various drugs and pesticides)—Status: Various drugs and pesticides (azamethiphos or Salmosan™, cypermethrin or Excis™) were previously pursued by the United States 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.

- On November 22, 2005, Veterinary Drugs Directorate of Health Canada amended the Maximum Residue Limit for Slice® to 42 ppb and revised the withdrawal time to 68 days under the Emergency Drug Release Program.

Trichlorfon (external parasite control)—Status: Some interest on the part of potential sponsor in a NADA approval in the United States; has approvals in several countries; several Special Local Need registrations obtained in 1998 for control of predaceous insects.

ANESTHETICS AND SEDATIVES

AQUACALM®—Status: Preliminary development by sponsor (Syndel Laboratories Ltd.).

- On August 26, 2005, the National Aquaculture NADA Coordinator and Syndel Laboratories Ltd. met with CVM to discuss the development of Aquacalm® for ornamental fish.

AQUI-S®—Status: Was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor (AQUI-S New Zealand LTD.), UMESC, and AADAPP; two label claims in progress: zero withdrawal anesthetic and sedative in (1) all freshwater finfish and (2) saltwater salmonids for short-exposure handling (rested harvest, spawning, marking, tagging, measuring, and sexing).

Progress on AQUI-S® (May 15, 2005 to November 9, 2005):

- The Center for Veterinary Medicine (CVM) accepted from the Aquatic Animal Drug Approval Partnership Program (AADAPP) as pivotal studies on juvenile and adult channel catfish and tilapia (June 17, 2005) and on subadult pallid sturgeon, juvenile largemouth bass, and adult smallmouth bass (July 1, 2005). CVM accepted as supportive studies on juvenile pallid sturgeon, adult largemouth bass, and juvenile smallmouth bass (July 1, 2005).

- On June 24, 2005, CVM concurred with the no-observed-adverse-effect level of 230 mg/kg/day that the National Toxicology Program (NTP) had established from the continuous breeding study in rats.

- On September 1, 2005, the North Central Regional Aquaculture Center (NCRAC) sent for review the Upper Midwest Environmental Sciences Center (UMESC) proposal entitled “Drug approval research on AQUI-S®”. Comments were received on October 7, 2005 and the National Aquaculture NADA Coordinator provided a review of the UMESC response to those comments on October 19, 2005. The proposal is awaiting final approval from the US Department of Agriculture.

- On September 16, 2005, the International Association of Fish and Wildlife Agencies (IAFWA) voted to fund a Multi-State Conservation Grant for (1) residue depletion studies on coolwater and warmwater fish species to be conducted by UMESC, (2) target animal safety studies on coolwater and warmwater fish species to be conducted by AADAPP, and (3) coordination of these efforts by the National Aquaculture NADA Coordinator.

Current status of technical sections on AQUI-S®:

- *Product Chemistry*—The sponsor (AQUI-S New Zealand LTD.) submitted studies on activity of AQUI-S® to CVM (October 2003); the complete manufacturing package is in progress.
- *Environmental Safety*—The sponsor submitted a summary to CVM in the late 1990s and environmental biodegradation studies in freshwater and saltwater (November 24, 2003). The sponsor is conducting a series of Ecotoxicity and physico-chemical studies in 2004 and 2005.
- *Human Food Safety–Toxicology*—The sponsor conducted a review of the mammalian safety literature to determine whether to continue with the original active ingredient in light of National Toxicology Program (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 but the final report will not be available until late 2006 or early 2007. The sponsor 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 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 and accepted June 7, 2005) and continuous breeding study (November 26, 2004 and accepted June 24, 2005).
- *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 is planning to conduct a pivotal total residue depletion study after the pilot studies are completed and radiolabeled material has been obtained. The National Aquaculture NADA Coordinator obtained funding from NCRAC (February 7, 2004) for the radiolabeled material that is needed to the total residue depletion study on rainbow trout, a surrogate for all salmonids. UMESC conducted the laboratory phase of the total residue depletion study and is in the process of writing up the final report.
- *Target Animal Safety*—Preliminary toxicity studies have been completed at UMESC on a variety of fish species but UMESC will not perform any other studies because funds were diverted to fulfill the need for human food safety studies. Pivotal target animal safety studies on salmonids were started in March 2005 by AADAPP. The sponsor 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).
- *Efficacy*—Preliminary efficacy studies were completed at UMESC on a variety of fish species. Pivotal efficacy studies will be performed by AADAPP on a variety of fish species but UMESC will not perform any other studies because funds were diverted to fulfill the need for human food safety studies. The sponsor submitted to CVM pivotal efficacy studies on Atlantic salmon completed in Canada (July 6, 2004) and CVM declared them as supportive (May 17, 2005). CVM accepted as pivotal one study on shovelnose sturgeon (June 24, 2004), one on hybrid striped bass (September 23, 2004), one on rainbow trout (November 12, 2004), studies on juvenile and adult channel catfish and tilapia (June 17, 2005) and subadult pallid sturgeon and juvenile largemouth and smallmouth bass (July 1, 2005). CVM accepted as supportive (1) five efficacy studies on salmonids (January 29, 2004 and July 30, 2004), (2) two on hybrid striped bass (January 29, 2004 and August 13, 2004), (3) largemouth bass (October 12, 2004), (4) tilapia (August 13, 2004), (5) hybrid carp/goldfish (August 13, 2004,), and (6) juvenile pallid sturgeon and adult largemouth and smallmouth bass (July 1, 2005). AADAPP submitted additional efficacy studies on a variety of species in 2005.

Benzocaine—Status: Major effort by IAFWA Project for NADA approval terminated because of decision by IAFWA Project stakeholders to select AQUI-S® as the candidate anesthetic in the U.S. public aquaculture sector; no known drug approval activities underway.

Clove oil—Status: Oil of cloves (eugenol) is considered Generally Recognized as Safe (GRAS) 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 and no sponsor

has come forward; no known drug approval activities underway. CVM provided guidance on the use of clove oil in Guidance for Industry #150: Status of Clove Oil and Eugenol for Anesthesia of Fish.

The National Aquaculture NADA Coordinator has provided CVM with information from the literature regarding detailed composition of clove oil (May and June 2004).

MS-222—Status: Two approved NADAs for MS-222 as an anesthetic with a 21-day withdrawal time.

SPAWNING AND GENDER MANIPULATION AIDS

Crude Carp Pituitary (CCP)—Status: 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, 2005 to November 9, 2005): 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 not decided 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 for crude carp pituitary to the National Research Support Project-7 (NRSP-7) for transmittal to CVM.
- *Efficacy*—Accepted as complete from NRSP-7 by CVM as a spawning aid in freshwater-reared female finfish (July 17, 2002).

Human Chorionic Gonadotropin (hCG)—Status: 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)—Status: Auburn University gained an INAD for LHRHa in the Spring 2003; early development stage.

17 α-methyltestosterone (MT)—Status: Sponsor, Rangen, Inc. is developing NADA package; INAD sponsors actively pursuing a NADA approval; one label claim close to completion: masculinization of female early life-stage tilapia.

Progress on MT (May 15, 2005 to November 9, 2005):

- The University of Wisconsin-Madison submitted protocols through UMESC to CVM for the following: (1) MT stability feed studies (July 20, 2005; revision November 4, 2005)) and (2) MT biodegradation study (July 20, 2005; revision October 26, 2005).

- On August 30, 2005, Southern Illinois University submitted a MT protocol through AADAPP for a pivotal target animal safety in tilapia to CVM for review.

- On July 22, 2005, CVM established an INAD (#11-395) for MT at UMESC.

- On December 2, 2005, CVM accepted the analytical method to detect MT in the feed developed by UW-M. The method now needs to be written in a Standard Operating Procedure format by UW-M for the method to be transferred to another testing laboratory.

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. The University of Wisconsin-Madison was selected as the contractor to complete these requirements and is conducting the studies starting in fall 2004. CVM accepted the analytical method to detect MT in feed (December 2, 2005).
- *Environmental Safety*—Auburn University received a response from CVM on November 8, 1999 regarding the revised environmental assessment for MT that requested additional information, a biodegradation study, and a more sensitive method to detect MT in water. The University of Wisconsin-Madison was selected as the contractor to complete these requirements and is conducting the studies starting in fall 2004.
- *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 Southern Illinois University 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; Southern Illinois University was selected to perform the target animal safety study on tilapia and the protocol is under development.
- *Efficacy*— Cornell University submitted to CVM a final report on the efficacy 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; AADAPP received authorization for a INAD to collect pivotal and supportive efficacy data on June 4, 2004; North Central Regional Aquaculture Center representatives are coordinating a compassionate INAD on percids.

Ovaplant™ and Ovaprim™C—**S**tatus: Sponsor recently submitted INAD letter of intent; early development stage.

- On January 19, 2005, the National Aquaculture NADA Coordinator met with Syndel Laboratories Ltd. to discuss the development of Ovaprim™ for ornamental fish.

CHEMICAL MARKING AGENTS

Calcein—Status: Have sponsor (Western Chemicals Inc.); early development stage.

Oxytetracycline (immersion)—Status: APPROVED: marking aid by immersion for all fish with three NADA sponsors.

- On June 13, 2005, CVM approved the supplemental NADA for Pfizer, Inc.'s oxytetracycline product (TERRAMYCIN-343®) as an otolith marking aid for all fish fry and fingerlings.

Strontium Chloride—Status: Western Chemical Inc. is the sponsor; some work completed in Alaska; some efficacy studies underway under Western NRSP-7.

PISCICIDES—Rotenone and antimycin are used by hatcheries in resource agencies and private aquaculture facilities to control diseases in cultured fish and undesirable fish in ponds.

- The Fishery Management Chemicals Subcommittee (FMCS) of the American Fisheries Society (AFS) gave a training course for piscicide use with aid from the FWS National Conservation Training Center in West Virginia in October 2005. FMCS is working with FWS to develop a national accreditation for piscicide applicator certification using completion of this course as the standard.

- The National Aquaculture NADA Coordinator, a FMCS representative, and a FWS representative met with the U.S. Environmental Protection Agency on October 31, 2005 to discuss the reregistration of antimycin and rotenone and the remaining data requirements.

- FMCS sponsored a symposium at the AFS annual meeting on September 13, 2005 entitled "National and International Challenges and Lessons Learned on Fish Management Chemicals."

PUBLIC INFORMATION AND MEETINGS

Meeting on Microbial Food Safety Data Requirements for Oral OTC and Chloramine-T

The National Aquaculture NADA Coordinator arranged a meeting on October 5, 2005 with the CVM Microbial Food Safety Team, other CVM divisions and offices, UMESC, AADAPP, University of Arizona, and the oral OTC sponsor (Phibro) to discuss the data requirements for microbial food safety for oral OTC and chloramine-T. CVM provided guidance on how to proceed on each drug. The National Aquaculture NADA Coordinator will develop the microbial food safety documents for chloramine-T and developed strategic plans to address the microbiological toxicology of residues and microbial food safety data requirements for changes to the oral OTC NADAs.

IAFWA Drug Approval Working Group (DAWG) for the Federal-State Aquaculture Drug Approval Partnership Project; known as the IAFWA Project (includes nine drugs: AQUI-S®, chloramine-T, copper sulfate, florfenicol, formalin, hydrogen peroxide, oral oxytetracycline, immersion oxytetracycline, and potassium permanganate)

The DAWG held a meeting on September 16, 2005 in Nashville, Tennessee. The National Aquaculture NADA Coordinator provided documents before the meeting on the following:

Agenda for the Pre-DAWG meeting (8:30 AM to 12 noon, Thursday, September 15, 2005)
Agenda for the DAWG meeting (1:00 PM to 5:00 PM, Thursday, September 15, 2005)
Final submissions projected for IAFWA Project drugs: Label claims with final submissions projected for 2005-2007 and Label claims with final submissions projected for 2008-2009
IAFWA Project: Progress September 2004 to August 2005
IAFWA Project: Remaining requirements as of September 15, 2005
Responsibilities and acceptances for public partners for planned IAFWA Project drug label claims (July 1994 to August 2005)
Total public funding for the IAFWA Project by partner and funding sources (1994-2005) and Actual (1994-2005) and estimated (2006-2009) public funding for the IAFWA Project
Statement of continued support for the Federal-State Aquaculture Drug Approval Partnership Project
Status of DAWG Action Items—Recently completed (March 2005 to August 2005) and in progress
DAWG Action Items completed (March 2004 to February 2005)
Survey on unmet label claim needs for the IAFWA Project Exit Strategy
Original proposal for "Approval of Drugs for Public Fish Production" (March 4, 1994)

The National Aquaculture NADA Coordinator indicated that approvals are very near because administrative NADAs will be submitted soon for initial approvals of IAFWA Project drugs. She noted that there should be final submissions for original or supplemental approvals for (1) one drug with one label claim in 2005 (florfenicol approved for ESC on October 24, 2005), (2) one drug with three label claims in early 2006, (3) six drugs and 12 label claims in late 2006 through 2007, and (3) three drugs and four label claims in 2008 to 2009. CVM indicated that the past six months have been exceedingly productive toward drug approvals. AADAPP, UMESC, and the National Aquaculture NADA Coordinator presented their work plans for 2006.

In her mailing of August 29, 2005, the National Aquaculture NADA Coordinator provided a draft of the "Survey on Unmet Label Claim Needs for the IAFWA Project Exit Strategy." The revised survey was sent to state stakeholders who had funded the IAFWA Project to determine if the IAFWA Project is meeting their label claim needs. The National Aquaculture NADA Coordinator wrote the cover letter and the survey was sent out by Doug Hansen under the IAFWA umbrella on September 21, 2005. [As of December 22, 2005, 36 surveys (only CA and LA remain) have been returned. The due date was October 28, 2005.]

Doug Hansen reported that the Multi-State Conservation Grant proposal on AQUI-S® was approved for funding by the IAFWA. It was the third highest rated proposal out of 60. The scoring was 45.4 of a possible 50 points. The Chair of the Grants Committee asked for assurances from Doug that this would be the last aquaculture drug project and Doug assured him it would be. The funds will be made available starting January 1, 2006. The Midwest Fish and Wildlife Association is feeling really good about the voting and the fact that they put forward such a good proposal.

Annual Drug Approval Coordination Workshop

On August 2-3, 2005, AADAPP and UMESC hosted the 11th Annual Drug Approval Coordination Workshop in Bozeman, Montana that centered on the progress being made on the drugs in the Federal-State Aquaculture Drug Approval Partnership Project (a project under the auspices of the International Association of Fish and Wildlife Agencies=IAFWA; project known as the IAFWA Project). The presentations included (1) history and partnerships of the IAFWA Project, (2) update on MUMS, (3) environmental assessment requirements for approval, (4) regulation of biologics, (5) update on NRSP-7 Minor Use Animal Drug Program, (6) completing a Technical Section, ((7) overview of microbial food safety evaluation, (8) human food safety for approval of antimicrobial new animal drugs, (9) ecological risk assessment for veterinary products, and (10) progress being made toward approval of all aquaculture drugs.

Joint Subcommittee on Aquaculture (JSA) Working Group on Quality Assurance in Aquaculture Production

The JSA Working Group on Quality Assurance in Aquaculture Production met on October 12, 2005 in Washington, DC. The topics of discussion were (1) Federal Advisory committee guidelines, (2) EPA registered pesticides and related topics, (3) dialogue relating to products as drugs or pesticides, (3) report on new Biologics Forum activities and issues, (4) report on National Research Forum, (5) plans to update the Guide to Drug, vaccine, and pesticide use in aquaculture, (6) JSA Aquaculture Resource Guide, (7) use of aquaculture drug approval status matrix, (8) restructuring the 5-year Strategic Plan, and (9) updates from agencies.

Meeting on PEROX-AID®

On November 9, 2005, the sponsor, Eka Chemicals, Inc., met with the National Aquaculture NADA Coordinator to discuss the final arrangements for an Administrative NADA on PEROX-AID® (hydrogen peroxide) for the first three broad label claims: (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.

Minor Use and Minor Species Animal Health Act of 2004 (MUMS)

The provision of the new MUMS Act is currently being implemented by CVM is the designation provision that gives sponsors seven years of marketing exclusivity. Schering-Plough Animal Health obtained final MUMS designation shortly before it obtained the approval of florfenicol for control of mortality due to enteric septicemia in catfish and Eka Chemicals, Inc. received final MUMS designation for three label claims on December 1, 2005.

The National Aquaculture NADA Coordinator is providing guidance and draft response letters for the final designations for several sponsors.

Animal Drug User Fee Act of 2003 (ADUFA)

The National Aquaculture NADA Coordinator is providing guidance and draft response letters to several sponsors because ADUFA requires that each sponsor send in a renewal letter annually.

Funding Needs

The National Aquaculture NADA Coordinator stayed 35 hours per week on May 15, 2005 because her special appeal to adequately support this position was heard. Contributions totaled $117,500 for Year 11 (May 15, 2005 to May 14, 2006).

PUBLICATIONS, MANUSCRIPTS, PAPERS PRESENTED, AND SPECIAL REPORTS

PUBLICATIONS

MacMillan, J.R., R.A. Schnick, and G. Fornshell. 2005. U.S. aquaculture. Alliance for the Prudent Use of Antibiotics, Facts about Antibiotics in Animals and their Impact on Resistance (FAAIR) Project. Perspectives in Veterinary Medicine. In press.

Schnick, R.A. 2005. Zero withdrawal anesthetic for all fish and shellfish: Need and candidates. Fisheries. In press.

PAPERS PRESENTED

Schnick, R.A. 2005. Upcoming Aquaculture Drug Approvals. American Fisheries Society, Fish Health Section Annual Meeting, Bloomington, Minnesota, July 27-29, 2005.

Schwaab, E. and R.A. Schnick. 2005. Summary of IAFWA Project: History and Partnerships. 11th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 2-3, 2005.

MacMillan, R. and R.A. Schnick. 2005. MUMS Update. 11th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 2-3, 2005.

Schnick, R.A. 2005. NADA Coordinator Perspective (All Drugs). 11th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 2-3, 2005.

Schnick, R.A. 2005. Challenges in the Approval/Registration Process for Fish Management Chemicals: Stakeholders' Perspectives. Symposium on National and International Challenges and Lessons Learned on Fish Management Chemicals. American Fisheries Society Annual Meeting, Anchorage, Alaska, September 11-15, 2005.

Schnick, R.A. 2005. Brief Overview—Recent Developments and Highlights on Drug Approval Progress. Drug Approval Working Group Meeting, Nashville, Tennessee, September 15, 2005.

Schnick, R.A. 2005. Overview of the Status of (1) Expansion and Extension of the Oxytetracycline (OTC) Label Claims, (2) Initial Label Claims for Chloramine-T, (3) Microbial Food Safety Submissions on These and Other Aquaculture Drugs, and (4) Information on Public and Private aquaculture Production statistics. Meeting on Microbial Food Safety Data Requirements for Oral Oxytetracycline and Chloramine-T for Approval in U.S. Commercial and Public Freshwater Aquaculture, Rockville, Maryland, October 5, 2005.

SPECIAL REPORTS

Schnick, R.A. 2005. MUMS designation requests for aquaculture drugs. Submitted to CVM. June 16, 2005. 2 pp.

Schnick, R.A. 2005. Statement on need for change in NCRAC and WRAC funded studies. Submitted to Ted Batterson, NCRAC and Graham Young, WRAC. June 16, 2005. 3 pp.

Schnick, R.A. 2005. National Coordinator for Aquaculture New Animal Drug Applications (NADAs). Tenth annual report of activities, May 15, 2004 to May 14, 2005. Submitted to Ted Batterson, North Central Regional Aquaculture Center, East Lansing, Michigan. June 20, 2005. 27 pp.

Schnick, R.A. 2005. Revised Call for Statements of Interest: Drug approval research on AQUI-S®. Submitted to Ted Batterson for distribution to researchers. June 23, 2005. 3 pp.

Schnick, R.A. 2005. Draft label claims for IAFWA Project drugs. Submitted to AADAPP and UMESC for the upcoming Drug Approval Coordination Workshop. July 13, 2005. 5 pp.

Schnick, R.A. 2005. 2005 annual report of the AFS Task Force on Fishery Chemicals. Submitted to the Governing Board and AFS President, Barb Knuth, Bethesda, Maryland. August 16, 2005. 4 pp.

Schnick, R.A. 2005. Request for meeting to discuss the microbial food safety data requirements for the expansion and extension of the oxytetracycline (OTC) label claims (Terramycin for Fish®); NADA #038-439, #008-804, INAD #11-368) and the initial label claims for chloramine-T (Halamid®; INAD #8086). Submitted to Microbial Food Safety Team (HFV-157), CVM. August 17, 2005. 3 pp.

Schnick, R.A. 2005. (1) Agenda for the Pre-DAWG meeting (1 pp.); (2) Agenda for the DAWG meeting (1 pp.); (3) Final submissions projected for IAFWA Project drugs: Label claims with final submissions projected for 2005-2007 and Label claims with final submissions projected for 2008-2009 (1 pp.); (4) IAFWA Project: Progress September 2004 to August 2005 (4 pp.); (5) IAFWA Project: Remaining requirements as of September 15, 2005 (4 pp.); (6) Responsibilities and acceptances for public partners for planned IAFWA Project drug label claims (July 1994 to August 2005) (3 pp.); (7) Total public funding for the IAFWA Project by partner and funding sources (1994-2005) and Actual (1994-2005) and estimated (2006-2009) public funding for the IAFWA Project (1 pp.); (8) Statement of continued support for the Federal-State Aquaculture Drug Approval Partnership Project (1 pp.); (9) Status of DAWG Action Items—Recently completed (March 2005 to August 2005) and in progress (3 pp.); (10) DAWG Action Items completed (March 2004 to February 2005) (2 pp.); (11) Survey on unmet label claim needs for the IAFWA Project Exit Strategy (11 pp.); and (12) Original proposal for "Approval of Drugs for Public Fish Production" (March 4, 1994) (1 pp.). Submitted to the Drug Approval Working Group members in preparation for September 16, 2005 meeting. August 29, 2005.

Schnick, R.A. 2005. Table 1. Approvals gained and final submissions projected for IAFWA Project drugs (as of September 20, 2005. Submitted to Drug Approval Working Group members and state supporters. September 20, 2005. 1 pp.

Schnick, R.A. 2005. 2005 Survey on Unmet Label Claim Needs for the IAFWA Project Exit Strategy. Sent to 38 state natural resources agencies that supported the IAFWA Project. September 21, 2005. 10 pp.

Schnick, R.A. 2005. Matrices for tracking major aquaculture drug approval development (9/30/05). Submitted to National Aquaculture NADA Coordinator website. October 9, 2005. 26 pp.

Schnick, R.A. 2005. Roz's Corner: AADAP Newsletter Contribution. Submitted to AADAP. October 10, 2005. 1 pp.

Schnick, R.A. 2005. Response to NCRAC Contamination Information Project Review Committee. Submitted to Ted Batterson, North Central Regional Aquaculture Center. October 10, 2005. 3 pp.

Schnick, R.A. 2005. Contribution to Fish Health Section Newsletter. Submitted to the AFS, Fish Health Section. October 24, 2005. 1 pp.

Schnick, R.A. 2005. Annual report for NCRAC funding: National Coordinator for Aquaculture New Animal Drug Applications, September 1, 2004 to August 31, 2005. Submitted to Ted Batterson, North Central Regional Aquaculture Center. October 29, 2005. 6 pp.

Schnick, R.A. 2005. News Release: Major Aquaculture Drug Approval: Great news!!! Florfenicol (AQUAFLOR®) was approved for control of mortality due to enteric septicemia in catfish (October 24, 2005). Submitted to National Aquaculture NADA Coordinator website. November 1, 2005. 1 pp.

Schnick, R.A. 2005. Study and activity schedules for 17 α-methyltestosterone (MT). Submitted to interested MT entities. November 7, 2005. 4 pp.

Schnick, R.A. 2005. Draft Administrative NADA for PEROX-AID®. Submitted to Eka Chemicals, Inc. November 9, 2005 (revised December 5, 2005). 38 pp.

Schnick, R.A. 2005. Final minutes to Drug Approval Working Group Meeting, Nashville, Tennessee. Submitted to Drug Approval Working Group Members. November 28, 2005. 12 pp.

Schnick, R.A. 2005. Presubmission conference agreements from October 5, 2005 Microbial Food Safety Meeting on oxytetracycline (OTC). Submitted to participants in the Microbial Food Safety Meeting of October 5, 2005. December 1, 2005. 3 pp.

Schnick, R.A. 2005. Strategic plans to address the microbiological toxicology of residues and microbial food safety data requirements for changes to the oxytetracycline (OTC) New Animal Drug Applications. Submitted to participants of the Microbial Food Safety Meeting of October 5, 2005. December 9, 2005. 4 pp.

Schnick, R.A. 2005. Response for specific changes to the Memorandum of Conference on October 5, 2005. Submitted to CVM's Microbial Food Safety Team (HFV-157). December 9, 2005. 4 pp.

Schnick, R.A. 2005. Eleventh mid-year report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2005 to November 9, 2005). Submitted to Ted Batterson, North Central Regional Aquaculture Center for distribution to contributors to this position. December 23, 2005. 20 pp.