

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

THIRTEENTH MID-YEAR REPORT OF ACTIVITIES

May 15, 2007 to November 9, 2007

Submitted by

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ACRONYMS AND ABBREVIATIONS USED

AADAP	Aquatic Animal Drug Approval Partnership Program
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)
°C	degrees Celsius
CCP	crude carp pituitary
CVM	Center for Veterinary Medicine
DAWG	Drug Approval Work Group
EA	environmental assessment
EPA	U.S. Environmental Protection Agency
ESC	enteric septicemia of catfish
FOI	Freedom of Information
FMCS	Fishery Management Chemicals Subcommittee
FWS	U.S. Fish and Wildlife Service
g	gram
GFI	Guidance for Industry document
GRAS	Generally Recognized as Safe
INAD	Investigational New Animal Drug
kg	kilogram(s)
lb	pound(s)
mg	milligram(s)
MOC	Memorandum of Conference
MT	17 α -methyltestosterone
MUMS	Minor Use and Minor Species
NADA	New Animal Drug Application
NCRAC	North Central Regional Aquaculture Center
NHP	necrotizing hepatopancreatitis
NRSP-7	National Research Support Project Number Seven (7)
NTP	National Toxicology Program
OTC	oxytetracycline
ppm, ppb	parts per million, parts per billion
p-TSA	para-toluenesulfonamide
®	Registered name
SNARC	Harry K. Dupree Stuttgart National Aquaculture Research Center
SPAH	Schering-Plough Animal Health
™	trademark
UMESC	Upper Midwest Environmental Sciences Center
UW-M	University of Wisconsin-Madison

**THIRTEENTH MID-YEAR SUMMARY OF ACTIVITY HIGHLIGHTS FOR THE NATIONAL
COORDINATOR FOR AQUACULTURE NEW ANIMAL DRUG APPLICATIONS (NATIONAL
AQUACULTURE NADA COORDINATOR)
(May 15, 2007 to November 9, 2007)**

MAY 15, 2007 TO NOVEMBER 9, 2007 APPROVALS!!

- (1) ABBREVIATED NADA APPROVAL: FORMACIDE-B[®] 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: AQUAFLO[®]R (FLORFENICOL) FOR CONTROL OF FURUNCULOSIS ON FRESHWATER-REARED SALMONIDS (APPROVED OCTOBER 26, 2007)

CHLORAMINE-T (HALAMID[®])—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 largemouth bass

- (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[®] (chloramine-T) prepared by the National Aquaculture NADA Coordinator with input from UMESC. The revision was based on the agency's comments.
- (2) On September 25, 2007, AADAP submitted pivotal effectiveness studies on Halamid[®] (chloramine-T) to CVM for control of mortality in largemouth bass due to external columnaris disease.
- (3) On October 12, 2007, UMESC received word that its final EA on Halamid[®] (chloramine-T) is acceptable 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) CVM reviewed the copper sulfate final EA for earthen pond systems from SNARC and required additional changes.

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 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 (AQUAFLO[®]R)—ORAL ANTIBACTERIAL

Several label claims under development

- (1) On April 19, 2007, CVM accepted from AADAP as complete the Effectiveness Technical Section 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 to be complete for control of mortality in hybrid striped bass due to *Streptococcus iniae*.
- (3) ON OCTOBER 26, 2007, CVM APPROVED AQUAFLO[®]R FOR A SUPPLEMENTAL APPROVAL FOR CONTROL OF MORTALITY IN FRESHWATER-REARED SALMONIDS DUE TO FURUNCULOSIS. AQUAFLO[®]R IS SPONSORED BY SCHERING-PLOUGH ANIMAL HEALTH.

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) The CVM Office of Research conducted formalin pivotal effectiveness studies 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.

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

One label claim in progress: (1) control of mortality on all warmwater fish due to saprolegniasis

- (1) On April 20, 2007, Eka Chemicals, Inc. submitted a Special Supplement on minor changes to the labeling 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 Kona Blue Aquatic Farms in Kona, Hawaii to discuss developing data to support a label claim for controlling certain external parasites with 35% PEROX-AID[®] (hydrogen peroxide) on the major fish species reared by Kona Blue, Kona Kampachi[®].
- (3) On October 15, 2007, CVM accepted the special supplement for minor changes in the 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[®].

ISOEUGENOL (AQUI-S[®])—ANESTHETIC

One initial label claim in progress: (1) zero withdrawal anesthetic for sedation to handleable condition of all freshwater fish

- (1) On April 27, 2007, AADAP and UMESC announced they were suspending all research until the completion of the NTP review scheduled for February 2008 on studies conducted on mice and rats. The review had originally been scheduled for May 2007 but due to other priorities was delayed.
- (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 to be complete for freshwater salmonids.

17 α -METHYLTESTOSTERONE=MT (MASCULINIZING FEED FOR TILAPIA[®])—GENDER MANIPULATION AID

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

- 1) On July 30, 2007, interested parties met in Bozeman, Montana to discuss EA issues and to determine a course of action.

- 2) On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17 α -methyltestosterone that were conducted and developed by the University of Wisconsin-Madison.
- 3) On November 5, 2007, AADAP requested that CVM consider the Effectiveness Technical Section to be complete for the use of MT to produce predominantly male populations of tilapia.

OXYTETRACYCLINE DIHYDRATE (TERRAMYCIN[®] 200 FOR FISH)—ORAL ANTIBACTERIAL
Three supplemental label claims close to completion: control of mortality due to (1) systemic columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) systemic 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 April 13, 2007, UMESC submitted the final amended EA on oxytetracycline dihydrate to CVM. CVM requested additional information and UMESC provided it on August 7, 2007.
- (2) 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.
- (3) On July 23, 2007, Phibro Animal Health submitted to CVM a Labeling Technical Section to add the three new label claims and request the removal of the warning statement concerning use below 9 degrees C.
- (4) On July 25, 2007, CVM accepted the justification for accepting the effectiveness studies on freshwater-reared steelhead trout to be sufficient to satisfy the effectiveness requirements for all freshwater-reared *Oncorhynchus mykiss*.

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 Syndel Laboratories, LTD, the sponsor of Ovaprim[®], for the induction of spawning in ornamental fish.

GENERAL

- (1) On July 18, 2007, the National Aquaculture NADA Coordinator gave an eight-hour presentation 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 USA, (2) our experience with various successful partnerships, and (3) insight into expediting the aquaculture drug approval processes in Canada.

- (2) The designation provision of the Minor Use and Minor Species Animal Health Act of 2004 (MUMS) gives sponsors seven years of marketing exclusivity. So far, the MUMS Office has granted 50 designations, 44 of those are to aquaculture drug sponsors who received extensive help from the National Coordinator for Aquaculture NADAs. The most recent MUMS designations are three for Pfizer Animal Health's Terramycin 343[®] (oxytetracycline hydrochloride) on June 7, 2007 and one for Aquatic Life Sciences, Inc.'s Ovaplant[®] (salmon gonadotropin releasing hormone analog) on May 25, 2007. There have been three NADA approvals of MUMS designations for Eka Chemicals, Inc.'s 35%PEROX-AID[®] and two NADA approvals and one Conditional Approval of MUMS designations for Schering-Plough Animal Health's Aquaflor[®].
- (3) The National Aquaculture NADA Coordinator, as Chair of the AFS Task Force on Fishery Chemicals, provided comments in July 2007 to the U.S. Environmental Protection Agency (EPA) on the Reregistration Eligibility Decisions regarding rotenone and antimycin, the piscicides used in controlling unwanted fish in aquaculture ponds.
- (4) From July to September 2007, the National Aquaculture NADA Coordinator gave presentations on innovations and status of aquaculture drug approvals at the 144th American Veterinary Medical Association Convention (Washington, DC), 13th Annual Drug Approval Coordination Workshop (Bozeman, Montana), Disease Management Strategies for the Aquatic Environment: Alternative and Innovations Symposium (San Francisco, California), and the Association of Fish and Wildlife Agencies, Drug Approval Working Group meetings (Louisville, Kentucky).

PUBLICATIONS, PRESENTATIONS, AND SPECIAL REPORTS

- The National Coordinator for Aquaculture New Animal Drug Applications had one publication in press, presented 9 papers, and wrote 27 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 November 9, 2007 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 November 9, 2007):

- (1) No progress to report.

CHLORAMINE-T (HALAMID®)—EXTERNAL ANTIBACTERIAL

Was an AFWA Project drug and now under development by the sponsor (Axcentive SARL), AADAP, and UMESC; 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 hybrid striped bass

Progress on chloramine-T (May 15, 2007 to November 9, 2007):

- (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® (chloramine-T) prepared by the National Aquaculture NADA Coordinator with input from UMESC. The revision was based on the agency's comments.
- (2) On September 25, 2007, AADAP submitted pivotal effectiveness studies to CVM for control of mortality in largemouth bass due to external columnaris disease.
- (3) On October 12, 2007, UMESC received word that its final EA on Halamid® (chloramine-T) is acceptable to CVM.

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® to CVM on May 22, 2006. The complete package is scheduled for December 2007.
- *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. CVM declared that para-toluenesulfonamide (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 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 in November 2006 to CVM; Accepted from Axcentive SARL GFI #152 (May 2007). The GFI #159 revision was submitted by Axcentive on July 27, 2007.
- *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) and (2) 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 and now under development by the sponsor (Phelps Dodge Sales Company) and SNARC; 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 November 9, 2007):

- (1) CVM reviewed the copper sulfate final EA for earthen pond systems from SNARC and required additional changes.

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 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.
- *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. SNARC submitted to CVM the label claim and other information on June 30, 2006 to complete this technical section.
- *Effectiveness*—CVM accepted as complete from SNARC the effectiveness technical section for control of ichthyophthiriasis on all fish. 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.

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 November 9, 2007):

- (1) On January 11, 2007, CVM accepted as complete the GFI document #159 on the safety of 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.

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 (AQUAFLO[®])—ORAL ANTIBACTERIAL

The sponsor, SPAH, recently gained Aquaflor[®] original and supplemental approvals to control mortality due to: (1) enteric septicemia in catfish (October 24, 2005), (2) coldwater disease in freshwater-reared salmonids (March 19, 2007), and (3) furunculosis in freshwater-reared salmonids (October 26, 2007); and one conditional approval for the control of mortality in catfish due to columnaris disease (April 18, 2007); was an AFWA Project drug and now under development by the sponsor, UMESC, AADAP, and Mississippi State University; Several label claims under development

Progress on florfenicol (May 15, 2007 to November 9, 2007):

- (1) On April 19, 2007, CVM accepted from AADAP as complete the Effectiveness Technical Section 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 to be complete for control of mortality in hybrid striped bass due to *Streptococcus iniae*.
- (3) ON OCTOBER 26, 2007, CVM APPROVED AQUAFLO[®] FOR A SUPPLEMENTAL APPROVAL FOR CONTROL OF MORTALITY IN FRESHWATER-REARED SALMONIDS DUE TO FURUNCULOSIS.

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 a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsors (Natchez Animal Supply Company, Western Chemical Inc., Argent Chemical Laboratories, B.L. Mitchell, Inc.), UMESC, and CVM's Office of Research; 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 November 9, 2007):

- (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 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 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! Low regulatory priority drug for use as a fungicide on fish and fish eggs was rescinded May 2, 2007; was an AFWA Project drug and now under development by the sponsor (Eka Chemicals Inc.) and UMESC; one additional label claim close to completion: control of mortality due to (1) saprolegniasis on all finfish.

Progress on hydrogen peroxide (May 15, 2007 to November 9, 2007):

- (1) On April 20, 2007, Eka Chemicals, Inc. submitted a Special Supplement on minor changes to the labeling 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 Kona Blue Aquatic Farms in Kona, Hawaii to discuss developing data to support a label claim for controlling certain external parasites with 35% PEROX-AID[®] (hydrogen peroxide) on the major fish species reared by Kona Blue, Kona Kampachi[®].
- (3) On October 15, 2007, CVM accepted the special supplement for minor changes in the 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[®].

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 and now under development by the sponsor (Phibro Animal Health, formerly Pfizer, Inc.), UMESC, and AADAP; three supplemental label claims close to completion: control of mortality due to (1) systemic columnaris disease in freshwater-reared *Oncorhynchus mykiss* and (2) systemic 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 November 9, 2007):

- (1) On April 13, 2007, UMESC submitted the final amended EA on oxytetracycline dihydrate to CVM. CVM requested additional information and UMESC provided it on August 7, 2007.

- (2) 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.
- (3) On July 23, 2007, Phibro Animal Health submitted to CVM a Labeling Technical Section to add the three new label claims and request the removal of the warning statement concerning use below 9 degrees C.
- (4) On July 25, 2007, CVM accepted the justification for accepting the effectiveness studies on freshwater-reared steelhead trout to be sufficient to satisfy the effectiveness requirements for all freshwater-reared *Oncorhynchus mykiss*.

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 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 submitted an EA on oxytetracycline to CVM on April 3, 2006 and a final EA on April 13, 2007. 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) a high performance liquid chromatography (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. Phibro submitted request for Technical Section Complete Letter (July 2, 2007). 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); 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) systemic columnaris disease in steelhead trout and (2) systemic coldwater disease in fingerling coho salmon. 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. 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 and now under development by the sponsor (Pfizer Animal Health) and UMESC; 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 November 9, 2007):

- (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 and now under development by the sponsor (Carus Chemical Company) and SNARC; one label claim in progress: control of mortality in channel catfish due to external columnaris disease.

Progress on potassium permanganate (May 15, 2007 to November 9, 2007):

- (1) 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 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 Multi-State Conservation Grant 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; early development stage.

ROMET® 30 AND ROMET® TC—ORAL ANTIBACTERIAL

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, 2007 to November 9, 2007):

- (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 (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 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 sponsor 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; no known drug approval activities underway.

CLOVE OIL

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 GFI #150: Status of Clove Oil and Eugenol for Anesthesia of Fish (updated April 24, 2007).

ISOEUGENOL (AQUI-S®)

Was an AFWA Project drug and now under development by the sponsor (AQUI-S New Zealand Ltd.), UMESC, and AADAP; one label claim suspended until February 2008: zero withdrawal anesthetic for sedation to (1) handleable condition in all freshwater finfish.

Progress on AQUI-S® (May 15, 2007 to November 9, 2007):

- (1) On April 27, 2007, AADAP and UMESC announced they were suspending all research until the completion of the NTP review scheduled for February 2008 on studies conducted on mice and rats. The review had originally been scheduled for May 2007 but due to other priorities was delayed.
- (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 to be complete for freshwater salmonids.
- (4) 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.

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*—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 is conducting 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 will not be available until late 2006 or early 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 will be reviewed in February 2008.
- *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. Resolution will occur after the toxicological data are reviewed.
- *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)

TRICAINE METHANESULFONATE (FINQUEL®, TRICAINE-S®)

Has 21-day withdrawal time.

SPAWNING AND GENDER MANIPULATION AIDS

CRUDE CARP PITUITARY (CCP)

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

Progress on CCP (May 15, 2007 to November 9, 2007):

- (1) No progress to report.

Current status of technical sections on CCP:

- *Product Chemistry*—The sponsor submitted the product chemistry technical section for CCP to CVM on September 21, 1999. The sponsor received a response on November 22, 1999 from CVM that asked for more information. The sponsor has decided not to pursue a response.
- *Environmental Safety*—Accepted by CVM.
- *Human Food Safety-Toxicology*—Accepted by CVM.
- *Human Food Safety-Residue Chemistry*—Accepted by CVM.
- *Target Animal Safety*—A literature review on target animal safety of CCP was completed, presented on August 5, 1998 in Bozeman, Montana, and submitted to CVM in summer 1999 by the Southeastern region of NRSP-7. On October 12, 2004, Southern Illinois University submitted the final report for the target animal safety study to NRSP-7 and this report was submitted to CVM.
- *Effectiveness*—Accepted as complete from NRSP-7 by CVM as a spawning aid in freshwater-reared female finfish (July 17, 2002). CVM has requested additional information.

HUMAN CHORIONIC GONADOTROPIN (CHORULON®)

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

LUTEINIZING HORMONE-RELEASING HORMONE ANALOG (LHRHA)

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

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

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

Progress on MT (May 15, 2007 to November 9, 2007):

- 1) On July 30, 2007, interested parties met in Bozeman, Montana to discuss EA issues and to determine a course of action.
- 2) On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17 α -methyltestosterone that were conducted and developed by the University of Wisconsin-Madison.
- 3) On November 5, 2007, AADAP requested that CVM consider the Effectiveness Technical Section to be complete for the use of MT to produce predominantly male populations of tilapia.

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).
- *Environmental Safety*—Auburn University received a response from CVM on November 8, 1999 regarding the revised EA for MT that requested additional information, a biodegradation study, and a more sensitive method to detect MT in water. On October 1, 2007, UMESC submitted to CVM the environmental safety studies and the water method for 17 α -methyltestosterone that were conducted and developed by the University of Wisconsin-Madison.
- *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.

- *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

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, the sponsor of Ovaplant®, for the induction of spawning in ornamental fish.

CHEMICAL MARKING AGENTS

CALCEIN (E-MARK®)

Early development stage as chemical marking aid.

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

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

STRONTIUM CHLORIDE

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

PISCICIDES (ROTENONE AND ANTIMYCIN)

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

- (1) The National Aquaculture NADA Coordinator, as Chair of the AFS Task Force on Fishery Chemicals, attended a meeting in June 2007 with the registrants and EPA to discuss the requirements for label changes and mitigation measures for rotenone. She also provided comments in July 2007 to EPA on the Reregistration Eligibility Decisions regarding both rotenone and antimycin.

PUBLIC INFORMATION AND MEETINGS

- (1) On July 18, 2007, the National Aquaculture NADA Coordinator gave an eight-hour presentation 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 USA, (2) our experience with various successful partnerships, and (3) insight into expediting the aquaculture drug approval processes in Canada.
- (2) The designation provision of the Minor Use and Minor Species Animal Health Act of 2004 (MUMS) gives sponsors seven years of marketing exclusivity. So far, the MUMS Office has granted 50 designations, 44 of those are to aquaculture drug sponsors who received extensive help from the National Coordinator for Aquaculture NADAs. The most recent MUMS designations are three for Pfizer Animal Health's Terramycin 343® (oxytetracycline hydrochloride) on June 7, 2007 and one for Aquatic Life Sciences, Inc.'s Ovaplant® (salmon gonadotropin releasing hormone analog) on May 25, 2007. There have been three NADA approvals of MUMS designations for Eka Chemicals, Inc.'s 35%PEROX-AID® and two NADA approvals and one Conditional Approval of MUMS designations for Schering-Plough Animal Health's Aquaflor®.
- (3) From July to September 2007, the National Aquaculture NADA Coordinator gave presentations on

innovations and status of aquaculture drug approvals at the 144th American Veterinary Medical Association Convention (Washington, DC), 13th Annual Drug Approval Coordination Workshop (Bozeman, Montana), Disease Management Strategies for the Aquatic Environment: Alternative and Innovations Symposium (San Francisco, California), and the Association of Fish and Wildlife Agencies, Drug Approval Working Group meetings (Louisville, Kentucky).

Funding Needs

The National Aquaculture NADA Coordinator position stayed at 35 hours per week to maintain adequate funding. Contributions totaled \$142,700 for Year 13 (May 15, 2007 to May 14, 2008).

PUBLICATIONS, MANUSCRIPTS, PAPERS PRESENTED, AND SPECIAL REPORTS

PUBLICATIONS

AFS Fish Management Chemicals Subcommittee. In press. Update on piscicides rotenone and antimycin. Fisheries.

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.

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, 17 α -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 the Drug Approval Working Group. 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 (I-008086-P-0056) 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. 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.
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