

**NATIONAL COORDINATOR FOR AQUACULTURE
NEW ANIMAL DRUG APPLICATIONS (NADAs)**

TENTH ANNUAL REPORT OF ACTIVITIES

May 15, 2004 to May 14, 2005

Submitted by

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TENTH ANNUAL SUMMARY OF ACTIVITY HIGHLIGHTS FOR THE NATIONAL COORDINATOR FOR
AQUACULTURE NEW ANIMAL DRUG APPLICATIONS (NATIONAL AQUACULTURE NADA
COORDINATOR)
(May 15, 2004 to May 14, 2005)

AQUI-S®—ANESTHETIC (two initial label claims in progress: zero withdrawal anesthetic for all salmonids and coolwater and warmwater fish)

- The National Toxicology Program (NTP) completed a two-year carcinogenicity study in spring 2004 but the final report will not be available until late 2006 or early 2007.
- The Center for Veterinary Medicine (CVM) accepted from the Aquatic Animal Drug Approval Partnership Program (AADAPP) as pivotal studies on shovelnose sturgeon (June 24, 2004), hybrid striped bass (September 23, 2004), and rainbow trout (November 12, 2004). CVM accepted as supportive studies on Chinook salmon (July 30, 2004), largemouth bass (October 12, 2004), and tilapia, hybrid carp/goldfish, and hybrid striped bass (August 13, 2004).
- The National Aquaculture NADA Coordinator prepared a fact sheet on the need for a zero withdrawal anesthetic and compared the approval efforts on AQUI-S® with the regulatory status of MS-222, clove oil, sodium bicarbonate, and carbon dioxide gas. This fact sheet along with a cover letter was sent to all International Association of Fish and Wildlife Agencies (IAFWA) Drug Approval Working Group members, state Fish Chiefs, and aquaculture organizations in October 2004.
- On November 5, 2004, CVM sent its review to AQUI-S New Zealand LTD concerning the method to detect AQUI-S® in water.
- On February 12, 2005, the National Aquaculture NADA Coordinator requested \$150,000 in funding from the North Central Regional Aquaculture Center (NCRAC) for the AQUI-S® marker residue depletion studies in coolwater and warmwater finfish. The request was granted pending additional funds from other sources.
- On February 16, 2005, the National Aquaculture NADA Coordinator developed a request for funding for AQUI-S® residue chemistry studies and columnaris disease efficacy studies using a disease model to the IAFWA National Conservation Need (NCN). The NCN was accepted on March 17, 2005.
- On April 18, 2005, AQUI-S New Zealand LTD submitted a response to CVM concerning the method to detect AQUI-S® in water during efficacy and target animal safety studies.
- On May 17, 2005, CVM found the target animal safety and efficacy studies on Atlantic salmon from the sponsor to be supportive.
- On June 3, 2005, the NCRAC Board of Directors agree to fund the development and validation of the determinative method for AQUI-S® instead of the AQUI-S® marker residue depletion studies in coolwater and warmwater finfish because the method was needed before the depletion studies could begin and the NCN funds were phased in for too long a period of time to allow for the development of the method. The NCN will fund the marker residue studies instead along with target animal safety studies on coolwater and warmwater fish and coordination effects on AQUI-S®.
- On June 7, 2005, CVM concurred with the fetal no-observed-adverse-effect level of 500 mg/kg/day that the NTP established from the teratology study in rats.
- On June 8, 2005, the National Aquaculture NADA Coordinator submitted a proposal to IAFWA for NCN funding entitled "Complete the marker residue depletion portion of the Human Food Safety Technical Section, complete the Target Animal Safety Technical Section, and coordinate and oversee all activities toward the approval of AQUI-S® as a zero-withdrawal anesthetic for short-exposure handling of all freshwater fish".

CHLORAMINE-T—EXTERNAL ANTIBACTERIAL (two label claims close to completion: control of mortalities associated with (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye)

- On September 17, 2004, CVM sent its review to the sponsor, Axcentive bv, on the proprietary environmental assessment (EA) on chloramine-T to CVM. The Upper Midwest Environmental Sciences Center (UMESC) developed the EA for the sponsor with funds from the company. The sponsor, UMESC, and the National Aquaculture NADA Coordinator are working on a response.
- On October 22, 2004, the sponsor of Halamid® (a chloramine-T product), Axcentive BV, announced that it and its mother company PNP Holding BV transferred to Axcentive SARL and to Bouc Bel Air, France.
- On March 4, 2005, CVM accepted the confirmatory method p-TSA, the marker residue for chloramine-T.
- On March 11, 2005, CVM accepted the hybrid striped bass target animal safety data from UMESC to complete the Target Animal Safety Technical Section for all freshwater-reared finfish.

COPPER SULFATE—EXTERNAL MICROBICIDE—(one label claim close to completion: control of Ichthyophthirius on channel catfish in earthen ponds with no outflows)

- On May 25, 2005, CVM accepted as complete from the sponsor the target animal safety study on channel catfish for use in ponds.

CRUDE CARP PITUITARY—SPAWNING AID

- 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.

ERYTHROMYCIN—ORAL ANTIBACTERIAL (one label claim in progress: bacterial kidney disease in salmonids)

- Bimeda, Inc. obtained an Investigational New Animal Drug Application (INAD) #11-360.
- On May 23, 2005, Bimeda, Inc., the National Aquaculture NADA Coordinator, and the Principal Investigator at Idaho met with CVM for a pre-submission meeting to discuss the manufacturing processes and the requirements to complete this Technical Section.

FLORFENICOL—ORAL ANTIBACTERIAL (four label claims close to completion: control of mortalities associated with (1) furunculosis in freshwater-reared salmonids, (2) coldwater disease in freshwater-reared salmonids, (3) systemic columnaris disease in freshwater-reared salmonids and catfish, and (4) enteric septicemia in catfish)

- Since May 2004, CVM accepted from the sponsor the following technical sections: (1) Product Chemistry and (2) Environmental Safety.
- On December 9, 2004, CVM accepted as complete from AADAPP the efficacy technical section for control of mortalities caused by *Streptococcus iniae* in hybrid striped bass.

FORMALIN—EXTERNAL MICROBICIDE (one additional label claim close to completion: control of mortalities associated with saprolegniasis on all fish)

- On November 16, 2004, CVM accepted as supportive efficacy studies for the control of saprolegniasis on channel catfish by UMESC.

- On November 5, 2004, CVM Office of Research submitted to CVM a final report on the pivotal efficacy studies on the control of saprolegniasis on rainbow trout

HYDROGEN PEROXIDE—EXTERNAL MICROBICIDE (four label claims close to completion: control of mortalities associated with (1) saprolegniasis on all finfish eggs, (2) saprolegniasis on all finfish, (3) bacterial gill disease on all freshwater-reared salmonids, and (4) external columnaris disease on all coolwater fish and channel catfish)

- On November 24, 2004, CVM accepted as pivotal efficacy data on hydrogen peroxide from UMESC for the control of mortalities associated with saprolegniasis on catfish but requested additional supportive data before this Technical Section can be considered as complete.
- On December 10, 2004, the sponsor, Eka Chemicals, Inc., met with UMESC and the National Aquaculture NADA Coordinator to discuss the final requirements to be met before an Administrative NADA is submitted to CVM on hydrogen peroxide for three broad label claims.
- On February 16, 2005, UMESC submitted to CVM a summary of the pivotal 21-day Daphnia study along with a preliminary revision of the environmental assessment on hydrogen peroxide.
- On March 29, 2005, Eka Chemicals, Inc. submitted to CVM the microbial food safety information and data on hydrogen peroxide to meet the requirements of Guidance Documents #52 and #152.
- On April 20, 2005, UMESC and the National Aquaculture NADA Coordinator met with CVM and resolved the remaining issues surrounding the environmental assessment on hydrogen peroxide. The EA is in the final stages for submission.
- On May 11, 2005, UMESC submitted to CVM a draft FOI summary for three label claims for hydrogen peroxide in all freshwater-reared finfish and finfish eggs.
- On May 20, 2005, the National Aquaculture NADA Coordinator met with CVM to discuss the remaining data requirements and labeling for approval of hydrogen peroxide. Results of two efficacy studies were identified that needed to be added to the FOI summaries.
- On June 1, 2005, UMESC submitted a revised draft FOI summary to include the results of the two efficacy studies that had been identified at the May 20, 2005 meeting with CVM.
- On June 6, 2005, CVM accepted the Microbial Food Safety submission for Guidance Document #52 saying that if used according to label claim directions “would probably not cause any adverse effect on the human intestinal flora”.

17 α -METHYLTESTOSTERONE (MT)—GENDER MANIPULATION AID (one label claim close to completion: gender manipulation aid for tilapia)

- The University of Wisconsin-Madison was selected as the contractor to complete the remaining Product Chemistry and Environmental Safety data requirements for MT and is conducting the studies that started in the fall of 2004.
- Southern Illinois University was selected in summer 2004 to perform the target animal safety study on tilapia with MT and the protocol is under development.
- On June 4, 2004, AADAPP received authorization for an INAD (#11-236) to collect pivotal and supportive efficacy data.

OXYTETRACYCLINE—ORAL ANTIBACTERIAL (two label claims close to completion: control of mortalities associated with (1) systemic columnaris disease in steelhead trout and (2) systemic coldwater disease in all freshwater-reared salmonids)

- In August 2004, the University of Arizona submitted to CVM a target animal safety study in penaeid shrimp.
- On October 15, 2004, UMESC submitted an EA written to meet current guidelines and requirements to CVM.

OXYTETRACYCLINE—IMMERSION ANTIBACTERIAL AND MARKING AID (one label claim approved=marking all fish and three label claims close to completion: control of mortalities associated with (1) bacterial gill disease, (2) external columnaris disease, and (3) systemic columnaris disease on coolwater and warmwater fish)

- In July 2004, Pharmaq AS of Oslo, Norway, performed a management buyout of the sponsor, Alpharma Animal Health, for its oxytetracycline immersion product.
- On October 14, 2004, CVM established INAD # 11-308 for UMESC to use in development of data on oxytetracycline immersion.
- On August 5, 2004, CVM accepted the HPLC method provided by UMESC as suitable to verify oxytetracycline concentrations in water during efficacy studies.
- On October 22, 2004, CVM approved the supplemental NADA for Phoenix Scientific, Inc.'s oxytetracycline product (Oxytetracycline HCl Soluble Powder-343®) as an otolith marking aid for all finfish fry and fingerlings.
- On October 27, 2004, CVM accepted from UMESC the bridging of the liquid chromatographic method to the official microbial inhibition method in fish tissue.

ROMET®—ORAL ANTIBACTERIAL (previously approved for control of enteric septicemia in catfish and furunculosis in salmonids)

- In July 2004, Pharmaq AS of Oslo, Norway, performed a management buyout of the sponsor, Alpharma Animal Health, for all Romet® products.

WORKSHOPS AND ROUNDTABLES

- The National Aquaculture NADA Coordinator organized a Roundtable on the Need for a Zero Withdrawal Anesthetic (with emphasis on approval effort toward AQUI-S®) at the annual meeting of the American Fisheries Society, August 22, 2004. A report on the results of the roundtable was sent to attendees and other interested parties.
- The National Aquaculture NADA Coordinator organized a Workshop on Marine Aquaculture Drug and Chemotherapeutant Issues and Needs on Southern United States that was held in Sarasota, Florida on November 16, 2004. This Workshop featured the need for marine aquaculture and fisheries entities to become involved in the approval efforts on AQUI-S®.

EFFLUENTS

EPA signed the final rule for national effluent limitation guidelines and standards on June 30, 2004. Among others, the rule will apply to the use, storage, and reporting requirements of drugs and chemicals at selected facilities where the water is released into public waters.

MUMS

The bill entitled "Minor Use Minor Species Animal Health Act" (MUMS) passed Congress on July 20, 2004 and the President signed it into law on August 2, 2004. Aquaculture sector representatives meet with CVM on December 6, 2004 to discuss implementing regulations and details of the new law.

- The National Aquaculture NADA Coordinator provided draft designation letters and designation packages for 14 drugs, 26 requests, and 34 label claims from December 2004 to February 2005.
- The National Aquaculture NADA Coordinator met with the MUMS Office on April 21 and May 20, 2005 to discuss the status of the MUMS requests for designation from the aquaculture drug sponsors.

PUBLICATIONS, PRESENTATIONS, AND SPECIAL REPORTS

- The National Coordinator for Aquaculture New Animal Drug Applications had one publication, one publication in press, and one in review, presented 25 papers, and wrote 31 special reports.

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, 2004 to May 14, 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 mortalities associated with (1) bacterial gill disease on all freshwater-reared salmonids and (2) external columnaris disease on walleye. Progress on chloramine-T (May 15, 2004 to May 14, 2005):

- Through an interagency agreement with UMESC, CVM's Office of Research developed a confirmatory method for p-TSA in fish tissue to satisfy an all fish label claim. This final report was submitted by UMESC to CVM (July 21, 2004).
- On July 30, 2004, UMESC submitted to CVM data and information on the target animal safety of chloramine-T to hybrid striped bass.
- On September 17, 2004, CVM sent a response to the sponsor, Axcentive bv, on the proprietary environmental assessment (EA) on chloramine-T to CVM. UMESC developed the EA for the sponsor with funds from the company. The sponsor, UMESC, and the National Aquaculture NADA Coordinator are working on a response.
- On October 22, 2004, the sponsor of Halamid®, Axcentive BV, announced that it and its mother company PNP Holding BV transferred to Axcentive SARL and to Bouc Bel Air, France.
- On March 4, 2005, CVM accepted the confirmatory method p-TSA, the marker residue for chloramine-T.
- On March 11, 2005, CVM accepted the hybrid striped bass target animal safety data to complete the Target Animal Safety Technical Section for all freshwater-reared finfish.
- On April 21, 2005, UMESC and the National Aquaculture NADA Coordinator met with CVM to discuss and resolve issues related to the environmental assessment.
- On May 11, 2005, UMESC submitted a draft label and a supplemental FOI summary for chloramine-T to support all freshwater-reared finfish label claims.

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 mortalities associated with bacterial gill disease on (1) tiger muskie (November 29, 1999) and (2) salmonids (July 12, 2000). CVM accepted as complete from (1) AADAPP the efficacy technical section for control of mortalities associated with 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 Refining Corporation) and SNARC; one label claim close to completion: control of *Ichthyophthirius* on channel catfish in earthen ponds with no outflows.

Progress on copper sulfate (May 15, 2004 to May 14, 2005):

- On July 1, 2004, the sponsor submitted to CVM a target animal safety study on channel catfish that was conducted by SNARC.
- On May 25, 2005, CVM accepted as complete the target animal safety study on channel catfish for use in ponds.

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 *Ichthyophthirius* 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.

Enrofloxacin (oral antibacterial)—Status: INADs inactive in the United States because of fluoroquinolone and antimicrobial resistance issues; no sponsor interest.

Erythromycin (oral antibacterial)—Status: A sponsor is available for erythromycin—Bimeda Inc.; most technical sections submitted by University of Idaho; sponsor needs to submit product chemistry; University of Idaho: risk assessment needed on potential for microbial food safety in humans and hazard in the environment (to complete the Environmental Safety and Human Food Safety Technical Sections); near NADA approval for bacterial kidney disease in salmonids if can resolve the antimicrobial resistance issue.

- Bimeda, Inc. obtained an Investigational New Animal Drug Application (INAD) #11-360.
- On May 23, 2005, Bimeda, Inc., the National Aquaculture NADA Coordinator, and the Principal Investigator at Idaho met with CVM for a pre-submission meeting to discuss the manufacturing processes and the requirements to complete this Technical Section.

Florfenicol (oral antibacterial)—Status: The sponsor, Schering-Plough Animal Health, gained florfenicol (Aquaflor®) approval in Canada in August 1997 to control furunculosis in Atlantic salmon; sponsor is developing data for aquaculture approval for control of diseases in salmonids and catfish; was a Federal-State Aquaculture Drug Approval Partnership Project drug and now under development by the sponsor, UMESC, and AADAPP; four label claims close to completion: control of (1) enteric septicemia in catfish, (2) coldwater disease in freshwater-reared salmonids, (3) furunculosis in freshwater-reared salmonids, and (4) systemic columnaris disease in freshwater-reared salmonids and catfish.

Progress on florfenicol (May 15, 2004 to May 14, 2005):

- CVM accepted from the sponsor the following technical sections: (1) Product Chemistry and (2) Environmental Safety.
- On December 9, 2004, CVM accepted as complete from AADAPP the efficacy technical section for control of mortalities caused by *Streptococcus iniae* in hybrid striped bass.

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—final acceptance pending
- *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 mortalities associated with saprolegniasis on all fish.

Progress on formalin (May 15, 2004 to May 14, 2005):

- On November 16, 2004, CVM accepted as supportive efficacy studies for the control of saprolegniasis on channel catfish by UMESC.

- On November 5, 2004, CVM Office of Research submitted to CVM a final report on the pivotal efficacy studies on the control of saprolegniasis on rainbow trout.
- In early 2005, CVM Office of Research submitted to CVM a protocol for a pivotal efficacy study on the control of saprolegniasis on channel catfish.
- On April 11, 2005, CVM established an INAD (11-365) for formalin at UMESC.

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). CVM Office of Research submitted pivotal efficacy studies for the control of saprolegniasis on rainbow trout (November 5, 2004).

Fumagillin (microsporidiosis control)—Status: No recent sponsor activity; several efforts to collect efficacy data in public and private sector; early development stage.

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 mortalities from (1) saprolegniasis on all finfish eggs, (2) saprolegniasis on all finfish, (3) bacterial gill disease on all freshwater-reared salmonids, and (4) external columnaris disease on all freshwater-reared coolwater finfish and channel catfish.

Progress on hydrogen peroxide (May 15, 2004 to May 14, 2005):

- On November 24, 2004, CVM accepted as pivotal efficacy data on hydrogen peroxide from UMESC for the control of mortalities associated with saprolegniasis on catfish but requested additional supportive data before this Technical Section can be considered as complete.
- On December 10, 2004, the sponsor, Eka Chemicals, Inc., met with UMESC and the National Aquaculture NADA Coordinator to discuss the final requirements to be met before an Administrative NADA is submitted to CVM on hydrogen peroxide for three broad label claims.
- On February 16, 2005, UMESC submitted to CVM a summary of the pivotal 21-day Daphnia study along with a preliminary revision of the environmental assessment on hydrogen peroxide.
- On March 29, 2005, Eka Chemicals, Inc. submitted to CVM the microbial food safety information and data on hydrogen peroxide to meet the requirements of Guidance Documents #52 and #152.
- On April 20, 2005, UMESC and the National Aquaculture NADA Coordinator met with CVM and resolved the remaining issues surrounding the environmental assessment on hydrogen peroxide. The EA is in the final stages for submission.
- On May 11, 2005, UMESC submitted to CVM a draft FOI summary for three label claims for hydrogen peroxide in all freshwater-reared finfish and finfish eggs.

- On May 20, 2005, the National Aquaculture NADA Coordinator met with CVM to discuss the remaining data requirements and labeling for approval of hydrogen peroxide. Results of two efficacy studies were identified that needed to be added to the FOI summaries.
- On June 1, 2005, UMESC submitted a revised draft FOI summary to include the results of the two efficacy studies that had been identified at the May 20, 2005 meeting with CVM.
- On June 6, 2005, CVM accepted the Microbial Food Safety submission for Guidance Document #52 saying that if used according to label claim directions “would probably not cause any adverse effect on the human intestinal flora.”

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 revision of the environmental assessment (preliminary revision submitted to CVM February 16, 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 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—CVM review in progress.
- *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 mortalities associated with (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 mortalities associated with 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 mortalities associated with (1) systemic columnaris disease in steelhead trout and (2) systemic coldwater disease in all freshwater-reared salmonids.

Progress on oral oxytetracycline (May 15, 2004 to May 14, 2005):

- In August 2004, University of Arizona submitted to CVM a target animal safety study in penaeid shrimp.
- On October 15, 2004, UMESC submitted an EA written to meet current guidelines and requirements to CVM.

- On April 11, 2005, CVM established an INAD (11-366) for oxytetracycline at UMESC.

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 lbs of fish for 10 days as effective in reducing mortalities 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 mortalities associated with necrotizing hepatopancreatitis in penaeid shrimp (June 28, 2000).

Oxytetracycline (OTC, immersion antibacterial)—Status: No current sponsor for antibacterial use; three label claims close to completion: control of mortalities associated with (1) bacterial gill disease, (2) external columnaris disease, and (3) systemic columnaris disease on coolwater and warmwater fish.

Progress on immersion OTC (May 15, 2004 to May 14, 2005):

- UMESC is conducting pivotal efficacy studies on coolwater and warmwater fish for control of mortalities associated with (1) bacterial gill disease, (2) external columnaris disease, and (3) systemic columnaris disease.

- On October 14, 2004, CVM established INAD # 11-308 for UMESC to use in development of data on oxytetracycline immersion.
- On August 5, 2004, CVM accepted the HPLC method provided by UMESC as suitable to verify oxytetracycline concentrations in water during efficacy studies.
- On October 27, 2004, CVM accepted from UMESC the bridging of the liquid chromatographic method to the official microbial inhibition method in fish tissue.

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; label claim in progress: control of Ichthyophthirius on channel catfish in earthen ponds with no outflows

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.

- In June and July 2004, Kona Blue Water Farms pursued with Bayer USA, Bayer Japan, and the National Aquaculture NADA Coordinator the possibility of developing data for approval of praziquantel for control of

monogenean capsalid trematodes on amberjack. Because no mammalian safety data are available for this purpose, the effort was abandoned.

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, 2004 to May 14, 2005):

- In July 2004, Pharmaq AS of Oslo, Norway, performed a management buyout of the sponsor, Alpharma Animal Health, for all Romet® products.

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.

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

AQUACALM®--Status: Preliminary development by sponsor.

- On January 19, 2005, the National Aquaculture NADA Coordinator met with Syndel Laboratories Ltd. 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; label claim in progress: zero withdrawal anesthetic in all salmonids for short-exposure handling (rested harvest, spawning, marking, tagging, measuring, and sexing).

Progress on AQUI-S® (May 15, 2004 to May 14, 2005):

- NTP completed a two-year carcinogenicity study in Spring 2004 but the final report will not be available until late 2006 or early 2007.
- The sponsor submitted to CVM target animal safety and efficacy studies on Atlantic salmon completed in Canada (July 6, 2004).
- CVM accepted as pivotal one study on shovelnose sturgeon (June 24, 2004), one on hybrid striped bass (September 23, 2004), and one on rainbow trout (November 12, 2004). CVM accepted as supportive studies on Chinook salmon (July 30, 2004), largemouth bass (October 12, 2004), and tilapia, hybrid carp/goldfish, and hybrid striped bass (August 13, 2004).
- Radiolabeled material has been delivered and being checked by UMESC for purity before the total residue depletion study begins in early 2005.
- On August 22, 2004, the National Aquaculture NADA Coordinator organized a Roundtable on the Need for a Zero Withdrawal Anesthetic (with emphasis on approval effort toward AQUI-S®) at the annual meeting of the American Fisheries Society. A report on the results of the roundtable was sent to attendees and other interested parties.
- The National Aquaculture NADA Coordinator prepared a fact sheet on the need for a zero withdrawal anesthetic and compared the approval efforts on AQUI-S® with the regulatory status of MS-222, clove oil, sodium bicarbonate, and carbon dioxide gas. This fact sheet along with a cover letter was sent to all Drug Approval Working Group members, state Fish Chiefs, and aquaculture organizations in October 2004.
- AADAPP submitted the following efficacy studies to CVM: (1) pallid sturgeon (October 5, 2004), (2) smallmouth bass (October 26, 2004), and (3) largemouth bass (November 9, 2005).
- On November 1, 2004, AQUI-S New Zealand LTD submitted a NTP teratology study on isoeugenol in rats to CVM for review.
- On November 5, 2004, CVM sent a response to AQUI-S New Zealand LTD concerning the method to detect AQUI-S® in water.
- On November 16, 2004, the National Aquaculture NADA Coordinator organized a Workshop on Marine Aquaculture Drug and Chemotherapeutant Issues and Needs on Southern United States that was held in Sarasota, Florida. This Workshop featured the need for marine aquaculture and fisheries entities to become involved in the approval efforts on AQUI-S®.
- On November 29, 2004, AQUI-S New Zealand LTD submitted a NTP continuous breeding study on isoeugenol in rats to CVM for review.
- On February 12, 2005, the National Aquaculture NADA Coordinator requested \$150,000 in funding from the North Central Regional Aquaculture Center (NCRAC) for the AQUI-S® marker residue depletion studies in coolwater and warmwater finfish. The request was granted pending additional funds from other sources.
- On February 16, 2005, the National Aquaculture NADA Coordinator developed a proposal for funding for AQUI-S® residue chemistry studies and columnaris disease efficacy studies using a disease model to the International Association for Fish and Wildlife Agencies National Conservation Need. The NCN was accepted on March 17, 2005.
- On April 18, 2005, AQUI-S New Zealand LTD submitted a response to CVM concerning the method to detect AQUI-S® in water during efficacy and target animal safety studies.

- On May 17, 2005, CVM found the target animal safety and efficacy studies on Atlantic salmon from the sponsor to be supportive.
- On June 3, 2005, the NCRAC Board of Directors agree to fund the development and validation of the determinative method for AQUI-S® instead of the AQUI-S® marker residue depletion studies in coolwater and warmwater finfish because the method was needed before the depletion studies could begin and the NCN funds were phased in for too long a period of time to allow for the development of the method. The NCN will fund the marker residue studies instead along with target animal safety studies on coolwater and warmwater fish and coordination effects on AQUI-S®.
- On June 7, 2005, CVM concurred with the fetal no-observed-adverse-effect level of 500 mg/kg/day that the NTP established from the teratology study in rats.
- On June 8, 2005, the National Aquaculture NADA Coordinator submitted a proposal to IAFWA for NCN funding entitled "Complete the marker residue depletion portion of the Human Food Safety Technical Section, complete the Target Animal Safety Technical Section, and coordinate and oversee all activities toward the approval of AQUI-S® as a zero-withdrawal anesthetic for short-exposure handling of all freshwater fish."

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).
- *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), and one on rainbow trout (November 12, 2004). 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), and (5) hybrid carp/goldfish (August 13, 2004). AADAPP submitted additional efficacy studies on a variety of species in 2004.

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, 2004 to May 14, 2005):

- 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.

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: September 1999 NADA approval in the United States. 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. This approval is significant because it is the first original NADA approval since 1986 when formalin was first approved for fish and because it was approved for all fish.

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: gender manipulation aid for tilapia.

Progress on MT (May 15, 2004 to May 14, 2005):

- The University of Wisconsin-Madison was selected as the contractor to complete the remaining Product Chemistry and Environmental Safety data requirements and is conducting the studies that started in the fall of 2004.
- Southern Illinois University was selected in summer 2004 to perform the target animal safety study on tilapia and the protocol is under development.
- On June 4, 2004, AADAPP received authorization for an INAD to collect pivotal and supportive efficacy data.
- On February 18, 2005, schedules were set up for all the studies and activities on MT at a Mini-Session held at Aquaculture America.
- On March 31, 2005, University of Wisconsin submitted the analytical method to detect MT in the feed to CVM through a PMF at UMESC. On April 4, 2005, Rangen, Inc. requested a review of the method.
- On April 6, 2005, CVM established a PMF (005-835) for MT at UMESC.
- On May 4, 2005, AADAPP submitted a MT pivotal efficacy study protocol for review to CVM.

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.
- *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™—Status: 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.

- On August 3, 2004, the sponsor and several researchers presented efficacy data at the FWS 10th Annual Drug Approval Coordination Workshop, Bozeman, Montana.

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

- On October 22, 2004, CVM approved the supplemental NADA for Phoenix Scientific, Inc.'s oxytetracycline product (Oxytetracycline HCl Soluble Powder-343®) as an otolith marking aid for all finfish 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—Both 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 Arizona in April 2004, in West Virginia in October 2004, and in Utah in May 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 November 1, 2004 to discuss the reregistration of antimycin and the remaining data requirements.
- FMCS is sponsoring 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, WORKSHOPS AND PRESENTATIONS

Annual Drug Approval Workshop

AADAPP and the National Aquaculture NADA Coordinator hosted the 10th Annual Drug Approval Workshop on August 3-4, 2004 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) progress being made on the IAFWA Project drugs, (2) overviews of activities by the National Aquaculture NADA Coordinator, AADAPP, SNARC, UMESC, CVM's Office of Research, CVM's Aquaculture Drugs Team, and NRSP-7, (3) Strategic Plan for the JSA Working Group on Quality Assurance in Aquaculture Production (4) status and impacts of MUMS legislation, (5) the role of the American Veterinary Medical Association in aquatic animal drug approvals, (6) overview of EPA's hatchery effluent guidelines, and (7) progress on other drugs under development including erythromycin, calcein, and Slice®.

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 meetings on September 27, 2004 in Atlantic City, New Jersey and on March 16, 2005 in Arlington, Virginia. The National Aquaculture NADA Coordinator provided documents before the meeting on the technical progress toward drug approvals and at the meeting, presented a brief overview of recent efforts toward initial

approvals of project drugs. She also developed a Strategic Plan for and endpoint to the IAFWA Project. Her other presentations included (1) update from CVM on drug approval progress, (2) review of March 2004 and September 2004 Action Items, (3) action items from the Roundtable on the Need for a Zero Withdrawal Anesthetic, and (4) need for statement for funding under the National Conservation Need (NCN) program. At the March 2005 meeting, the DAWG determined that funding should be provided for the National Aquaculture NADA Coordinator through the NCN for AQUI-S® if the NCN for AQUI-S® was accepted. At the Pre- and Post-DAWG meetings, on September 27, 2004 and March 16, 2005, the group discussed Work Plans for AQUI-S®, chloramine-T, copper sulfate, florfenicol, formalin, hydrogen peroxide, oxytetracycline, and potassium permanganate, and the proposed Memorandum of Agreement.

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 August 2, 2004 in Bozeman, Montana and on January 17, 2005 in New Orleans, Louisiana. The topics of discussion at the 2004 were (1) progress reports on Strategic Plan goals, (2) Environmental Safety Technical Section for NADAs, and (3) presentation and discussion of the National Research Forum Strategic Plan. At the 2005 meeting, the topics of discussion were (1) vaccines and biologics, (2) Research Forum, (3) guide to Federal programs, (4) drug matrix database, (5) field sampling activities, (6) NRSP-7 International Harmonization Workshop, and (8) Strategic Plan activities. At both meetings, the National Aquaculture NADA Coordinator presented (1) a review and status of the priority drugs, (2) latest matrices for all the drugs under development (Goal #2), (3) strategies for funding research on drug approvals (Goal #3), and (4) status of funding for her position (Goal #6). On August 5, 2004, the first meeting of the National Research Forum took place. The areas of studies that were discussed included (1) target animal safety, (2) Efficacy, (3) environmental safety, and (4) human food safety (both residue chemistry and microbial safety). Teams were organized in each discipline to address the issues and objects of the Strategic Plan.

Roundtable on the Need for a Zero Withdrawal Anesthetic

The National Aquaculture NADA Coordinator organized a Roundtable on the Need for a Zero Withdrawal Anesthetic (with emphasis on approval effort toward AQUI-S®) at the annual meeting of the American Fisheries Society, August 22, 2004 in Madison, Wisconsin. The umbrella organization unit was the AFS Aquaculture Chemicals Subcommittee of the Task Force on Fishery Chemicals. A report on the results of the roundtable was sent to attendees and other interested parties. An abbreviated version is presented below:

The purposes of the Roundtable were as follows:

1. Identify anesthesial procedures needing a zero withdrawal time anesthetic
2. Identify potential candidates for a zero withdrawal anesthetic
3. Identify current efforts and data gaps for approval of a potential zero withdrawal anesthetic—AQUI-S®
4. Determine ways and means to secure
5. Additional research support for AQUI-S® for the label claims currently underway and funded
6. Additional funding for the label claims not covered by current efforts and funding for AQUI-S®
7. Determine ways and means of alerting the fisheries communities to the need for approval, support, and additional funding for AQUI-S®

The first two purposes were easily accomplished. The third purpose centered on AQUI-S® label claims currently underway and funded for the initial new animal drug application approvals. These label claims include (1) short-exposure procedures for all freshwater and saltwater salmonids and (2) short-exposure procedures for all coolwater and warmwater freshwater fish. One of the two presentations centered on the data that have been generated showing the effectiveness of AQUI-S® to help perform procedures needing short-exposures to the handeable stage for freshwater fish. The Roundtable group discussed the last two purposes in great detail.

The ways and means for securing additional research support for supportive efficacy data for the initial label claims underway included:

- Get additional persons to sign up for the investigational new animal drug (INAD) exemption on AQUI-S®
- Obtain information on supportive efficacy data needs for the AQUI-S® INAD through the International Association of Fish and Wildlife Agencies Drug Approval Working Group

The ways and means for securing additional funding for potential, additional label claims (e.g., transport) included:

- Advocate the continued funding of the entities currently involved in the drug approval effort on AQUI-S®
- Re-establish aquaculture drug approvals as a National Conservation Need through IAFWA, U.S. Fish and Wildlife Service, and the states
- Determine need for potential, additional label claims (e.g., transport) through a survey of all potential stakeholders
- Address the label claims not discussed at the Roundtable (i.e., surgical anesthesia/all fish & shellfish and short-exposure/marine fish (not salmonids) & shellfish by determining the need and potential support from its stakeholders

The ways and means of alerting the fisheries communities to the need for approval, support, and additional funding for AQUI-S® included:

- Meetings involving stakeholders
- Article on this issue in Fisheries
- Fact sheets on AQUI-S®
- Pertinent Websites
- Newsletters from societies and associations involved in fisheries and aquaculture
- Seminars with stakeholders needing AQUI-S®

Workshop on Marine Aquaculture Drug and Chemotherapeutant Issues and Needs on Southern United States

The National Aquaculture NADA Coordinator organized a Workshop on Marine Aquaculture Drug and Chemotherapeutant Issues and Needs on Southern United States that was held in Sarasota, Florida on November 16, 2004. This Workshop featured the need for marine aquaculture and fisheries entities to become involved in the approval efforts on AQUI-S®. The Workshop goals were to (1) alert the southern United States marine and fisheries industries to the impacts of the lack of drug approvals and potential solutions and (2) develop strategic plans to gain drug approvals for these groups. The PowerPoint presentation was distributed to attendees and other entities involved in marine aquaculture and fisheries.

Funding Needs

The National Aquaculture NADA Coordinator went from fulltime to three-quarter time due to lack of funds starting October 1, 2003 and then went up to 35 hours per week on May 15, 2004 because her special appeal to adequately support this position was heard. Contributions totaled \$107,476 for Year 10 (May 15, 2004 to May 14, 2005) and \$117,500 for Year 11.

EPA Effluent Guidelines Plan

EPA signed the final rule for national effluent limitation guidelines and standards on June 30, 2004. Among others, the rule will apply to the use, storage, and reporting requirements of drugs and chemicals at selected facilities where the water is released into public waters.

Minor Use Minor Species Legislation

The bill entitled "Minor Use Minor Species Animal Health Act" (MUMS) passed Congress on July 20, 2004 and the President signed it into law on August 2, 2004. Aquaculture sector representatives meet with CVM on December 6, 2004 to discuss implementing regulations and details of the new law.

The National Aquaculture NADA Coordinator provided draft designation letters and designation packages for 14 drugs, 26 requests, and 34 label claims from December 2004 to February 2005.

The National Aquaculture NADA Coordinator met with the MUMS Office on April 21 and May 20, 2005 to discuss the status of the MUMS requests for designation from the aquaculture drug sponsors.

Animal Drug User Fee Act Of 2003

The Animal Drug User Fee Act of 2003 (Public Law 108-130) requires that each sponsor send in a renewal letter annually.

PUBLICATIONS, MANUSCRIPTS, PAPERS PRESENTED, AND SPECIAL REPORTS

PUBLICATIONS

Schnick, R.A. 2005. The need for a zero withdrawal fish anesthetic (February 16, 2005). North Central Regional Aquaculture Center Website (<http://ag.ansc.purdue.edu/aquanic/ncrac/pubs/AQUI-S.pdf>). February 16, 2005. 2 pp.

MacMillan, J.R., R.A. Schnick, and G. Fornshell. 2003. 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. Need for a zero withdrawal anesthetic for all finfish and shellfish. Fisheries. In review.

PAPERS PRESENTED

Schnick, R.A. 2004. Matrices for tracking major aquaculture drug approval development. JSA Working Group on Quality Assurance in Aquaculture Production, Bozeman, Montana, August 2, 2004.

Schnick, R.A. 2004. JSA Working Group on Quality Assurance in Aquaculture Production: 5-Year Plan. JSA Working Group on Quality Assurance in Aquaculture Production, Bozeman, Montana, August 2, 2004.

Schnick, R.A. 2004. Recent efforts for initial Federal-State Aquaculture Drug Approval Partnership Project drug approvals. 10th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 3-4, 2004.

Schnick, R.A. 2004. Overview of progress toward aquaculture drug approvals for non-IAFWA Project drugs. 10th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 3-4, 2004.

Schnick, R.A. 2004. Initial original or supplemental new animal drug application approvals for the Federal-State Aquaculture Drug Approval Partnership Project. 10th Annual Drug Approval Coordination Workshop, Bozeman, Montana, August 3-4, 2004.

Schnick, R.A. 2004. Roundtable on the need for a zero withdrawal anesthetic. American Fisheries Society Annual Meeting, Madison, Wisconsin, August 22, 2004.

Schnick, R.A. 2004. Brief overview—Recent developments and highlights on drug approval progress. Drug Approval Working Group Meeting, Atlantic City, New Jersey, September 27, 2004.

Schnick, R.A. 2004. Review and Policy Guidance #5—Strategic plan for end point to IAFWA Project. Drug Approval Working Group Meeting, Atlantic City, New Jersey, September 27, 2004.

Schnick, R.A. 2004. IAFWA Project Work Plan—National Coordinator for Aquaculture New Animal Drug Applications. Post-Drug Approval Working Group Meeting, Atlantic City, New Jersey, September 27, 2004.

- Schnick, R.A. 2004. Aquaculture outside of NRSP-7. NRSP-7 Fall 2004 Meeting, Rockville, Maryland, October 6, 2004.
- Schnick, R.A. 2004. Drug issue & needs for Southern US Marine Aquaculture. Workshop on Marine Aquaculture Drug and Chemotherapeutant Issues and Needs on Southern United States, Sarasota, Florida, November 16, 2004. PowerPoint presentation distributed to interested entities and placed on the National Aquaculture NADA Coordinator website.
- Schnick, R.A. 2005. An update on the approval of therapeutants for use in aquaculture. Coolwater Fish Culture Workshop, Cherry Valley Lodge, Ohio, January 9-11, 2005.
- Schnick, R.A. 2005. Need for a zero withdrawal anesthetic for coolwater fish culture. Coolwater Fish Culture Workshop, Cherry Valley Lodge, Ohio, January 9-11, 2005.
- Schnick, R.A. 2005. Drug Matrix Database. JSA Working Group on Quality Assurance in Aquaculture Production, Aquaculture America 2005, New Orleans, Louisiana, January 17, 2005.
- Schnick, R.A. 2005. INAD/NADA Overview—17 α -methyltestosterone. 17-MT Mini-Session, Aquaculture America 2005, New Orleans, Louisiana, January 18, 2005.
- Schnick, R.A. 2005. Responsible use of therapeutants drugs in aquaculture. Environmental and Ethical Issues in Aquaculture, Aquaculture America 2005, New Orleans, Louisiana, January 19, 2005.
- Schnick, R.A. 2005. Update on product approvals for fish health. Striped Bass Industry Forum, Aquaculture America 2005, New Orleans, Louisiana, January 19, 2005.
- Schnick, R.A. 2005. Highlights and progress toward aquaculture drug approvals. Producer Session “Successes in Drug Approvals”, Aquaculture America 2005, New Orleans, Louisiana, January 20, 2005.
- Schnick, R.A. 2005. Aquaculture drugs. North Central Regional Aquaculture Center Board of Directors and 2005 Program Planning Meeting, East Lansing, Michigan, February 11-13, 2005.
- Schnick, R.A. 2005. Aquaculture drug research schedules for AQUIS[®] & 17 α -methyltestosterone. North Central Regional Aquaculture Center Board of Directors and 2005 Program Planning Meeting, East Lansing, Michigan, February 11-13, 2005.
- Schnick, R.A. 2005. Highlights on IAFWA Project drug approval progress. Drug Approval Working Group Meeting, Arlington, Virginia, March 16, 2005.
- Schnick, R.A. 2005. Questions in Strategic Plan for End Point to the IAFWA Project. Drug Approval Working Group Meeting, Arlington, Virginia, March 16, 2005.
- Schnick, R.A. 2005. IAFWA Project Work Plan—National Coordinator for Aquaculture New Animal Drug Applications. Drug Approval Working Group Meeting, Arlington, Virginia, March 16, 2005.
- Laurenson, J.P., B.L. Baxter, R.M. Kauffman, J.C. Cleland, and R.A. Schnick. 2005. Development and use of the Aquaculture Risk information System (AQRIS) and Risk Ranking Tool (AQRRT) for prioritizing import sampling and other activities (poster). 2005 FDA Science Forum, Washington, DC, April 27-29, 2005.
- Schnick, R.A. 2005. Aquaculture drug approval progress. NRSP-7 Meeting, Rockville, Maryland, May 19, 2005.

SPECIAL REPORTS

- Schnick, R.A. 2004. National Coordinator for Aquaculture New Animal Drug Applications (NADAs). Ninth annual report of activities, May 15, 2003 to May 14, 2004. Submitted to Ted Batterson, North Central Regional Aquaculture Center, East Lansing, Michigan. July 6, 2004. 21 pp.
- Schnick, R.A. 2004. 2004 annual report of the AFS Task Force on Fishery Chemicals. Submitted to the Governing Board and AFS President, Ira Adelman, Bethesda, Maryland. July 8, 2004. 7 pp.
- Schnick, R.A. 2004. Potential supplemental new animal drug application (NADA) approvals for oxytetracycline. Submitted to National Aquaculture NADA Coordinator website. July 9, 2004. 5 pp.
- Schnick, R.A. 2004. Initial new animal drug application (NADA) approval for AQUI-S®, zero withdrawal anesthetic, for (1) short-exposure handling for all freshwater- & saltwater-reared salmonids, and supplemental NADA approvals for AQUI-S® for (1) short-exposure handling for all cool & warm freshwater fish, (2) short-exposure handling for all marine fish, (3) long-exposure handling for all fish, and (4) surgical anesthesia for all fish. Submitted to National Aquaculture NADA Coordinator website. July 21, 2004. 7 pp.
- Schnick, R.A. 2004. Notes on FWS Annual Drug Approval Coordination Workshop, August 3-4, 2004, Bozeman, Montana. Submitted to organizers of on FWS Annual Drug Approval Coordination Workshop. August 18, 2004. 8 pp.
- Schnick, R.A. 2004. AADAP Newsletter Contribution. Submitted to AADAP. September 14, 2004. 1 pp.
- Schnick, R.A. 2004. Report on Roundtable on the Need for a Zero Withdrawal Anesthetic. Submitted to various groups with interest in a zero withdrawal anesthetic. September 16, 2004. 2 pp.
- Schnick, R.A. 2004. Commercial fish production. Submitted to the Center for Veterinary Medicine and the Drug Approval Working Group. October 14, 2004. 1 p.
- Schnick, R.A. 2004. Zero withdrawal anesthetic: AQUI-S® versus clove oil versus MS-222. Submitted to Mike Gibson for distribution to all state Fish Chiefs. October 26, 2004. 2 pp.
- Schnick, R.A. 2004. The need for a zero withdrawal fish anesthetic. Submitted to aquaculture organizations. November 5, 2004. 2 pp.
- Schnick, R.A. 2004. Minutes to Drug Approval Working Group Meeting, Atlantic City, New Jersey, September 27, 2004. Submitted to Drug Approval Working Group. November 5, 2004. 9 pp.
- Schnick, R.A. 2004. Tenth mid-year report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2004 to November 9, 2004). Submitted to Ted Batterson, North Central Regional Aquaculture Center for distribution to contributors to this position. December 30, 2004. 22 pp.
- Schnick, R.A. 2005. Table 1. Commercial and public finfish production (1,000). Prepared for consumption of U.S. aquaculture products. January 6, 2005. 1 pp.
- Schnick, R.A. 2005. Technical Section Submission on Hydrogen Peroxide (PEROX-AID®, INAD #9671) Related to Guidance Document #52—Assessment of the effects of antimicrobial drug residues from food of animal origin on the human intestinal flora. Submitted to Eka Chemicals, Inc. for forwarding to CVM. January 25, 2005. 2 pp.
- Schnick, R.A. 2005. Technical Section Submission on Hydrogen Peroxide (PEROX-AID®, INAD #9671) Related to Guidance Document #152—Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects of human health concern. Submitted to Eka Chemicals, Inc. for forwarding to CVM. January 25, 2005. 2 pp.

- Schnick, R.A. 2005. Midyear report to AFS Governing Board, March 2005. Submitted to AFS, January 27, 2005. 5 pp.
- Schnick, R.A. 2005. Draft Communiqué: Aquaculture Drug Approval Development Matrices. Submitted to JSA Working Group on Drugs, Pesticides, and Biologics. January 29, 2005. 1 pp.
- Schnick, R.A. 2005. Draft—General information document: Aquaculture Drug Approval Development Matrices. Submitted to JSA Working Group on Drugs, Pesticides, and Biologics. January 29, 2005. 1 pp.
- Schnick, R.A. 2005. Status of drug approval for 17 α -methyltestosterone, October 2, 2003 (updated February 4, 2005). Prepared for entities interested in 17 α -methyltestosterone approval. January 28, 2005. 6 pp.
- Schnick, R.A. 2005. Roz's Corner: AADAP Newsletter Contribution. Submitted to AADAP. February 10, 2005. 1 pp.
- Schnick, R.A. 2005. Report on AQUI-S® funding needs, February 15, 2005. Submitted to the NCRAC Board. February 15, 2005. 3 pp.
- Schnick, R.A. 2005. Proposed 2005 National Conservation Need for the Multistate Conservation Grant Program: Complete the Approval Requirements for AQUI-S®, the Candidate Zero Withdrawal Anesthetic, and Oral and Waterborne Antibacterials to Control Columnaris Disease. Submitted to the International Association of Fish and Wildlife Agencies. February 16, 2005. 1 pp.
- Schnick, R.A. 2005. Report on background, justification, and efforts to gain additional funding for AQUI-S® studies, April 7, 2005. Submitted to the NCRAC Board. April 12, 2005. 3 pp.
- Schnick, R.A. 2005. Draft label claim for 35% hydrogen peroxide (PEROX-AID®). Submitted to Eka Chemicals, Inc. for development into final labeling. April 12, 2005. 5 pp.
- Schnick, R.A. 2005. Call for Statements of Interest: Drug Approval Research on 17 Alpha-Methyltestosterone. Submitted to Ted Batterson, North Central Regional Aquaculture Center for distribution to potential contractors. April 26, 2005. 3 pp.
- Schnick, R.A. 2005. Final minutes to Drug Approval Working Group meeting, Arlington, Virginia. Submitted to Drug Approval Working Group members. April 26, 2005. 10 pp.
- Schnick, R.A. 2005. Draft label claims for Halamid®. Submitted to Axcentive SARL. May 9, 2005. 1 pp.
- Schnick, R.A. 2005. Roz's Corner: AADAP Newsletter Contribution. Submitted to AADAP. May 13, 2005. 1 pp.
- Schnick, R.A. 2005. MUMS designation requests for aquaculture drugs (May 14, 2005). Submitted to CVM. May 14, 2005. 2 pp.
- Schnick, R.A., J.J. Meinertz, and J.D. Bowker 2005. Complete the marker residue depletion portion of the Human Food Safety Technical Section, complete the Target Animal Safety Technical Section, and coordinate and oversee all activities toward the approval of AQUI-S® as a zero-withdrawal anesthetic for short-exposure handling of all freshwater fish. Submitted to the International Association of Fish and Wildlife Agencies. June 8, 2005. 15 pp.
- Schnick, R.A. 2004. Tenth annual report of activities—National Coordinator for Aquaculture New Animal Drug Applications (May 15, 2004 to May 14, 2005). Submitted to Ted Batterson, North Central Regional Aquaculture Center for distribution to contributors to this position. June 20, 2005. 27 pp.