Eighth Annual IAFWA Project Summary Report

(Performance Period: July 1, 2001 to June 30, 2002)

Approval of Drugs for Public Fish Production

a project of the

International Association of Fish and Wildlife Agencies (IAFWA)

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Research Study Number 1: Formalin

Objectives: To develop suitable efficacy and target animal safety data to extend the current NADA for formalin to include its use to control saprolegniasis on eggs and adults of publicly cultured freshwater fish.

Efficacy:

Progress: UMESC completed two trials evaluating the efficacy of formalin to control mortality associated with saprolegniasis on channel catfish. In each study, the mortality in treated fish was not significantly different from the mortality in untreated fish. The apparent failure of formalin to control mortality was more likely a result of an inconsistent performance of the disease model, i.e. variations in lesion severity and variations in the extent of fungal infections, rather than ineffective formalin treatments. UMESC is continuing to work with CVM's Office of Research (OR) to develop a fungal infection model in fish in order to use that model to conduct pivotal efficacy studies with formalin and hydrogen peroxide.

Current Status: UMESC and OR plan to complete fungal disease model development; UMESC will conduct a pivotal efficacy trial with channel catfish by December 31, 2002. OR will conduct similar pivotal efficacy studies in rainbow trout.

Research Study Number 2: Oxytetracycline

Objectives: (1) Extend the feed additive label for treatment of certain bacterial diseases on cool and warm water fish species of importance to public fish production and to cover marking of fish species not covered by a current approval. (2) Expand the feed additive label for control of flavobacteriosis on cold, cool, and warm water fishes.

Environmental Assessment

Progress: The development of an Environmental Assessment for the amended use of oxytetracycline in aquaculture is in progress. A literature search for information associated with the aquatic fate and environmental toxicity of oxytetracycline is in progress and will include a risk assessment to aquatic life from aquaculture use of oxytetracycline based on estimated introduced environmental concentrations from a comprehensive UMESC hatchery survey.

Current Status: The environmental assessment report will be submitted to CVM by December 31, 2002. A model to describe the fate of oxytetracycline released into the environment from aquaculture facilities is being prepared under contract with a researcher at the University of Wisconsin – Madison. Validation of the estimated model concentrations will be conducted at an aquaculture facility in spring 2003, and the results will be submitted as an amendment to the environmental assessment report by June 30, 2003.

Target Animal Safety

Progress: Studies describing oxytetracycline target animal safety with cool and scaled warm water fish are complete. Oxytetracycline (TM-100F) was administered in the medicated feed to hybrid striped bass, walleye, and yellow perch. Fish were dosed at 0, 1, 3, and 5X the

current maximum label dose of 82.5 mg/kg body weight/day for 10 (hybrid striped bass and yellow perch) or 20 days (walleye). No fish died during the dosing period and specimens submitted for histological assessment were generally unremarkable. Draft pathology reports from a private pathology laboratory have been submitted to UMESC for review.
Current Status: Data collection is considered complete for target animal safety studies. A final report will be submitted to CVM by December 31, 2002. Pending acceptance of the data by CVM, all Project obligations for oxytetracycline target animal safety with cool and scaled warm water fish will be fulfilled.

Efficacy

Progress: A pivotal efficacy trial was conducted using the U.S. Fish and Wildlife Service (Bozeman, MT) protocol for feed additive oxytetracycline at Spirit Lake SFH in Spirit Lake, Iowa. A UMESC scientist served as study monitor and assisted in the trial.
Current Status: Data was reviewed by a UMESC scientist and forwarded to the Bozeman NIO.

FOI Document Preparation

Progress: Draft Freedom of Information documents describing residue depletion studies conducted by UMESC in coho salmon, walleye and northern pike were forwarded to CVM on May 30, 2001. A Federal Register notice was published on November 16, 2001 concerning the availability of residue depletion data in support of new approved uses of feed additive oxytetracycline.
Current Status: The animal safety section of the freedom of information summary for oxytetracycline will be submitted to CVM by December 31, 2002. The effectiveness section of the freedom of information summary will be submitted to CVM if efficacy trials are declared pivotal by CVM.

Responses to CVM

Progress: A letter dated September 9, 2002 was received from CVM concerning a response and submission of additional data associated with the analytical method for oxytetracycline in edible fish tissue from several species of fish.
Current Status: Comments from the letter dated September 9, 2002 concerning the analytical method for oxytetracycline in fish edible tissue are currently being evaluated and a response is being developed. These correspondences will not affect the pending label amendments.

Research Study Number 3: Copper Sulfate

Objectives: To gain approval of copper sulfate as a therapeutic drug to control external protozoan and metazoan parasites, bacterial, and fungal diseases of cultured food fish.

Environmental Assessment

Progress: Two reports were submitted to CVM. After reviewing the reports, CVM requested additional data.

Current Status: The additional data requested by CVM has been collected and a report presenting the data is in preparation. The report will be submitted to CVM by December 31, 2002.

Target Animal Safety

Progress: Two reports were submitted to CVM. After reviewing the reports, CVM requested additional data.

Current Status: The additional data requested by CVM has been collected and a report presenting the data is in preparation. The report will be submitted to CVM by December 31, 2002.

FOI Document Preparation

Progress: The effectiveness and animal safety sections of the freedom of information summary for copper sulfate are in preparation.

Current Status: The effectiveness and animal safety sections of the freedom of information summary for copper sulfate will be submitted to CVM by December 31, 2002.

Research Study Number 4: Chloramine-T

Objectives: Develop data on mutagenicity, environmental fate, residue chemistry, efficacy, and target animal safety that satisfy CVM requirements to support the approval of chloramine-T to BGD and external flavobacteriosis on cultured freshwater fish.

Environmental Assessment

Progress: An environmental summary of chloramine-T discharged from aquaculture facilities based on a literature search has been prepared. The report includes a risk assessment to aquatic life based on estimated environmental concentrations from a UMESC hatchery survey and validation of those estimates by a formal study at the UMESC aquaculture facility.

Current Status: The environmental assessment report will be submitted to CVM by September 30, 2002. Pending acceptance of the report by CVM, all Project obligations for the environmental assessment of chloramine-T will be fulfilled.

Human Food Safety

Progress: Six final reports were submitted to CVM. Three reports presented data validating the proposed determinative method for p-TSA in fish fillet tissue and three reports presented data from p-TSA depletion studies conducted with rainbow trout, yellow perch, and hybrid striped bass. A confirmatory method for p-TSA in fish fillet tissue was developed by CVM.

Current Status: Data submissions associated with the determinative method are complete. Pending acceptance of the data by CVM, all Project obligations for the determinative method will be fulfilled. Chloramine-T residue depletion studies are complete. CVM concluded that the studies were conducted satisfactorily and that the data provided in each submission can be used to calculate a withdrawal time after a tolerance is assigned for p-TSA. Validation of the confirmatory method by CVM is nearing completion. A final report describing validation

of the confirmatory method will be complete by December 31, 2002. Pending acceptance of the data by CVM, all Project obligations for the confirmatory method will be fulfilled.

Target Animal Safety

Progress: A final report presenting data from the chloramine-T target animal safety studies with cool and warm water fish was submitted to CVM on August 25, 2002. The report described the results of target animal safety studies conducted with walleye, lake sturgeon, northern pike, channel catfish, and largemouth bass. Based on a minimum 3X safety margin for the representative species tested in this study, chloramine-T administered at concentrations of up to 20 mg/L administered once daily for 60 min on four consecutive days is likely to be considered safe for the fry and fingerling stages of all freshwater cool and warm water fish.

NIO submitted a report to CVM describing the toxicity of chloramine-T to salmonids on April 1, 2002; CVM accepted these data in September 2002. The NIO recommended approval of a NADA for the use of chloramine-T administered as a 60 min bath at a concentration up to 20 mg/L on three consecutive or alternate days to freshwater-reared salmonids.

Current Status: Data submissions associated with chloramine-T target animal safety studies are complete. Pending acceptance of the data by CVM, all Project obligations for chloramine-T target animal safety studies with cold, cool and warm freshwater fish will be fulfilled.

Efficacy

Progress: UMESC completed two trials that evaluated the efficacy of chloramine-T to control mortality on channel catfish and walleye infected with external columnaris. The mortality of treated channel catfish was not significantly different than the mortality of untreated control channel catfish. The mortality of treated walleye was significantly less than the mortality of untreated control walleye.

Current Status: Final reports from the channel catfish and walleye efficacy trials will be submitted to CVM by December 31, 2002. Pending CVM's acceptance of data from the walleye trial, all Project obligations for chloramine-T efficacy studies with cool water fish will be fulfilled. The NIO will attempt to conduct or coordinate additional pivotal efficacy trials to broaden the pending approval of chloramines-T using base funds.

FOI Document Preparation

Progress: The animal safety (April 26, 2002) and human safety (April 23, 2002) sections of the freedom of information summary for Halamid® (chloramine-T) were submitted to CVM.

Current Status: The effectiveness section of the freedom of information summary for Halamid® will be submitted to CVM by December 31, 2002.

Research Study Number 5: Florfenicol

Objectives: Develop efficacy, target animal safety, and total residue and metabolism data required for the use of florfenicol to control furunculosis and other susceptible systemic bacterial

diseases in freshwater cold, cool, and warm water fish.

Efficacy

Progress: NIO initiated 13 and completed 12 trials that evaluated the efficacy of florfenicol-medicated feed to control mortality of coho salmon, steelhead trout, cutthroat trout, muskellunge, and hybrid striped bass infected with a variety of fish pathogens. Results from three studies showed that the mortality of treated fish was significantly less than the mortality of untreated fish. Results from five studies showed that the mortality of treated fish was less than mortality of untreated fish, but differences were not significant. Results from the remaining four trials were inconclusive.

Current Status: Final reports that demonstrate conclusive results will be submitted to CVM by December 31, 2002.

Research Study Number 6: Potassium Permanganate

Objectives: Gain approval of potassium permanganate as a therapeutant to control external protozoan and metazoan parasites and bacterial and fungal diseases of cultured food fish.

Environmental Assessment

Progress: Tier 1 studies are near completion.

Current Status: A report will be submitted to CVM by December 31, 2002.

Target Animal Safety

Progress: A target animal safety study was completed for potassium permanganate.

Current Status: A report presenting the data is in preparation. The report will be submitted to CVM by December 31, 2002.

Efficacy

Progress: Two controlled efficacy studies are complete for control of ichthyophthiriasis in channel catfish and tilapia.

Current Status: A pivotal efficacy study will be conducted when seasonal water temperature is optimal.

Research Study Number 7: AQUI-S™

Objectives: Submission of efficacy, target animal safety, and residue depletion technical data required for the approval of AQUI-S™ as an anesthetic/sedative with a short withdrawal time for several species of freshwater fish.

Environmental Assessment

Progress: A literature search for information associated with the aquatic fate and toxicity of AQUI-S™ is under development. Based on a preliminary search for aquatic fate and toxicity information, the environmental assessment report is expected to be deficient. CVM will most likely require additional information from aquatic fate and toxicity studies.

Current Status: The environmental assessment report will be submitted to CVM by December 31, 2002.

Human Food Safety

Progress: A pilot total residue depletion study is in progress to define sampling times, techniques for extraction and analysis of residues, and to identify the marker residue resulting from exposure of rainbow trout to AQUI-S™. A protocol for the definitive total residue depletion study was forwarded to CVM on July 3, 2002 for review and comments were received on August 8, 2002.

Current Status: A definitive total residue depletion study will be completed and a report will be submitted to CVM by December 31, 2002.

Target Animal Safety

Progress: Preliminary toxicity studies have been completed at UMESC on a variety of fish species. 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 will be performed by the FWS.

Current Status: The sponsor is ready to submit to CVM target animal safety and efficacy studies on salmonids completed in Canada. NIO will submit to CVM salmonid target animal safety study protocols by December 31, 2002. NIO will conduct pivotal target animal safety studies with salmonids using base funds.

Efficacy

Progress: Preliminary efficacy studies were completed at UMESC on a variety of fish species. UMESC will not perform any other studies because funds were diverted to fulfill the need for human food safety studies. NIO will conduct pivotal efficacy studies with a variety of cold, cool, and warm water fish species using base funds. FWS has an INAD to treat up to 100 million fish with 5 to 60 mg/L AQUI-S™ in static baths for up to 1 h.

Current Status: The sponsor is ready to submit to CVM efficacy studies on salmonids completed in Canada.

Research Study Number 8: Hydrogen Peroxide

Objectives: Develop efficacy and target animal safety data to provide fish culturists with effective, safe treatment regimens for hydrogen peroxide to control saprolegniasis on fish and fish eggs and for controlling external parasitic infestations and mortalities associated with external bacterial infections on freshwater fish.

Environmental Assessment

Progress: Review of the hydrogen peroxide environmental assessment report was completed by CVM. During subsequent UMESC discussions with CVM concerning the review, CVM indicated the need for data from a 21-day chronic toxicity study with *Daphnia magna*. CVM recommended revising the environmental assessment report after completing the chronic toxicity study and resubmitting the revised report.

Current Status: The chronic toxicity study will be conducted at the UMESC with a target completion date of December 31, 2002. A final report describing the results of the study and a revised environmental assessment report will be submitted to CVM by March 31, 2003.

Target Animal Safety

Progress: Two final reports were submitted to CVM. One report described the safety of hydrogen peroxide to non-eyed and eyed rainbow trout eggs and the other described the safety of hydrogen peroxide to paddlefish and rainbow trout eggs. The reports are in review by CVM.

Data from target animal safety studies with fish was accepted by CVM on October 4, 2001.

Current Status: Pending CVM's acceptance of data from the egg reports, all Project obligations for hydrogen peroxide target animal safety studies with cold, cool, and warm water fish eggs and fish will be fulfilled.

Efficacy (eggs)

Progress: CVM accepted pivotal efficacy data for treatment of salmonid eggs to control mortalities associated with saprolegniasis by a 15-minute treatment at 500 mg/L of hydrogen peroxide.

A report describing the efficacy of hydrogen peroxide to control mortality associated with saprolegniasis on paddlefish, walleye, and white sucker eggs was submitted to CVM. A trial to evaluate the efficacy of hydrogen peroxide to control mortality associated with saprolegniasis on channel catfish eggs was conducted at the Lost Valley Hatchery (Warsaw, MO). The mortality of treated channel catfish eggs was significantly less than the mortality of untreated control eggs.

Current Status: A final report from the Lost Valley Hatchery efficacy study will be submitted to CVM by December 31, 2002. Pending CVM's acceptance of data from the two final reports, all Project obligations for hydrogen peroxide efficacy studies with cold, cool, and warm water fish eggs will be fulfilled.

Efficacy (fish)

Progress: CVM accepted pivotal efficacy data for treatment of all salmonids reared in freshwater to control mortalities associated with bacterial gill disease by a 60-minute treatment at 50 mg/L or 30-minute treatment at 100 mg/L of hydrogen peroxide. CVM accepted the following as supporting data: (1) 60-minute treatments to control mortalities associated with external columnaris disease in yellow perch and (2) treatment of external parasitic infestations in fish.

UMESC completed two trials with channel catfish and one with rainbow trout evaluating the efficacy of hydrogen peroxide to control mortality associated with saprolegniasis. In each trial, the mortality of treated fish was not significantly different from the mortality of untreated control fish. The apparent failure of hydrogen peroxide to control mortality was likely a result of an inconsistent disease model caused by variations in lesion severity and variations in the extent of fungal infections among test fish.

UMESC completed two field trials to evaluate the efficacy of hydrogen peroxide to

control mortality associated with external columnaris infections on channel catfish and walleye. In each trial, the mortality of treated fish was not significantly different from the mortality of untreated control fish.

Current Status: UMESC will continue efficacy work with channel catfish to develop a consistent model that will cause fungal infections with subsequent mortality. If a disease model is successfully developed, an efficacy trial with hydrogen peroxide will be conducted. Pending successful development of a disease model, a final report will be submitted to CVM by December 31, 2002.

Final reports from channel catfish and walleye field trials will be submitted to CVM by December 31, 2002. Pending CVM's acceptance of data from the field trials, Project obligations for efficacy studies with cool and warm water fish infected with columnaris will be fulfilled.

FOI Document Preparation

Progress: The following three documents summarizing data for effectiveness and animal safety sections of the freedom of information document for hydrogen peroxide (Perox-Aid®) were submitted to CVM: (1) Perox-Aid® for the Treatment of Fungal Infections on Finfish Eggs; (2) Perox-Aid® for the Treatment of External Flavobacter Infections on Freshwater Finfish; and (3) Perox-Aid® for the Treatment of External Parasitic Infestations on Freshwater Finfish.

Current Status: Additional documents summarizing data for the effectiveness section of the freedom of information document will be submitted to CVM by December 31, 2002.

Research Study Number 9: Crop Grouping

Objectives: (1) Develop cooperative studies with CVM scientists and university investigators that will result in a reasonable approach to solving problems related to developing extensive residue chemistry data for minor species drug approvals. (2) Develop a course of study to demonstrate similarities and differences in the metabolism and residue chemistry of aquaculture drugs by a broad range of cultured freshwater fish.

Progress: The remaining work on crop grouping was conducted in the first quarter of FY02. A final report and associated data from the analysis of florfenicol in plasma from different species of fish were submitted to the UMESC archives on November 20, 2001. A manuscript describing the analysis of florfenicol in fish plasma was accepted for publication in the Journal of Chromatography.

Current Status: All amended Project obligations for florfenicol have been be fulfilled.

Research Study Number 10: Negotiations and Contract Coordination

Objectives: (1) Ensure that all data required by CVM for approval through NADAs are developed for the eight priority drugs in a timely, logical, and efficient manner. (2) Coordinate the administration of all contracts by CVM's Office of Science to ensure efficiency, timeliness, and acceptability of data to CVM. (3) Track and report the progress of all studies and ensure that

they are proceeding toward approval in a timely, logical, and efficient manner. (4) Assemble and submit NADA technical sections for approval by CVM.

(1) Ensure that all data required by CVM for approval through NADA's are developed for the eight priority drugs in a timely, logical, and efficient manner.

General progress: UMESC obtained funding for an oxytetracycline environmental assessment from the Wallop-Breaux Sport Fish Restoration Funds on July 25, 2001. The project includes measurement of oxytetracycline in water and sediment in and around a hatchery with a typical treatment for a disease episode.

In September 2001, the Multi-State Conservation Grant Program indicated it funded UMESC to develop (1) a model to infect fish with external columnaris disease, (2) data toward oxytetracycline immersion therapy, and (3) a determinative analytical method for the marker residue for AQUI-S™.

In September 2001, the Multi-State Conservation Grant Program indicated it funded a study at Arkansas State University on the environmental fate and effect of potassium permanganate.

Progress by drug:

AQUI-SÔ

Status: The sponsor (AQUI-S New Zealand LTD.) is currently proceeding with worldwide drug approval; in June 2001, the sponsor decided to proceed with the old formulation and not develop a new formulation for the U.S. market

Bottom Line: The late decision of whether to change the formulation of AQUI-S™ delayed data generation on all technical sections and impacts the submission of all technical sections by 2002.

The sponsor, AQUI-S New Zealand LTD., reversed a business decision to reformulate their product. The product to be developed in the United States is the same formulation that the company has approved as a fish anesthetic in several countries.

At their meeting at Bozeman, MT on August 2-3, 2001, members of the DAWG verbally agreed to the redirection of UMESC Year 8 funds originally intended for efficacy and target animal safety studies, to studies necessary to determine the marker residue of AQUI-S™?

In September 2001, the Multi-State Conservation Grant Program indicated it would fund UMESC to develop a determinative analytical method for the marker residue for AQUI-S™.

USDA did not fund the proposal submitted by the U.S. representative of AQUI™ for mammalian safety studies that would substitute for NTP studies.

CLOVE OIL--CVM issued Guidance for Industry Document #150 on June 11, 2002 on the use of clove oil or eugenol as anesthetics for fish. CVM reiterated that the Generally Recognized As Safe (GRAS) status of clove oil or eugenol as food additives does not justify their use as animal drugs and both substances are considered as an unapproved new animal drugs. These substances also cannot be used for routine clinical use on laboratory animals but they can be used in teaching settings under restricted regulations.

No disclosable INAD activity is known for gaining approval of clove oil or eugenol but there is an effort to gain approval of AQUI-S™ (active ingredient is isoeugenol) by the sponsor (AQUI-S New Zealand LTD), International Association of Fish and Wildlife

Agencies, UMESC and NIO. The FWS INAD requires a 21-day withdrawal time as part of the INAD but the withdrawal time could be lowered to zero if ongoing tests prove that isoeugenol is safe at concentrations present at time of release for slaughter.

Chloramine-T

Status: Sponsor (Axcentive bv; formerly Akzo Nobel Chemicals, Inc.) committed to INAD/NADA.

Bottom Line: All submissions should be completed by 2002 for control of mortalities associated with bacterial gill disease and external columnaris disease on all freshwater-reared salmonids and all technical sections except efficacy for bacterial gill disease and external columnaris disease on cool and warm water fish.

Axcentive bv through its U.S. representative held a meeting with CVM on October 31, 2001 to discuss the genotoxicity concerns that CVM has on marker residue of its chloramine-T product Halamid®. Resolution to mammalian safety issues is possible if Axcentive bv provides acceptable evidence that p-TSA is not genotoxic.

In September 2001, the Multi-State Conservation Grant Program indicated it would fund UMESC to development of a model to infect fish with external columnaris disease.

Axcentive bv requested a meeting with the National Aquaculture NADA Coordinator in Chicago, Illinois on June 3, 2002 to discuss progress on mammalian safety and environmental safety issues.

Axcentive bv submitted genotoxicity studies and information to CVM on June 18, 2002 and CVM declared that p-TSA is not genotoxic on July 19, 2002.

The U.S. representative for Axcentive bv and the National Aquaculture NADA Coordinator prepared documents in August 2002 to refute the nomination of chloramine-T and p-TSA for study under NTP.

Copper Sulfate

Status: Sponsor Phelps Dodge Refining Corporation has an acceptable product chemistry technical section.

Bottom Line: All submissions should soon be completed for the control of *Ichthyophthirius* sp. on catfish in earthen ponds. The claims for control of *Ichthyophthirius* sp. on all fish and other external microbes on all fish would be based on additional efficacy and target animal safety studies that would be completed in 2002, if stakeholders were interested.

Florfenicol

Status: The sponsor, Schering-Plough Animal Health, recently allowed the development of florfenicol for approval in the United States; approved in Canada in August 1997 to control furunculosis in Atlantic salmon.

Bottom Line: Sponsor will continue to develop data for aquaculture approval but the efforts by the IAFWA Project on florfenicol were redirected by the DAWG to other IAFWA Project drugs.

The florfenicol INAD exemption (INAD 10-697) has been granted by CVM to FWS. The INAD stipulates a 21-day withdrawal period. Efficacy studies are underway at the NIO on a variety of cold, cool, and warm water fish species. UMESC scientists were trained by

Schering-Plough Animal Health personnel to perform the analytical method for the determination of florfenicol in fish feed to support efficacy studies.

Multi-State Conservation Grant Proposal "Analytical Support of Pivotal Efficacy Trials for Use in Public Fisheries" was funded under the Federal Aid in Sport Fish Restoration Act on May 16, 2001. The proposal provides for analyses of fish feed for florfenicol content from pivotal efficacy trials conducted under the INAD held by FWS. In addition, the proposal includes validation of the analytical method on fish feeds not previously completed by the sponsor and used in pivotal trials.

A Cooperative Research and Development Agreement (CRADA) between SPAH and USGS was signed on April 10, 2001. UMESC completed a target animal safety study for florfenicol in channel catfish under that CRADA.

Formalin

Status: Supplemental NADA by Western Chemical Inc. approved on June 18, 1998 for control of certain fungi on the eggs of all fish and certain external protozoa and monogenetic trematodes on all fish.

Bottom Line: All submissions should be completed in 2002 for control of mortalities associated with saprolegniasis on all fish.

Natchez Animal Supply Company submitted a supplemental NADA to CVM on June 5, 2001 for its formalin product, Formalin-F®, to control certain fungi on the eggs of all fish and certain external protozoa and monogenetic trematodes on all fish.

Hydrogen peroxide

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; human food safety data requirements are met.

Bottom Line: All submissions should be completed in 2002 for control of mortalities from saprolegniasis on all fish eggs; for control of mortalities from saprolegniasis on all fish, for control of mortalities from external bacterial gill disease and external columnaris disease on salmonids, and for control of parasites on all fish.

On July 18, 2001, CVM accepted as supporting efficacy data for treatment of external parasitic infestations in fish.

On October 4, 2001, CVM accepted target animal safety data at concentrations from 50 to 100 mg/L for a variety of fish exposed to hydrogen peroxide from 30 to 60 minutes.

In September 2001, the Multi-State Conservation Grant Program indicated it would fund UMESC to develop a model to infect fish with external columnaris disease.

UMESC has continued to expand its coordination and collaboration to develop additional efficacy data to support the use of hydrogen peroxide by initiating three compassionate INADs. Participation in the three INAD protocols has increased immensely over the past year from 24 INAD cooperators in 2000 to 115 in 2001 and 2002.

Eka Chemicals, Inc. submitted a revised Product Chemistry Technical Section on June 28, 2002.

Oxytetracycline

Status: Currently approved for control of certain bacterial diseases in catfish, salmonids, and lobsters and as a marking agent in Pacific salmon.

Bottom Line: All submissions are considered complete for otolith marking on all fish by immersion. By 2002, all submissions should be complete for control of (1) systemic coldwater disease in salmonids and (2) mortalities associated with systemic columnaris disease in salmonids.

On October 5, 2001, UMESC submitted a response to CVM regarding data to support human food safety technical section for an analytical method for oxytetracycline in the edible tissue of fish used in residue depletion studies.

On May 21, 2002, CVM accepted the Public Master File for the use of oxytetracycline immersion for skeletal marking of fry and fingerling finfish.

UMESC obtained funding for an oxytetracycline (OTC) environmental assessment (EA) from the Wallop-Breaux Sport Fish Restoration Funds on July 25, 2001. The project includes measurement of OTC in water and sediment in and around a hatchery with a typical treatment for a disease episode.

In September 2001, the Multi-State Conservation Grant Program indicated it would fund UMESC to develop data toward oxytetracycline immersion therapy.

On October 5, 2001, UMESC submitted a response to CVM regarding data to support human food safety technical section for an analytical method for oxytetracycline in the edible tissue of fish used in residue depletion studies.

Potassium permanganate

Status: The sponsor, Carus Chemical Company, submitted a product chemistry technical section and a request for categorical exclusion for environmental safety; CVM has requested additional data for both technical sections.

Bottom Line: All submissions should be completed by 2004 for control of *Ichthyophthirius* sp. on all fish.

In September 2001, the Multi-State Conservation Grant Program indicated it would fund a study on the environmental fate and effect of potassium permanganate. This study was initiated January 2002 at Arkansas State University.

The National Aquaculture NADA Coordinator met with Carus Chemical Company on February 12, 2002 to discuss the role that the company can play in the final development of potassium permanganate as an aquaculture drug.

(2) Coordinate the administration of all contracts by CVM's Office of Science to ensure efficiency, timeliness, and acceptability of data.

Progress: In May 2002, an interagency agreement was approved to fund a portion ($20,100) of the National Coordinator for Aquaculture New Animal Drug Applications for the period July 01, 2002 to September 30, 2002

Current Status: The position of National Coordinator for Aquaculture New Animal Drug Applications was funded through to September 30, 2002 by the existing interagency agreement.

(3) Track and report progress of all studies and ensure that they are proceeding toward approval in a timely, logical and efficient manner.

Progress: Major advances were made toward communication and coordination of INAD/NADAs of high priority drugs important to public fish production at workshops held by NIO in Bozeman, Montana in 2001 and 2002.

The DAWG held a meeting in Bozeman, Montana on August 2-3, 2001 to (1) discuss the progress being made on the IAFWA Project drugs, (2) work plans for the final year of the IAFWA Project, (3) discuss new funding proposals on florfenicol, AQUI-S™, disease model for external columnaris disease, and environmental assessment for oxytetracycline, and (4) the future of public drug approval efforts after 2002.

The DAWG had three other meetings during this period of time–December 4, 2001 in Wichita, Kansas, April 4, 2002 in Dallas, Texas, and September 19, 2002 in Big Sky, Montana. At the Wichita meeting, several action items were developed. Listed below are those action items and the response:

1) The National Aquaculture NADA Coordinator and Bill Gingerich. Request a meeting in February 2002 with CVM regarding the data gaps for the remaining technical sections. Such a meeting was held March 14, 2002.

2) The National Aquaculture NADA Coordinator. Write a letter to CVM requesting a high-level meeting before the April DAWG meeting but after the technical section meeting to discuss progress and impediments to approvals for IAFWA Project drugs. It was decided by the DAWG that a letter should be written instead. The National Aquaculture NADA Coordinator wrote a draft letter that was finalized and signed by Bob Miles on March 6, 2002.

3) The National Aquaculture NADA Coordinator. Develop a brief survey of the states on their priority label claims for the eight IAFWA Project drugs. The National Aquaculture NADA Coordinator sent out a survey to the states on December 27, 2001. Results were analyzed and presented at the meeting in Dallas on April 4, 2002.

4) Dave Erdahl and the National Aquaculture NADA Coordinator. Obtain and compile annual fish production figures for each state for information to be sent to sponsors and potential sponsors. The National Aquaculture NADA Coordinator sent surveys on December 28, 2002 to all 50 states and followed up with another mailing on February 9, 2002. The Bozeman NIO is collating the responses into a database.

5) Celebration Steering Committee (Bob Miles, Doug Hanson, Roz Schnick, and Dave Erdahl). Plan the celebration of the success of the IAFWA Project. The celebration luncheon was set for September 18, 2002 at Big Sky, Montana. Doug Hanson coordinated a series of conference calls in April and May 2002. The National Aquaculture NADA Coordinator prepared lists of invitees and awardees, wrote a brochure, arranged for a speaker, and contacted and secured sponsors for the event.

6) Bill Gingerich. Draft letter to Mike Gibson to partially support the National Aquaculture NADA Coordinator's position from May to September 2002 based a her budget needs for coordinating the IAFWA Project during that time. The National Aquaculture NADA Coordinator provided information on a budget to Bill Gingerich.

7) Bob Miles and Bill Gingerich. Obtain radiolabeled AQUI-S™ in an expeditious manner

through IAFWA, thus by-stepping the Federal Register notice. UMESC was able to obtain the material without assistance from IAFWA.

8) The National Aquaculture NADA Coordinator. Distribute the DAWG minutes from the August 2001 meeting in Bozeman by December 18, 2001. The National Aquaculture NADA Coordinator sent out the final minutes on December 17, 2001.

9) Bob Miles. Draft letters to USGS, USDA, and FWS for Max Peterson's signature to indicate the great job that UMESC, HKD-SNARC, and Bozeman have done on the IAFWA Project drugs. No known action.

10) Bob Miles and Doug Hanson. Plan the April 2002 meeting of the DAWG to be held in Dallas, Texas. Meeting was held April 4, 2002.

Follow-up items to the Dallas meeting are as follows:

1) Follow-up to fish production survey. The National Aquaculture NADA Coordinator worked with Dave Erdahl to determine which states have not responded and informed Mike Gibson. Dave Erdahl is contacting the remaining states for the production data.

2) Current status of the technical sections for IAFWA Project drugs. UMESC volunteered to clarify the status with new graphics.

3) Remaining funds available for the IAFWA Project. USGS offered to provide the final figures for the funds available form the states for the remaining data gaps at the FWS INAD Workshop in August 2002.

4) Prioritization of unmet label claim needs. The National Aquaculture NADA Coordinator prepared an assessment of the major unmet label claim needs for the control of external bacterial infections on cool water and warm water species on April 7, 2002 and for oral drugs on April 15, 2002.

5) Clarification of the projected status of label claims. The National Aquaculture NADA Coordinator provided such a clarification on April 8, 2002.

6) MUMS status. The National Aquaculture NADA Coordinator provided the most current status of the Minor Use Minor Species legislation to the DAWG on April 13, 2002.Next DAWG meeting–Bob Miles and Mike Gibson scheduled a meeting of the DAWGs for the morning of August 2, 2002 in Bozeman, Montana.

7) Funds from state contributions for Program Manager of the IAFWA Project (i.e., the National Aquaculture NADA Coordinator). The National Aquaculture NADA Coordinator provided a budget to Mike Gibson for FY 2003 with a copy to Bob Miles on April 7, 2002.

The Celebration Luncheon on September 18, 2002 at the Big Sky Resort, Montana for the Project was a huge success. More than 80 persons attended and certificates and plaques were provided to those individuals, agencies, organizations, and companies that contributed to the successes.

The DAWG held a meeting at the 100th anniversary celebration of the IAFWA at Big Sky Resort, Montana on September 19, 2002. The National Aquaculture NADA Coordinator gave a report on (1) general outline of what needs to be done and the cost, (2) what to do next to complete the label claims, and (3) how to systematically march to end points. The DAWG voted to have UMESC use the remaining Federal Aid funds for Year 8 Work Plan studies and to provide partial funding for the position of the National Aquaculture NADA Coordinator. The

DAWG will remain in place for another year at least to direct the remaining studies. Dr. Bill Gingerich provided the status of all submissions made to CVM since the Federal-State Aquaculture Drug Approval Partnership Project began.
Current Status: Appropriate progress reports have been and will continue to be presented to the IAFWA Project participants and stakeholders. Continuing efforts will be made to inform the entire aquaculture community of the progress being made on IAFWA Project.

(4) Assemble and submit NADA technical sections for approval by CVM.

From July 1, 2001 to June 30, 2002, IAFWA Project personnel submitted 25 data packages to CVM (see **Products Inventory, Submissions to Regulatory Agencies**).

(5) (New Title) Address national aquaculture issues

Progress: The Joint Subcommittee on Aquaculture formed the Aquaculture Effluents Task Force (AETF) to coordinate and facilitate input of science-based information to assist in the development of national effluent limitation guidelines and standards for aquaculture facilities by EPA. The AETF met on October 17-18, 2001 to discuss the status of EPA's Effluent Guidelines Plan for aquaculture facilities. A conference call was convened on May 30, 2001 to discuss drug and chemical issues with EPA and a response was prepared after a conference call on October 11, 2001 with AETF members. The latest meeting of the AETF was held on January 27, 2002. The purpose of the meeting was to discuss the status of EPA's Effluent Guidelines Plan for aquaculture facilities. The latest direction that EPA plans to go are Best Management Practices for drugs and chemicals; however, recent attempts at gaining a discharge permit from EPA in Maine have illustrated that INADs and extra label use would not be allowed. The National Aquaculture NADA Coordinator wrote a response to this extreme proposed permit in Maine and interacted with CVM on this issue. EPA issued its proposed rule for aquaculture effluents on September 12, 2002 and comments are due December 11, 2002. EPA will host its first public meeting to discuss the proposed rule on October 30, 2002 in Washington, DC.

A bill entitled "Minor Animal Species Health and Welfare Act of 2000" was introduced in the U.S. Congress into the House on June 27, 2000 (HR-4780) and into the Senate on October 5, 2000 (S-3169). The MUMS Act will facilitate and accelerate the approvals of aquaculture drugs. The bill includes provisions for early life stages that should help expedite the approvals of aquaculture drugs that are of interest to public and private fish production. A revised bill "Minor Use Minor Species Animal Health Act of 2001" was reintroduced into the House on May 24, 2001 (HR-1956) and into the Senate on August 2, 2001 (S-1346). The MUMS Coalition met on June 22, 2001 to coordinate the legislative effort on the bill, present information to legislative staff, and contact individual congressmen and senators for their support and sponsorship. The MUMS bill was attached to the Bioterrorism Bill but it was removed from the bill shortly before its passage on May 22, 2002. The MUMS bill picked up additional supporters who attached it to the "Animal Drug User Fee Act of 2002" (ADUFA - HR#4955 and S#2665). On August 9, 2002, the MUMS Coalition was requested to render immediate assistance in moving the MUMS bill through Congress under ADUFA.

On August 2-3, 2001, nine sponsors or potential sponsors invited by the National

Aquaculture NADA Coordinator attended a meeting of the Federal-State Aquaculture Drug Approval Partnership Project. These sponsors were interested in the development of their products for aquaculture. These sponsors included the major pharmaceutical firms of Alpharma, Bayer, Intervet, Novartis, and Schering-Plough and chemical or niche companies of Akzo Nobel Chemicals Inc., AQUI-S New Zealand LTD, Phelps Dodge Refining Corporation, and Carus Chemical Company.

Syngenta Crop Protection, Inc., expressed an interest in developing their diquat product for use as a drug in aquaculture. The National Aquaculture NADA Coordinator provided information on diseases, fish species, and potential market from August to October 2001. The National Aquaculture NADA Coordinator met with Syngenta Crop Protection, Inc. on December 18-19, 2001 in Greensboro, North Carolina to provide information on how to proceed with an INAD that would lead to an NADA approval. Syngenta Crop Protection, Inc. requested an INAD exemption for their diquat product on March 4, 2002 and was granted an INAD by CVM on March 11, 2002. The Drug Approval Working Group for the public aquaculture sector expressed an interest in the development of diquat at its meeting on April 4, 2002. Syngenta Crop Protection, Inc. and the National Aquaculture NADA Coordinator met with CVM on August 28, 2002 to discuss development of diquat as a therapeutant. Dr. Bill Gingerich and the National Aquaculture NADA Coordinator met with a Syngenta Crop Protection, Inc. representative on September 18, 2002 to discuss development of data and a CRADA.

The National Aquaculture NADA Coordinator met with the Alpharma Animal Health product manager for Romet-30® and UMESC in August 2001 in Bozeman, Montana to discuss potential extensions and expansions of the NADA for publicly cultured finfish. The National Aquaculture NADA Coordinator met with the Alpharma Animal Health product manager for Romet-30® on April 16 and May 1-2, 2002 to develop a plan for the extensions and expansions of the NADA. Alpharma has made a commitment to expand and extend Romet-30® to other species and other diseases in the near future. Alpharma may also consider extensions and expansions of sulfamerazine.

Current Status: Progress is being made toward gaining approval of the MUMS legislation, resolving the issues with EPA on aquaculture effluents, addressing the antimicrobial resistance issues, and gaining additional and active company sponsors for drugs of importance to public aquaculture.

Product Inventory

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