

MID-YEAR PROGRESS REPORT
FOR
JULY 1, 1994 TO DECEMBER 31, 1994

Approval of Drugs for Public Fish Production

International Association of Fish and
Wildlife Agencies (IAFWA) Project

by

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IAFWA Project Report Number 1

INTRODUCTION

A partnership was developed between the National Biological Service (NBS), the U.S. Fish and Wildlife Service (FWS), and the International Association of Fish and Wildlife Agencies (IAFWA) on behalf of state fish and wildlife agencies to conduct research for the approval of aquaculture drugs with the U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM).

Research to gain new animal drug application (NADA) approvals or extensions of approvals for eight drugs identified as high priority by the states and to establish crop grouping was initiated July 1, 1994 and will extend until June 30, 1999. During that 5-year period, at least 39 states will contribute a total of \$3.9 million, NBS's Upper Mississippi Science Center (UMSC, formerly National Fisheries Research Center, La Crosse, Wisconsin) will provide \$4.3 million, and the Fish Farming Experimental Laboratory, Stuttgart, Arkansas (FFEL) will provide some base funding toward: a) development of data under GLP provisions to gain CVM approval of NADAs for use in aquaculture for the following essential drugs; 1) extension of formalin to other species, 2) expansion to other diseases and extension to other species for oxytetracycline, 3) copper sulfate, 4) chloramine-T, 5) sarafloxacin hydrochloride (sarafloxacin), 6) potassium permanganate, and 7) benzocaine; b) development of safety and efficacy data to delineate concentrations of hydrogen peroxide for control of fungi on various fish species and eggs and efficacy data to expand the low regulatory priority status of hydrogen peroxide for potential control of external parasitic infestations and external bacterial infections on freshwater fishes; and c) development of research information to allow acceptance of a crop grouping concept by CVM. Data will be generated to allow CVM to assess whether a few selected fish species can be used as surrogates for all or most of the cultured fishes in the United States.

The development of aquaculture NADAs through the IAFWA project is contingent upon continued base funding at UMSC of \$867,000 per year designated for chemical and drug registration activities, contribution of some base funding from FFEL, and state funding of at least \$780,000 per year under a five-year agreement through the IAFWA. A portion of the state contribution (\$50,000 to \$160,000 per year) and FFEL base funding will be used by FFEL for research on copper sulfate and potassium permanganate. The remainder of the state funding (\$620,000 to \$655,000 per year) and UMSC base funding will be used by UMSC (or contracted out) to achieve original or extended NADAs. The proposed studies to be conducted by UMSC and FFEL are estimated to cost \$8.9 million and only \$8.2 million is available, resulting in a need for an additional \$700,000.

GENERAL SUMMARY OF PROGRESS (JULY 1, 1994 TO DECEMBER 31, 1994)

Some progress has been on all the Research Study Plans in the IAFWA Project. Most of the effort has centered on administering and coordinating IAFWA Project efforts, identifying the data requirements, determining strategies for implementation, writing protocols, and initiating the research. Efforts have been made to keep CVM and all aquaculture interests informed of the IAFWA Project's activities and goals.

SUMMARY OF PROGRESS BY RESEARCH STUDY PLAN

A summary follows on the progress made during the period from July 1, 1994 to December 31, 1994 for each of the ten Research Study Plans in the IAFWA Project.

STUDY NO. 1: FORMALIN

Objectives: To develop suitable efficacy and target animal safety data to extend the current New Animal Drug Application (NADA) for formalin to include its use to control fungal infections on eggs and adults of cultured freshwater fish.

Job No. 1: Contract supervision of the formalin compassionate investigational new animal drug (INAD) request.

Progress: A protocol for the FWS's INAD for formalin to support the expanded use of formalin as a fungicide on fish eggs cultured on public hatcheries was written by NBS's UMSC and submitted to the Center for Veterinary Medicine (CVM) for review. The protocol has been approved and the INAD study is scheduled to begin in January 1995. The sponsorship of the FWS INAD is now under administration of the FWS's facility in Bozeman, Montana. In addition, UMSC met on October 28, 1994 with the coordinator for the Western Regional INAD Project to coordinate data transfer to UMSC for a NADA. Several workshops and coordination meetings have been conducted involving FWS's study director, study monitors, and INAD coordinators.

Job No. 2: Conduct controlled laboratory studies on a variety of fish species to evaluate the efficacy of formalin as a fungicide on cultured freshwater fish.

Progress: Formalin is currently approved by CVM for use on trout, salmon, and esocid eggs as a fungicide. Research underway at UMSC is necessary to support the extension of the formalin NADA to include fungicidal treatment of eggs of additional species of cultured freshwater fish. Treatments on a variety of fish species have shown that formalin is effective for controlling fungus even when 10% of the eggs are intentionally infected with fungus (*Saprolegnia parasitica*).

Job No. 3: Conduct target animal safety studies on adult fish and fish eggs with formalin in support of its expanded use as an antifungal agent in public aquaculture.

Progress: Toxicity tests to evaluate the safety of formalin to a variety of species of fish and fish eggs have been conducted at UMSC. Eggs of walleye, white sucker, channel catfish, and lake sturgeon were cultured in miniature egg hatching jars. The eggs were treated for 45 min (3X normal exposure) every-other-day with formalin concentrations of 1,500, 4,500, or 7,500 mg/L to evaluate target animal safety. All species had greater percent hatch in the 1,500 mg/L concentration than in the controls. The walleye were the most resistant with good survival even at 7,500 mg/L. There was no survival among the channel catfish or white suckers at 7,500 mg/L. Lake sturgeon were the most sensitive with no survival even at 4,500 mg/L; however, this treatment is 3X the normal treatment concentration and 3X the normal exposure time as required by CVM.

STUDY NO. 2: OXYTETRACYCLINE

Objectives: To extend the feed additive label for treatment of certain bacterial diseases on cool- and warmwater fish species of importance to public fish production and to cover marking of fish species not covered by the current label. To expand the feed additive label for control of flexibacteriosis on cold, cool, and warmwater species.

Job No. 1: Develop efficacy data or determine whether the data on oxytetracycline is adequate to expand and extend the current label.

Progress: UMSC personnel discussed coordination of data acquisition from INADs for oxytetracycline that are being conducted by FWS and the Western Regional INAD Project. UMSC will continue to work with these groups and other INAD holders on the collection of efficacy data as it is generated.

Job No. 2: Develop residue chemistry data on oxytetracycline in cool- and warmwater species.

Progress: A protocol has been developed by UMSC and is in review for the adaptation of an analytical method for oxytetracycline in muscle for rainbow trout and chinook salmon edible tissue. The protocol will also determine the accuracy, precision, recovery, method detection limit, and limit of quantitation for the edible fillets for these species. Work effort originally intended for Research Study Plan No. 5 on sarafloxacin will be shifted to oxytetracycline because of questions on the development of resistant bacteria to fluoroquinolones. Residue chemistry studies will likely focus on expansion of the lower temperature limits of oxytetracycline in salmonids. Currently oxytetracycline use is restricted below 9°C in salmonids.

Job No. 3: Develop target animal safety data on oxytetracycline in cool- and warmwater species.

Progress: No activity during July 1, 1994 to December 31, 1994.

STUDY NO. 3: COPPER SULFATE

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

Progress: On September 30, 1994, final approval was granted by CVM and FDA's National Center for Toxicological Research (NCTR) for the research protocol from FFEL to determine the accumulation of copper in edible muscle of channel catfish following exposure to water borne copper sulfate. On November 1, 1994, the research described in that protocol was started. Approximately 400 to 600 gram fish (100 per tank, 50 of each sex) were stocked into experimental tanks and given a two-week acclimation period. Copper sulfate dosing began on November 15, 1994; one group of controls received no copper sulfate exposure and three other groups received one of three graded doses of copper sulfate.

On November 15, 1994 and at two-week intervals thereafter, six fish from each group were sacrificed for collection of muscle and liver samples for copper analysis. Sampling is to continue until an equilibrium has been established between uptake and elimination of copper from liver tissue. Daily water samples have been collected and analyzed for copper content.

The accumulation of copper in liver tissue is used as the indicator of when equilibrium has been reached; therefore, efforts have concentrated on completing liver analysis as quickly as possible after collection of tissues. Preliminary results of analysis of copper residues in liver tissues indicate that equilibrium has not been established after six weeks of exposure to the doses used in this study.

STUDY NO. 4: CHLORAMINE-T

Objectives: To 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 control bacterial gill disease (BGD) and flexibacteriosis on cultured freshwater fish.

Job No. 1: A mutagenicity study in support of the approval of chloramine-T as a drug.

Progress: No activity during July 1, 1994 to December 31, 1994.

Job No. 2: Environmental fate and effect studies in support of the approval of chloramine-T as a drug.

Progress: No activity during July 1, 1994 to December 31, 1994.

Job No. 3: Contract supervision, data collection and analysis of efficacy data collected from the FWS compassionate INAD for use of chloramine-T on FWS hatcheries.

Progress: A protocol for the FWS's INAD for chloramine-T to support its use for treatment of BGD and flexibacteriosis on fish raised on public aquaculture facilities was written by UMSC and submitted to CVM for review. The protocol has been approved and the INAD study has been initiated. The protocol has been used as a template for other INAD applications. Several workshops and coordination meetings have been conducted involving FWS's study director, study monitors, and INAD coordinators.

Job No. 4: Residue chemistry studies to support the approval of chloramine-T as a drug.

Progress: Two chloramine-T residue studies have been completed at UMSC. One entitled "Accumulation and clearance of chloramine-T residues in rainbow trout after use-pattern treatment with [ring UL-¹⁴C]chloramine-T" has been submitted to CVM. A second study entitled "Isolation and characterization of chloramine-T

metabolites in rainbow trout after use-pattern treatment with [ring UL-¹⁴C]chloramine-T" had been completed and the completion report is in the process of being submitted to CVM.

Job No. 5: Target animal safety studies in freshwater fish to support the approval of chloramine-T as a drug.

Progress: No activity during July 1, 1994 to December 31, 1994.

STUDY NO. 5: SARAFLOXACIN

Objectives: To develop efficacy, target animal safety, and total residue depletion and metabolism data required for the use of sarafloxacin in the control of furunculosis and flexibacteriosis in freshwater cold-, cool, and warmwater fish. Expansion of the label to include other diseases is beyond the scope of the current protocol.

Job No. 1: Contract supervision of the sarafloxacin compassionate investigational new animal drug (INAD) request.

Progress: No activity during July 1, 1994 and December 31, 1994. Because of concern for the development of resistant bacteria resulting from the use of fluoroquinolones, INADs for these compounds are not being considered by CVM at this time. Work on Job No. 1 by UMSC will depend on decisions by CVM to allow use of this class of antibacterials in animals.

Job No. 2: Residue chemistry studies in freshwater rainbow trout to support the use of sarafloxacin to control furunculosis and flexibacteriosis. In years four and five of this proposal, residue chemistry for a cool- and warmwater fish or additional salmonids will be completed.

Progress: A protocol for the adaptation of an analytical method in catfish to rainbow trout has been developed by UMSC and is ready for review. Further progress will depend on resolving the question of bacterial resistance discussed in Job 1.

Job No. 3: Target animal safety studies in rainbow trout to support its approval as a drug to control furunculosis and flexibacteriosis. Target animal safety studies for approval in cool- or warmwater fish or other salmonids.

Progress: No activity during July 1, 1994 to December 31, 1994; see Job 1 above.

Job No. 4: Environmental studies for flowing water applications in support of sarafloxacin as a therapeutant to control furunculosis and flexibacteriosis in cold-, cool-, and warmwater fish.

Progress: No activity during July 1, 1994 to December 31, 1994; see Job 1 above.

STUDY NO. 6: POTASSIUM PERMANGANATE

Objectives: To gain approval of potassium permanganate as a therapeutant to control external protozoan and metazoan parasitic, bacterial, and fungal diseases of cultured food fish.

Progress: A protocol titled, "Accumulation of manganese in edible muscle of channel catfish (Ictalurus punctatus) following exposure to water borne potassium permanganate," is in preparation at FFEL and will be submitted to CVM and FDA-NCTR by February 15, 1995. An ideal final approval time for that protocol would be July to October 1995 to coincide with the time when the experimental fish are ready to be introduced into the study.

Preliminary range finding studies have been set up to determine more accurately the tolerance of channel catfish to potassium permanganate before submitting exposure levels in a protocol for CVM approval. These are simply exposure/tolerance tests to provide guidelines for the study and are not intended to gather preliminary data on tissue residues of manganese.

Contacts have been made with Clear Springs Food Company (Buhl, Idaho) to expose rainbow trout to potassium permanganate and have the samples analyzed through FFEL.

STUDY NO. 7: BENZOCAINE

Objectives: To develop efficacy, target animal safety, and residue depletion data required for the approval of benzocaine as a anesthetic/sedative with a short withdrawal time for several species of freshwater fish.

Job No. 1: Develop a compassionate investigational new animal drug (INAD) request to evaluate the efficacy of benzocaine as an anesthetic/sedative for cultured freshwater fish.

Progress: No activity during July 1, 1994 to December 31, 1994.

Job No. 2: Residue chemistry studies in rainbow trout to support the use of benzocaine as an anesthetic/sedative.

Progress: UMSC is investigating the effect of acclimation temperature on the loss of benzocaine and acetylated benzocaine from the edible tissues of rainbow trout. Pilot studies have been conducted but results are not available. The definitive study will include analysis of 8 time points after exposure to benzocaine at 7° and 16°C acclimation temperatures.

Job No. 3: Target animal safety studies in rainbow trout and a second species (cool- or warmwater) to support the approval of benzocaine as an anesthetic/sedative.

Progress: No activity during July 1, 1994 to December 31, 1994.

Job No. 4: Mutagenicity testing in support of the approval of benzocaine as an anesthetic/sedative for all fish in public production.

Progress: Based on discussions with CVM officials at a November 15, 1994 meeting, CVM will not require these data.

Job No. 5: To execute 90-day feeding study in rodents, 90-day feeding study in non-rodents, and two-generation reproduction study with teratology in support of the approval of benzocaine as an anesthetic/sedative for cultured freshwater fish.

Progress: Based on discussions with CVM officials at the November 15, 1994 meeting, only the two 90-day feeding studies will be required. UMSC is in the process of developing a Memorandum of Agreement with CVM's Office of Science to contract for these studies in fiscal year 1996.

Job No. 6: Environmental fate and effects studies in support of the approval of benzocaine as an anesthetic/sedative for cultured freshwater fish.

Progress: Based on discussions with CVM officials at the November 15, 1994 meeting, CVM encouraged UMSC to provide environmental information on benzocaine as soon as is feasible to the Environmental Sciences Staff for review and recommendations for a draft environmental assessment.

STUDY NO. 8: HYDROGEN PEROXIDE

Objectives: To develop efficacy and target animal safety data to provide fish culturists with effective, safe treatment regimes of hydrogen peroxide for controlling fungal infections on fish and fish eggs and, potentially, for controlling external parasitic infestations and external bacterial infections on freshwater fish.

Job No. 1: Conduct efficacy studies on the use of hydrogen peroxide to control fungal infections of freshwater fish and fish eggs.

Progress: Studies at UMSC have indicated that hydrogen peroxide is as or more effective than formalin for the control of fungus on incubating eggs. Hydrogen peroxide and its primary decomposition products, oxygen and water, are considered environmentally compatible. CVM recently approved a petition from UMSC that hydrogen peroxide be classified as a low regulatory priority (LRP) drug when used to control fungi on all species and life stages of fish, including eggs. Protocols are being developed to delineate the efficacy of hydrogen peroxide for controlling fungal infections on juvenile and adult fish.

Job No. 2: Conduct efficacy studies on the use of hydrogen peroxide to control external parasitic infestations and external bacterial infections of freshwater fish on public hatcheries.

Progress: Protocols are being developed by UMSC to study the efficacy of hydrogen peroxide for controlling external parasitic infestations and external bacterial infections of freshwater fish. Contacts are being established with

federal and state fish hatcheries and technical centers to carry out cooperative, on-site studies of the efficacy of hydrogen peroxide for controlling parasitic and bacterial diseases of freshwater fish.

Job No. 3: Conduct target animal safety studies on adult fish and fish eggs with hydrogen peroxide in support of its intended use as an antifungal agent and therapeutic to control external parasitic infestations and external bacterial infections on cultured freshwater fish.

Progress: Toxicity tests to evaluate the safety of hydrogen peroxide to a variety of species of fish and fish eggs have been conducted at UMSC. Hydrogen peroxide concentrations of 250 to 500 mg/L (ppm) have been classified as a low regulatory priority (LRP) drug when used to control fungi on all species and life stages of fish, including eggs. Concentrations well above 500 mg/L have been shown to be non-toxic to a variety of species of fish eggs. Eggs are generally more resistant to hydrogen peroxide than fish. However, treatments as high as 1,000 mg/L for 15 min have not caused mortalities among most species and life stages of fish. Additional target animal safety studies are underway.

STUDY NO. 9: CROP GROUPING

Objectives:

1. To 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. To 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.

Job No. 1: Develop comparative pharmacokinetic and metabolism data for sarafloxacin in rainbow trout and channel catfish.

Progress: Work plans for comparative pharmacokinetic and metabolism studies for sarafloxacin in rainbow trout are being developed at the present time.

Job No. 2: Develop comparative pharmacokinetic and metabolism data for sarafloxacin in phylogenetically diverse fish species cultured in U.S. public aquaculture.

Progress: No activity in the period July 1, 1994 to December 31, 1994.

Job No. 3: Develop comparative pharmacokinetic and metabolism data for benzocaine in rainbow trout and channel catfish.

Progress: The first of two contracts to develop the required data for this study was initiated by UMSC with Dr. William Hayton, College of Pharmacy and Pharmaceutical Sciences, Ohio State University, through a research work order with the Ohio State Cooperative Fish and Wildlife Unit. The research work order will fund a cooperative education agreement to support the research of a doctoral candidate. A research study plan and proposal for the project has been drafted and equipment for the project is being ordered. Preliminary method development work to detect benzocaine and metabolites in trout tissues has begun.

Job No. 4: Develop comparative pharmacokinetic and metabolism data for benzocaine in phylogenetically diverse freshwater fish.

Progress: No activity in the period July 1, 1994 to December 31, 1994.

STUDY NO. 10: NEGOTIATIONS AND CONTRACT COORDINATION

Objectives:

1. To ensure that all data required by CVM for approval through NADAs are developed for the seven priority drugs in a timely, logical, and efficient manner.
2. To coordinate the administration of all contracts by CVM's Office of Science to ensure efficiency, timelessness, and acceptability of data to CVM.
3. To track and report the progress of all of studies and ensure that they are proceeding for approval in a timely, logical, and efficient manner.
4. To assemble and submit NADA's for approval to CVM.

Job No. 1: Determine data requirements for approval of each candidate drug.

Progress:

1. UMSC personnel met with CVM personnel on November 15, 1994 to determine the data requirements for the following IAFWA priority drugs and to discuss strategies for gaining approvals.

Benzocaine vs MS-222. A full human safety package would likely have to be developed on MS-222 (Finquel) for any opportunity to reduce the 21-day withdrawal time. The requirements for residue chemistry studies on MS-222 would depend on the results of the human food safety studies (battery of mutagenicity studies, two 90-day feed studies and a rat reproduction study with a teratology component). On the other hand, only two-90 day feeding studies most likely would be required for the free-base form of benzocaine because of its extensive safe epidemiological record as an over-the-counter human drug. (The only adverse toxicological effects that have been observed are allergic responses.) Data generated under a CVM contract at Ohio State University would provide much, but not all, of the residue chemistry data necessary to complete the human food safety requirements for benzocaine in fish.

Benzocaine Formulation. Discussions on the formulation of benzocaine centered on its being not readily soluble in water. A formulation that provides the drug to the fish in the water needs to be developed. Previous studies performed at UMSC on benzocaine involved the use of ethanol as the solvent. UMSC will ascertain the feasibility of using methanesulfonate salt (used with MS-222) to gain that solubility. One problem with abandoning the ethanol formulation is that some of the data UMSC and Ohio State University have developed (efficacy, residue chemistry) may have to be repeated. This switch may be worth the effort if the new formulation were easier to use and to transport in field operations. The formulation that is selected must also be commercially viable to attract a sponsor.

Benzocaine Environmental and User Safety. CVM recommended that UMSC provide the following background information on benzocaine:

- a) anticipated worst case environmental exposures: how the drug is intended to be used and in what dosages, estimations of the drug

concentrations that would be expected to be released in effluents, and the reasoning used to arrive at the concentration. These estimations should be based on the assumption that all drug used to treat fish will end up in the effluent. Reductions in concentration through degradation, etc., will be considered in the environmental assessment (EA).

- b) existing fate and effects data.

Once this information is collected, the environmental staff will work with UMSC on a strategy for the EA. CVM provided an outline and data sheet for the information CVM needs. CVM also stated that the issue of user safety is being looked at more systematically and CVM is starting earlier in the approval process to identify any potential hazards to the user (ocular, dermal, inhalation). UMSC was encouraged to contact CVM for details.

Benzocaine Sponsor. A sponsor for benzocaine is not yet known. UMSC plans to work with the private aquaculture sector to identify a sponsor using appropriate criteria. The sponsor needs to provide data on stability and solubility, prove that they can manufacture the product under Good Manufacturing Practices provisions, have the ability to market the product to the aquaculture community, and have data in their files that can be used in a NADA. CVM discussed the issue of exclusivity as an incentive to attract a sponsor for benzocaine and, potentially, sponsors for other aquaculture drugs. Dr. Andrew Beaulieu of CVM suggested that a sponsor may be able to gain exclusivity for an extended period of time based on the type of data in their files. This incentive might be a way to stimulate minor use development beyond aquaculture issues. Currently, exclusivity is granted when an NADA sponsor funds safety or efficacy studies; if all studies were publicly funded, as currently planned, an original NADA sponsor would not qualify for exclusivity. CVM suggested UMSC write a letter to the Office of General Council at CVM requesting an opinion about whether any marketing exclusivity could be offered in exchange for sponsor development of a manufacturing package for a minor use application or even just a submission of a minor use application. There is precedent for this concept through the principle of orphan drugs for human use.

Sarafloxacin. Aquaculture use of fluoroquinolones was singled out in the fluoroquinolone hearing held November 9-10, 1994. Concern over bacterial resistance developing under net pens has led to the probability that fluoroquinolones will be restricted to prescription only; however, CVM felt that the use of fluoroquinolones in aquaculture could be worked out over time. Thus, it would be better to delay development of a new animal drug application for sarafloxacin, but sarafloxacin may still be used as the model oral drug in the croup grouping research.

Oxytetracycline. CVM discussed the fluorometric HPLC method for oxytetracycline that is being tested as a regulatory method in comparison with the microbial assay that is currently used as the analytical method for the product, Terramycin For Fish. It would be relatively easy to extend the label use of oxytetracycline to other fish species and to different temperatures since it is already approved for use on fish. Additional studies should be conducted to determine withdrawal times for fish species dosed at temperatures below 9°C.

2. Rosalie A. Schnick met with Dr. Stephen Sundlof (Director of Center for Veterinary Medicine) and Dr. Andrew Beaulieu (Deputy Director, Therapeutic and Production Drug Review) at the NRSP-7/FDA Workshop for Minor Use Drugs: Drugs in Aquaculture: Current Status - Future Goals, September 29-30, 1994, Bethesda, Maryland. In her

discussions, she emphasized the important role of the IAFWA Project and the need to know the specific data requirements for each priority drug. Both individuals are very supportive of the IAFWA Project.

Job No. 2: Coordinate the administration of contracts by CVM's Office of Science.

Progress: UMSC personnel discussed the development of a Memorandum of Agreement (MOA) with the Office of Science (OS) for the administration and monitoring of any contracted studies. The Office of Science personnel noted that any funds transferred to their office must be spent the year they are obligated; therefore, the MOA should be in place after the start of fiscal year 1996 (starting October 1995) to avoid having to return funds. It will take some time to develop the MOA, write the Requests for Proposals, and issue the contracts. UMSC needs to determine the timing of the contracted studies. UMSC will work with the Office of Science to establish a MOA for administration of contract work as soon as it is feasible.

Job No. 3: Track the progress of all studies and summarize and report the data.

Progress:

UMSC has established a system to track the use of funds from UMSC base funding (\$867,000 annually) and state contributions (Year 1 = \$680,000 for UMSC, \$100,000 for FFEL).

UMSC reallocated the Sport Fish Restoration Contributed funds to reflect revisions in the study plans based on discussions with CVM.

UMSC is in the final stages of recruiting for an assistant to help the Registration and Quality Assurance Officers at UMSC with their roles and responsibilities with the IAFWA Project.

Rosalie A. Schnick and William H. Gingerich presented information on the IAFWA Project at the Seventh NRSP-7/FDA Workshop for Minor Use Drugs: Drugs in Aquaculture: Current Status - Future Goals. September 29-30, 1994, Bethesda, Maryland.

UMSC sent a letter to FDA outlining UMSC's roles and responsibilities as they relate to INADs and NADAs associated with the IAFWA Project.

Ms. Schnick is providing information on the IAFWA Project and leadership to the aquaculture drug approval process by being an active member of the Working Group on Quality Assurance in Aquaculture Production and as chairman of the Task Force on Fishery Chemicals, American Fisheries Society.

Job No. 4: Assemble and submit NADA packages to FDA for approval.

Progress:

UMSC personnel met with the coordinator, Western Regional Investigational New Animal Drug (INAD) Project on October 28, 1994 to discuss collaborative efforts for INAD studies on oxytetracycline, chloramine-T, and formalin that will lead to development of NADAs supported by the IAFWA Project. The format for data submitted to UMSC and the parameters needed for NADAs were presented to the coordinator to implement in the Western Regional INAD Project.

UMSC personnel met with the FWS INAD Coordinator and the FWS Study Monitors on December 13-14, 1994 in Denver, Colorado. The objective of the meeting was to troubleshoot and streamline the INAD process that will lead to NADA for drugs important to public aquaculture and the IAFWA Project. The following items were discussed:

1. Current status of aquaculture drugs and chemicals;
2. IAFWA Project for approval of drugs for public fish production;
3. Current status of FWS INADs; and,
4. Roles and responsibilities for INADs and NADAs as they relate to the IAFWA Project.

A list of INAD holders for formalin, oxytetracycline, and chloramine-T has been developed by UMSC. They will be contacted in the near future concerning their roles and responsibilities related to IAFWA NADAs.