Chemical Use Manual
Idaho Dept of Fish and Game
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Table of Contents

A MANUAL OF CHEMICALS
COMMONLY USED IN FISH CULTURE
AT IDAHO DEPT. OF FISH AND GAME HATCHERIES

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Grace Fish Hatchery

2008

This booklet was put together to provide a quick reference to the spectrum of chemicals and drugs used at the various IDFG hatcheries around the state. These chemicals are used for keeping fit fish healthy, treating sick fish, cleaning and disinfecting equipment and various other uses. It is modeled after a publication put together by Elwood Vedvig, IDFG fish disease biologist, in 1971. Some of the hatcheries use only a few different chemicals which meet all of their needs while other hatcheries have an assortment of chemicals utilized for various purposes at a multi-role hatchery.

This booklet is also meant to be an evolving guide, as new chemicals or techniques are found. This booklet is certainly not all inclusive. More specific information can be found on a host of internet sites. Our own pathology people are also great sources of information.

The concentrations of the chemical used are the label-recommended mixtures, and should be strictly adhered to. In extraordinary circumstances, "extra-label" use of a drug may be approved by a licensed veterinarian. Use of this option should only be considered after consultation with a fish pathologist, the appropriate hatchery supervisor and an IDFG veterinarian. When the chemical is used for treating fish, there are variables which may alter the amount of chemical needed at your hatchery. Water chemistry factors such as water hardness, pH, temperature, oxygen content and organic materials present as wells as fish type, stage and health are all variables in what may be an acceptable treatment level, so treat conservatively before assuming the chosen concentration will suffice. At least two people should independently calculate the quantity of a chemical to use for an intended treatment and then compare their results before treatment is started. A missed decimal point can easily be missed resulting in under-treating or killing the fish

with an overdose. The Department's fish pathologists should always be notified before any treatment of fish occurs. It is their job to know the history of disease at your hatchery and recommend a successful treatment regimen. If a chemical has not been used at your hatchery, if it has not been used for some time, or is being used for the first time on a new lot of fish, a bioassay should be done. To do a bioassay, a small group of fish should be placed in an isolated container and exposed to the target dose and duration before all of the fish to be treated are subjected to the chemical. If the level used proves toxic, the concentration of the chemical, duration of treatment or the chemical used can be changed until an acceptable therapeutic treatment is found.

Material Safety Data Sheet (MSDS) information is available for all chemicals, and by law, every hatchery must keep a copy on hand for every chemical in used on the station. Every employee should read the MSDS **before** handling any chemical. The hatchery manager is responsible for assuring every employee complies with this. Do not assume information passed from employee to employee is correct. Look up this information for yourself before using any chemical. Sources for all the chemicals mentioned in this booklet are listed in the appendices.

In the current EPA permit to operate (effective 12/1/2007-11/30/2012), page 42, there is a list of occurrences that must be reported to EPA's hotline phone,

206-553-1846,

and the regional IDEQ office, within 24 hours of the event. Regional IDEQ phone numbers are:

Boise - - - - - - - 373-0550
Twin Falls - - - - 736-2190
Pocatello - - - - - 236-6160
Idaho Falls - - - - 528-2650
Lewiston - - - - - 799-4370
Coeur d'Alene - -769-1422

Local sources, private and governmental, that may be able to help in an emergency should be contacted ahead to know exactly what resources are available and

to familiarize them to the hatchery's operation and possible emergency situations. These phone numbers need to be kept with other emergency numbers in conspicuous display.

FORMALIN

Formalin is the most widely used and most used by volume chemical found in IDFG hatcheries. It is used in the control of external parasites and for control of fungus on eggs, fingerling and adults. Formalin is approved for use in controlling external parasites on all finfish and in controlling fungi on fin fish eggs (see Drugs Approved for Aquaculture Species).

Formalin comes as a 37% formaldehyde solution. The FDA approved brands of formalin are Formalin-F, Paracide-F and Parasite-S. Formalin always contains 15% methanol to inhibit the formation of the highly toxic paraformaldehyde, the white precipitate found in formalin that has gotten too cold or is very old. Never store formalin where the temperature can go above 90°F or below 40°F. There are specific regulations about storing formalin that will have to be met in the future. For now, storage should be in a well-ventilated, heated area with little usage.

For controlling fungus growth on eggs, a 1,667 ppm flow for 15 minutes is the most common treatment. To control external parasites, different solutions are used specific to the hatchery and parasite. These vary from 40 ppm to 170 ppm in a flow-through treatment. To control external parasites, different solutions are used specific to the hatchery and parasite. Be sure to read the actual label directions on the container prior to starting any treatment. Formalin use will temporarily reduce the feeding response in fish by burning their taste buds.

Safety Concerns for the User

Formaldehyde, which is the active ingredient in formalin, is a known carcinogen. Formaldehyde is a noxious gas. Exposure to fumes will cause eye and respiratory irritation. Protective eyewear and gloves are mandatory. A respirator with formaldehyde filtration is mandatory. The full face respirators fog up quickly and make handling formalin more difficult, thus increasing the possibility of a spill or personnel not using

the mask. The half-face respirators, combined with appropriate eye protection, are the best choice. You do not want formalin on your clothes or boots because it will continue to release fumes until the clothes are washed, so wear protective gear. When decanting or pumping formalin, do it in a well-ventilated area to keep fume exposure to a minimum. Any spilled formalin must be soaked up with a spill kit and the remainder flushed with water. Unused portions must be kept in a sealed container. While no one likes handling formalin, some people develop sensitivity to it over time. A chronic skin irritation can develop, thus, they should avoid handling the chemical. Preexisting respiratory problems or skin conditions may be aggravated by exposure.

The addition of a dye to formalin helps in identifying if any formalin has spilled onto surfaces or the user. It also helps seeing where the product is in the incubator, raceway or pond. Aquashade or Admiral Liquid-Dye work well for this purpose.

Safety Concerns for the Fish

Formalin becomes more toxic as the water temperature increases. Hatcheries that treat fingerling or adult fish with formalin should do it in the morning when DO's are higher, water temperatures are lower and while there is a minimum of metabolic waste and food in the water.

Do not use any formalin that is suspected to have been stored at temperatures below 40°F. The paraformaldehyde precipitate lies on the bottom of a barrel and may not be readily visible. If you use a questionable barrel, fish may be dead before it is realized the product is toxic.

Mortality from formalin treatments can be a delayed response. Bioassay your treatment on a small group of fish and wait at least one day before mass treatment.

SALT

Sodium chloride is one of the most commonly used chemicals in aquaculture. While not approved for use on aquatic animals, it is of a low regulatory priority (LRP) which makes it legal for use as specified for parasite control and handling stress (see the reference for LRP drugs). Several kinds of salt can be used. Sodium chloride is the most commonly utilized, followed by sodium bicarbonate. It is important to use only feed mixing or solar salt. **DO NOT** use water softener salt because it has non-caking chemicals added to it that can react with sunlight to make hydrogen cyanide, which is highly toxic to fish. Iodized salt exposes the fish to iodine which is also toxic. **ONLY USE SODIUM CHLORIDE ON FISH.**

Fish and other vertebrates share a common trait: the salt content of their blood is almost identical, about 9 g/l (0.9 %) and a pH of 7.4. Approximately 77% of the salt in blood is sodium chloride. The remainder is made up of bicarbonate, potassium and calcium salts. Sodium and potassium salts are needed for normal function of heart, nerve and muscle. An 8.5 g/l (8500 ppm) salt solution made with sodium chloride would match the sodium content of blood.

Fish Transportation

Fish are moved around the hatchery at different times of their life. They are transferred from raceway to raceway, raceways to clipping tank to raceway and finally into stocking tanks. To accomplish this, the fish are crowded, netted, pumped and manually handled. The thin layer of mucous coating slows the loss of salts from the fish's blood to the surrounding water. With any handling, some of the mucous layer is removed. In addition, handling increases the loss of salt by increasing the metabolism of the fish. If too much salt is lost, muscle and nerve tetany or heart failure may occur. The increased stress may cause a disease outbreak in a marginally healthy fish. The addition of sodium chloride can help reduce or eliminate the loss of salts, which in turn, should reduce the adverse effects on the fish from movement and handling..

If fish are placed in an 8.5 g/l salt solution, no salt loss will occur because the salt solution and blood are equal concentrations. This reduces energy demands upon the fish in trying to meet salt output by input. But if a 10 g/l solution is used, the fish would be harmed as the fish would become lethally dehydrated by loss of water from the blood by

osmosis. So, transport solutions should contain less than 9 g/l of salt. An 8 g/l (30 g/gal) sodium chloride solution matches blood sodium content, preventing dehydration and shock by keeping kidneys active and salt loss low. Traditionally, 0.5 to 2 g/l (1.9 to 7.5 g/gal) sodium chloride solutions have been used to reduce stress during transport.

The other salt that can be used to improve the quality of fish transport water is sodium bicarbonate. The pH of transport water should be around 7-8. The accumulation of carbon dioxide can lower the pH of transport water below an optimum of pH 7-8. The addition of sodium bicarbonate (baking soda) will help keep the pH at a healthy level. A side effect of sodium bicarbonate at 140-642 ppm is the introduction of carbon dioxide as an anesthetic (LRP use). Prolonged exposure at these concentrations may be harmful to the fish due to oxygen deprivation. The amounts of each of these salts needed are below.

Table 1. Types, concentrations and quantities* of food grade salts used in live fish transport water.

Chemical name	Common name	Concentration	Teaspoons per gallon	Cups per 100 gallons	Pounds per 100 gallons
Sodium chloride	feed mixing or non-iodized table salt	8 g/l (0.8% salt)	4 3/4	9 3/4	6.4
Sodium bicarbonate	baking soda	100-200 mg/l (as CaCO3)	1/8 - 1/4	1/4 - 1/2	0.14-0.28

- Amounts listed assume a starting concentration of zero (none present). For accuracy, concentrations should be checked before, during and after the addition of each salt. Use level household measures.

Table taken from *Using Salt to Tranport Live Fish* by *William A. Wurts, Senior State Specialist for Aquaculture, Kentucky State University Cooperative Extension Program,*

Parasite Control

Sodium chloride solutions from 1-3% are effective in removing external parasites from the skin, gills and fins. Recommended treatment times are 30 minutes or less. Parasites subjected to the salt are osmotically killed when exposed to the rapid change in salinity. They quickly dehydrate and implode. *Costia, Epistylis, Trichodina, Dactylogyrus and Gyrodactylus* are some of the parasites that can be removed. A dip or prolonged bath are the most effective ways to administer the salt. This treatment method is limited to smaller containers as a large raceway would require a lot of salt and labor to

get that salt into solution to make it practical. In cases that treatment with salt doesn't work, it is likely that the concentration was too low to be effective. Treatment methods are in Table 2.

Table 2. Specific Treatments and methods of using salt for treating various diseases or as a remedial treatment of stress.

Disease	Concentration and duration of treatment for control of disease
External parasites of brood fish	30,000 ppm (3%) as quick dip (15 seconds or until signs of stress
External parasites *Costia, Epistylis, Trichodina, flukes Datylogyrus and Gyrodatylus*	10,000-30,000 ppm (1-3%) prolonged treatment (30 minutes or until signs of stress) or 1,000-2,000 ppm in hauling tanks as an indefinite treatment
Stress during transport and handling	Indefinite treatment using 1,000 -10,000 ppm (0.1-1%) while
Gill disease in fry or fingerling	20,000 ppm (2%) bath for 30 minutes or until sign of stress early

Other Uses of Salt around the Hatchery

The use of salt before a formalin treatment will reduce the chances of mortality and increase the effectiveness of the treatment for parasite control. A salt flush right after a formalin treatment will help recondition the damaged gills and reduce the chances of delayed mortality. One pound of salt for every four gallons per minute water flow is adequate for both treatments.

Salt is used to float dead eggs up and away from live fish eggs at eye-up. This speeds up machine or hand picking. A concentration of around 5% will separate most of the dead eggs from good eggs.

Salt blocks can be added to the head of the raceway for 2 to 3 days to relieve the stress of handling while netting, crowding, grading, or to aid newly arrived fish at the hatchery.

Salt can be used to removal algae in emptied raceways or can be used to kill weeds or sterilize the ground in areas that herbicides can't be used.

POTASSIUM PERMANGANATE

Potassium permanganate (POPM) is used as an external parasiticide, fungicide and bactericide. It is a strong oxidizing agent, highly caustic, tissue-destroying chemical. In water, it forms the permanganate ion, manganese oxide and oxygen, which is freed. It works by permanganate ion (MnO_4) destroying the cell wall by oxidation. The manganese dioxide molecule forms protein complexes on surface epithelium, creating the characteristic brown color seen on the fish and fins. These protein complexes also form on the respiratory structures of the parasites, resulting in their death. It was thought at one time to have added oxygen to water, but can actually take oxygen from the water by destroying oxygen producing algae in pond situations. Potassium permanganate temporarily reduces the feeding response in fish by burning their taste receptors. It is used now as an alternative to copper sulfate in treating *Icthyophthirius*. It's very effective against flukes such as *Gyrodactylus*. Treatment levels start at 0.5 ppm, and go on up to 3 or 4 ppm, depending on water parameters. POPM is currently on the FDA's deferred regulatory status list and is exempt from registration by the EPA. However, this may change, so regulatory status should be checked before initiating each new course of treatment. Be sure to read and follow the label directions on the container you are using. Use of POPM to treat any warm-water fish species is regulated under an Investigational New Animal Drug (INAD) protocol. The warm-water INAD lists a 7-day withdrawal period before fish should be released for possible human consumption. Lacking further information for salmonids, this minimum 7-day withdrawal should be observed.

Safety Concerns for the User

Potassium permanganate will burn your skin and eyes. It will also stain your hands and clothing. Protective gear is a must. POPM can have a strong chemical reaction with other aquaculture chemicals, (hydrogen peroxide, for example). Drip bottles used to apply POPM should not be used for any other chemical treatments.

Safety Concerns for the Fish

The safety margin between an effective concentration and a lethal concentration can be as little as 1 ppm. A bioassay is recommended upon each use as the organic content of the water can change between treatments. Overuse, especially multiple uses in

a short time, will kill fish. Once a week seems safe for most fish. Water with an elevated organic load requires a higher concentration as the potassium permanganate is non-specific as to what it is oxidizing. Treatment should be in the morning before feeding. It should not be used on eggs or fry. Its mixture with formalin creates a toxic combination.

HYDROGEN PEROXIDE 35%

Hydrogen peroxide 35% (HP) is a caustic oxidizer. As with any oxidizer, it is non-selective in what it oxidizes. Organic and inorganic matter in the water will cause it to be less effective. HP will kill most microbes within 20 seconds of contact. Only PEROX-AID, by EKA chemicals, is approved by the FDA for use fungal control on eggs and a treatment for bacterial gill disease. Columnaris infections in catfish and other coolwater finfish species can also be treated. HP can be used on all freshwater finfish eggs at concentrations of 500-1000 mg/l for 15 minutes in a continuous flow system, once per day con consecutive or alternate days until hatch. For bacterial gill disease, a 50-100 mg/l solution can be used in a 30-60 daily bath or flow-through treatment. Treatments should be bio-assayed to ensure safe treatment levels. Always read and follow the label directions on the container you are using.

Safety Concerns for the User

As a strong oxidizer, HP will burn skin upon contact. Eye damage can be delayed, causing blindness, so protection is a must. Inhalation must be avoided. **DO NOT** use metal containers to transport or dispense undiluted hydrogen peroxide 35%. **DO NOT** use transport or dispensing containers that have been previously used with other aquaculture chemicals. Reaction with other chemicals or metal may result in the release of dangerous gases or high heat (fire).

Safety Concerns for the Fish

Some fish species and life stages are more sensitive to HP than others. Some strains of rainbow trout eggs have shown sensitivity to treatment around 70-140 CTU's, so no HP treatment should be used during this time. Other treatments can be used, though.

BENZALKONIUM CHLORIDE

Benzalkonium chloride (BC) is a generic name for a class of quaternary ammonium compounds which includes Hyamine 3500 and Roccal. The FDA recognizes it as a pesticide meant for disinfection of water and equipment. BC may no longer be used in aquaculture as a therapeutic for any food fish, but can only be used as a surface/equipment disinfectant. It can not be discharged into effluent waters. BC is a long lasting disinfectant effective against bacteria, fungi, protozoa, and some viruses. It will not destroy bacterial spores. BC is found in hundreds of products used daily, from eye drops and dishwashing detergent to baby-wipes. Its use around hospitals is widespread. Solutions are bacteriostatic or bactericidal according to their concentration. Gram-positive bacteria are more susceptible than gram-negative. The cationic surfactants disrupt intermolecular activity and breaks down the tertiary structures of microbes. Activity increases with higher temperature and exposure times. Activity decreases with temperature, with little action below 4°C. Organic and inorganic material will render the solution less effective. Surfaces should be free of visible contamination for maximum disinfection. Some newer studies are blaming its wide use for causing new strains of resistant bacteria. The labeled concentration is 1:1250 (800 ppm) for equipment disinfection. Always read and follow the label direction on the container you are using.

Safety Concerns for the User

Some people have or may develop allergies to the chemical. A dermatitis condition will develop with use. It can cause genetic damage at low concentrations. Gloves and eye protection are a must.

Safety Concerns for the Fish

BC is illegal for any use in food fish production. It is extremely toxic to salmon: 100% mortality on fry and fingerlings at 4 ppm or less in low alkalinity/soft water. Equipment disinfected with BC must be well rinsed away from raceways to avoid discharge. If the equipment is not well rinsed, a built-up layering of BC may occur that has the potential of killing fish at some point.

CHLORINE

Chlorine is a broad spectrum surface disinfectant effective against almost all microorganisms. It will even kill bacterial spores that the other hatchery disinfectants won't. Household chlorine bought at the store is a 5.25% solution. A 12.5% solution is available for general disinfection. A 68% powdered form is also available. Chlorine solutions lose their effectiveness rather quickly so must be replaced frequently. Sunlight, the presence of organic materials, higher temperatures and an alkaline pH will degrade its ability to disinfect. A 200 ppm solution for 30 to 60 minutes is recommended for equipment disinfection. A 10 ppm solution is effective in a 24 hour bath. Chlorine solutions are corrosive to metals so they must be rinsed off metallic equipment immediately after the exposure time.

Chlorine solutions must be neutralized before being disposed of. For every gallon of 200 ppm chlorine solution, 5.6 grams of sodium thiosulfate can be added to neutralize the chlorine. Some literature recommends 7 grams of sodium thiosulfate per gallon. Several days of sunlight exposure will neutralize surfaces that were disinfected with chlorine. Release of unneutralized chlorine into any surface water is illegal. Release of chlorine into a septic system will kill the microorganisms that make the system work. Always read and follow the label directions on the container you are using.

Safety Concerns for the User

Chlorine will cause irritation to the eyes, skin and lungs. Permanent eye damage can occur. Wear eye, hand and clothing protection. Face masks with organic vapor filters must be used when vapors are present. Proper ventilation of work areas is essential. Large quantities of high concentration chlorine are considered hazardous material and require special handling during transportation and storage.

Safety Concerns for the Fish

Chlorine is toxic to all fish at levels above 0.03 ppm. This amounts to only 0.454 ml of 12.5% chlorine in a 500 gal tank. In poorly vented rooms, fumes from liquid bleach may cause mortality in adjacent tanks. No release of unneutralized chlorine can occur.

SODIUM THIOSULFATE

Some of the uses for sodium thiosulfate (ST) are: as an antidote for cyanide poisoning, a fixative agent for photograph negatives and as a hand warmer ingredient. In hatcheries, it is used to neutralize chlorine solutions and can be used to neutralize iodine solutions. It acts by binding the chloride ion. It works best to dissolve the ST crystals in warm water and then add that solution into the chlorine solution rather than to add the ST crystals directly into the chlorine. For each gallon of 200 ppm chlorine, 5.6 grams of ST must be used. Some literature recommends 7 grams of ST for each gallon. Insure the ST is well mixed with the chlorine solution by stirring the container or driving the tank truck being neutralized around the hatchery to induce mixing. Allow the solution several minutes to fully neutralize the chlorine. Always read and follow the label directions on the container that you are using.

Safety Concerns for the User

Eye and skin irritation will develop on contact with ST. There are warnings against inhaling the dust or mist, so the chemical should always be handled with caution and in areas with good ventilation.

Safety Concerns for the Fish

It's hard to overdose using ST, but it does become toxic around 24,000 ppm. It is exempt from the EPA's maximum residual residue list.

TRICAINE METHANESULFONATE (MS-222)

Tricaine methanesulfonate (MS) is FDA approved for use as a sedative and anesthetic while handling fish. It should be used when measuring, clipping, tagging or sorting fish. Concentrations between 50-100 ppm are generally used although some species are more sensitive to it than others. Start with lower concentrations and increase the concentration until the desired effect is achieved. Sedation and recovery waters can be oxygenated to relieve stress. MS solutions degrade over time, especially if exposed to sunlight. Degraded solutions develop a brownish color and should be disposed of. Because it is an acid a stock solution should be buffered by 2 parts sodium bicarbonate by weight to 1 part MS. It can not be used within 21 days of fish release. Always read and follow the directions on the container you are using.

Safety Concerns for the User

It is an eye, skin and lung irritant. There is one report that prolonged (years) daily exposure to the skin can lead to vision problems (American Journal of Ophthalmology, Vo. 124, no.6, Dec. 1997).

Safety Concerns for the Fish

Fish should be taken off feed 24 hours prior to anesthesia to reduce fecal contamination and the risk of regurgitation. If opercle movement ceases, move the fish to clean, oxygenated water immediately. A standard dosage squeeze bottle ensures consistent concentrations.

VIRKON AQUATIC

Virkon Aquatic (Virkon) is a broad spectrum aquaculture disinfectant effective against bacteria, virus, fungi and many microbial spores. It is a mixture of six different disinfectants working synergistically. There is a Virkon-S, which is formulated for warm-blooded animals and can not be used on fish. The chemical works by oxidizing proteins and other components of cell protoplasm required for metabolism. Surfaces to be disinfected should be free of organic material. Hard surfaces, boots and clothing can be disinfected with a 1% solution for ten minutes. A Virkon footbath is viable as long as it retains a reddish-pink color (around 4 days). Once the color is grayish-brown, the solution is failing and should be replaced. Low concentrations (1-4 ppm) have been experimentally used on fish with the effect of lowering bacterial and viral counts to non-infective levels; however, there is no current legal avenue to use this product on food fish. The Hagerman Fish Culture Experiment Station has conducted research on the product and may provide more independent results. Virkon may not be directly discharge into surface water unless approved on the hatchery NPDES permit. Always read and follow the directions on the label on the container that you are using.

Safety Concerns for the User

The powder causes skin burns and irreversible eye damage. Inhalation may cause irritation of the upper respiratory passages. Face/eye shields, respirators, protective clothing and proper ventilation are recommended by the MSDS.

Safety Concerns for the Fish

Virkon is reported lethal to first feeding fry at 6 ppm. Virkon is not approved for use on any food fish.

CHLORAMINE-T

Chloramine-T (CT) is used as an algicide, bactericide, germicide and parasite control in the food, beverage, poultry, dairy and drinking water industries. Hatchery use is limited to treatment of bacterial gill disease and columnaris disease under INAD guidelines. The current INAD lists no withdrawal period, but recent communications (Feb. 2008) indicate that the FDA may impose an 11-day withdrawal on the final approved label. CT is a strong oxidizer, unstable in an aqueous solution. CT should not be dispensed from a metal container. Treatment levels range from 10-20 ppm, one hour treatments on three alternate days. Dosage depends on the size of fish, water hardness, organic load and water temperature. A bioassay should be conducted before general treatment is undertaken. Morning treatments, while the water is cooler and organic load less, are recommended. The fish should be taken off feed during treatment days. Always read and follow the directions on the container that you are using.

Safety Concerns for the User

CT will cause skin, eye and respiratory irritation. A respiratory sensitization will cause asthma symptoms. Protective eye/face gear, respirator and clothing are mandatory.

Safety Concerns for the Fish

Dosages at less than 10 ppm usually have little therapeutic value. Dosages higher than 20 ppm started causing increased mortality.

OXYTETRACYCLINE

Oxytetracycline (OTC) is a FDA approved antibiotic for feed use in salmonids to treat furunculosis (*Aeromonas* salmonicida), bacterial hemorrhagic septicemia (motile *Aeromonas* sp.) and *Pseudomonas* disease at temperatures above 48.2°F (9°C). OTC is also used under INAD protocols to treat bacterial coldwater disease (*Flavobacterium psychrophilum*). Terramycin is the Pfizer Co. trade name for the antibiotic. The withdrawal time is 21 days. There are three different forms of OTC that can be used to mark otoliths. It can also be used to mark fish otoliths by immersing juvenile fish in a bath. The mark remains visible under UV light. The FDA has ruled this usage as drug usage and must comply with the normal regulations. (http://www.fda.gov/cvm/Policy_Procedures/4230.pdf).

There's growing concern about the development of OTC-resistant bacteria because of antibiotic use at hatcheries. The concerns are incomplete control of the pathogen and the antibiotic residues downstream of hatchery effluent. Residues of the antibiotics are finding their way into the gut of many other organisms, including humans. Both of these subjects are being studied by private and governmental groups.

Safety Concerns for the User

The medicated feed should be handled with protective gloves. After handling, hands and clothing should be washed.

Safety Concerns for the Fish

Trout appetites are often stimulated by the drug but salmon may not eat it very well.

ERYTHROMYCIN

Erythromycin (ERY) is a much used drug still seeking to gain FDA approval to treat bacterial kidney disease (BKD). Aquamycin is the trade name of the drug. Use of ERY in medicated feed is regulated under an INAD, while an injectable form (Gallimycin) is used in adult Chinook salmon under a veterinary extra-label prescription. Adults are injected with ET to reduce pre-spawn mortality and pass the drug into the yolk of the developing egg which has proven effective.

Salmon populations have been fed two and sometimes three metaphylactic feedings of ERY to prevent the onset of BKD but this protocol is changing. Some hatcheries aren't feeding any medicated feed prior to smolt release.

Safety Concerns for the User

Wash hands and clothing after handling.

Safety Concerns for the Fish

Tetany (convulsive muscle contractions) can occur during feeding cycles, particularly if the fish are stressed, become excited or are handled. Fish condition and behavior must be closely monitored during treatment.

FLORFENICOL

Florfenicol is a broad spectrum antibiotic effective against many gram-negative and gram-positive bacteria. Its trade name is Aquaflor, made by Schering-Plough. Unlike all the other antibiotics used by aquaculture, this one is specifically designed for aquacultural use. Florfenicol was approved by the FDA in 2007 for use in salmonids against coldwater and furunculosis disease, and in catfish with columnaris disease or Edwardsiella infection. An INAD is still available to use Aquaflor in fish that have other bacterial infections besides those specified in the FDA label. A veterinary feed directive (VFD) is required for its use. A VFD is essentially a prescription written by a licensed veterinarian. No fish food manufacturer can release Aquaflor-medicated feed to a buyer without it. The VFD will specify the concentration of drug in the feed and the proper feeding rate to meet a target dose of 10 mg/kg of fish /day for 10 consecutive days. There is a 15-day withdrawal period after feeding.

Safety Concerns for the User

Wash hands and clothing after use.

Safety Concerns for the Fish

The feed is highly palatable and well tolerated by the fish.

Treatment Methods

Treatment methods	
Bath	A bath treatment is carried out by stopping the flow of water to a tank and adding the chemical. After a predetermined amount of time, the water flow is restarted. In tanks and ponds with a large volume, the level of the pond will be lowered to approximately half and the pond then treated. The water flow will then be turned on and the pond allowed to fill up and then run as normal. This reduces the amount of chemical used. Bath treatments are also used in cages, where a tarpaulin is pulled around the cage to enclose it and the chemical added. At the end of the treatment period the tarpaulin is removed.
Flush	A slug of chemical is added to a raceway or trough and allowed to pass down through the raceway with clean freshwater following behind. This is used in applications where it is impossible to turn the water off for a bath treatment due to limitations such as a lack of oxygen. This is used to good effect with eggs but with fish, their ability to swim through the chemical into the clean water, above gives variable results as the contact time cannot be guaranteed.

Drip	A constant supply of chemical at a low concentration (usually from a dosing pump, but sometimes form a simple device like a bucket with a hole in it) into tank over a long period. Drips are sometimes with the antifungal chemicals used for eggs. Care must always be taken not to overdose the animals/ova, especially if the chemical used is one which can build up in the bloodstream (such as the copper in copper sulphate)
Dip	A quick (usually lasting less than one minute) treatment where fish are immersed in a chemical solution (usually of a high concentration). The easiest method for this is to net the fish from the tank and immerse the whole net and fish into the chemical. Used primarily for immersion vaccination, but also for the treatment of some parasites.
Swab	A piece of cloth or cotton wool is dipped into a high concentration of chemical and wiped of the fish. Impractical for large numbers of fish but sometimes used for the treatment of localized infections on valuable broodfish.
Injection	Injection of chemicals into the body of the fish is a process used by many farms for the administration of vaccines. Vaccines fall into one of four categories: 1. Intramuscular -where the chemical is injected into the muscle of the fish, improved results are gained if it is injected into the red muscle as the greater blood supply to this area ensures quick distribution round the body, 2.Intraperitonal - where the chemical is injected into the body cavity. 3. Intravenous - Injected into the bloodstream, which is largely impractical in most fish as locating the site is difficult, 4. Subcutaneous - Injected beneath the skin but not into the muscle. Both methods 1 and 2 give the best results with methods 3 and 4 not as effective. Injection of chemicals makes them act much faster than other types of administration and so are often used for valuable fish such as broodstock.
Oral	Mixing of chemicals such as antibiotics with the feed is an effective method of treating large numbers of fish. The feed is usually sprayed or coated with oil before mixing the chemicals in as this makes them stick to the pellets and prevents them being washed off as soon as the pellet hits the water. As appetite is often reduced as a result of infections, there can be difficulties in getting the fish to eat the medicated feed if treatment is left too late. This is particularly so with some antibiotics such as sulphonimides which impart an unpleasant flavor to the fish and so reduce the appetite even more.

Table source: www.aquattext.com/tables/treatment%20methods.htm

Best practices for chemical storage

Labeling

- Label all containers. Include chemical name, formula, expiration date, storage requirements and primary hazards.
- Ensure labels are colorfast and permanent.
- Replace labels if they become damaged or faded.

Storage

- Keep containers closed when not in use with threaded caps.
- Segregate incompatible chemicals by storing acids, bases, and flammable liquids in separate cabinets, and separating oxidizers, pure metals, reactives from other compounds on shelves.
- Consult chemical supplier for suggested systems for chemical storage.
- Store chemicals so that labels are visible.
- Ensure chemicals are stored in appropriate storage cabinets.
- Store flammable liquids in certified flammable storage cabinets and acids in corrosion resistant non-metal cabinets.
- Store volatile chemicals requiring refrigeration, in explosion-proof refrigerators. A spark from the thermostat or light switch in a traditional unit could be enough to set off volatile fumes from the chemical and cause an explosion.
- Store chemicals at or below eye level (but not on the floor).
- Never stack chemicals top of each other.
- Stock small quantities of chemicals. Small bottles are less likely to break than large ones.
- Monitor the integrity of shelves. For example, are the chemicals too heavy for the shelf? Is the shelf sagging? Do the shelves show signs of wear? Are support clips corroded?
- Use secondary containment for liquids in storage to contain spills. Ensure the materials in a secondary container are compatible with each other and with the containment tub.
- Anchor storage cabinets to walls and doors so that earthquakes or other hazards do not topple cabinets.
- Monitor chemical containers to ensure container integrity remains intact. Signs of wear may include bulging, cracks, leaks, or rust.
- Monitor container tops for cracks, especially on bottles of nitric acid. Replace if degraded.

Chemical storage area

- Acid fumes can eat away at metals. Note corrosion residue below metal shelf holders.
- Labels should include chemical name, formula, expiration date, storage requirements, and primary hazards.
- Monitor caps and replace when worn to prevent evaporation, leaks, and spills.

- Monitor volumes of chemicals. If chemical reductions are noted, this could be a sign of evaporation or theft.
- Monitor the stored chemicals for crystal buildup or formation of a liquid above a solid. These could indicate a leaking cap or the formation of potentially unstable and dangerous by-products.
- If hazardous potential is unknown, contact a local hazardous waste management company (look in phone book under Environmental Services) or the State Communications Center (800) 632-8000 for assistance.
- Monitor expiration dates on chemicals. Use chemicals on a first-in, first-out basis to prevent accumulation of expired materials.

Security

- Lock chemical cabinets or storage rooms to prevent theft.
- Restrict student access to chemical cabinets and storage rooms.
- Monitor chemical volumes. Unanticipated reductions in volume could be a sign of theft.
- Conduct routine inventories of chemicals and monitor wastes.
- Provide copies of updated chemical inventories to school management and the local fire station.

Other

- Ensure staff are trained in the hazards of chemicals, spill clean up response, and safety procedures.
- Have Material Safety Data Sheets (MSDS) onsite for all chemicals.
- Purge unneeded, older chemicals yearly to prevent chemical stockpiles.

Chemical Sources

Formalin - annual contract purchase- Western Chemical 800-283-5292

Salt - local ranch or feed stores

Potassium Permanganate - Western Chemical 800-283-529

Iodine - 1.75% - Durvet 800-821-5570; Western Chemical 800-283-5292
- PVP - Western Chemical 800-282-5292; Argent 800-426-6258

Hydrogen Peroxide - Western Chemical 800-282-5292

Benzalkonium Chloride -10% - Western Chemical 800-283-5292
-50% - Argent 800-426-6258

Chlorine - 12.5% liquid - Univar – Nampa – 466-7019; Pocatello – 238-8319
- 65% granule - Univar – Nampa – 466-7019; Pocatello – 238-8319

Sodium Thiosulfate – contract through 8/29/08 - Western Chemical 800-283-5292

Tricaine Methanesulfonate – contract through 8/28/09 – Western Chemical

Virkon Aquatic – contract through 8/28/08 - Western Chemical 800-283-5292

Aquashade – Eagar 800-423-6249

Admiral Liquid Blue Dye - Aquatechnex 208-338-8490

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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: sGnRHa/Ovaplant INAD 11-375

[For detailed information see INAD Study Protocol]

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of sGnRHa/Ovaplant® to induce gamete maturation in a variety of fish species.
Drug name:	Ovaplant®; salmon Gonadotropin - Releasing Hormone analogue (des-Gly^{10}, [D-Arg^{6}, Trp^{7}, Leu^{8}]- LHRH, ethyl amide)
Source of drug:	Western Chemical, Inc.
Address:	1269 Lattimore Road Ferndale, WA 98248 USA
Contact:	Attention: Jim Brackett Toll Free: 800-283-5292; Tel: 360-384-5898 email: brackett@wchemical.com
Target pathogen(s):	Not Applicable
Method of administration:	Pellet-implant treatment
Treatment dosage:	10 - 75 micrograms sGnRHa per kilogram body weight
Treatment regimen:	Implant:: Single treatment
Withdrawal period:	Implant:: No Release. All treated broodfish must be maintained indefinitely or destroyed.
Required test parameters:	Investigator must collect data reporting percent ovulation and/or percent spermiation in treated fish. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 11-375 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Calcein INAD 10-987

INAD objective/purpose:	Collect supportive and/or pivotal data needed to establish the effectiveness of calcein to mark fin rays, scales, otoliths, and other calcified fish or selected mussel tissues, via immersion bath.
Drug name:	Calcein (SE-MARK®)
Source of drug:	Western Chemical, Inc.
Address:	1269 Lattimore Road Ferndale, WA 98248
Contact:	Attention: Ron Malnor Phone: 1-800-283-5292; Fax: 360-384-0270; email: ronm@wchemical.com
Target pathogen(s):	Not applicable
Method of administration:	Immersion: standing-bath treatment only
Treatment dosage:	***Option A:*** 125 - 250milligrams calcein per liter ***Option B:*** 2.5 - 5.0 grams calcein per liter (finfish only)
Treatment regimen:	***Option A:*** Treatment duration is 1 - 6 hr ***Option B:*** Treatment duration is 1 - 7 min (Note: Treatment may include a pretreatment with a 1 -5% salt solution for ~3.5 min.) Calcein may be applied as a single treatment, or repeated treatments.
Withdrawal period:	None for fish; they may be released immediately following treatment for those treated at less than 2 grams and for Federally Threatened and Endangered species. None for mussels; due to their treatment at an early life stage and the limited human consumption
Required test parameters:	Investigator must collect mark retention and mortality data. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Treatment is restricted to finfish having a body weight of 2 grams or less. Treatment of mussels is restricted to the following species: Higgins eye, hickory nut, black sandshell, pocketbook, fat mucket, sheepnose and maple leaf. Repeated treatments may be conducted to establish mutltiple marks. However, an interval of at least 2 days should be observed between treatment events. No discharge of calcein marking solution is allowed. Although used calcein marking solution may be stored on station in a secure, leak-proof container, it must ultimately be disposed of according to procedures detailed in a general Waste-stream profile (see INAD Study Protocol for specific instructions). Investigator must follow all instructions in the Study Protocol for INAD 10-987 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements.
Required INAD fee:	$400.00 per facility per year
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: CCP INAD 8391

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of CCP to induce gamete maturation in a variety of fish species.	
Drug name:	Common Carp Pituitary	
Source of drug:	Stoller Fisheries	Argent Laboratories
Address:	1301 18th St; P.O. Box B Spirit Lake, IA 51360	8702 152nd Avenue, N.E. Redmond, WA 98052
Contact:	Phone: 800-831-5174 email: stollerfisheries@mchsi.com	Phone: 800-426-6258 email: email@argent-labs.com
Target pathogen(s):	Not applicable	
Method of administration:	IP or IM injection	
Treatment dosage:	up to 25 milligrams (mg) CCP per kilogram (kg) body weight. Although certain situations may require a higher dose rate, dosage should never exceed 25 mg CCP per kg body weight	
Treatment regimen:	Single or multiple treatment. Multiple treatment will generally consist of a single "priming dose," followed by a single "resolving dose."	
Withdrawal period:	No withdrawal period is required for treated fish.	
Required test parameters:	Investigator must collect data reporting percent ovulation and/or percent spermiation in treated fish. Investigator should also report general fish behavior and any adverse effects relating to treatment.	
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 8391 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.	
Required INAD fee:	$400.00 per facility per year	
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov	
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Chloramine-T INAD 9321

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of chloramine-T to control mortality caused by certain bacterial diseases.	
Drug name:	Chloramine-T (Halamid®)	Chloramine-T (Actamide)
Source of drug:	Axcentive SARL/International Specialty Chemicals, Inc.	B.L. Mitchell, Inc.
Address:	303 South Broadway Suite 425 Tarrytown, NY 10591	1774 E Azalea Dr. Greenville, MS 38701-7505
Contact:	Larry Holzman Telephone: 914-333-0606 Telefax: 914-333-0333 email: lbh@ischem.com	Betty Mitchell Phone: 662-686-9002 Fax: 662-686-9020 email: blmitchell@bellsouth.net
Target pathogen(s):	External flavobacteriosis (e.g. bacteria responsible for BGD and external columnaris)	
Method of administration:	Immersion: flow-through or standing bath treatment	
Treatment dosage:	10, 15 or 20 mg/L for BGD & external columnaris in cold, cool & warmwater fish.	
Treatment regimen:	60 minutes per day for up to 3 days.	
Withdrawal period:	None. Fish may be released or harvested for market immediately following treatment.	
Required test parameters:	Investigator must collect mortality data throughout the 5 day pre-treatment, treatment, and 14 day post-treatment periods. Investigator should also report general fish behavior and any adverse effects relating to treatment.	
Limitations or restrictions on use of drug:	Not for use on fish in culture systems with no outflows . Investigator must follow all instructions in the Study Protocol for INAD 9321 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements.	
Required INAD fee:	$400.00/facility	
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov	
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: CP INAD 11-468

INAD objective/purpose:	Collect scientific data necessary to establish the efficacy of Channel Catfish Pituitary (CP) on gamete maturation in a variety of catfish species.
Drug name:	Channel Catfish Pituitary
Source of drug:	Hybrid Catfish Company
Address:	1233 Montgomery Dr Inverness, MS 38753
Contact:	Attn: Roger Yant Phone: 662-265-5308 FAX: 662-207-0461 email: yant@technoinfo.com
Target pathogen(s):	Not applicable
Method of administration:	IP or IM injection in sterile saline
Treatment dosage:	Up to 25 mg per kg body weight within a 12 hour period. Although certain situations may require a higher dosage rate, dosage will never exceed 25 mg CP/kg body weight.
Treatment regimen:	1 or 2 treatments total within a 12 hour period. A dual treatment will generally consist of a single "priming dose", followed by a single "resolving dose."
Withdrawal period:	3 days. No withdrawal period is required for treated fish that will not be susceptible to legal harvest for 3 days posttreatment. No withdrawal period is required for offspring of fish receiving channel catfish pituitary.
Required test parameters:	Investigator must collect data reporting percent ovulation and/or percent spermiation in treated fish. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 11-468 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements.
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Copper Sulfate INAD 9101

[For detailed information see INAD Study Protocol]

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of copper sulfate to control external protozoan and metazoan parasites, and bacterial and fungal infections in a variety of warmwater fish species.
Drug name:	Copper sulfate
Source of drug:	Phelps Dodge Refining Corporation
Address:	P.O Box 20001 El Paso, TX 79998
Contact:	David Fisher Phone: 915-775-8853; Fax: 915-775-8350; email: dfisher@phelpsdodge.com
Target pathogen(s):	external parasites, bacteria, and fungi
Method of administration:	Immersion: standing-bath or flow-through treatment
Treatment dosage:	Variable (dependent upon total alkalinity). See Study Protocol for calculations.
Treatment regimen:	Treatment duration is 1 hour. Although a single treatment event is generally efficacious, repeated treatments may be used.
Withdrawal period:	7 days No withdrawal period is required for fish that are not susceptible to legal harvest for a period of 7 days posttreatment.
Required test parameters:	Investigator must collect data indicating pretreatment pathogen level, and pathogen level at 1, 4, and 18 hours posttreatment. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9101 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	None
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Florfenicol INAD 10-697

INAD objective/purpose:	Collect supportive and/or pivotal data needed to establish the effectiveness of florfenicol to control mortality caused by certain bacterial diseases.
Drug name:	Florfenicol (Aquaflor®)
Source of drug:	Schering-Plough Animal Health
Address:	1095 Morris Avenue Union, NJ 07083-1982
Contact:	Dr. Richard Endris Phone: 908-473-3133; Fax: 908-629-3654; email: richard.endris@spcorp.com
Target pathogen(s):	Bacterial pathogens susceptible to florfenicol, exclusive of already approved claims (i.e., *Edwardsiella ictaluri* and *Flavobacterium columnare* in catfish, and *Aeromonas salmonicida* and *Flavobacterium psychrophilum* in freshwater-reared salmonids).
Method of administration:	Medicated feed treatment
Treatment dosage:	10 milligrams florfenicol per kilogram fish body weight per day
Treatment regimen:	10 days (consecutive)
Withdrawal period:	21 days all salmonids 28 days all non-salmonids No withdrawal period is required for fish that are not susceptible to legal harvest for a period posttreatment equal to the withdrawal periods noted above or are illegal for harvest during those same periods.
Required test parameters:	Investigator must collect mortality data throughout the 10 day pretreatment, treatment, and 21-day posttreatment period. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 10-697 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$400/facility
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Formalin (fungicide) INAD 9013

[For detailed information see INAD Study Protocol]

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of formalin to control mortality caused by external fungal infections on a variety of fish species and their eggs.
Drug name:	Formalin (formaldehyde solution)
Source of drug:	Natchez Animal Supply Co., 201 John R. Junkin Dr., Natchez, MS 39120 Phone: 800-647-6760 Western Chemical Inc., 1269 Lattimore Road, Ferndale, WA 98248 Phone: 206-384-5898 Argent Chemical Laboratories, 8702 152nd Ave. NE, Redmond, WA 98052 Phone: 800-426-6258
Target pathogen(s):	external fungi
Method of administration:	Immersion: standing-bath or flow-through treatment
Treatment dosage:	15 - 2000 milligrams formalin per liter
Treatment regimen:	Treatment duration is variable. See Study Protocol for details. Treatments may be repeated at various intervals.
Withdrawal period:	5 days No withdrawal period is required for fish that are not susceptible to legal harvest for a period of 5 days post-treatment.
Required test parameters:	Investigator must collect mortality data throughout the 10-day pretreatment, treatment, and 14day post-treatment period. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9013 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	None
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: 35% PEROX-AID® INAD 11-669

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness and safety of hydrogen peroxide to control mortality caused by ectoparasites in a variety of fish species.
Drug name:	35% PEROX-AID® (hydrogen peroxide)
Source of drug:	Eka Chemical Inc.
Address:	1269 Lattimore Road Ferndale, WA 98248 USA
Contact:	Attention: Ron Malnor Toll Free: 800.283.5292 Tel: 360.384.5898 email: ronm@wchemical.com
Target pathogen(s):	Ectoparasites of the genera *Ambiphrya, Chilodonella, Dactylogyrus, Epistylis, Gyrodactylus, Ichthyobodo, Ichthyophthirius, Trichodina, Trichophrya, Argulus, Salmincola, Lernaea,* and *Ergasilus* in freshwater fish species; and of the genera *Neobenedenia, Amyloodinium, Cryptocaryon,* and *Uronema* in marine fish species.
Method of administration:	Immersion bath
Treatment dosage:	***Option A***: 100 or 150 milligrams per liter ***Option B:*** 50, 75 or 100 milligrams per liter ***Option C:*** 200 milligrams per liter
Treatment regimen:	***Option A:*** Treatment duration is 30 min; 3 consecutive or alternate days ***Option B:*** Treatment duration is 60 min; 3 consecutive or alternate days ***Option C:*** Treatment duration is 30 min; 3 consecutive or alternate days
Withdrawal period:	None. Fish may be allowed to enter the food chain immediately after treatment.
Required test parameters:	Investigator must collect mortality data throughout the 5 day pretreatment, treatment, and 10 day posttreatment periods. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 11-669 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements.
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
Disclaimer:	Product and company names mentioned in this website, or mentioned in materials accessed via this website, are for informational purposes only. The mention of such does not imply endorsement by the Aquatic Animal Drug Approval Partnership, the U.S. Fish & Wildlife Service or any other organization of the U.S. Government.

U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Potassium Permanganate INAD 9246

[For detailed information see INAD Study Protocol]

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of potassium permanganate to control external protozoan and metazoan parasites, and bacterial and fungal infections in a variety of warmwater fish species.
Drug name:	Potassium permanganate (Cairox)
Source of drug:	Carus Chemical Company
Address:	315 5th Street Peru, IL 61354-0599
Contact:	Brenda Veronda Phone: 815-224-6557; Fax: 815-224-6697; email: brenda.veronda@caruschem.com
Target pathogen(s):	external parasites, bacteria, and fungi
Method of administration:	Immersion: standing-bath or flow-through treatment
Treatment dosage:	1 - 10 milligrams potassium permanganate per liter
Treatment regimen:	Treatment duration is 1 hour. Although a single treatment event is generally efficacious, repeated treatments may be used.
Withdrawal period:	7 days No withdrawal period is required for fish that are not susceptible to legal harvest for a period of 7 days posttreatment.
Required test parameters:	Investigator must collect data indicating pretreatment pathogen level, and pathogen level at 1, 4, and 18 hours posttreatment. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9246 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	None
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: LHRHa INAD 8061

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of LHRHa to induce gamete maturation in a variety of fish species.
Drug name:	Luteinizing-Hormone - Releasing Hormone analogue (des-Gly^{10}, [D-Ala^{6}] LH-RH Ethylamide) - LHRHa
Source of drug:	Western Chemical, Inc.
Address:	1269 Lattimore Road Ferndale, WA 98248 USA
Contact:	Attention: Jim Brackett Toll Free: 800-283-5292 Tel: 360-384-5898 email: brackett@wchemical.com
Target pathogen(s):	Not Applicable
Method of administration:	Injectable only, implants not permitted
Treatment dosage:	5 - 100 micrograms LHRHa per kilogram body weight
Treatment regimen:	Single or multiple treatment. Multiple treatment will generally consist of a single "priming dose," followed by a single "resolving dose." Administered IP or IM.
Withdrawal period:	14 days for all fish; no withdrawal period is required for injected fish that will not be susceptible to legal harvest for at least 14 days posttreatment.
Required test parameters:	Investigator must collect data reporting percent ovulation and/or percent spermiation in treated fish. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 8061 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Use of LHRHa implants is not authorized
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: 17-α Methyltestosterone INAD 11-236

[For detailed information see INAD Study Protocol]

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of 17-α methyltestosterone when fed as a feed additive to larval tilapia to produce populations comprising over 90% male fish.
Drug name:	17-α methyltestosterone (MT)
Source of drug/feed:	Rangen Inc.
Address:	P.O. Box 706 Buhl, ID 83316
Contact:	Attention: David Brock Phone: 1-800-657-6446 x 3332 Fax: 208-543-8037 email: dbrock@rangen.com
Target pathogen(s):	Not Applicable
Method of administration:	Medicated-feed treatment
Treatment dosage:	9 milligrams (mg) MT per kilogram (kg) fish per day Note: MT will typically be incorporated into standard tilapia feed at a rate of 60 mg MT per kg feed
Treatment regimen:	28 consecutive days
Withdrawal period:	Batch Culture: 120 days (from last day of treatment) Note: Batch culture is defined as when all fish in a group/lot enter and leave the lot at the same time. Partial Harvest/Restock Culture: individual minimum weight of 350 grams per fish Note: Partial harvest/restock culture is defined as the mixing of different lots of fish during the grow-out period and selective harvest from the production unit at various times.
Required test parameters:	A minimum of once per calendar year, a minimum of 60 fish must be sampled from a specific treatment lot to determine the sex ration of the population. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	No re-treatment of fish is allowed. Investigator must follow all instructions in the Study Protocol for INAD 11-236 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$600.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-587-9265 ext 136 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Oxytetracycline Immersion INAD 9033

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of oxytetracycline (OTC) immersion therapy to control mortality caused by certain bacterial diseases.
Drug name:	Terramycin-343®
Source of drug:	Pfizer, Inc.
Address:	Pfizer Animal Health 700 Portage Road RIC-190-43 Kalamazoo, MI 49001-0199
Contact:	Dr. Mark Subramanyam Phone: 269-833-3388; Fax: 269-833-2707; Email: mark.subramanyam@pfizer.com
Target pathogen(s):	Bacterial pathogens susceptible to oxytetracycline.
Method of administration:	Immersion treatment
Treatment dosage:	***Options A & B:*** single treatment of 20 milligrams OTC per liter. ***Options C & D:*** up to multiple treatments at 20 milligrams OTC per liter.
Treatment regimen:	***Option A:*** 1-hour treatment for salmonids. ***Option B:*** 1-hour treatment for various cool and warmwater fish. ***Option C:*** 1-hour treatment on 1 to 4 consecutive days for salmonids. ***Option D:*** 1-hour treatment on 1 to 4 consecutive days for various cool and warmwater fish.
Withdrawal period:	***Options A & B:*** 21 days. No withdrawal period is required for fish that will not be catchable for 21 or more days after release, or are illegal for harvest. ***Options C & D:*** 60 days. No withdrawal period is required for fish that will not be catchable for 60 or more days after release, or are illegal for harvest.
Required test parameters:	Investigator must collect mortality data throughout the 5 day pretreatment, treatment, and 30 day posttreatment periods. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9033 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Oxytetracycline Injectable INAD 9027

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of oxytetracycline (OTC) injectable therapy to control mortality caused by certain bacterial diseases.
Drug name:	Liquamycin® LA-200®
Source of drug:	Pfizer, Inc.
Address:	Pfizer Animal Health 700 Portage Road RIC-190-43 Kalamazoo, MI 49001-0199
Contact:	Dr. Mark Subramanyam Phone: 269-833-3388; Fax: 269-833-2707 Email: mark.subramanyam@pfizer.com
Target pathogen(s):	Bacterial pathogens susceptible to oxytetracycline.
Method of administration:	IP or IM injection
Treatment dosage:	20 milligrams per kilogram body weight
Treatment regimen:	***Option A:*** Single injection; all salmonids ***Option B:*** Single injection; all non-salmonids
Withdrawal period:	30 days No withdrawal period is required for treated fish that will not be susceptible to legal harvest for at least 30 days posttreatment.
Required test parameters:	Investigator must collect mortality data throughout the 5 day pretreatment, treatment, and 30 day posttreatment periods. Investigator should also report general fish behavior and any adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9027 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$400.00 per facility per year
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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U.S. Fish & Wildlife Service

The Aquatic Animal Drug Approval Partnership Program

Fact Sheet: Oxytetracycline Medicated Feed INAD 9332

INAD objective/purpose:	Collect supportive and pivotal data needed to establish the effectiveness of oxytetracycline (OTC) when fed as a feed additive to 1) control mortality caused by bacterial diseases in a variety of freshwater and marine fish, and abalone; and 2) mark skeletal tissue of finfish.
Drug name:	Oxytetracycline dihydrate (Terramycin 200® for Fish)
Source of drug:	Phibro Animal Health
Address:	65 Challenger Road; Ridgefield, NJ 07660
Contact:	Paul Duquette; Phone: 973-575-5255; Fax: 973-575-4354; email: paul.duquette@pahc.com
Target pathogen(s):	Bacterial pathogens susceptible to oxytetracycline.
Method of administration:	Medicated-feed treatment
Treatment dosage:	**Standard therapeutic finfish dose:** 2.5 - 3.75 g OTC per 100 pounds fish per day. **High therapeutic finfish dose:** 10 g OTC per 100 pounds fish body weight per day. **Standard abalone dose:** up to 6.0 g OTC per 100 pound abalone body weight per day. **Skeletal marking dose:** same as standard or high therapeutic finfish dose.
Treatment regimen:	**Option A**: standard therapeutic finfish dose; 10-day treatment duration (all salmonids). **Option B:** high therapeutic finfish dose; 14-day treatment duration; temp > 4°C (all finfish). **Option C:** standard therapeutic finfish dose; 10-day treatment duration (non-salmonid freshwater and marine fish). **Option D:** standard abalone dose; 14-day treatment duration. **Option E:** skeletal marking at standard therapeutic dose, 10-day treatment duration; skeletal marking at high therapeutic dose, 14-day treatment duration.
Withdrawal period:	**Option A:** 21 days. **Option B:** 70 days. **Option C:** 40 days. **Option D:** 35 days. **Option E (standard dose):** 21 days (salmonids); 40 days (non-salmonids). **Option E (high dose):** 70 days (all finfish). No withdrawal period is required for treated fish that will not be susceptible to legal harvest or slaughtered for market for the appropriate number of days as specified in the Options listed above.
Required test parameters:	Investigator must collect mortality data throughout the 5 day pre-treatment, treatment, and 21 day post-treatment periods. Investigator should also report general fish behavior and any possible adverse effects relating to treatment.
Limitations or restrictions on use of drug:	Investigator must follow all instructions in the Study Protocol for INAD 9332 regarding drug acquisition and handling, fish treatment and disposition, and data reporting requirements. Drug discharge must be in compliance with local NPDES permitting requirements.
Required INAD fee:	$400.00/facility
AADAP Contact Information:	Ms. Bonnie Johnson, FWS-AADAP Phone: 406-994-9905 Fax: 406-582-0242 email: bonnie_johnson@fws.gov
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Drugs Approved for Aquaculture Species

updated: 21 July 2008

Drug	Product Name, Supplier & FOI Summary	Species	Indication	Dosage regimen	Limitations & Comments
Immersion					

Formalin	Parasite-S® by Western Chemical; FOI Summary and Formalin-F ™ by Natchez Animal Supply Co.; FOI Summary and Formacide-B by B.L. Mitchell, Inc. FOI Summary (not yet available)	All finfish	Control external protozoa *(Chilodonella, Costia, Epistylis, Ichthyophthirius, Scyphidia, Trichodina spp.)* and monogenetic trematodes *(Cleidodiscus, Dactylogyrus, Gyrodactylus spp.)*	• Salmon & trout in tanks and raceways:
				  • Above 50°F: up to 170 µl/L for up to 1 hr
				  • Below 50°F: up to 250 µl/L for up to 1 hr
				• All other finfish up to 250 µl/L for up to 1 hr
				• Earthen ponds: 15 to 25 µl/L indefinitely
					• Drug must not be subjected to temperature below 40°F
					• Do not apply to ponds when water is warmer than 80°F, there is a heavy phytoplankton bloom, or dissolved oxygen is less than 5 mg/L
					• Ponds may be retreated in 5 to 10 days if needed
					• Do not treat ponds containing striped bass
					• Test on a small number from each lot to check for any unusual sensitivity to formalin before proceeding

		All finfish eggs	Control fungi of the family Saprolegniaceae	• All finfish eggs: 1000-2000 ppm for 15 min. • Acipenseriformes up to 1500 ppm for 15 min.	• Preliminary bioassay should be conducted to determine species sensitivity
		Penaeid shrimp	Control protozoan parasites *(Bodo, Epistylis and Zoothamnium spp.)*	• Tanks and raceways: 50 to 100 µl/L for up to and 4 hours daily • Earthen ponds: 25 µl/L as single treatment	• Drug must not be subjected to temperature below 40°F • Do not apply to ponds when water is warmer than 80°F, when there is a heavy phytoplankton bloom, or when dissolved oxygen is less than 5 mg/L • Ponds may be retreated in 5 to 10 days if needed

	Paracide-F® by Argent Laboratories; FOI Summary	Salmon, trout, catfish, largemouth bass, and bluegill	Control external protozoa *(Chilodonella, Costia, Epistylis, Ichthyophthirius, Scyphidia, Trichodina spp.)* and monogenetic trematodes *(Cleidodiscus, Dactylogyrus, Gyrodactylus spp.)*	• Salmon & trout in tanks and raceways:
				  • Above 50 °F: up to 170 µl/L for up to 1 hr
				  • Below 50 °F: up to 250 µl/L for up to 1 hr
				• Catfish, largemouth bass and bluegill: up to 250 µl/L for up to 1 hr
				• Earthen ponds: 15 to 25 µl/L indefinitely
					• Drug must not be subjected to temperature below 40°F
					• Do not apply to ponds when water is warmer than 80 ° F, when there is a heavy phytoplankton bloom, or when dissolved oxygen is less than 5 mg/L
					• Ponds may be retreated in 5 to 10 days if needed
					• Do not treat ponds containing striped bass

		Salmon, trout, and esocid eggs	Control fungi of the family Saprolegniaceae	• 1000-2000 ppm for 15 min.	• Preliminary bioassay should be conducted to determine species sensitivity
Hydrogen Peroxide	35% PEROX-AID® by Eka Chemicals Inc.; FOI Summary	Freshwater-reared finfish eggs	Control mortality due to saprolegniasis	• Coldwater and coolwater: 500 to 1000 mg/L for 15 minutes in a continuous flow system once per day on consecutive or alternate days until hatch • Warmwater: 750 to 1000 mg/L for 15 minutes in a continuous flow system once per day on consecutive or alternate days until hatch	• Initial bioassay on a small number is recommended before treating the entire group
		Freshwater-reared salmonids	Control mortality due to bacterial gill disease *(Flavobacterium branchiophilum)*	• 100 mg/L (30 minutes) or 50 to 100 mg/L (60 minutes) once per day on alternate days for three treatments	• Initial bioassay on a small number is recommended before treating the entire group
		Freshwater-reared coolwater finfish and channel catfish	Control mortality due to external columnaris disease *(Flavobacterium columnare/ Flexibacter columnaris)*	• Fingerling and adults (except northern pike and paddlefish): 50 to 75 mg/L (60 minutes) once per day on alternate days for three treatments • Fry (except northern pike, paillid sturgeon, and paddlefish): 50 mg/L (60 minutes) once per day on alternate days for three treatments	• Use with caution on walleye • Initial bioassay on a small number is recommended before treating the entire group

Drug	Product Name, Supplier & FOI Summary	Species	Indication	Dosage regimen	Limitations & Comments
Immersion (con't)					
Oxytetracycline hydrochloride	OxyMarine by Alpharma Inc.; FOI Summary & Oxytetracycline HCl Soluble Powder-343 by Phoenix Scientific, Inc FOI Summary & TERRAMYCIN-343 Soluble Powder by Pfizer, Inc. FOI Summary & TETROXY Aquatic Soluble Powder by Cross Vetpharm Group Ltd.	Finfish fry and fingerlings	Mark skeletal tissues	• 200 to 700 mg oxytetracycline hydrochloride (buffered) per liter of water for 2 to 6 hours	
Tricaine methanesulfonate	Finquel® by Argent Laboratories FOI Summary and Tricaine-S by Western Chemical, Inc. FOI Summary	Fish (Ictaluridae, Salmonidae, Esocidae, Percidae), aquatic amphibians, and other aquatic poikilotherms	Temporary immobilization	• 15 to 330 mg/L (fish) • 1:1,000 to 1:20,000 (other poikilotherms)	• Powder is added to water • Concentration depends upon desired degree of anesthesia, species, size, water temperature and softness, stage of development; preliminary tests of solution should be made with a few fish • 21 day withdrawal time (fish); laboratory or hatchery use only in other poikilotherms –Water temperature over 50° F (10° C)
Injectable					
Chorionic Gonadotropin	Chorulon® by Intervet Inc.; FOI Summary	Male and female brood finfish	Aid in improving spawning function	• 50 to 510 IU/lb males • 67 to 1816 IU/lb females	• Intramuscular injection • Up to three doses. Total dose not to exceed 25,000 IU in fish intended for human consumption • Prescription product restricted to use by or on the order of a licensed veterinarian
Medicated Article/Feed					
Oxytetracycline dihydrate	Terramycin® 200 for Fish by Phibro Animal Health FOI Summary (coming soon)	Pacific salmon	Mark skeletal tissue	• 250 mg/kg/day for 4 days	• salmon < 30 g • In feed as sole ration • 7 day withdrawal time
		Salmonids	Control ulcer disease, furunculosis, bacterial hemorrhagic septicemia, and pseudomonas disease *(Hemophilus piscium, Aeromonas salmonicida, A. liquefaciens, Pseudomonas spp.)*	• 2.5 to 3.75 g/100 lb/day for 10 days	• In mixed ration • 21 day withdrawal time
		Freshwater-reared salmonids	Control of mortality due to coldwater disease caused by *Flavobacterium psychrophilum*	• 3.75 g/100 lb/day for 10 days	• In mixed ration • 21 day withdrawal time
		All freshwater-reared *Oncorhynchus mykiss*	Control of mortality due to columnaris associated with *Flavobacterium columnare*	• 3.75 g/100 lb/day for 10 days	• In mixed ration • 21 day withdrawal time
		Catfish	Control of bacterial hemorrhagic septicemia and pseudomonas disease *(A. liquefaciens, Pseudomonas)*	• 2.5 to 3.75 g/100 lb/day for 10 days	• In mixed ration • Water temperature not below 62°F • 21 day withdrawal time
		Lobster	Control of gaffkemia *(Aerococcus viridans)*	• 1 g/lb medicated feed for 5 days	• In feed as sole ration • 30 day withdrawal time
Sulfadimethoxine & ormetoprim	Romet®-30 & Romet®TC by Pharmaq AS	Salmonids	Control furunculosis *(Aeromonas salmonicida)*	• 50 mg/kg/days for 5 days	• In feed • 42 day withdrawal time
		Catfish	Control enteric septicemia *(Edwardsiella ictaluri)*		• In feed • 3 day withdrawal time
Sulfamerazine	Alpharma, Inc.	Rainbow, brook, and brown trout	Control furunculosis	• 10 g/100 lb/day for up to 14 days	• In feed • 21 day withdrawal time • **Not currently available**

Drug	Product Name, Supplier & FOI Summary	Species	Indication	Dosage regimen	Limitations & Comments
Medicated Article/Feed (con't)					
Florfenicol	Aquaflor® by Schering-Plough Animal Health Corporation; FOI Summary	Catfish	Control of mortality due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*	• 10 mg/kg/day for 10 consecutive days	• Veterinary Feed Directive (VFD) drug • 12 day withdrawal time
			Control of mortality due to columnaris associated with *Flavobacterium columnare*		• Veterinary Feed Directive (VFD) drug • 12 day withdrawal time • Conditional Approval • Must use Aquaflor®-CA1 product
		Freshwater-reared salmonids	control of mortality due to furunculosis associated with *Aeromonas salmonicida*	• 10 mg/kg/day for 10 consecutive days	• Veterinary Feed Directive (VFD) drug • 15 day withdrawal time
			Control of mortality due to coldwater disease associated with *Flavobacterium psychrophilum*		

Extra Label Drug Use ...

Certain drugs approved by FDA's Center for Veterinary Medicine (CVM) for other animals or other conditions of use (i.e., treatment claims) may, under very specific circumstances, be legally used on aquatic species for which the drugs are not approved. Any such use is referred to as "extra-label" or "off-label" drug use.

All of the following general conditions must be true before extra-label drug use (ELDU) is permissible.

- ELDU may only be prescribed by a licensed veterinarian.
- The prescribing veterinarian must have established a valid veterinarian - client - patient relationship as it relates to the specific situation under which the ELDU is being prescribed.
- Under most circumstances, ELDU does not apply to medicated feed.
- The drug being extra-labeled must be an FDA-approved drug
- There can be no FDA-approved drug for the particular species and condition of use for which the ELDU is being prescribed. However, there is one exception. If there is an approved drug for the species and condition of use, **but** that particular drug is ineffective for that species/condition, then another drug may be extra-labelled.
- ELDU is only applicable to therapeutic claims; i.e., a production drug such as a spawning hormone could not be extra-labeled.
- ELDU does not apply to apply to Veterinary Feed Directive (VFD) drugs (see CVM Update on VFD Final Regulations.

A pivotal law was passed in 1994, the Animal Medicinal Drug Use Clarification Act, which essentially legalized extra-label drug use. The following information has been excerpted from another page on AADAP's website, and provides valuable links to information about ELDU.

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA): FDA's Center for Veterinary Medicine states that "...[AMDUCA] allows veterinarians to prescribe extra-label uses of certain approved animal drugs and approved human drugs for animals under certain conditions. Extralabel (or extra-label) use refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. The key constraints of AMDUCA are that any extralabel use must be by or on the order of a veterinarian within the context of a veterinarian client patient relationship, must not result in violative residues in food-producing animals, and the use must be in conformance with the implementing regulations published at 21 CFR Part 530."

The table below summarizes several key sources of information, from CVM and the American Veterinary Medical Association (AVMA)documents, that provide extensive information about AMDUCA and should be consulted for details. In essence, AMDUCA converts (or codifies) what was once a case of regulatory discretion (i.e., it was illegal, but something that CVM would normally choose not to take regulatory action against) into a law, which now means that extra-labeling by veterinarians is legal if conducted per the conditions of the Act. Click on document number to view actual document.

Document Number	Title
view CVM web page	Webpage for the Animal Medicinal Drug Use Clarification Act of 1994
Title 21 of the Code of Federal Regulations, Section 530 (21CFR530)	Code of Federal Regulations covering Extralabel Drug Use in Animals
CPG Section 615.115	Extra-label Use of Medicated Feeds for Minor Species
PPPM 1240.4210	Extralabel Use of Approved Drugs in Aquaculture
AVMA-1	An Informational Outline of the Animal Medicinal Drug Use Clarification Act (AMDUCA)

SUPPLEMENTAL POLICIES

EXTRALABEL USE OF APPROVED DRUGS IN AQUACULTURE

I. Purpose:

The purpose of this document is to summarize acceptable conditions for extralabel use of approved drugs in aquaculture.

II. Policy:

A. Extralabel use in animals of approved animal and human drugs is provided for in the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). FDA implementing regulations are at 21 CFR 530, and were published in the FEDERAL REGISTER, November 7, 1996 (61 FR 57732).

B. Extralabel drug use is required to be under the supervision of a veterinarian.

C. Provided that all requirements of the implementing regulations are met, drugs approved for terrestrial animals can be used in aquaculture.

D. AMDUCA does not permit extralabel use of an approved drug for nontherapeutic uses, including reproductive uses. Enforcement discretion may be considered on a case-by-case basis.

E. FDA will not object to the extra-label use of approved aquaculture medicated feeds for other indications of use and/or other aquaculture species if all the conditions in Compliance Policy Guide, 615.115, Extra-label Use of Medicated Feeds for Minor Species, are followed. For fish, this applies only to the two Type A medicated articles currently approved for use in fish, Romet and Terramycin.

CVM Update

<<Back

June 23, 2006

REMINDER TO AQUACULTURE PRODUCERS ABOUT THE USE OF FORMALDEHYDE

FDA's Center for Veterinary Medicine (CVM) has received reports that some aquaculture producers are using chemical grade formaldehyde as a parasiticide drug for their fish. The use of the chemical grade product is not approved by CVM. Using a formaldehyde compound other than the approved product can be unsafe for fish and the effectiveness of an unapproved compound is questionable. CVM would like to remind aquaculture producers to read veterinary drug labels carefully and follow label directions to help avoid causing illegal residues in their products.
There are three drug sponsors with approved new animal drug applications for formaldehyde including: Western Chemical, PARASITE-S (NADA 140-989), Argent Chemical Laboratories, Inc., Paracide-F (NADA 140-831), and Natchez Animal Supply Company, Formalin-F (NADA 137-687).

Parasite-S and Formalin-F are approved for the control of:

- external protozoa (*Chilodonella, Costia, Epistylis, Ichthyophthirius, Scyphidia*, and *Trichodina* spp.) and the monogenetic trematodes (*Cleidodiscus, Dactylogyrus*, and *Gyrodactylus* spp.) on all finfish,
- fungi of the family Saprolegniaceae on all finfish eggs, and
- protozoan parasites (*Bodo, Epistylis*, and *Zoothamnium* spp.) on penaeid shrimp.

Paracide-F is approved for the control of:

- external protozoa and monogenetic trematodes (as above) on salmon, trout, catfish, largemouth bass, and bluegill, and
- fungi (as above) on salmon, trout, and esocid eggs.

Paracide-F is not currently approved for use on penaeid shrimp.

The sponsors of the above drugs have approved applications filed with the Agency and have demonstrated that their products are safe and effective for the approved uses. Approved formaldehyde products are manufactured to strict good manufacturing practices (GMP) standard that ensures their quality, purity and strength. The specifications ensuring these attributes are tightly controlled. The standards by which approved formaldehyde and chemical grade formaldehyde is manufactured are different. Aquaculture producers are producing food for human consumption and should be mindful of these considerations. They should not use the chemical grade formaldehyde in place of these approved products.

Any questions about the use of formaldehyde in aquaculture may be directed to Fran Pell, Consumer Safety Officer, FDA/Center for Veterinary Medicine, Division of Compliance, 240-276-9211, e-mail frances.pell@fda.hhs.gov.

Issued by:
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Web page updated by hd - June 23, 2006, 2:24 PM ET

150

Guidance for Industry

Concerns Related to the use of Clove Oil as an Anesthetic for Fish

(This version of the guidance replaces the version that was made available in June 11, 2002. This guidance document has been revised to clarify our position on the use of clove oil as an anesthetic for fish.)

This level 2 guidance document provides information regarding the use of clove oil and its components as an anesthetic for fish.

Comments and suggestions regarding this guidance document should be submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. All comments should be identified with the exact title of the document.

For questions regarding information about regulatory discretion, contact Ms. Fran Pell, Center for Veterinary Medicine (HFV-235), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9211.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
April 24, 2007

Concerns Related to the use Clove Oil as an Anesthetic for Fish

This document represents the Agency's current thinking on concerns related to the use of clove oil as an anesthetic for fish. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used as long as it satisfies the requirements of the applicable statute and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

Introduction

The Food and Drug Administration's Center for Veterinary Medicine (FDA/CVM) has had many inquiries regarding the use of clove oil, and/or the active components of clove oil, as an anesthetic for use in fish. This guidance document provides information regarding CVM's position for the use of clove oil and its components as an anesthetic for fish.

Background

Current scientific information suggests that clove oil is actually a mixture of different compounds. Some of the ingredients of clove oil include eugenol, isoeugenol and methyleugenol. Although clove oil is generally 85 to 95% eugenol, the remaining components may vary. Isoeugenol is the compound considered by some aquaculturists to have the best anesthetic effect. However, neither clove oil nor any individual active ingredient of clove oil (including eugenol, isoeugenol, or methyleugenol) is the subject of an FDA approved new animal drug application.

Although clove oil and some of its components are generally recognized as safe (GRAS) for use in dental cement or as food additives, neither clove oil nor any of its components are GRAS for use as an anesthetic for fish.

The only new animal drug approved for use as an anesthetic in fish as of the date of publication of this guidance document, is MS-222 (Finquel® or Tricaine-S®), also known as tricaine methanesulfonate. This drug has a 21-day withdrawal time. The conditions of use for this drug can be viewed at http://dil.vetmed.vt.edu/AdvancedNADA/NadaPrint.cfm?NadaString=042-427 and http://dil.vetmed.vt.edu/AdvancedNADA/NadaPrint.cfm?NadaString=200-226.

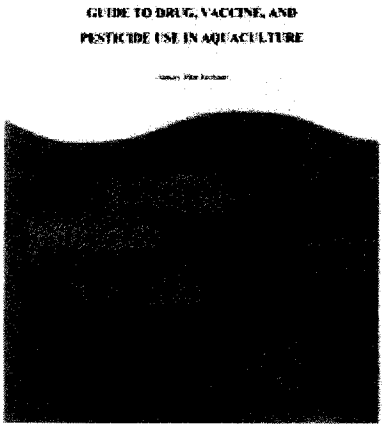
Safety Concerns over the Use of Clove Oil and its Components in Fish

Historically, clove oil and isoeugenol have been used in foods and eugenol has been used in animal foods. However, concerns regarding this class of chemical compounds led to the nomination of eugenol, isoeugenol, and methyleugenol for investigation under the National Toxicology Program (NTP). The NTP conducts studies in nominated drugs and chemicals to determine their potential to cause cancer. Studies have been completed for

eugenol, isoeugenol, and methyleugenol. NTP determined that eugenol is an equivocal carcinogen and methyleugenol is carcinogenic to rodents. While the in-life studies are complete for isoeugenol, the NTP has not yet reached a conclusion regarding its carcinogenicity. The status of toxicology studies conducted on these compounds can be found on the NTP website at http://ntp-server.niehs.nih.gov/. A search for 'eugenol' brings up all the related test results.

Because some clove oil products may contain or include either methyleugenol or isoeugenol, or both, CVM is concerned that the use of clove oil or its components in fish may adversely affect human food safety and animal food safety. This concern especially applies to the use of Clove Oil or any of its components in fish intended for use in human or animal food, and from use in those fish that may be released into public waters where they would be available as food for other aquatic species, or could be caught and end up in the human food supply. In addition, because clove oil and its components have not been evaluated for target animal safety, CVM is also concerned that the use of any of these compounds may adversely affect fish, including endangered aquatic species.

This guidance is intended to remind producers that neither clove oil nor any of its components are the subject of an approved new animal drug application and, because of safety concerns, should not be used as an anesthetic in fish. For more information on drugs that are acceptable for use as an anesthetic for fish, contact Ms. Fran Pell, at (240) 276-9211.



JSA

GUIDE TO DRUG, VACCINE, AND PESTICIDE USE IN AQUACULTURE

(April, 2007 Revision)
.pdf version

Prepared by
The Federal Joint Subcommittee on Aquaculture
Working Group on Quality Assurance in Aquaculture Production

in cooperation with the
Animal and Plant Health Inspection Service (APHIS)
and the
Cooperative State Research, Education, and Extension Service (CSREES)
United States Department of Agriculture

Center for Veterinary Medicine
and
Center for Food Safety and Applied Nutrition
Food and Drug Administration
United States Department of Health and Human Services

and the
Office of Pesticide Programs
United States Environmental Protection Agency

This revision of the original GUIDE TO DRUG, VACCINE, AND PESTICIDE USE IN AQUACULTURE (Texas Agricultural Extension Service Publication No.: B-5085, 1994), has been prepared by the Working Group on Quality Assurance in Aquaculture Production, which was established by the Federal Joint Subcommittee on Aquaculture (JSA) in November, 1990. This publication provides current information on federally regulated drugs, vaccines, and pesticides that may be used in aquaculture production and in aquatic sites according to product label directions. Sources of additional information and assistance are also presented.

PREFACE

The Working Group on Quality Assurance in Aquaculture Production provides a national forum for addressing drug, biologics, and pesticide use in aquaculture through education and the coordination of related efforts in government, industry, and academia. The Working Group, co-chaired by Kevin Greenlees of the Center for Veterinary Medicine (CVM), Food and Drug Administration (FDA) and Gary Jensen of the Cooperative State Research, Education, and Extension Service (CSREES), United States Department of Agriculture (USDA), is composed of representatives of the following agencies and organizations:

Federal and State Agencies

State Departments of Wildlife and Fisheries	U.S. Department of Health and Human Services	Fish and Wildlife Service (FWS)
U.S. Department of Agriculture	Food and Drug Administration (FDA)	U.S. Geological Service (USGS)
Agricultural Research Service (ARS)	Center for Food Safety and Applied Nutrition (CFSAN)	U.S. Environmental Protection Agency
Animal and Plant Health Inspection Service (APHIS)	Center for Veterinary Medicine (CVM)	
Cooperative State Research, Education, and Extension Service (CSREES)	U.S. Department of the Interior	

Trade, Industry, Professional, and Private Organizations

American Feed Industry Association	Baitfish Industry	National Association of State Aquaculture Coordinators
American Fisheries Society	Catfish Farmers of America	National Ornamental Goldfish Growers Association, Inc.
AFS Fish Culture Section	Florida Tropical Fish Farms Association	Striped Bass Growers Association
AFS Fish Health Section	Louisiana Crawfish Farmers Association	U.S. Trout Farmers Association
American Tilapia Association	Marine Shrimp Industry	Washington Fish Growers Association
American Veterinary Medical Association *Guide for the Use of Antimicrobial Drugs in Aquaculture* *Aquatic Animal Veterinarians and Diagnostic Laboratories Database*	National Aquaculture Association	
Animal Health Institute	National Aquaculture Council	

United Nations Food and Agriculture Organization (FAO)

The responsible use of antibiotics in aquaculture

ACKNOWLEDGEMENTS

Special appreciation is expressed to Gary Jensen and Max Mayeaux, CSREES/USDA for providing leadership for this revision of the *Guide*. The assistance of the following individuals in providing information and obtaining agency approvals and clearances is also acknowledged: Melisse Schilling, USDA Animal and Plant Health Inspection Service; Chuck Eirkson, Kevin Greenlees, Julia Oriani, Joan Gotthardt, Meg Oller, Ben Puyot, Don Prater, Fran Pell, Susan Storey, and Margaret Zabriski, FDA Center for Veterinary Medicine, ONADE Aquaculture Working Group; William Jones and Barbara Montwill, FDA Center for Food Safety and Applied Nutrition; and Linda Murray and Dayton Eckerson, EPA Office of Prevention, Pesticides, and Toxic Substances. Special appreciation is extended to: Joe Hogue, who coordinated EPA's review and product update; John Dupuy, EPA, who updated the pesticide listing after extensive reviews of product labels; and Jim Beech, who conducted numerous searches of EPA pesticide databases. Patricia Gaunt, Gary Jensen, Kal Knickerbacker, Michael Masser, Rosalie Schnick and David Straus assisted EPA by selecting appropriate codes for aquatic sites and pests of interest to aquaculture. Rosalie Schnick, National Coordinator for Aquaculture New Animal Drug Applications, contributed valuable comments and suggestions.

CONTENTS

INTRODUCTION

The aquaculture industry in the United States has grown considerably in recent years and is now recognized as a significant supplier of food products for U.S. consumers. Aquaculture also provides aquatic stocks for recreational fishing, the restoration of threatened and endangered species, wild-stock enhancement, as well as for the bait, aquarium, and ornamental fish trades. In order to ensure the safety of aquatic food products, the integrity of the environment, the safety of cultured animals, and the safety of persons who administer various compounds, it is critical that all regulated aquaculture products be used correctly and responsibly.

An important initiative is the development and implementation of aquaculture-producer, quality-assurance programs. These industry-driven and industry-developed programs are essential for U.S. producers and the entire U.S. aquaculture industry, regardless of type of system, location, size of operation, and species grown, to insure the safety and quality of the nation's food supply. These programs identify potential safety hazards associated with drugs and chemicals and directly support mandatory U.S. Hazard Analysis Critical Control Point (HACCP)-based regulations for processors and importers. Additionally, private and public aquaculture producers should use Best Management Practices (BMP) to provide consumers with safe, wholesome food products and attempt to minimize the use of federally regulated products whenever possible. This *Guide* serves as an important resource to assist aquaculture producers and others to use federally approved products legally, correctly, and responsibly.

On some occasions, various drugs, pesticides, and veterinary biologics are needed to ensure the health, productivity, and well-being of cultured aquatic stocks and to maintain production efficiency. These regulated products must be used in such a manner as to avoid risks to public safety, the environment, and animal health, as well as potential loss of consumer trust.

IT IS THE RESPONSIBILITY OF EVERYONE USING, PRESCRIBING, AND/OR RECOMMENDING THE USE OF REGULATED PRODUCTS TO KNOW WHICH PRODUCTS CAN BE LEGALLY USED, AND WITH WHAT RESTRICTIONS, UNDER FEDERAL, STATE, AND LOCAL REGULATIONS. REGULATED PRODUCT USES MAY VARY WITH DIFFERENT SITES, LIFE STAGES, AND CULTURE CONDITIONS.

This *Guide* presents information that can assist U.S. aquaculture producers in providing high-quality, wholesome products. Information is included on drugs, pesticides, vaccines, and other veterinary biologics that currently may be used in commercial or non-commercial aquaculture production.

The reader is encouraged to note the information presented in the Appendices. Appendix A addresses FDA-regulated drugs for use in aquaculture. In Appendix B, EPA-registered pesticides for aquaculture and aquatic sites are listed. USDA-licensed biologics for fish are presented in Appendix C. Readers may find the glossary of common terms listed in Appendix D to be a handy reference. For sources of further information and assistance, see Appendix E. Appendix F lists sponsors, registrants, licensees, and permittees for the federally regulated products included in the *Guide*.

Although food additives, color additives, and disinfectants are used in aquaculture, they are not within the scope of this publication. More information on these products may be obtained by contacting the U.S. Food and Drug Administration's Center for Food Safety and Nutrition (CFSAN), or Center for Veterinary Medicine (CVM), or U.S. Environmental Protection Agency's Office of Pesticide Programs (OPP), or other sources of assistance in Appendix E.

UPDATING THE *GUIDE*

This electronic version of the *Guide* will be updated periodically. Individuals wishing current updates on specific products may contact the individual federal regulatory agencies responsible for these products. Contact information for federal agencies responsible for these products can be found in Appendix E.

REGULATORY AGENCIES

Several federal and state agencies are involved in regulating drugs, vaccines, pesticides, and other products used in aquaculture. Each federal agency has specific responsibilities, mandated by Congress, to regulate the products under their respective jurisdictions.

U.S. Food and Drug Administration

The Food and Drug Administration is responsible for ensuring the safety, wholesomeness, and proper labeling of food products; ensuring the safety and effectiveness of human and animal drugs; and protecting consumers from economic fraud. The Federal Food, Drug, and Cosmetic Act (FFDCA), the basic food and drug law of the United States, includes provisions for regulating the manufacture, distribution, and use of new animal drugs and animal feed. This law applies to public agencies and organizations as well as to private industry.

FDA's regulatory programs are intended to ensure compliance with existing laws. Enforcement activities include actions to correct and prevent violations; remove illegal products or goods from the market; and punish offenders. The testing of domestic and imported aquacultural products for drug and pesticide residues is part of these enforcement activities. The range of enforcement action includes warning letters, seizures, injunctions, and criminal prosecution. FDA's field offices are responsible for initiating and recommending regulatory action. These field offices use guidance provided by FDA headquarters, including the various FDA Centers, to determine whether violations have occurred and, if so, what enforcement action is warranted.

Center for Veterinary Medicine

FDA's Center for Veterinary Medicine (CVM) regulates the manufacture, distribution, and use of animal drugs. CVM is responsible for ensuring that drugs used in food-producing animals are safe and effective and that food products derived from treated animals are free from potentially harmful residues.

CVM approves new animal drugs based on data usually provided by a sponsor (usually a drug company). To be approved, an animal drug must be effective for the claim on the label and safe when used as directed for: treated animals; persons administering treatment; the environment, including non-target organisms; and consumers. CVM establishes tolerances and withdrawal periods as needed for all drugs approved for use in food-producing animals. CVM has the authority to grant Investigational New Animal Drug (INAD) exemptions so that data can be generated to support the approval of a new animal drug.

CVM guide to judicious use of antimicrobials for aquatic veterinarians

CENTER FOR FOOD SAFETY & APPLIED NUTRITION
5100 PAINT BRANCH PARKWAY COLLEGE PARK, MARYLAND 20740-3835

Center for Food Safety and Applied Nutrition

FDA's Center for Food Safety and Applied Nutrition (CFSAN) conducts research on and develops standards for the composition, quality, nutrition, labeling, and safety of food, food additives, and color additives. The Center's responsibilities include domestic and imported seafood inspection, and the development of seafood policies, standards, and programs, along with seafood research and educational activities. One ongoing program involves the annual pesticide and contaminant sampling of food items, including domestic and imported aquacultural products. CFSAN also reviews and approves industry petitions for the safe use of food and color additives. The Center's Office of Seafood has implemented mandatory seafood inspection regulations for the nation's seafood processors and seafood importers based on HACCP principles (effective date, November 25, 1997). This is important for producers because the first critical control point is the quality of the raw product.

U.S. Environmental Protection Agency

The Environmental Protection Agency (EPA) is responsible for registering or licensing all pesticides used in the United States under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA requires that EPA register pesticides for specific uses, provided that the use does not pose an unreasonable risk to human health or the environment, when used according to label restrictions. Any pesticide sold or distributed in the United States must be registered by EPA. It is illegal to use a pesticide in a manner inconsistent with its product label, which must be approved by the Agency during the registration process. Places or establishments where pesticides are produced or formulated are also subject to registration. In addition, EPA sets tolerances or maximum legal limits for pesticide residues in food commodities and animal feed under the FFDCA. The purpose of the tolerance program is to ensure a reasonable certainty of no harm to consumers from pesticide residues in food.

EPA is required by law to re-register those pesticides registered prior to 1984 in order to ensure that such pesticides meet current scientific and regulatory standards for the protection of human health and the environment. Furthermore, EPA must re-assess tolerances to ensure a reasonable certainty of no harm from pesticide residues in food. Products regarded as pesticides include (but are not limited to) algicides, fish toxicants, aquatic herbicides, and toxicants for controlling invertebrates.

[redacted]

Animal and Plant Health Inspection Service

The Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture regulates all veterinary biologics distributed in the United States. This includes vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, certain immunostimulants and cytokines, natural or synthetic immunizing substances such as carbohydrates, proteins, genes or genetic sequences, and test kits for the diagnosis of disease.

IT IS UNLAWFUL TO PREPARE, SELL, BARTER, OR EXCHANGE WORTHLESS, CONTAMINATED, DANGEROUS, OR HARMFUL VETERINARY BIOLOGICS OR TO SHIP UNLICENSED VETERINARY BIOLOGICS FOR EXPERIMENTAL USE IN ANIMALS.

States may impose additional requirements on the use of veterinary biologics. For example, APHIS requires that state approval for distribution of products be obtained before APHIS authorizes field trials with experimental products or before a conditionally licensed product is marketed in the state.

An extensive inspection program involves the monitoring of manufacturing site activities, the testing and release of product batches, and the monitoring of veterinary biologics after licensing to ensure that they are pure, safe, potent, and effective. Every batch of a product offered for distribution and sale in the United States is tested by the manufacturer. In addition, samples are sent to APHIS, and each batch is subject to general and/or specific testing by APHIS to ensure that high quality is maintained.

INTERAGENCY JURISDICTION

FDA and EPA share some areas of mutual regulatory responsibility. A memorandum of understanding sets forth the responsibilities of each agency under FFDCA and FIFRA. The memorandum also provides guidance in the area of aquaculture, particularly as to which agency has jurisdiction over a particular substance for its intended use.

EPA has jurisdiction over disinfectants, sanitizers, and aquatic treatments used solely for the control of algae or bacterial slime and over any other aquatic treatments used solely for pest control that do not include claims for control of parasites or diseases of fish.

FDA has jurisdiction over new animal drugs, including products intended to treat or prevent parasites or diseases of fish, anesthetize aquatic species, and alter the sex or regulate the reproduction of aquatic species. FDA has taken the position that if a pesticide registered by EPA for aquaculture or aquatic site use is being used properly (i.e., the labeled conditions in fact exist in the facility or site at the time the pesticide is used, and the compound is not misused under FIFRA), FDA will not step in to regulate such proper use even though the pesticide may have a secondary therapeutic benefit.

STATE REGULATORY AGENCIES

State Departments of Agriculture or other designated state agencies may also register federally approved pesticides to permit their legal distribution and sale within a state or territory. States may have additional regulatory requirements, including additional data and/or additional restrictions on use and licensing. These requirements can affect the distribution and use of pesticides that are purchased from a distributor in one state for intended use in another. States can provide registration for additional uses of federally registered pesticides to meet special local needs under section 24(c) of FIFRA. Products registered for special local needs under section 24(c) are listed separately in each table of EPA-registered products in Appendix B.

Some states license or impose additional regulations on the use of certain veterinary biologics. Some states may not allow the use of specific products or may require that they be administered only by

licensed veterinarians. States also participate in the approval of field trials of veterinary biologics in their respective jurisdictions and in the experimental use of certain veterinary biologics.

The use of a drug under an Investigational New Animal Drug (INAD) exemption may require approval by a state agency to comply with any local, state, and/or regional EPA discharge regulations. Discharge approval is intended to ensure that the possible impacts of a discharge (effluent) containing a specific compound or its residues are addressed.

USE OF FEDERALLY REGULATED PRODUCTS

The proper use of regulated products in aquacultural production, handling, and processing promotes human, cultured organism, and environmental safety; ensures, to the greatest extent possible, the effectiveness of the products used; reduces overuse, expense, and possible undesirable side effects; and prevents harmful and illegal residues in edible products available for human consumption. Food safety and quality are critical factors that influence the long-term development and economic competitiveness of all food production.

Public perception of the safety of food is also very important. Through the proper use of regulated products, the U.S. aquaculture industry can benefit while ensuring public trust and consumer confidence in the safety of U.S. aquacultural products in domestic and international markets.

SAFETY CONSIDERATIONS

Producers need to establish systems and adopt controls in production and processing that ensure the proper use of regulated products. Producers should evaluate the need for the products carefully and should use them in a way that maximize product effectiveness and minimize the amount of the product used. **They should also keep detailed chronological records of treatment and amounts of the product used.**

USERS SHOULD NOT MIX DIFFERENT REGULATED PRODUCTS UNLESS THIS IS SPECIFICALLY RECOMMENDED ON THE PRODUCT LABEL.

Combining products can have many, mostly undesirable, effects. One or both products can be inactivated, and chemical reactions can produce harmful gases or other reaction products and by-products, some of them toxic.

Applicators and persons near treatment areas can be affected by various regulated products through contact, exposure to evaporated material in the air, or exposure to dusts or aerosols. Treated waters or airborne drift can carry restricted products to distant locations where the products may affect non-target organisms and sites.

Accidental self-injection of some veterinary biologics and injectable drugs can cause local tissue reactions, allergic reactions, or infections. Use of common sense and strict compliance with product label directions can minimize undesirable effects in humans, non-target plants and animals, and the environment. Seek professional advice when in doubt.

ALWAYS READ AND UNDERSTAND THE PRODUCT LABEL BEFORE USING ANY COMPOUND.

Label directions and information are important for two reasons. First, they describe the conditions of use under which the product can be expected to be effective and safe. Second, labels for approved products describe uses allowed by law. Any departure from the directions and conditions on the product label or on special state labels could mean a violation of law.

The product label and package inserts provided with regulated products present information on proper storage, mixing, dosage, and administration; date of expiration; diluting or reconstituting the product; safe disposal of the unused product and product containers; and withdrawal times. Pesticide product labels describe how, when, and where the product may be applied, as well as the target pests they are intended to control. Pesticide labels also list precautionary statements on environmental, physical, and chemical hazards. Pesticide toxicity is identified by signal words on the product label. The terms "DANGER" and "POISON" are used with the most acutely toxic products, whereas "WARNING" and "CAUTION" are associated with those that are less acutely toxic. The label also identifies Restricted-use Pesticides (RUP).

Prescribed aquatic-use information is usually not found on the product labels of those substances determined by FDA to be unapproved new animal drugs of Low Regulatory Priority (LRP). These compounds are listed in Appendix A (Table 2), as are the specific treatment rates and uses allowed by FDA. Generally, LRP substances are not marketed specifically for aquaculture use.

ECONOMIC CONSIDERATIONS

Drugs, pesticides, and vaccines are used to control or prevent specific diseases, water quality conditions, and pest (e.g., weed) or stress problems.

THESE TREATMENTS SHOULD BE USED ONLY WHEN NEEDED.

Each treatment has an economic value in terms of treatment cost and expected economic benefit. The proper use of regulated products, some of which are quite costly, can be important in preventing significant economic losses. Such losses are more likely to occur if the actual problem is incorrectly diagnosed, if precautions for treatment are ignored, or if treatments are improperly applied.

The use of best management practices in aquatic animal husbandry and water quality maintenance can reduce the use of regulated products and thereby increase profitability. Higher production based upon increased dependence on chemicals does not necessarily mean higher profits. Such short-term goals may lead to long-term problems.

Using regulated products at less than the concentrations or dosages specified on the label can cause the treatment to be ineffective or only partially effective. For example, water quality may not be sufficiently improved, pests may not be controlled, vaccines may not protect adequately, and resistant strains of disease organisms may develop. Some pesticide product labels may give maximum allowable application rates. Depending on the target pest and environmental conditions, something less than the maximum rate may be sufficient. Users are encouraged to practice Integrated Pest Management techniques in an effort to minimize the frequency and rate of pesticide applications and considering the best means for control of multiple pests.

Using these compounds at concentrations or in dosages greater than those specified on the label (overdosing or overtreating) is illegal for pesticides, wastes the product and can cause unwanted side effects, including stress and toxicity problems in aquatic stocks and non-target organisms as well as environmental damage. Persons applying regulated products should recognize their legal responsibility for any harm to non-target aquatic and non-aquatic species and for off-site damage.

OPTIONS FOR PROPER DRUG USE

According to the FFDCA, a drug is defined as an article that is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; an article (other than food) intended to affect the structure or any function of the body of man or other animals; or an article that is recognized in official drug compendia. (See Appendix D.) A new animal drug is a drug intended for animals that is not generally recognized by qualified experts as safe and effective for the uses recommended on the label.

NEW ANIMAL DRUGS ARE CONSIDERED ADULTERATED, AND THEREFORE IN VIOLATION OF THE LAW, UNLESS THEY HAVE BEEN APPROVED BY FDA OR ARE THE SUBJECT OF AN INAD EXEMPTION.

At present, no drugs used in aquaculture are considered by FDA to be Generally Recognized as Safe (GRAS) or Generally Recognized as Effective (GRAE) for their proposed uses. For a drug to be classified as GRAS or GRAE, general recognition by experts must be supported by published scientific studies that meet strict FDA standards.

There are several options for properly obtaining and using drugs and chemicals:

1. **FDA-approved or Conditionally-approved New Animal Drugs.** A limited number of new animal drugs are currently approved by FDA for use in food-producing aquatic species. Each drug is approved for specific species, for specific disease conditions, and at specific dosages. Refer to Appendix A (Table 1) for a listing of these approved drugs. Conditional approvals have recently been authorized under the Minor Use and Minor Species Animal Health Act. Conditional approvals will be recognized by clear statements on the label identifying them as such. Conditional approvals are granted to products that have demonstrated all safety components of the New Animal Drug Application, but have yet to complete the effectiveness component. At the time of conditional approval, the drug must only have been shown to have a

death would result from failure to treat the affected animals. The extra-label regulations do not allow the use of drugs to prevent diseases (prophylactic use), improve growth rates, or enhance reproduction or fertility. Spawning hormones cannot be used under the extra-label policy. The veterinarian assumes responsibility for drug safety and efficacy and for potential drug residues in the animal. For further information regarding extra-label drug use, producers should contact their veterinarian.

USE OF DRUGS IN A MANNER OTHER THAN THE OPTIONS DISCUSSED IS SUBJECT TO REGULATORY ACTION BY FDA.

DRUGS IN AQUACULTURE FEED

In the November 19, 1999, Federal Register FDA published a final rule amending the new animal drug regulations to implement the medicated-feed mill licensing requirements of the Animal Drug Availability Act of 1996 (ADAA). The ADAA replaced the requirement for feed mills to have an approved medicated feed application (MFA) for the manufacture of each medicated feed with the need for medicated feed mills to be licensed by FDA. Licensed facilities are allowed to manufacture animal feeds containing Category II, Type A medicated articles. In addition, the ADAA amended the Federal, Food, Drug, and Cosmetic Act to provide the Agency with the authority, to the extent consistent with the public health, to exempt facilities that manufacture certain types of medicated feed from the requirement of obtaining a medicated feed mill license. This rule removed the medicated feed procedural regulations from Title 21, Part 514 of the CFR and adds a new section, Title 21, Part 515 of the Code of Federal Regulations (CFR). The final rule became effective on December 20, 1999. There are more details on these regulations on the CVM website at: http://www.fda.gov/cvm/feedmilltoc.htm.

The FDA published a Compliance Policy Guide (CPG), effective April 23, 2001, to allow regulatory discretion for the extra-label use of medicated feeds in minor species (any species other than cattle, horses, pigs, dogs, cats, chickens, or turkeys). All aquatic species are minor species. A CPG is FDA's direction to its field inspectors. It describes the actions that they should take when they encounter a given situation. This CPG lets inspectors know that FDA will not ordinarily take regulatory action against producers, veterinarians, or feed mills who use or produce medicated feeds for extra-label use in minor species. This does not make the use legal, it simply means that, at this time, the FDA has chosen not to take action when medicated feeds are used under the conditions described in the CPG.

The policy applies only to minor species. The medicated feed must already be approved for use in a major species. The feed must be formulated and labeled at the feed mill according to its approved labeling for the major species. If the medicated feed is to be used for a food-producing minor species, the medicated feed must be one approved for use in another food-producing species. If the medicated feed is to be used in an aquaculture species, the medicated feed must be one approved for use in another aquaculture species. The policy applies to farmed wildlife species, but not to unconfined wildlife. The medicated feed may be used in an extra-label manner only under the written recommendation and oversight of a licensed veterinarian. Only therapeutic extra-label uses of medicated feed are included. This excludes production claims such as increased weight gain or feed efficiency. The specific responsibilities of the animal producer, veterinarian, and the feed mill are all outlined in the text of the

CPG. If the conditions of the CPG are not met or if tissue-residue violations occur, then regulatory action may be taken against the producer or the veterinarian, or in some cases against the feed mill.

The full text of the CPG is the version that you should consult. A copy of the full text of the CPG is available on the FDA Home Page at: http://www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg615-115.html

If you prefer a paper copy, you may submit a written request for a copy of CPG number 615.115 to the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855. Please send one self-addressed adhesive label or envelope with your request.

WATER TREATMENTS

Many of the chemicals used in aquaculture are applied directly to water. The federal agency (either FDA or EPA) with jurisdiction over chemicals applied to the water is determined by the intended use of the product. Fish and other aquatic species are exposed to any compound present in the water. An off-flavor is an example of a condition that can develop when fish are exposed to certain compounds, even those found naturally in water.

Although some products may be beneficial when applied to aquaculture systems at low concentrations, they may also act as irritants or even become toxic at higher concentrations. The improper use or application of water treatments can cause severe stress, which can lead to an animal disease outbreak or even death. Some compounds can accumulate in the animal and may cause illegal chemical residues in tissues intended for human consumption. Illegal residues can also result from the improper use of products to control weeds or unwanted fish or to alter water quality. To prevent possible fish losses and illegal chemical residues from excessive treatment levels, always read and strictly follow product label directions.

RECORD KEEPING

Record keeping is essential for any aquaculture business and is a critical element of quality assurance programs. Record keeping may also be required of producers by processors purchasing fish from them to comply with HACCP requirements. A good record keeping system helps producers keep track of specific treatments and their results with identifiable, known populations or stocks of aquatic animals, as well as the specific water and land areas involved.

Good records provide a basis for sound, cost-effective management decisions. The treatment status of animals, ponds, and other areas is known at all times. Records are needed to determine dosage rates and certify withdrawal times. Processors may require records to demonstrate that all drugs and chemicals have been used properly. Federal seafood processing inspection regulations may also require such record keeping. Records provide valuable evidence and protection in liability cases.

Accurate record keeping is required for any producer using an INAD exemption in clinical field trials. In case of crop loss resulting from a natural disaster, proper records are necessary for eligibility and possible compensation under federal programs. Lenders may require that production input and output records be kept for at least 2 years.

Pesticide record keeping regulations for pesticides designated as "restricted use" require that private, as well as commercial users, keep records of the use of these compounds. There are no mandatory record keeping requirements for pesticides, that do not have the restricted-use pesticide designation, but there might be merit in keeping some records for documenting beneficial effects, as well as non-efficacious treatments. The records for restricted-use pesticides must indicate the date of use, the product name, the EPA product registration number, the size of the area treated, and the amount of the product used on the site, as well as the name and license number of the applicator. Records must be kept for 2 years from the date of application.

Check with your county agricultural Extension office for record keeping help and record keeping requirements, such as those for restricted-use pesticides. States may also mandate additional record keeping requirements. Assistance is also available for other farm record- keeping systems.

CALCULATING WITHDRAWAL TIMES

Product withdrawal times must be observed to ensure that a product used in an aquatic site or on animals does not exceed legal tolerance levels in the animal tissue. Using proper withdrawal times helps to ensure that products reaching consumers are safe and wholesome.

All federally approved products list any specific required withdrawal times. Withdrawal information is found on the product label, package insert, or feed tag. An exception to withdrawal requirements is made for drug and vaccine products used in an extra-label manner. Extra-label use may require the same or a different withdrawal time from that listed on the label, depending on the species, treatment, and other conditions. Withdrawal times for the extra-label use of an approved product are not listed on the label and must be determined by the prescribing licensed veterinarian.

Withdrawal times are usually reported as a specific number of days. Each withdrawal day is a full 24 hours, starting from the last time an animal receives or is exposed to a drug, pesticide, or vaccine. For example, a treatment with a product that has a 5-day withdrawal time is completed at 9:00 a.m. on Friday. At 9:00 a.m. on Saturday, the treated animals have completed their first withdrawal day. The fifth withdrawal day will end at 9:00 a.m. on Wednesday. Waiting restrictions may apply not only to the slaughter time for treated aquaculture stocks but also to treated water used for swimming, livestock watering, crop or turf irrigation, a potable drinking supply, or other purposes.

STORAGE, HANDLING, MIXING, AND DISPOSAL

Always follow label directions for storing, handling, mixing, diluting, reconstituting, and disposing of regulated products and their containers. This preserves the activity and quality of the product and helps prevent misuse, damaging effects on plants and animals, human injury, and environmental contamination.

Pesticides and most drugs should be stored in a locked cabinet in a dry, well-ventilated utility area located away from children, animals, food, feed, and living areas. Some drugs and veterinary biologics require refrigerated storage; other products require storage in a freezer or at room temperature. All pesticides, drugs, and veterinary biologics should be stored away from bright light, because light can cause inactivation or deterioration of the product. Most of these compounds should be stored in a dark area, or at least in a closed carton.

Regulated products should be stored in their original containers, with the original label left attached to the container. Dampness in storage areas can cause paper packages to deteriorate, metal containers to rust, and metal and glass containers to lose their labels. Disinfectants, pesticides, and drugs should not be stored where flooding is possible or in sites where they might spill or leak into the environment. High-temperature storage (above 80 or 90 degrees Fahrenheit) can cause excessive pressure in and bursting of sealed containers. Exposure to high temperatures can also result in product deterioration, shortened shelf-life, premature inactivity, and inactivation.

Proper mixing, diluting, and reconstituting are essential for the effectiveness of products requiring such steps as well as for reasons of safety. Powders may be harmful or toxic if they are inhaled as dusts; fumes and evaporating ingredients may also be harmful or toxic. Improper dilution may cause the concentration or dosage administered to be too great or too small. Incomplete mixing can cause variations in the concentration or dosage applied or administered, with uneven effects ranging from ineffectiveness to overdose and toxicity. Some veterinary biologics are supplied with accompanying diluents that are necessary for reconstitution and the proper concentration of materials.

The use of any pesticide (and some other regulated products) requires adequate protection from exposure. Users should always read the product label for information on required or recommended personal protective equipment. Common-sense precautions should be followed, such as wearing gloves, long-sleeved shirts, and long pants, socks, shoes or boots, a hat and goggles, protective glasses, and/or a face shield. Some pesticides may require use of a respirator. Persons mixing and/or applying pesticides, or working in an area where pesticides are being applied or have recently been applied, should shower and wash their clothes after actual or possible exposure. Contaminated work clothing should be washed separately from household laundry.

As emphasized earlier,

USERS SHOULD NOT MIX DIFFERENT REGULATED PRODUCTS UNLESS THIS IS SPECIFICALLY RECOMMENDED ON THE LABEL.

The combining of products can have many, mostly undesirable, effects. One or both products can be inactivated, and chemical reactions can produce harmful gases or other reaction products and by-

IMPORTATION OF REGULATED PRODUCTS

To be imported, a new animal drug must either be approved by FDA or be intended for investigational use under an INAD exemption. Without approval or proper identification as an investigational new animal drug, a compound can be refused entry into the United States. If the drug is imported under false pretenses, the responsible person(s) involved are subject to enforcement action by FDA as well as the U.S. Customs Service.

Veterinary biologics may be imported only under a permit, and veterinary biologics for sale must meet U.S. requirements. To ensure compliance, manufacturing specifications are monitored, and manufacturing facilities are inspected. Manufacturers of veterinary biologics for experimental use or field testing must meet strict permit requirements and must have provided extensive information to APHIS prior to the issuance of a permit. Permits are not issued for preventive products if the organism in question does not exist in this country.

Pesticides produced by foreign manufacturers and imported into the United States must comply with all requirements applicable to domestic manufacturers including registration and labeling requirements. In addition, the regulations require an importer to submit to EPA a Notice of Arrival of Pesticides and Devices for review and for a determination as to whether the shipment should be sampled and/or permitted entry into the United States.

TIPS FOR USE OF REGULATED PRODUCTS

There are numerous actions and practices that producers can take to use regulated products safely and also achieve desired results in both managing targeted pests or diseases economically and minimizing any potential impact on the environment. The following list provides recommendations and guidance to users of federally regulated products in aquaculture.

1. Obtain a diagnosis of the problem(s) before applying any treatment.
2. Seek professional advice if ever in doubt as to when or how to use regulated products.
3. Use regulated products only for those species and indications listed on the label, unless extra-label use is specifically prescribed by a licensed veterinarian.
4. Read and follow directions for use on the product label carefully.
5. Use the proper dosage, amount, or concentration for the species, area, and/or specific condition.
6. Use the correct method and route of application or administration, whether by spraying aquatic vegetation, water treatment (ponds, tanks, or immersion), injection, or oral administration (used with medicated feed and some biologics).
7. Calculate withdrawal times accurately.
8. Identify treated populations or stocks with clear markings of production and holding units.
9. Do not use antibiotic drugs or medicated feed for disease prevention unless they are specifically approved for that use.
10. Do not substitute unlabeled or generic products or trade-name products that are labeled and approved for aquaculture or aquatic site uses.
11. Keep accurate records.

12. Consider the environmental impact of discharging treated water, including possible effects on non-target organisms.
13. Adopt a producer quality assurance program or a HACCP program that provides guidelines for preventing tissue residue violations and for producing high-quality, wholesome products for consumer use.
14. Be aware of requirements concerning personal safety measures and proper procedures for farm workers and pesticide applicators who handle or apply regulated products.
15. Consider the economic consequences, both short- and long-term, of treatment before using a regulated product.

CITATION

Texas Agricultural Extension Service. Publication No.: B-5085. 1994. *Guide to Drug, Vaccine, and Pesticide Use in Aquaculture*. The Texas A&M University System.

To cite the web-based revised *Guide*, Please cite the URL: http://aquanic.org/jsa/wgqaap/drugguide/drugguide.htm and the time and date the *Guide* was accessed. For example:

Guide to Drug, Vaccine, and Pesticide Use in Aquaculture. 2004 revision, http://aquanic.org/jsa/wgqaap/drugguide/drugguide.htm . Accessed (month, day, year).

APPENDICES: FEDERALLY REGULATED PRODUCTS AND DIAGNOSTIC TEST KITS

The legal status of regulated products approved, registered, or licensed for aquaculture or for aquatic site uses can change for a variety of reasons, such as new or terminated approvals, re-registrations, or new data. The drug and vaccine product listings in this section are based on data provided by the Food and Animal Residue Avoidance Databank (FARAD). For updated information on the status of a regulated drug and vaccine product, contact any FARAD Regional Access Center or other organizations and agencies listed in Appendix E. The listings of registered pesticides were compiled by the U.S. Environmental Protection Agency's Office of Pesticide Programs.

It is especially important to avoid introducing potentially harmful chemicals into the food chain through improper product use. This can occur not only through direct exposure of food fish to such chemicals, but also through indirect means (for example, livestock contact with contaminated water).

Some products may be approved only for use with non-food fish or for certain life stages of aquatic species. The use of products may also be restricted to specified aquatic sites (for example, drainage ditches) rather than sites containing aquatic food species.

IT IS THE USER'S RESPONSIBILITY TO KNOW WHETHER A PARTICULAR PRODUCT IS APPROVED FOR AN INTENDED USE IN AQUACULTURE.

Refer to the product label for information on dosages, conditions of use, withdrawal times, and other instructions for product use. Be sure to read the entire label and adhere strictly to its requirements and restrictions for use.

APPENDIX A: FDA-REGULATED DRUGS FOR AQUACULTURE

The drugs listed in this section include FDA-approved new animal drugs as well as unapproved new animal drugs of low regulatory priority for FDA. Federal approval of new animal drugs applies only to specific products that are the subject of approved new animal drug applications.

Active ingredients from sources other than the listed sponsors are not considered approved new animal drugs. Such products cannot legally be marketed or used. FDA approved products are listed in the publication FDA Approved Animal Drug Products (Green Book) available online at http://www.fda.gov/cvm/Green_Book/greenbook.html. Specific new animal drugs can be looked up using the Database of Approved Animal Drug Products available online at http://dil.vetmed.vt.edu/NADA/

States and other jurisdictions may impose additional regulatory requirements and restrictions on FDA-regulated drugs for aquaculture.

Table 1. FDA-Approved New Animal Drugs (.pdf version)
Table 2. Unapproved New Animal Drugs of Low Regulatory Priority for FDA (* See NOTE at bottom of table.) (.pdf version)

APPENDIX B: EPA-REGISTERED PESTICIDES FOR AQUACULTURE/AQUATIC SITES

The pesticide products listed in this section are registered by EPA for application and use in aquatic sites, as of January, 2004. Before purchasing or using any commercial product, read the label carefully to make certain that the product is approved for its intended use.

IT IS THE RESPONSIBILITY OF THE APPLICATOR TO USE THE PROPER COMPOUND(S) AND TO READ AND FOLLOW LABEL DIRECTIONS.

This listing of pesticide products in this appendix is intended as a guide to help potential pesticide users identify products which may be legally used in aquacultural applications. However, it is not an entirely complete listing of all products for all possible uses in aquaculture.

In addition, it is possible that some products may be listed here that may not be legally used in aquaculture in the manner desired or intended by a potential user. If the label of any pesticide product listed herein does not indicate that the product is legal for use on the site or in the manner the user intends to use it, the listing of that product in this *Guide* **DOES NOT** make it legal for that or any other non-labeled use.

The reason that this appendix may unintentionally exclude or include some EPA-registered pesticide products legal for use in aquaculture, stems from the way pesticide products are registered. Any pesticide active ingredient may be the active ingredient in many different pesticide products. Each product has its own separate directions for use, which include what use site(s) it may be used on and what target pest(s) it may be used to control. The label is consistent with the use site(s) and pest(s) for which the product is registered. A pesticide use site is the term used to describe what the product is intended to protect (from the pest), or, in some cases, where the product is to be used (description of type of physical setting, not geographical location). Although for most agricultural uses, the use site is of the former type, meaning a crop, (e.g., corn) for most aquatic uses, the use site is the latter type, (e.g., lakes, ponds, or fish hatcheries). In many cases the site is defined even more narrowly, (e.g., "ponds (farm) (water treatment)," or, "oyster ponds (water treatment))." However, under EPA's current use-site nomenclature, in no case is the use site termed "aquaculture." Suitability for use in aquaculture must be determined by carefully reading the product label. Therefore, it is difficult to find a precise list of all possible products, from among the over 19,000 pesticide products registered (as of January, 2004), which may be used in some manner in aquaculture.

For this reason, a small group of individuals knowledgeable in aquaculture was selected by Gary Jensen, co-chair of the Working Group on Quality Assurance in Aquaculture Production, to assist EPA in selecting which products to include in this *Guide*. To include all products registered for any aquatic site would have included many products which are clearly not for aquacultural uses. EPA supplied the group of aquaculture experts with its complete list of site codes and pest codes used for registration of pesticides. The group selected the sites and the pests which they felt are of significant interest to the aquaculture industry in the U.S. and supplied that listing to EPA. EPA then searched its database of registered products to determine a listing of all products which are registered for use on at least one of the sites AND for control of at least one of the pests which were on the site and pest listings supplied by the group. Finally, EPA refined the list of products resulting from the search through a review of those product labels. Again, however, EPA cannot guarantee that this process and review resulted in a 100% accurate listing of pesticide products legal for use in aquaculture.

All of the pests selected by the group discussed above to be included in this *Guide* fell into the categories of pests controlled by algicides, fish toxicants, aquatic herbicides, and invertebrate toxicants. In order to limit the scope of the pesticide product listings to those of primary interest to the aquaculture industry, we excluded disinfectants, terrestrial herbicides, and lampreycides unless such products also fit into one of the other above categories. For example, if an aquatic herbicide also is registered for use as a terrestrial herbicide, it is included under aquatic herbicide listings, but terrestrial weed pests are not listed under it's target pests. EPA decided not to include a large number of products which are registered

pesticide type, active ingredient, and product name of a particular pesticide, they can easily find that product listing to obtain further information about the product (EPA registration number, registrant name, whether the product is designated as restricted use, the applicable registered use sites, and the applicable registered target pests). The user may simply find the appropriate table (e.g., aquatic herbicides), then find the active ingredient alphabetically, then find the product alphabetically within the listings for that active ingredient. If a user does not know the active ingredient or product name, but wants to find aquatic herbicides for certain weeds, for example, they may scan the use sites and target pests listed under each product listing in the aquatic herbicide table, to find available products.

After a user has identified a product which they are interested in using, they should obtain and review a copy of the product label to be certain the product is registered for the specific use they intend to use it for, prior to buying the product.

ALWAYS REFER TO THE PRODUCT LABEL FOR DETAILS ON RECOMMENDED OR APPROVED TREATMENT RATES AND USAGE AS WELL AS FOR ANY RESTRICTIONS ON USE.

The best way to identify a particular product is with the EPA registration number. For most pesticide products, the user should be able to access a copy of the label through the Pesticide Product Label System (PPLS) on EPA's website at http://www.epa.gov/pesticides/pestlabels. PPLS is a collection of images of pesticide labels which have been approved by EPA. If for any reason a user is not able to access the label for a particular product through PPLS, they should find another source. Users may wish to contact the registrant for the product to obtain a copy of the label. The registrant for each product is also listed in the tables. A list of all registrants, with addresses and telephone numbers, is included in Appendix F. Pesticide distributors may provide copies of some product labels. A copy of a pesticide product label may also be obtained through a request under the Freedom of Information Act (FOIA). Interested parties should first pursue the sources of labels discussed above, but as a last resort (because it may take longer) a FOIA request may be made. Instructions for making a FOIA request by mail or e-mail can be found in Appendix E, under U.S. Environmental Protection Agency.

Some listed products are of more than one pesticide type, meaning that they control pests in more than one group. For example, many products included in the following tables are both algicides and fish toxicants. Some are for various other combinations of pesticide types addressed in this *Guide*. In order to include a complete listing of identified products for each pesticide type, products which are of multiple-pesticide types are listed repeatedly, once in each applicable table. Each time a product is listed, all applicable pesticide types are indicated under "type." Only the four pesticide types included in this appendix (algicides, fish toxicants, aquatic herbicides, and invertebrate toxicants) are indicated for each product. Some products included here may also be of other types, but those types were determined to be not of significant interest to the aquaculture industry, or not within the scope of this *Guide*. Likewise, each time a product is repeated in another table (pesticide type), all of the use sites and target pests applicable to aquaculture are listed, regardless of pesticide type.

Appendix B -Table 1. EPA-Registered Algicides (.pdf version)

Appendix B - Table 2. EPA-Registered Fish Toxicants (.pdf version)

Appendix B - Table 3. EPA-Registered Aquatic Herbicides (.pdf version)

Appendix B - Table 4. EPA-Registered Invertebrate Toxicants (.pdf version)

Appendix F EPA-Registrant Contact List (.pdf version)

Definition of terms used in pesticide product tables in Appendix B

Product name: The trade name under which a pesticide product is sold.

EPA registration #: A hyphenated, two-part unique number assigned by EPA to identify each product registration. The first part of the number is the assigned company number (called the establishment number), which is specific to a given chemical company, or registrant; the second part is the specific product number. The registration number must appear on the product's label.

Type: This refers to pesticide type, and describes the type (or group) of organism which the product is targeted for control, e.g., algicide, aquatic herbicide. A product is of a type if it is registered for control of one or more target pests within that pest group.

Common name A.I.: The common name (as opposed to the chemical name) of the active ingredient. The active ingredient is the chemical or substance in a pesticide product that prevents, destroys, repels, or mitigates a pest, or is a plant regulator, defoliant, desiccant, or nitrogen stabilizer.

Registrant: The term given to a person or company that has registered a pesticide product under FIFRA.

Restricted use: A pesticide that is available for purchase and use only by certified pesticide applicators or persons under their direct supervision. This designation is assigned to a pesticide product because of its relatively high degree of potential human and/or environmental hazard.

Use site: The term used to describe where, or on what, a pesticide product is registered for use, and may therefore be legally used. A use site is what the product is intended to protect (from the pest), or, in some cases, where the product is to be used (description of type of physical setting, not geographical location).

Target pest: A pest for which a pesticide product is registered to control; the pest which is intended to be controlled by a pesticide. A pest is defined in FIFRA as any insect, rodent, nematode, fungus, weed or any other form of terrestrial or aquatic plant or animal life, or any virus, bacteria, or other micro-organism which the Administrator of EPA declares to be a pest.

PARASITE-S

Formalin (aqueous formaldehyde solution)

For control of External Protozoa and Monogenetic Trematodes on all Finfish, and External Protozoans on Penaeid Shrimp, and for control of Fungi on all Finfish eggs

DESCRIPTION

PARASITE-S is the aqueous solution of formaldehyde gas (this is equivalent to formalin 37% or 37 grams of formaldehyde in 100 mL of solution). U.S.P. grade PARASITE-S contains not less than 37% (by weight) of formaldehyde gas per weight of water and 6 to 14% methanol. In solution, formaldehyde is present chiefly as $HO(CH_2)OH$. Its molecular weight is 30.03. PARASITE-S is readily miscible with water, methanol, and ethanol and is slightly soluble in ether. It is a clear colorless liquid (Heyden Newport Chemical Corporation, 1961).

FISH AND SHRIMP TOXICITY STUDIES

The toxicity of PARASITE-S was measured by standard methods in laboratory bioassays with rainbow trout, Atlantic salmon, lake trout, black bullhead, channel catfish, green sunfish, bluegill, smallmouth bass, largemouth bass, and striped bass. The 3, 6, 24, and 96-hour LC_{50} (lethal concentration for 50% of the animals) values for trout range from 1,230 to 106 µL/L (455 to 47 ppm formaldehyde), for catfish: from 495 to 65.8 µL/L (183 to 24 ppm formaldehyde); for bluegill, from 2,290 to 100 µL/L (847 to 37 ppm formaldehyde), for largemouth bass, the values for 6 to 96-hour LC_{50} range from 1,030 to 143 µL/L (381 to 53 ppm formaldehyde) (Bill et al., 1977) and for striped bass the values for 6 to 96-hour LC_{50} range from 940 to 30 µL/L (347 to 11 ppm formaldehyde) (Bills, Marking & Howe-1993). The 24, 48, 72, and 96-hour LC_{50} values for penaeid shrimp range from 712 to 235 µL/L (ppm) (Johnson, 1974 and Williams, 1980).

INDICATIONS FOR USE:

1. **Parasiticide for Finfish:** for the control of external protozoa (*Chilodonella* spp., *Costia* spp., *Epistylis* spp., *Ichthyophthirius* spp., *Scyphidia* spp. and *Trichodina* spp.) and the monogenetic trematode parasites (*Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.)
2. **Parasiticide for Penaeid Shrimp:** for the control of external protozoan parasites (*Bodo* spp., *Epistylis* spp., and *Zoothamnium* spp.)
3. **Fungicide for Finfish Eggs:** for the control of fungi of the family Saprolegniaceae

DIRECTIONS FOR USE:

1. Parasiticide for Finfish

Concentrations of Formalin

Aquatic species	Administer in Tanks & Raceways for up to 1 hr (µL/L)*	Administer in Earthen Ponds indefinitely (µL/L)*
Salmon & trout		
above 50° F	up to 170	15-25** ***
below 50° F	up to 250	15-25** ***
All other finfish	up to 250	15-25** ***

* Microliter per liter (µL/L) = parts per million (ppm).

** Use the lower concentration when ponds, tanks or raceways are heavily loaded with phytoplankton, or fish, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternatively, a higher concentration might be used if dissolved oxygen is strictly monitored.

*** Although the indicated concentrations are considered safe for cold and warm water finfish, a small number of each lot or pond to be treated should always be used to check for any unusual sensitivity to formalin before proceeding.

2. Parasiticide for Penaeid Shrimp

Concentrations of Formalin

Aquatic species	Administer in Tanks and Raceways for up to 4 hours (µL/L)*	Administer in Earthen Ponds indefinitely (µL/L)*
Shrimp	50 to 100**	25***

* Microliter per liter (µL/L) = parts per million (ppm).

** Treat for up to 4 hours daily. Treatment may be repeated daily until parasite control is achieved. Use the lower concentration when ponds, tanks or raceways are heavily loaded with phytoplankton, or shrimp, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternatively, a higher concentration might be used if dissolved oxygen is strictly monitored.

*** Treatment may be repeated in 5 to 10 days if needed.

3. Fungicide for Finfish Eggs

Concentrations of Formalin

Aquatic species	Administer in Hatchery Systems (µL/L)*
Eggs of all finfish except Acipenseriformes	1000-2000 for 15 minutes**
Eggs of Acipenseriformes	up to 1500 for 15 minutes**

* Microliter per liter (µL/L) = parts per million (ppm).

** Apply in constant flow water supply of incubating facilities. A preliminary bioassay should be conducted on a small subsample of fish eggs to determine sensitivity before treating an entire group. This is necessary for all species because egg sensitivity can vary with species or strain and the unique conditions at each facility.

METHODS OF APPLICATION

APPLICATION TO TANKS AND RACEWAYS - Turn off water supply, provide aeration, apply appropriate amount of PARASITE-S, and thoroughly dilute and mix to assure equal distribution of PARASITE-S. Treat for up to 1 hour for fish and up to 4 hours for penaeid shrimp, then drain the solution and refill the tank with fresh, well-aerated water. While tank is under treatment, adequate oxygen must be present to maintain the fish or shrimp. If needed, aeration should be provided to prevent oxygen depletion. Treatments may be repeated daily until parasite control is achieved.

APPLICATION TO PONDS - Apply greatly diluted PARASITE-S to the pond evenly using a pump sprayer, boat bailer, or other suitable device to assure even distribution. Allow PARASITE-S to dissipate naturally. Single treatments usually control most parasites, but may be repeated in 5 to 10 days if needed. Treatments for *Ichthyophthirius* should be made at 2-day intervals until control is achieved.

APPLICATION TO EGG INCUBATORS - Apply PARASITE-S into a constant water supply flowing around the eggs. A drip or pressure system should be used and timed. Apply PARASITE-S under the surface of the water flow.

WARNING

Striped bass have been demonstrated to be hypersensitive to formalin; lethal toxicity has been noted to occur at levels approximately 2-3 times the recommended therapeutic concentration.

DANGER ☠ POISON

USER SAFETY WARNINGS

Exposure to high concentrations of formaldehyde vapor causes severe respiratory irritation which can be life threatening. Lower vapor levels can cause irritation to the eyes, respiratory tract, and skin. Swallowing formaldehyde can be life-threatening. Formaldehyde is an irritant when splashed on skin or into the eyes. It can cause severe eye damage, even blindness.

Keep out of reach of children.

Use only with adequate ventilation.

Keep container tightly closed when not in use.

May aggravate a pre-existing asthmatic condition and allergic rhinitis.

Moderate fire and explosion hazard exists when exposed to heat or flame.

Contains methanol - cannot be made non-poisonous. Prolonged exposure to methanol has been associated with reproduction disorders.

Potential Cancer Hazard: Formaldehyde vapor may be carcinogenic if inhaled. Use applicable safety protection. (Note: This drug, used as labeled, does not cause formaldehyde tissue residues in fish).

Employers: Refer to Occupational Safety and Health Administration (OSHA) regulation 29 CFR 1910.1048 for human safety guidance that may be applicable to your specific operation. OSHA's 'action level' concentration for airborne formaldehyde is 0.5 part per million (ppm), calculated as an **8-hour time-weighted average (TWA). Use respiratory, skin, and eye protection when needed (refer** to OSHA's regulation 29 CFR 1910.1048). OSHA's airborne exposure limits (without use of a respirator) for formaldehyde shall not exceed 1) 0.75 part per million (ppm) as an 8-hour time-weighted average (TWA) or 2) 2 parts per million (ppm) as a 15-minute, short term exposure limit (STEL). **NOTE:** The odor of formaldehyde in the air can generally be detected at about 0.5 to 0.8 ppm (range about 0.05 to 1 ppm).

USER EXPOSURE EMERGENCY AID

INHALATION (Breathing): Vacate exposure area and go to area of fresh air. If removing a victim from area of very high vapor concentrations, use a self-containing breathing apparatus. If the victim is not breathing, give artificial respiration, preferably mouth-to-mouth. Seek medical help immediately.

INGESTION (Swallowing): If the person is conscious, dilute, inactivate, or absorb the formaldehyde by giving milk, activated charcoal, or water. Get medical help immediately. If vomiting occurs, keep head lower than hips.

EYE CONTACT: Immediately flush eye(s) with large amounts of water for at least 15 minutes, lifting the lower and upper eyelids occasionally, until no evidence of chemical remains. Seek medical attention immediately.

SKIN CONTACT: Remove contaminated clothing (including shoes) immediately. Wash affected area of body with soap and large amounts of water until no evidence of chemical remains (at least 15 minutes). If there are chemical burns, or appreciable eye or respiratory irritation, get medical help immediately.

PRECAUTIONS

Store PARASITE-S indoors away from direct sunlight, heat, sparks, and open flames, and ventilate storage area. Do not subject PARASITE-S to temperatures below 40° F (4.4° C). PARASITE-S subjected to temperatures below 40° F causes the formation of paraformaldehyde, a substance which is toxic to fish. Paraformaldehyde can be recognized as a white precipitate at the bottom of, or on the walls of, the container.

Tolerance to PARASITE-S may vary with strain and species of fish, eggs and shrimp. While the indicated concentrations are considered safe for the indicated use, a small number of each lot to be treated should be used to check for any unusual sensitivity to PARASITE-S before proceeding.

Under some conditions, fish or penaeid shrimp may be stressed by normal treatment concentrations. Heavily parasitized or diseased fish or penaeid shrimp often have a greatly reduced tolerance to PARASITE-S. Such animals do not tolerate the normal tank treatment regimen the first time they are treated. Therefore, time and dosage may need to be reduced. If they show evidence of distress (by piping at the surface), the solution should be removed and replaced with fresh, well aerated water. Careful observations should always be made throughout the treatment period whenever tank or raceway treatments are made. Treatment should never exceed 1 hour for fish or 4 hours for penaeid shrimp (even if they show no sign of distress), nor should it exceed 15 minutes for fish eggs.

Do not apply PARASITE-S to fish ponds, tanks or raceways with water warmer than 27° C (80° F) when a heavy bloom of phytoplankton is present, or when the concentration of dissolved oxygen is less than 5 mg/L (5 ppm). Do not apply to penaeid shrimp ponds when the concentration of the dissolved oxygen is less than 3 to 4 mg/L (ppm). PARASITE-S may kill phytoplankton and can cause depletion of dissolved oxygen. If an oxygen depletion occurs, add fresh, well-aerated water to dilute the solution and to provide oxygen.

Because formalin may harm a biofilter, biofilters should be bypassed during treatment, and the system should be flushed and replaced with untreated water before reconnecting the biofilter.

Do not use PARASITE-S in a tank, pond or raceway in which methylene blue, or other dyes which are absorbed, have been recently used.

ENVIRONMENTAL PRECAUTIONS

Do not discharge the contents of fish treatment tanks into natural streams or ponds without thorough dilution (greater than or equal to 10X). Do not discharge the contents of egg treatment tanks without a 100X dilution. This will avoid damage to PARASITE-S sensitive phytoplankton, zooplankton, and fish populations and avoid depletion of dissolved oxygen.

Formaldehyde is identified by the U.S. Environmental Protection Agency (EPA) as a toxic pollutant and hazardous substance and is required by regulation (40 CFR, Part 122) to be identified as a **discharge for NPDES permits for aquatic animal production facilities, aquaculture projects and other** facilities. Formaldehyde is subject to SARA Title III, Section 313 reporting.

Use, storage, and disposal of this product must be handled in accordance with applicable local, state and Federal laws.

STORAGE

Recommended storage temperature 59° F (15° C). DO NOT EXPOSE TO DIRECT SUNLIGHT. Store PARASITE-S indoors away from direct sunlight, heat, spark, and open flame, and ventilate storage area. Do not subject PARASITE-S to temperatures below 40° F (4.4° C).

Manufactured for
Western Chemical Inc.
1269 Lattimore Rd., Ferndale, WA 98248
(360) 384-5898

NADA 140-989, Approved by FDA

HEXION
Specialty Chemicals

MATERIAL SAFETY DATA SHEET

FOR INDUSTRIAL USE ONLY

DESCRIPTION: PARASITE-S

1. Chemical Product and Company Identification

DESCRIPTION:	**PARASITE-S**
PRODUCT CODE:	04-1437.-.
PRODUCT TYPE:	Formaldehyde Solution
APPLICATION:	Multi Purpose

Manufacturer/Supplier Information

MSDS prepared by:
Hexion Specialty Chemicals, Inc.
155 West A Street, Bldg. A-1
Springfield, OR
97477

For Emergency Medical Assistance
Call Health & Safety Information Services
1-866-303-6949

For additional health and safety or regulatory information, call (541)744-3256.

2. Composition, Information on Ingredients

The ingredients listed below have been associated with one or more immediate and/or delayed(*) health hazards. Risk of damage and effects depends upon duration and level of exposure. BEFORE USING, HANDLING, OR EXPOSURE TO THESE INGREDIENTS, READ AND UNDERSTAND THE MSDS.

		% by weight
67-56-1	***Methanol**	**10.0 - 30.0**
50-00-0	***Formaldehyde**	**30.0 - 50.0**

Any applicable Canadian trade secret numbers will be listed in Section 15.2.

3. Hazards Identification

3.1 Emergency Overview

Appearance	Clear, colorless liquid
Odor	Pungent

WARNING!
COMBUSTIBLE
May further react at high temperatures to form methanol, formic acid or methylals. At low temperatures will self-polymerize to form paraformaldehyde.
Harmful if inhaled.
Can cause central nervous system depression.
Causes chemical burns to eyes.
May be harmful if swallowed.
Ingestion may cause blindness.
May be harmful if absorbed through skin.

50-00-0 Formaldehyde

May cause cancer. OSHA regulates formaldehyde as a potential human carcinogen. See the OSHA Formaldehyde Workplace Standard at 29CFR 1910.1048. Rats chronically exposed to 14 ppm formaldehyde contracted nasal cancer. The National Toxicology Program (NTP) has listed formaldehyde as a probable human carcinogen. The International Agency for Research on Cancer (IARC) has concluded formaldehyde is carcinogenic to humans.

Safe handling and use instructions are provided in this MSDS and in the OSHA Formaldehyde Workplace Standard at 29CFR1910.1048. OSHA has identified 0.5 ppm as the "Action Level". Please review and understand the guidance contained in this MSDS and refer to the OSHA Formaldehyde Standard for regulatory requirements that may be applicable to your operation and use.

For further information and a review of various studies, go to www.osha.gov/SLTC/formaldehyde, www.iarc.fr and other authoritative websites.

May cause allergic skin reaction. Some reports suggest that formaldehyde may cause respiratory sensitization, such as asthma, and that preexisting respiratory and skin disorders may be aggravated by exposure.

Footnote: As of the date of issuance of this document, this material has not been listed by NTP, classified by IARC nor regulated by OSHA as a carcinogen.

4. First Aid Measures

INGESTION: If accidentally swallowed, dilute by drinking large quantities of water. If the individual is drowsy or unconscious, do not give anything by mouth. Immediately contact poison control center or hospital emergency room for advice on whether to induce vomiting or for any other additional treatment directions.

INHALATION: If inhaled, remove to fresh air. If not breathing give artificial respiration, preferably mouth-to-mouth. If breathing is difficult, give oxygen. Get medical attention immediately.

SKIN: Immediately remove all contaminated clothing, including shoes. Wash the affected area of the body with soap or mild detergent and large quantities of water for at least 20 minutes. Contact a physician if irritation persists. If there are chemical burns, cover the area with sterile, dry dressings and get medical attention immediately.

EYES: Immediately flush eyes with plenty of water for at least 15 minutes. Eyelids should be held apart during irrigation to ensure water contact with entire surface of eyes and lids. Get medical attention immediately.

5. Fire Fighting Measures

Flash point	61.1 °C (142.0 °F) Setaflash Closed Cup ASTM D 3828
Lower explosion limit	Approx. 7 % (V)
Upper explosion limit	Approx. 70 % (V)
Autoignition temperature	Approx. 420 °C (788 °F)

COMBUSTIBLE. Keep away from heat and flame.
In case of fire, use water spray, dry chemical, "alcohol" foam or CO2. Use water to keep fire-exposed containers cool.

6. Accidental Release Measures

Always wear appropriate protective equipment. Eliminate all ignition sources and ventilate the area to reduce the potential for exposure, fire and explosion. Recover and reuse as much liquid as possible. Large quantities: Enclose with diking material to prevent seepage into sewer systems, surface/ground water or natural bodies of water. If possible neutralize with dilute(<5%) solutions of ammonium hydroxide, sodium hydroxide, sodium bisulfite or sodium sulfite. Small quantities: Soak up with absorbent material (vermiculite, dry sand, earth) and remove to a chemical disposal area. Follow all emergency notification and reporting regulations.

7. Handling and Storage

7.1 Handling

Handle in accordance with good industrial hygiene and safety practices. These practices include avoiding unnecessary exposure and removal of the material from eyes, skin and clothing. Wash thoroughly after handling. Always use appropriate Personal Protective Equipment (PPE).

INHALATION: Do not breathe vapor. Use with adequate ventilation.

SKIN: Avoid contact with skin and clothing.

EYES: Do not get in eyes.

7.2 Storage

Storage temperature depends on methanol content and should be controlled to avoid precipitation or vaporization. See technical bulletin for recommended storage temperatures. Remove plug slowly to relieve pressure.
Formaldehyde solutions will start to precipitate paraformaldehyde if stored below their recommended storage temperatures making the freezing point difficult to determine.

8. Exposure Controls/Personal Protection

8.1 Exposure Controls

ENGINEERING CONTROLS: The following exposure control techniques may be used to effectively minimize employee exposure: local exhaust ventilation, enclosed system design, process isolation and remote control in combination with appropriate use of personal protective equipment and prudent work practices. These techniques may not necessarily address all issues pertaining to your operations. We, therefore, recommend that you consult with experts of your choice to determine whether or not your programs are adequate.

If airborne contaminants are generated when the material is heated or handled, sufficient ventilation in volume and air flow patterns should be provided to keep air contaminant concentration levels below acceptable criteria.

8.2 Personal Protection

Where formaldehyde gas concentrations can exceed acceptable criteria, use NIOSH (42 CFR Part 84) approved full-facepiece respiratory protection equipment. Respirators should be selected based on the concentration of formaldehyde in air in accordance with the OSHA Formaldehyde Standard Respiratory Protection requirements at 29CFR 1910.1048?, and the OSHA Respiratory Protection Standard at 29CFR 1910.134 or other applicable standards or guidelines, including ANSI standards regarding respiratory protection. A full-facepiece respirator with cartridges or canisters specifically approved for formaldehyde may be used for exposure levels up to 7.5 ppm (10 times the PEL). Chemical safety goggles must be worn if there is a possibility of contact with liquid formaldehyde or excessive gas-phase exposures. A full-facepiece respirator complies with this requirement. Wear protective gloves as required to prevent skin contact. Protective gloves must be worn when handling formaldehyde solutions of 1% or higher. Consult your glove manufacturer for specific information on permeation, degradation and breakthrough data to ensure proper selection. Based on available information, butyl, nitrile and Viton appear to be quite impervious to various strengths of formaldehyde solutions. Other glove materials may be equally suitable depending on composition, thickness and use conditions. Where high concentrations of formaldehyde may be present, such as in an emergency, full body protection should be worn. Other protective equipment that must be available when handling formaldehyde solutions of 1% or higher include eye wash fountains and safety showers. Reusable protective clothing should be cleaned and ventilated after any formaldehyde contamination. See the OSHA Formaldehyde Standard requirements at 29CFR 1910.1048(h) Protective Equipment and Clothing and OSHA 29CFR 1910.1048(i) Hygiene Protection for other specific protective measures based on the form of formaldehyde, the conditions of use and the hazards to be prevented.

8.3 Exposure Guidelines

67-56-1	**Methanol**			
ACGIH TLV	8-hr TWA	200 ppm	262 mg/m3	Skin
	STEL (15 min)	250 ppm	328 mg/m3	
OSHA PEL	8-hr TWA	200 ppm	260 mg/m3	
	Remanded TWA	200 ppm	260 mg/m3	Skin; 1989 PEL remanded, but in effect in some states
	Remanded STEL	250 ppm	310 mg/m3	
50-00-0	**Formaldehyde**			
ACGIH TLV	Ceiling	0.3 ppm	0.37 mg/m3	A2 - Suspected Human Carcinogen; SEN
OSHA PEL	8-hr TWA	0.75 ppm	0.9 mg/m3	
	STEL (15 min)	2 ppm	2.5 mg/m3	

9. Physical and Chemical Properties

Appearance	Clear, colorless liquid
Odor	Pungent
Odor threshold	Not available
Specific gravity	1.0775 - 1.0865
pH	2.5 - 3.6
Freezing point	See storage section
Solubility in water	Infinite
Octanol/water partition coefficient	Pow 0.35
Vapor pressure	Approx. 40 mm Hg @39 °C (102 °F)
Vapor density	Approx. 1
Evaporation rate	Less than 1 (Butyl Acetate = 1)
Boiling point, 760 mm Hg	Approx. 100 °C (212 °F)

10. Stability and Reactivity

Normally stable, but may further react at high temperatures to form methanol, formic acid or methylals. At low temperatures will self-polymerize to form paraformaldehyde.

Incompatibilities:

Reacts with many compounds. Reaction with phenol, strong acids or alkalis may be violent. Reaction with hydrochloric acid may form bis-chloromethyl ether, an OSHA regulated carcinogen.

Decomposition products may include:

CO, CO2.

Hazardous polymerization:

Will not occur.

11. Toxicological Information

See Section 3 Hazards Identification information.
67-56-1 Methanol
LC50: rat=64,000 mg/l/4 h (Sax)
LD50: Oral-rat= 5,628 mg/kg (Sax); Skin-rabbit= 20,000 mg/kg (Sax)
50-00-0 Formaldehyde
LC50: rat=0.59 mg/l (Sax)
LD50: Oral-rat= 800 mg/kg (Merck); Skin-rabbit= 270 mg/kg (Sax)

12. Ecological Information

Formaldehyde is highly toxic to algae, protozoa and other unicellular organisms and slightly toxic to fish. In the atmosphere the material is rapidly degraded by photolysis and photooxidation. Formaldehyde is mobile in the soil. In water or soil, formaldehyde is biodegraded in a few days. Experiments performed on a variety of fish and shrimp show no bioconcentration of formaldehyde.

Ecotoxicity:
Algae(scenedesmus): toxic: 0.3-0.5 mg/l
Arthropoda(daphnia): toxic: 2 mg/l
Fish (guppies): TLm = 50-200 mg/l

Environmental Fate:
BOD5 = 60% of ThOD = 0.6-1.07 standard dilution at <260 mg/l
Octanol/Water Partition Coefficient = 0.35 (LKOW)

13. Disposal Considerations

Recover free liquid. Absorb residue and dispose of according to local, state/provincial, and federal requirements. Empty container: May contain explosive vapors. DO NOT cut, puncture or weld on or nearby.

14. Transport Information

14.1 U.S. Department of Transportation (DOT)

The data provided in this section is for information only and may not be specific to your package size. You will need to apply the appropriate regulations to properly classify your shipment for transportation.

Proper shipping name	FORMALDEHYDE SOLUTION
UN/NA number	2209
Class	8
Packing group	III
Label	8
RQ Ingredients	

14.2 Canadian Transportation of Dangerous Goods (TDG)

Proper shipping name	FORMALDEHYDE SOLUTION
UN number:	2209
Class	Class 8
Packing group	III
Label	8

15. Regulatory Information (Selected Regulations)

15.1 U.S. Federal Regulations

OSHA Hazards Communication Standard 29CFR1910.1200

This material is a "health hazard" and/or a "physical hazard" as determined when reviewed according to the requirements of the Occupational Safety and Health Administration 29 CFR Part 1910.1200 "Hazard Communication" Standard.

SARA Title III: Section 311/312

Immediate health hazard
Delayed health hazard
Fire hazard

SARA Title III: Section 313 and 40 CFR Part 372

This product contains the following toxic chemical(s) subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986, and Subpart C-Supplier Notification Requirement of 40 CFR Part 372.

Methanol	67-56-1	13.97%
Formaldehyde	50-00-0	37.00%

TSCA Section 8(b) Inventory

All reportable chemical substances are listed on the TSCA Inventory. We rely on certifications of compliance from our suppliers for chemical substances not manufactured by us.

15.2 Canadian Regulations

Workplace Hazardous Materials Information System (WHMIS)

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulation (CPR) and the MSDS contains all the information required by the CPR.

Class B3
Class D1A
Class D1B
Class D2A
Class D2B
Class E

Canadian Environmental Protection Act (CEPA)

All reportable chemical substances are listed on the Domestic Substances List (DSL) or otherwise comply with CEPA new substance notification requirements.

National Pollutant Release Inventory (NPRI)

This product contains the following chemical(s) subject to the reporting requirements of the Canadian Environmental Protection Act (CEPA) subsection 16(1), National Pollutant Release Inventory.

Methanol	67-56-1	13.97%
Formaldehyde	50-00-0	37.00%

16. Other Information

User's Responsibility

The OSHA Hazard Communication Standard 29CFR 1910.1200 and the Workplace Hazardous Materials Information System (WHMIS) require that the information contained on these sheets be made available to your workers. Educate and train your workers regarding OSHA and WHMIS precautions. Instruct your workers to handle this product properly. Consult with appropriate experts to guard against hazards associated with use of this product and its ingredients.

Disclaimer

SELLER MAKES NO WARRANTY, EXPRESS OR IMPLIED, CONCERNING THE PRODUCT OR THE MERCHANTABILITY OR FITNESS THEREOF FOR ANY PURPOSE, except that the product shall conform to contracted specifications, and that the product does not infringe any valid United States or Canadian patent. No claim of any kind shall be greater in amount than the purchase price of the quantity of product in respect of which damages are claimed. In no event shall Seller be liable for incidental or consequential damages, whether Buyer's claim is based on contract, breach of warranty, negligence or otherwise.

I. GENERAL INFORMATION

NADA Number: NADA 140-989

Sponsor: WESTERN CHEMICAL INC.
1269 Lattimore Road
Ferndale, WA. 98248

Accepted Name: Formalin

Trade Name: PARASITE-S

Marketing Status: Over-the-counter

Supplemental Effects: The approval will allow for the use of formalin to be expanded, as a parasiticide, to all finfish, and, as a fungicide, to the eggs of all finfish.

II. INDICATIONS FOR USE

PARASITE-S is added to the environmental water as follows: (a) for the control of external protozoa (*Chilodonella* spp., Costia spp., *Epistylis* spp., *Ichthyophthirius* spp., *Scyphidia* spp. and *Trichodina* spp.), and the monogenetic trematode parasites (*Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.) on all finfish, (b) for the control of fungi of the family Saprolegniaceae on all finfish eggs and (c) for the control of external protozoan parasites (*Bodo* spp., *Epistylis* spp., and *Zoothamnium* spp.) on penaeid shrimp.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

A. Dosage Form: Formalin is a solution of about 37% by weight of formaldehyde gas in water. (This is equivalent to formalin 37, or 37 grams of formaldehyde in 100 ml of solution.)

B. Route of Administration: In the environmental water

C. Recommended Concentrations: as represented in Table 1-3 below.

1. For the Control of External Parasites on Finfish

TABLE 1
Concentrations of Formalin

Aquatic Species	Administer in Tanks and Raceways for up to 1 hour (µL/L)*	Administer in Earthen Ponds Indefinitely (µL/L)*
Salmon & trout		
above 50°F	up to 170	15 to 25**, ***
below 50°F	up to 250	15 to 25**, ***
All other finfish	up to 250	15 to 25**, ***

* Microliter per liter (µL/L) = parts per million (ppm).

** Use the lower concentration when ponds, tanks or raceways are heavily loaded with phytoplankton, or finfish, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternatively, a higher concentration might be used if dissolved oxygen is strictly monitored.

*** Although the indicated concentrations are considered safe for cold and warm water finfish, a small number of each lot or pond to be treated should always be used to check for any unusual sensitivity to formalin before proceeding.

2. For the Control of Fungi of the Family Saprolegniaceae on Finfish Eggs

TABLE 2
Concentrations of Formalin

Aquatic Species	Administer in Hatchery Systems (μL/L)*
Eggs of all finfish except Acipenseriformes	1000 to 2000 for 15 minutes**
Eggs of Acipenseriformes	up to 1500 for 15 minutes**

* Microliter per liter (μL/L) = parts per million (ppm).

** Apply in constant flow water supply of incubating facilities. A preliminary bioassay should be conducted on a small subsample of finfish eggs to determine sensitivity before treating an entire group. This is necessary for all species because egg sensitivity can vary with species or strain and the unique conditions at each facility.

3. For the Control of External Protozoan Parasites on Penaeid Shrimp

TABLE 3
Concentrations of Formalin

Aquatic Species	Administer in Tanks and Raceways for up to 4 hours (μL/L)*	Administer in Earthen Ponds Indefinitely (μL/L)*
Shrimp	50 to 100**	25***

* Microliter per liter (μL/L) = parts per million (ppm).

** Treat for up to 4 hours daily. Treatment may be repeated daily until parasite control is achieved. Use the lower concentration when tanks or raceways are heavily loaded with phytoplankton, or shrimp, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternatively, a higher concentration might be used if dissolved oxygen is strictly monitored.

*** Treatment may be repeated in 5 to 10 days, if needed.

IV. PREVIOUS APPROVAL

Fish are minor species of animals defined under 21 CFR 514.1 (d). Formalin is presently approved for use as a parasiticide on catfish, largemouth bass, bluegill, salmon, trout, and shrimp, and a fungicide on salmon, trout and esocid eggs (21 CFR 529.1030).

V. EFFECTIVENESS

A. Striped Bass and all other Finfish

The need for additional efficacy studies has been waived because it was determined that interspecies extrapolation is appropriate to demonstrate the efficacy of formalin in striped bass (*Morone saxatilis*) and all other finfish for the control of the same ectoparasites for which the drug is currently approved.

Formalin is a water treatment where the primary effect results from localized action at the topical site of administration. The concentration of active drug at the topical site is a function of the administered concentration and water conditions. These latter two conditions and the pathogen's drug sensitivity are considered the primary determinants of efficacy. Although the drug may be slightly absorbed, systemic absorption is not believed to play a significant role in the drug's effectiveness at the topical site. Thus, drug concentration and the effects of the pathogen are considered to be the primary determinants of effectiveness, while differences in drug/host response among species is considered to be an insignificant factor.

Formalin is currently approved for its effectiveness against external protozoa (*Chilodonella* spp., *Costia* spp., *Epistylis* spp., *Icthyophthirius* spp., *Scyphidia* spp., and *Trichodina* spp.) and monogenetic trematode parasites (*Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.), in a wide range of cold and warm freshwater finfish (see 21 CFR 529.1030). Since, as discussed above, formalin's effectiveness is based on drug concentration and the drug effects on potentially pathogenic external protozoans rather than the *in vivo* drug/host response in various species, the effectiveness of formalin against these pathogens would be the same in all species of finfish. Therefore, the efficacy data summarized in the attached Public Master File (PMF) 3543 and PMF 5228 are adequate to support formalin's effectiveness against the same ectoparasites on striped bass and on all other finfish.

B. Eggs of all Finfish

The need for additional efficacy studies has been waived because it has been determined that interspecies extrapolation is appropriate to demonstrate the efficacy of formalin on the eggs of all finfish for the control of the same family of fungi (Saprolegniaceae) for which the drug is currently approved.

Formalin is a water treatment where the primary effect results from localized action at the topical site of administration. The concentration of active drug at the topical site is a function of the administered concentration and water conditions. Although the drug may be slightly absorbed, absorption of formalin by the eggs is not believed to play a significant role in the drug's effectiveness at the topical site. Thus, drug concentration and the effects on the fungi are considered to be the primary determinants of effectiveness, while differences in drug/host response among species is considered to be an insignificant factor.

Formalin is currently approved for its effectiveness against fungi of the family Saprolegniaceae on salmon, trout and esocid eggs (see 21 CFR 529.1030). Since, as discussed above, formalin's effectiveness is based on drug concentration and the drug effects on eggs rather than the individual drug/host response in various species, the effectiveness of formalin against the fungi would be the same in all species of eggs. Therefore, the efficacy data in PMF 3543 (attached) and data existing in the publicly-disclosable Investigational New Animal Drug (INAD) file 8886 are adequate to support formalin's effectiveness against the same fungi on all finfish eggs. Studies within INAD file 8886 address the safety of formalin when used on the eggs of several finfish species representing five families, including: walleye, common carp, channel catfish, white sucker and lake sturgeon. These same studies indirectly address the effectiveness of the treatment as measured by egg hatchability, because the presence of significant fungi on finfish eggs can severely reduce hatchability.

VI. ANIMAL SAFETY

A. Finfish

The data in PMF 3543 (attached) addressed the safety of formalin in salmon, trout, catfish, largemouth bass, bluegill (the originally approved set of species), as well as smallmouth bass, black bullhead and green sunfish. The results of additional studies (contained in PMF 5228)

demonstrating the safety of short-term and indefinite use of formalin in striped bass, a species known to be sensitive to formalin, are described below. The data in these studies show that use of the drug at the recommended concentration is safe in a wide range of cold and warm water finfish, including striped bass, the most sensitive species. Since, as discussed above, formalin safety has been demonstrated in a wide variety of species (nine species from four of the most important North American families of cultured finfish: Ictaluridae, Salmonidae, Centrarchidae and Percichthyidae), one species (striped bass) of which has been documented as an extremely sensitive species, the safety of formalin would be the same for all finfish species. Therefore, these studies are adequate to demonstrate that use of the drug at recommended concentrations is safe in all finfish.

As noted in the Freedom of Information summary for PMF 3543, tolerances to formalin may vary with strains and species of finfish. Health status may also affect formalin tolerance. Although the indicated concentrations are considered safe for cold and warm water finfish, a small number of each lot or pond to be treated should always be used to check for any unusual sensitivity to formalin before proceeding.

In addition, formalin may be harmful to biofilters, and care should be taken to avoid contamination of the biofilter with treatment solution.

1. Target Animal Safety Study #1

a. Name and Address of Investigator:

Wilmer A. Rogers, Ph.D.
Department of Fisheries and Allied Aquacultures
Auburn University, Alabama 36849

b. General Design of the Investigation:

i. **Purpose of the study:** To determine if formalin is safe when administered to healthy striped bass.

ii. **Test Animals:** Striped bass (*Morone saxatilis*) fingerlings averaging 46.7 mm in length and 0.9 g in body weight were used for this set of studies. One study was conducted at 18°C, while the other was conducted at 25°C. Sixteen aquaria (eight aerated and eight not aerated), with 20 fingerlings in each, were used in the study.

iii. **Dosage form:** Formalin solution

iv. **Route of Administration:** In the environmental water

v. **Dosages Used:** Untreated control, 250, 500, and 750 ppm formalin, respectively (1X, 2X, and 3X the maximum proposed concentration)

vi. **Test Duration:** 3 hours

vii. **Parameters:** Mortality at 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 hours of treatment

c. **Results:** Refer to Tables 4 and 5 below. No mortality occurred in fish exposed to 250 ppm formalin for up to 1.5 hour.

TABLE 4
Safety of Formalin in Striped Bass at 25°C

Formalin Concentration (ppm)	Mortalities (%), with/without Aeration					
	0.5 hr	1.0 hr	1.5 hr	2.0 hr	2.5 hr	3.0 hr
0	0/0	0/0	0/0	0/0	0/0	0/0
250	0/0	0/0	0/0	50/25	50/30	65/45
500	0/0	0/0	20/45	70/90	80/100	80/100
750	10/5	75/50	100/80	100/100	100/100	100/100

TABLE 5
Safety of Formalin in Striped Bass at 18°C

Formalin Concentration (ppm)	Mortalities (%), with/without Aeration					
	0.5 hr	1.0 hr	1.5 hr	2.0 hr	2.5 hr	3.0 hr
0	0/0	0/0	0/0	0/0	0/0	0/0
250	0/0	0/0	0/0	0/15	5/25	15/35
500	0/0	0/0	25/40	55/65	80/85	100/100
750	0/5	35/10	80/70	95/100	100/100	100/100

2. Target Animal Safety Study #2

a. Name and Address of Investigator:

Wilmer A. Rogers, Ph.D.
Department of Fisheries and Allied Aquacultures
Auburn University, Alabama 36849

b. General Design of the Investigation:

i. **Purpose of the study:** To determine if formalin is safe when administered to healthy striped bass.

ii. **Test animals:** Striped bass fingerlings averaging 46.5 mm in length and 0.9 g in body weight were used for this study. Twenty fish were allotted to each of six treatment groups. The study was conducted at 22°C.

iii. **Dosage form:** Formalin solution

iv. **Route of Administration:** In the environmental water

v. **Dosages Used:** Untreated control, 55.0, 57.5, 60.0, 62.5, and 65.0 ppm formalin. Formalin administered in flow-through aquaria with aeration.

vi. **Test Duration:** 96 hours

vii. **Parameters:** Cumulative mortality at 24, 48, 72, and 96 hours of treatment

c. **Results:** The 96-hour LC_{50} was 60.1 ppm. Refer to Table 6 below for mortality patterns.

TABLE 6
Safety of Formalin in Striped Bass at 22°C

Formalin Concentration (ppm)	Cumulative Mortalities (%) at Different Times after Formalin Application			
	24 hr	48 hr	72 hr	96 hr
0	0	0	0	0
55.0	0	0	0	0
57.5	5	40	40	40
60.0	20	45	55	55
62.5	15	35	55	60
65.0	5	70	90	90

3. Target Animal Safety Study #3

Bills, T.D., L.L. Marking, G.E. Howe. 1993. Sensitivity of juvenile striped bass to chemicals used in aquaculture. United States Department of the Interior, Fish and Wildlife Service, *Resource Publication 192.*

These studies determined LC_{50}'s (concentrations producing 50% mortality in a population) of formalin in striped bass. Ten juvenile (1.0 g) striped bass were exposed to each test concentration of formalin in 15 L glass jars. Tests were conducted at a water temperature of 12°C and at varying levels of water hardness. Observations on mortality were made at 1, 3, and 6 hours during the first day of exposure, and then once daily for 4 days. Tests were duplicated in different year class fish in waters of different temperature (12, 17, and 22°C), hardness, and pH. Mean LC_{50}'s in soft water of pH 7.5 at 12°C were as represented in Table 7:

TABLE 7
Mean 50% Lethal Concentrations (LC50's) of Formalin to Striped Bass (ppm)

Time (hours)	Test 1	Test 2
1	1230	>1000
3	1410	>1000
6	940	760
24	211	120
96	75	56

Toxicity of formalin was not affected by water hardness or pH. However, toxicity was greater in warm water than in cold water. Mean LC_{50}'s in soft water of pH 7.5 at three temperatures were as represented in Table 8.

TABLE 8
Mean 50% Lethal Concentrations (LC50's) of Formalin to Striped Bass (ppm)

Time (hours)	12°C	17°C	22°C
1	>1000	>1000	>1000
3	>1000	>1000	750
6	760	455	210
24	120	86	82
96	56	48	30

B. Eggs of Finfish

Formalin is currently approved for the control of fungi of the family Saprolegniaceae on salmon, trout, and esocid eggs (see 21 CFR 529.1030). Additional safety studies for the control of fungi of the family Saprolegniaceae on other finfish eggs are provided in INAD file 8886. The sponsor, U.S. National Biological Service, Upper Mississippi Science Center, La Crosse, Wisconsin, has authorized the public disclosure of all information within their INAD file 8886.

The data in these studies show that use of the drug at the recommended concentration is safe on the eggs of a wide range of cold and warm water fish. Since, as discussed above, formalin safety has been demonstrated in finfish eggs from a wide variety of species, the safety of formalin would be the same for the eggs of all finfish species. Therefore, these studies are adequate to demonstrate that use of the drug at the recommended concentration is safe on the eggs of all finfish. The following summarizes the finfish egg safety study in INAD 8886.

1. **Name and Address of Investigator:**

   National Fisheries Research Center
   National Biological Service
   Department of the Interior
   La Crosse, Wisconsin 54602-0818

2. **General Design of the Investigation:**

   a. **Purpose of the study:** To determine if formalin is safe when administered to finfish eggs of representative finfish species.

   b. **Test Animals:** Green eggs of walleye (*Stizostedion vitreum*), channel catfish (*Ictalurus punctatus*), white sucker (*Catostomus commersoni*), common carp (*Cyprinus carpio*) and lake sturgeon (*Acipenser transmontanus*) were tested. The study was conducted at 12±2°C for walleye and white sucker, at 17±2°C for common carp and lake sturgeon and at 22±2°C for channel catfish.

   c. **Dosage form:** Formalin solution

   d. **Route of Administration:** In the environmental water

   e. **Dosages Used:** 1500, 4500, and 7500 ppm formalin

   f. **Test Duration:** 45 minutes

   g. **Parameters:** percent hatch was calculated by the following formula:

   $$\% \text{ hatch} = (\text{number of hatched fry} \div \text{initial number of eggs}) \times 100$$

3. **Results:**

   This study demonstrated that standard formalin treatment, at a concentration of 1000 to 2000 ppm, is safe for finfish eggs of the orders Cypriniformes (common carp and white sucker), Perciformes (walleye) and Siluriformes (channel catfish) for 15 minutes daily, if necessary. Formalin is also safe, at a concentration of 1500 ppm or less, for finfish eggs of the order Acipenseriformes (lake sturgeon) for 15 minutes daily, if necessary. Because the species of finfish eggs treated in the study are representative of the variety of species of finfish eggs, it is determined that formalin is safe for other finfish eggs. Due to the varying sensitivity of finfish eggs, however, the following statement is included in the labeling.

   > "A preliminary bioassay should be conducted on a small subsample of finfish eggs to determine sensitivity before treating an entire group. This

is necessary for all species because egg sensitivity can vary with species or strain and the unique conditions at each facility."

VII. HUMAN FOOD SAFETY

Human food safety data for the use of formalin in salmon, trout, catfish, largemouth bass, and shrimp are found in PMF 3543. The results of four residue depletion studies of formalin in striped bass are summarized below (and found in PMF 5228). The use of formalin has not been shown by these studies to result in the accumulation of formaldehyde above naturally occurring levels in the edible tissue of any of these aquatic species. Because formalin treatment of this wide variety of aquatic species does not result in levels of formaldehyde in the edible tissue above the normal range of endogenous formaldehyde, formaldehyde is not expected to accumulate in additional finfish species which have not been specifically tested.

The studies summarized below (and found in detail in PMF 5228) were all conducted by Wilmer A. Rogers, Ph.D. at Auburn University, Auburn, Alabama. Formalin was administered in the environmental water in all studies and the following method of tissue analysis was used in all studies. Formaldehyde was measured in the muscle of treated and control fish by the Nash test (described in Castell and Smith, *J. Fisheries Research Board of Canada* 30:91, 1973). The Nash test also was used in the residue studies to support the prior approvals for formalin in salmon, trout, catfish, largemouth bass, and shrimp. The recovery of formaldehyde in striped bass muscle samples fortified with 5, 20, and 40 mg/kg formalin was 106.9%, 78.0%, and 70.9%, respectively. The limit of quantitation was 5 mg/kg formalin (1.85 mg formaldehyde/kg fish).

The studies differed from each other as follows:

A. Juvenile/Indefinite Exposure Period Study - a two-part experiment in which striped bass in tanks were exposed to formalin for an indefinite period of time at two water temperatures.

1. **Test Animal:** Striped bass; body weight was 23 grams for Part 1 and 39 grams for Part 2
2. **Water Temperature:** 12 to 14°C for Part 1 and 21 to 22°C for Part 2
3. **Dose Levels and Treatment Duration:** 0 (control) and 25 ppm formalin indefinitely.
4. **Results:** as represented in Table 9

TABLE 9
Mean Formaldehyde Residues (mg/kg) in Muscle of Juvenile Striped Bass

Hours of Exposure to 25 ppm Formalin	Part 1: 12-14°C		Part 2: 21-22°C	
	Treated Fish n= 2	Control Fish n = 2	Treated Fish n = 5	Control Fish n = 5
0	4.67	3.74	3.26	3.32
12	4.42	4.02	not collected	not collected
24	4.40	3.85	6.63	5.52
48	4.22	1.67	6.64	3.39
72	5.12	3.84	7.60	5.34
96	4.12	3.63	5.61	4.41
120	2.36	2.71	4.02	4.03
144	1.76	1.76	4.63	4.58
168	3.60	3.74	4.04	3.86

B. Fingerling/Short Duration Bath Study - striped bass in tanks were exposed to formalin for one hour.

1. **Test Animal:** Striped bass; body weight was 26 grams
2. **Water Temperature:** 21°C
3. **Dose Levels and Treatment Duration:** 0 ppm (control) and 250 ppm formalin for 1 hour
4. **Results:** as represented in Table 10

TABLE 10
Mean Formaldehyde Residues (mg/kg) in Muscle of Fingerling Striped Bass

Hours After Addition of 250 ppm Formalin	Treated Fish n = 4	Control Fish n = 4
0	2.86	3.57
12	3.67	3.17
24	3.73	3.61
48	2.65	2.97
72	3.37	3.38

C. Market size/Indefinite Exposure Period Study - market size striped bass in tanks were exposed to formalin indefinitely.

1. **Test Animal:** Striped bass; body weight was 435 grams
2. **Water Temperature:** 24°C
3. **Dose Levels and Treatment Duration:** 0 ppm (control) and 25 ppm formalin indefinitely
4. **Results:** as represented in Table 11

TABLE 11
Mean Formaldehyde Residues (mg/kg) in Muscle of Market-size Striped Bass

Hours of Exposure to 25 ppm Formalin	Treated Fish n = 2	Control Fish n = 2
0	3.29	4.00
48	3.98	4.42
96	3.85	3.85

D. Juvenile/Indefinite Exposure Study - striped bass in ponds were exposed to formalin indefinitely.

1. **Test Animal:** Striped bass; body weight was 137 grams
2. **Water Temperature:** 26 to 30°C
3. **Dose Levels and Treatment Duration:** 0 ppm (control) and 25 ppm formalin indefinitely
4. **Results:** as represented in Table 12

TABLE 12
Mean Formaldehyde Residues (mg/kg) in Muscle of Juvenile Striped Bass

(HFA-305), Park Building (Room 1-23), 12420 Parklawn Dr., Rockville, Maryland 20857 at the time of publication of approval in the FEDERAL REGISTER.

PARASITE-S is not under any unexpired U.S. patents.

X. APPROVED PRODUCT LABELING: See attached draft package insert and drum labeling.

Date of Approval: November 25, 2002

FREEDOM OF INFORMATION SUMMARY

NADA 137-687

FORMALIN-F™

(formalin: approximately 37% by weight of formaldehyde gas)

"...for the use of formalin to be expanded, as a parasiticide, to all finfish and penaeid shrimp, and, as a fungicide, to the eggs of all finfish"

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

Sponsored by:

Natchez Animal Supply Company

I. GENERAL INFORMATION

NADA Number:	137-687
Sponsor:	Natchez Animal Supply Company 201 John R. Junkin Drive Natchez, Mississippi 39120
Generic Name:	Formalin, approximately 37% by weight of formaldehyde gas
Trade Name:	FORMALIN-F™
Marketing Status:	Over-the-counter
Effect of Supplement:	Provides for the use of FORMALIN-F™ to be expanded, as a parasiticide, to all finfish and penaeid shrimp, and, as a fungicide, to the eggs of all finfish.

II. INDICATIONS FOR USE

FORMALIN-F™ is added to the environmental water as follows: (a) for the control of external protozoa (*Chilodonella* spp., *Costia* spp., *Epistylis* spp., *Ichthyophthirius* spp. *Scyphidia* spp. and *Trichodina* spp.) and the monogenetic trematode parasites (*Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.) on all finfish, (b) for the control of fungi of the family Saprolegniaceae on all finfish eggs, and (c) for the control of protozoan parasites (*Bodo* spp., *Epistylis* spp., and *Zoothamnium* spp.) on penaeid shrimp.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION AND RECOMMENDED DOSAGE

A. Dosage Form: Formalin is a solution of approximately 37% formaldehyde gas (by weight) in water. This is equivalent to 37 grams of formaldehyde in 100 ml of solution.

B. Route of Administration: In the environmental water

C. Recommended Concentrations: as shown in Tables 3.1 to 3.3.

1. For the Control of External Parasites on Finfish

TABLE 3.1 Concentrations of Formalin

Aquatic Species	Administer in Tanks and Raceways for up to 1 hour (μL/L)*	Administer in Earthen Ponds Indefinitely (μL/L)*
Salmon & trout		
above 50° F	up to 170	15-25**, ***
below 50° F	up to 250	15-25**, ***
All other finfish	up to 250	15-25**, ***

* Microliter per liter (μL/L) = parts per million (ppm).

** Use the lower concentration when ponds, tanks, or raceways are heavily loaded with phytoplankton, or finfish, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternately, a higher concentration might be used if dissolved oxygen is strictly monitored.

*** Although the indicated concentrations are considered safe for cold and warm water finfish, a small number of each lot or pond to be treated should always be used to check for any unusual sensitivity to formalin before proceeding.

2. For the Control of Fungi of the Family Saprolegniaceae on Finfish Eggs

TABLE 3.2 Concentrations of Formalin

Aquatic Species	Administer in Hatchery Systems (μL/L)*
Eggs of all finfish except Acipenseriformes	1000 to 2000 for 15 minutes**
Eggs of Acipenseriformes	Up to 1500 for 15 minutes**

* Microliter per liter (μL/L) = parts per million (ppm)

**Apply in constant flow water supply of incubating facilities. A preliminary bioassay should be conducted on a small sub sample of finfish eggs to determine sensitivity before treating an entire group. This is necessary for all species because egg sensitivity can vary with species or strain and the unique conditions at each facility.

3. For Control of External Protozoan Parasites on Penaeid Shrimp

Table 3.3 Concentrations of Formalin

Aquatic Species	Administer in Tanks and Raceways for up to 4 hours (μL/L)*	Administer in Earthen Ponds Indefinitely (μL/L)*
Shrimp	50 to 100**	25***

*Microliter per liter μL/L) = parts per million (ppm).

**Treat for up to 4 hours daily. Treatment may be repeated daily until parasite control is achieved. Use the lower concentration when tanks or raceways are heavily loaded with phytoplankton, or shrimp, to avoid oxygen depletion due to the biological oxygen demand created by decay of dead phytoplankton. Alternatively, a higher concentration might be used if dissolved oxygen is strictly monitored.

***Treatment may be repeated in 5 to 10 days, if needed.

IV. EFFECTIVENESS

A. Striped Bass and all other Finfish

Formalin is a water treatment where the primary effect results from localized action at the topical site of administration. The concentration of active drug at the topical site is a function of the administered concentration and water conditions. These latter two conditions and the pathogen's drug sensitivity are considered the primary determinants of effectiveness. Although the drug may be slightly absorbed, systemic absorption is not believed to play a significant role in the drug's effectiveness at the topical site. Thus, drug concentration and the effects of the pathogen are considered to be the primary determinants of effectiveness, while differences in drug/host response among species are considered to be an insignificant factor.

FORMALIN-F™ is currently approved for its effectiveness against external protozoa *(Chilodonella* spp., *Costia* spp., *Epistylis* spp., *Ichthyophthirius* spp., *Scyphidia* spp., and *Trichodina* spp.) and monogenetic trematode parasites *(Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.), in a wide range of cold and warm freshwater finfish (see 21 CFR 529.1030). Since, as discussed above, formalin's effectiveness is based on drug concentration and the drug effects on potentially pathogenic external protozoans rather than the *in vivo* drug/host response in various species, the effectiveness of formalin against these pathogens would be the same in all species of finfish.

Therefore, the effectiveness data summarized in the attached Public Master File (PMF) 3543 and PMF 5228 are adequate to support formalin's effectiveness against the same ectoparasites on striped bass and on all other finfish.

B. Eggs of All Finfish

FORMALIN-F™ is currently approved for its effectiveness against fungi of the family Saprolegniaceae on salmon, trout, and esocid eggs (see 21 CFR 529.1030). Since, as discussed above, formalin's effectiveness is based on drug concentration and the drug effects on eggs rather than the individual drug/host response in various species, the effectiveness of formalin against the fungi would be the same in all species of eggs. Therefore, the effectiveness data in PMF 3543 and data existing in the publicly disclosable investigational new animal drug (INAD) file 8886 are adequate to support formalin's effectiveness against the same fungi on all finfish eggs. Studies within INAD 8886 address the safety of formalin when used on the eggs of several finfish species representing five families, including: walleye, common carp, channel catfish, white sucker, and lake sturgeon. These same studies indirectly address the effectiveness of the treatment as measured by egg hatchability, because the presence of significant fungi on finfish eggs can severely reduce hatchability.

Additional effectiveness studies are not required because it is determined that interspecies extrapolation is appropriate to demonstrate the effectiveness of formalin on the eggs of all finfish for the control of the same family of fungi (Saprolegniaceae) for which the drug is currently approved.

C. Penaeid Shrimp

Effectiveness data from the Freedom of Information (FOI) summary for PMF 3543, 6 FR 20618, May 6, 1991, demonstrated that formalin, when used as directed, is effective in the treatment and control of external protozoan parasites on shrimp.

V. ANIMAL SAFETY

A. Finfish

The data summarized in the FOI summary for PMF 3543 addressed the safety of formalin in salmon, trout, catfish, largemouth bass, bluegill (the originally approved set of species), as well as smallmouth bass, black bullhead and green sunfish. The results of additional studies (contained in PMF 5228) demonstrating the safety of short-term and indefinite use of formalin in striped bass, a species known to be sensitive to formalin, are described below. The data in these studies show that use of the drug at the recommended concentration is safe in a wide range of cold and warm water finfish, including striped bass, the most sensitive species. Since, as discussed above, formalin safety has been demonstrated in a wide variety of species (nine species from four of the most important North American families of cultured finfish: Ictaluridae, Salmonidae, Centrarchidae and Percichthyidae), one species (striped bass) of which has been documented as an extremely sensitive species, the safety of formalin would be the same for all finfish species. Therefore, these studies are adequate to demonstrate that use of the drug at recommended concentrations is safe in all finfish.

As noted in the Freedom of Information summary for PMF 3543, tolerances to formalin may vary with strains and species of finfish. Health status may also affect formalin tolerance. Although the indicated concentrations are considered safe for cold and warm water finfish, a small number of each lot or pond to be treated should always be used to check for any unusual sensitivity to formalin before proceeding.

In addition, formalin may be harmful to biofilters, and care should be taken to avoid contamination of the biofilter with treatment solution.

1. Target Animal Safety Study #1

   a. Name and Address of Investigator:

      Wilmer A. Rogers, Ph.D.
      Department of Fisheries and Allied Aquaculture
      Auburn University, Alabama 36849

   b. General Design of the Investigation:

      i. Purpose of the study: To determine if formalin is safe when administered to healthy striped bass.

      ii. Test Animals: Striped bass *(Morone saxatilis)* fingerlings averaging 46.7 mm in length and 0.9 g in body weight were used for this set of studies. One study was conducted at 18°C, while the other was conducted at 25°C. Sixteen aquaria (eight aerated and eight not aerated), with 20 fingerlings in each, were used in the study.

iii. Dosage Form: Formalin solution

iv. Route of Administration: In the environmental water

v. Dosages Used: Untreated control, 250, 500, and 750 ppm formalin, respectively (1X, 2X, and 3X the maximum proposed concentration)

vi. Test Duration: 3 hours

vii. Parameters: Mortality at 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 hours of treatment

viii. Results: Refer to Tables 5.1 and 5.2 below. No mortality occurred in fish exposed to 250 ppm formalin for up to 1.5 hour.

TABLE 5.1 Safety of Formalin in Striped Bass at 25°C

Formalin Concentration (ppm)	Mortalities (%), with/without Aeration					
	0.5 hr	1.0 hr	1.5 hr	2.0 hr	2.5 hr	3.0 hr
0	0/0	0/0	0/0	0/0	0/0	0/0
250	0/0	0/0	0/0	50/25	50/30	65/45
500	0/0	0/0	20/45	70/90	80/100	80/100
750	10/5	75/50	100/80	100/100	100/100	100/100

TABLE 5.2 Safety of Formalin in Striped Bass at 18°C

Formalin Concentration (ppm)	Mortalities (%), with/without Aeration					
	0.5 hr	1.0 hr	1.5 hr	2.0 hr	2.5 hr	3.0 hr
0	0/0	0/0	0/0	0/0	0/0	0/0
250	0/0	0/0	0/0	0/15	5/25	15/35
500	0/0	0/0	25/40	55/65	80/85	100/100
750	0/5	35/10	80/70	95/100	100/100	100/100

2. Target Animal Safety Study #2

a. Name and Address of Investigator:

Wilmer A. Rogers, Ph.D.
Department of Fisheries and Allied Aquaculture
Auburn University, Alabama 36849

b. General Design of the Investigation:

i. Purpose of the study: To determine if formalin is safe when administered to healthy striped bass.

ii. Test Animals: Striped bass fingerlings averaging 46.5 mm in length and 0.9 g in body weight were used for this study. Twenty fish were allotted to each of six treatment groups. The study was conducted at 22°C.

iii. Dosage Form: Formalin solution

iv. Route of Administration: In the environmental water

v. Dosages Used: Untreated control, 55.0, 57.5, 60.0, 62.5, and 65.0 ppm formalin. Formalin was administered in flow-through aquaria with aeration.

vi. Test Duration: 96 hours

vii. Parameters: Cumulative mortality at 24, 48, 72, and 96 hours of treatment

viii. Results: The 96-hour LC50 was 60.0 ppm. Refer to Table 5.3 below for mortality patterns.

TABLE 5.3 Safety of Formalin in Striped Bass at 22°C

Formalin Concentration (ppm)	Cumulative Mortalities (%) at Different Times after Formalin Application			
	24 hr	48 hr	72 hr	96 hr
0	0	0	0	0
55.0	0	0	0	0
57.5.	5	40	40	40
60.0	20	45	55	55
62.5	15	35	55	60
65.0	5	70	90	90

3. Target Animal Safety Study #3

Bills, T.D., L.L. Marking, and G.E. Howe. 1993. Sensitivity of juvenile striped bass to chemicals used in aquaculture. United States Department of the Interior, Fish and Wildlife Service, *Resource Publication 192*.

These studies determined LC50's (concentrations producing 50% mortality in a population) of formalin in striped bass. Ten juvenile (1.0 g) striped bass were exposed to each test concentration of formalin in 15 L glass jars. Tests were conducted at a water temperature of 12°C and at varying levels of water hardness. Observations on mortality were made at 1, 3, and 6 hours during the first day of exposure, and then once daily for 4 days. Tests were duplicated in different year class fish in waters of different temperature (12, 17, and 22°C), hardness, and pH. Mean LC50's in soft water of pH 7.5 at 12°C were as shown in Table 5.4.

TABLE 5.4 Mean 50% Lethal Concentrations (LC50's) of Formalin to Striped Bass

Time (hours)	LC50 (ppm) Test 1	LC50 (ppm) Test 2
1	1230	>1000
3	1410	>1000
6	940	760
24	211	120
96	75	56

The Toxicity of formalin was not affected by water hardness or pH. However, the toxicity was greater in warm water than in cold water. Mean LC50's in soft water of pH 7.5 at three temperatures were as shown in Table 5.5.

TABLE 5.5 Mean 50% Lethal Concentrations (LC50's) of Formalin to Striped Bass

Time (hours)	LC50 (ppm) at 12°C	LC50 (ppm) at 17 °C	LC50 (ppm) at 22 °C
1	>1000	>1000	>1000
3	>1000	>1000	750
6	760	455	210
24	120	86	82
96	56	48	30

B. Finfish Eggs

FORMALIN-F™ is currently approved for the control of fungi of the family Saprolegniaceae on salmon, trout, and esocid eggs (see 21 CFR 529.1030). Additional safety studies for the control of fungi of the family Saprolegniaceae on other finfish eggs are provided in INAD file 8886. The sponsor, the Upper Midwest Environmental Sciences Center (formerly the U.S. National Biological

Service, Upper Mississippi Science Center), La Crosse, Wisconsin, has authorized the public disclosure of all information within their INAD file 8886.

The data in these studies show that use of the drug at the recommended concentration is safe on the eggs of a wide range of cold and warm water fish. Since, as discussed above, formalin safety has been demonstrated in finfish eggs from a wide variety of species, the safety of formalin would be the same for the eggs of all finfish species. Therefore, these studies are adequate to demonstrate that use of the drug at the recommended concentration is safe on the eggs of all finfish. The following summarizes the finfish egg safety study in INAD 8886.

1. Investigator: Jeffrey J. Rach, M.S.
   National Fisheries Research Center
   National Biological Service
   Department of the Interior
   La Crosse, Wisconsin 54609-0818

2. General Design of the Investigation:

   a. Purpose of the study: To determine if formalin is safe when administered to finfish eggs of representative finfish species.

   b. Test Animals: Green eggs of walleye *(Stizostedion vitreum)*, channel catfish *(Ictalurus punctatus)*, white sucker *(Catostomus commersoni)*, common carp *(Cyprinus carpio)*, and lake sturgeon *(Acipenser transmontanus)* were tested. The study was conducted at 12±2°C for walleye and white sucker, at 17±2°C for common carp and lake sturgeon and at 22±2°C for channel catfish.

   c. Dosage form: Formalin solution

   d. Route of Administration: In the environmental water

   e. Dosages Used: 1500, 4500, and 7500 ppm formalin

   f. Test Duration: 45 minute

   g. Parameters: percent hatch was calculated by the following formula:
   % hatch = (number of hatched fry ÷ initial number of eggs) x 100

3. Results:

   This study demonstrated that standard formalin treatment, at a concentration of 1000 to 2000 ppm, is safe for finfish eggs of the orders Cypriniformes (common carp and white sucker), Perciformes (walleye) and Siluriformes (channel catfish) for 15 minutes daily, if necessary. Formalin is also safe, at a concentration of 1500 ppm or less, for finfish eggs of the order Acipenseriformes (lake sturgeon) for up to 15 minutes daily. Because the species of finfish eggs treated in the study are representative of the variety of species of finfish eggs, it is determined that

formalin is safe for other finfish eggs. Due to the varying sensitivity of finfish eggs, however, the following statement is included in the labeling.

"A preliminary bioassay should be conducted on a small sub sample of finfish eggs to determine sensitivity before treating an entire group. This is necessary for all species because egg sensitivity can vary with species or strain and the unique conditions at each facility."

C. Penaeid Shrimp

Target animal safety data from the Freedom of Information (FOI) summary for PMF 3543, 56 FR 20618, May 6, 1991, demonstrated that an adequate margin of animal safety exists when formalin is used as directed by labeling in penaeid shrimp.

VI. HUMAN SAFETY

Human food safety data for the use of formalin in salmon, trout, catfish, largemouth bass, and shrimp are found in the FOI summary of PMF 3543. The results of four residue depletion studies of formalin in striped bass are summarized below (and found in PMF 5228). The use of formalin has not been shown by these studies to result in the accumulation of formaldehyde above naturally occurring levels in the edible tissue of any of these aquatic species. Because formalin treatment of this wide variety of aquatic species does not result in levels of formaldehyde in the edible tissue above the normal range of endogenous formaldehyde, formaldehyde is not expected to accumulate in additional finfish species, which have not been specifically tested.

Wilmer A. Rogers, Ph.D. at Auburn University, Auburn, Alabama conducted the studies summarized below (and found in detail in PMF 5228). Formalin was administered in the environmental water in all studies and the following method of tissue analysis was used in all studies. Formaldehyde was measured in the muscle of treated and control fish by the Nash test (described in Castell and Smith, *J. Fisheries Research Board of Canada* 30:91, 1973). The Nash test also was used in the residue studies to support the prior approvals for formalin in salmon, trout, catfish, largemouth bass, and shrimp. The recovery of formaldehyde in striped bass muscle samples fortified with 5, 20, and 40 mg/kg formalin was 106.9%, 78.0%, and 70.9%, respectively. The limit of quantitation was 5 mg/kg formalin (1.85 mg formaldehyde/kg fish).

The studies differed from each other as follows:

A. Juvenile/Indefinite Exposure Period Study - a two-part experiment in which striped bass in tanks were exposed to formalin for an indefinite period of time at two water temperatures.

   1. Test Animals: Striped bass; body weight was 23 grams for Part 1 and 39 grams for Part 2.

   2. Water Temperatures: 12 to 14°C for Part 1 and 21 to 22°C for Part 2

   3. Dose Levels and Treatment Duration: 0 (control) and 25 ppm formalin indefinitely

4. Results: as shown in Table 6.1.

TABLE 6.1 Mean Formaldehyde Residues (mg/kg) in Muscle of Juvenile Striped Bass

Hours of Exposure to 25 ppm Formalin	Part 1: 12-14 °C		Part 2: 21-22 °C	
	Treated Fish n=2	Control Fish n=2	Treated Fish n=5	Control Fish n=5
0	4.67	3.74	3.26	3.32
12	4.42	4.02	Not collected	not collected
24	4.40	3.85	6.63	5.52
48	4.22	1.67	6.64	3.39
72	5.12	3.84	7.60	5.34
96	4.12	3.63	5.61	4.41
120	2.36	2.71	4.02	4.03
144	1.76	1.76	4.63	4.58
168	3.60	3.74	4.04	3.86

B. Fingerling/Short Duration Bath Study - striped bass in tanks were exposed to formalin for one hour.

1. Test Animals: Striped bass; body weight was 26 grams
2. Water Temperature: 21°C
3. Dose Levels and Treatment Duration: 0 ppm (control) and 250 ppm formalin for 1 hour

4. Results: as shown in Table 6.2.

TABLE 6.2 Mean Formaldehyde Residues (mg/kg) in Muscle of Fingerling Striped Bass

Hours After Addition of 250 ppm Formalin	Treated Fish n = 4	Control Fish n = 4
0	2.86	3.57
12	3.67	3.17
24	3.73	3.61
48	2.65	2.97
72	3.37	3.38

C. Market Size/Indefinite Exposure Period Study - market size striped bass in tanks were exposed to formalin indefinitely.

1. Test Animals: Striped bass; body weight was 435 grams
2. Water Temperature: 24°C
3. Dose Levels and Treatment Duration: 0 ppm (control) and 25 ppm formalin indefinitely
4. Results: as shown in Table 6.3.

TABLE 6.3 Mean Formaldehyde Residues (mg/kg) in Muscle of Market-Size Striped Bass

Hours of Exposure to 25 ppm Formalin	Treated Fish n = 2	Control Fish n = 2
0	3.29	4.00
48	3.98	4.42
96	3.85	3.85

D. Juvenile/Indefinite Exposure Study - striped bass in ponds were exposed to formalin indefinitely.

1. Test Animals: Striped bass; body weight was 137 grams
2. Water Temperatures: 26 to 30°C
3. Dose Levels and Treatment Duration: 0 ppm (control) and 25 ppm formalin indefinitely

4. Results: as shown in Table 6.4.

TABLE 6.4 Mean Formaldehyde Residues (mg/kg) in Muscle of Juvenile Striped Bass

Hours of Exposure to 25 ppm Formalin	Treated Fish n = 8	Control Fish n = 8
24	3.60	3.78
48	3.50	3.43
72	3.53	3.50
96	3.43	3.37
120	3.63	3.53

Residue depletion data submitted under PMF 3543, 56 FR 20618, May 6, 1991, support a zero-hour pre-harvest withdrawal time for penaeid shrimp treated with the recommended dose of formalin.

E. Human Food Safety Conclusions: Formaldehyde residues in striped bass muscle did not differ between any of the test groups. Formaldehyde did not accumulate as a result of formalin treatment in juvenile or adult striped bass. Residue accumulation was not affected by dose or duration of exposure. Water temperatures between 12 and 30°C did not appear to affect accumulation of formaldehyde residues in striped bass muscle exposed to formalin.

By the studies in PMF 3543 and PMF 5528, the use of formalin at the recommended concentration has not been shown to result in the accumulation of formaldehyde above naturally occurring levels in the edible tissue of a wide range of cold and warm water fish, including striped bass, the most sensitive species or in shrimp. Therefore, these studies are considered adequate to demonstrate that use of the drug in all finfish, all finfish eggs, and on penaeid shrimp at the recommended concentrations will not result in the accumulation of formaldehyde above naturally occurring levels in their edible tissue.

VII. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that FORMALIN-F™, when used as recommended, is effective for the control of external parasites (*Chilodonella* spp., *Costia* spp., *Epistylis* spp., *Icthyophthirius* spp., *Scyphidia* spp., and *Trichodina* spp.) and monogenetic trematode parasites (*Cleidodiscus* spp., *Dactylogyrus* spp., and *Gyrodactylus* spp.) on all finfish, for the control of external protozoan parasites (Bodo spp., Epistylis spp., and Zoothamnium spp.) on penaeid shrimp, and for the control of fungi of the family Saprolegniaceae on the eggs of all finfish.

Fish are minor animal species as defined under 21 CFR 514.1(d). The data submitted (in PMF 5228 and INAD 8886) meet the requirements of that regulation and FDA's "Guidelines for the Preparation of Data to Satisfy the Requirements of Section 512 of the Act Regarding Minor use of Animal Drugs" (April 1986). FDA has considered these data, along with other required data, as support for this supplemental NADA (137-687) which was filed for the expansion of the use of formalin as a parasiticide in all finfish and penaeid shrimp, and as a fungicide on the eggs of all finfish.

Data found within PMF 5228 demonstrate that formaldehyde residues in the muscle of striped bass juveniles and adults did not differ between those treated with formalin and non-treated controls. By the studies in PMF 3543 and PMF 5528, the use of formalin at the recommended concentration has not been shown to result in the accumulation of formaldehyde in the muscle of striped bass, salmon, trout, catfish, largemouth bass, or shrimp. Therefore, additional residue depletion studies for other finfish species are not necessary, because these studies are considered adequate to demonstrate that use of the drug in all finfish at the recommended concentration will not result in the accumulation of formaldehyde.

According to the Center's supplemental approval policy, 21 CFR 514.106(b)(2)(vii), this is a Category II change that did not require a reevaluation of the safety and effectiveness data in the parent application.

This product remains an over-the-counter drug for use by a lay-person. Adequate instructions have been provided for its safe and effective use for the label indications.

The Agency has determined under 21CFR25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

VIII. APPROVED LABELING

A facsimile label to be used interchangeably with the 1 gallon, 5 gallon, and 55 gallon containers by stamping the appropriate Net Contents, Lot. No. and Expiration Date is attached along with the package insert.

NADA 140-831Approval Date: February 3, 1989

Freedom of Information Summary

NADA 140-831

I. GENERAL INFORMATION:

NADA140-831
Sponsor: Argent Chemical Laboratories, Inc.
8702 152nd Ave., N.E.
Redmond, WA 08052
Generic Name:formalin
Trade Name:Paracide-F
Marketing Status:

II. INDICATIONF FOR USE

a. Formalin is indicated for the control of external parasites on cultured sport and food fishes: salmon, trout, catfish, largemouth bass, and bluegill. Organisms controlled include the protozoa: Ichthyophthirius spp. ("Ich"), Chilodonella spp., Costia spp., Scyphidia spp., Epistylis spp., and Trichodina spp. and monogenetic trematodes: Cleidodiscus spp., Gyrodactylus spp., and Dactylogyrus spp.

b. For control of fungi of the family Saprolegniaceae on salmon, trout, and esocid eggs.

III. DOSAGE FORMS, ROUTE OF ADMINISTRATION, RECOMMENDED DOSAGE

As stated in the FOI Summary for Public Master File (PMF) 3543.

IV. ANIMAL EFFICACY

As discussed in the FOI Summary for PMF 3543.

V. ANIMAL SAFETY

As discussed in the FOI Summary for PMF 3543.

VI. HUMAN SAFETY

As discussed in the FOI Summary for PMF 3543.

VII. AGENCY CONCLUSIONS

The data submitted in support of this NADA comply with the requirements of 512 of the Act and demonstrate that formaldehyde when used under its proposed conditions of use is safe and effective for the control of external protozoa and monogenetic trematodes on trout, salmon, catfish, largemouth bass, and bluegil, and for control of fungi on salmon, trout, and esocid eggs. The proposed labeling is adequate to assure safe use of formalin by aquaculturists. Therefore, this product can be marketed over the counter (OTC).

Cargill Salt

Material Safety Data Sheet

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Chemical Product Name	Sodium Chloride (Salt)
Chemical Family	Alkali Metal/Halide
Chemical Name	Sodium Chloride
INCI Name	SODIUM CHLORIDE
INN Name	sodium chloride
Formula	NaCl
Molecular Weight	58.44
Commercial Name	Diamond Crystal® Solar Salt - Extra Coarse, Diamond Crystal® Solar Salt - Coarse

Manufacturer
Cargill Salt
P.O. Box 5621
Minneapolis, MN 55440

Emergency Telephone Numbers
CHEMTREC (800) 424-9300

2. COMPOSITION/INFORMATION ON INGREDIENTS

Description
White crystalline solid

Ingredient Name / **CAS Number**	**Exposure Limits**	**Concentration (%)**
Sodium Chloride 7647-14-5		100

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

None – GRAS Substance (Generally Recognized As Safe)

Potential Health Effects

Route(s) Of Entry: Ingestion, skin/eye contact, inhalation.

Human Effects and Symptoms of Overexposure:

Acute Inhalation: Irritation of the respiratory tract.

Chronic Inhalation: No applicable information found for chronic system effects.

Acute Skin Contact: Large amounts can cause irritation, and, if applied to damaged skin, absorption can occur with effects similar to those via ingestion.

Chronic Skin Contact: No applicable information found for chronic system effects.

Acute Eye Contact: Irritation with burning and tearing (salt concentrations greater than the normal saline present).

Chronic Eye Contact: No applicable information found for chronic systemic effects.

Acute Ingestion: Intake of large amounts has generally occurred for deliberate reasons: suicide, absorption, and to induce vomiting. The following effects were observed; nausea and vomiting, diarrhea, cramps, restlessness, irritability, dehydration, water retention, nose bleed, gastrointestinal tract damage, fever, sweating, sunken eyes, high blood pressure, muscle weakness, dry mouth and nose, shock, cerebral edema (fluid on brain), pulmonary edema (fluid in lungs), blood cell shrinkage, and brain damage (due to dehydration of brain cells). Death is generally due to cardiovascular collapse or CNS damage. Less than a few grams would not be harmful. For larger quantities, drink large amounts of water or milk.

Chronic Ingestion: No applicable information found for chronic systemic effects.

Carcinogenicity

NTP: Not listed as carcinogen or mutagen.
IARC: Not listed as carcinogen or mutagen.
OSHA: Not listed as carcinogen or mutagen.

Medical Conditions Aggravated by Exposure: In some cases of confirmed hypertension, ingestion may result in elevated blood pressure.

4. FIRST AID MEASURES

First Aid for Eyes: For eye contact, flush with water immediately, lifting eyelids occasionally.

First Aid for Skin: Remove clothing from affected area. Wash skin thoroughly. Rinse carefully.

First Aid for Inhalation: If person breathes large quantities, remove to fresh air at once. If breathing stops, apply artificial respiration immediately.

First Aid for Ingestion: Less than a few grams would not be harmful. For larger quantities, drink large amounts of water or milk.

5. FIRE AND MEASURES

Flash Point: N/A

Extinguishing Media: N/A. This product is nonflammable.

Special Fire Fighting Procedures: N/A

6. ACCIDENTAL RELEASE MEASURES

Spill or Leak Procedures: Contain spills to prevent contamination of water supply or sanitary sewer system. Vacuum or sweep into containers for proper disposal.

7. HANDLING AND STORAGE

Storage Temperature (min./max.): Avoid humid or wet conditions as product will cake and become hard.

Special Sensitivity: Avoid contact with strong acids.

Handling and Storage Precautions: Becomes hygroscopic at 75% relative humidity.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Eye Protection Requirements: Eyeglasses or goggles should be worn in dusty areas.

Skin Protection Requirements: Protective clothing may be worn in dusty areas, but is generally not required.

Respiratory/Ventilation Requirements: NIOSH/MSHA approved respirator for particulates.

Exposure Limits: Not listed.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Form: White crystalline solid with slight halogen odor.

Color: White to opaque.

Odor: Halogen odor when heated.

Boiling Point (760mm Hg)(°C): 1465

Melting Point/Freezing Point (°C): 801

pH: 6.7 – 10.0

Solubility in Water (g/cc)(%): 26.4

Specific Gravity (H_2O = 1): 2.16

Bulk Density (lbs./ft^3): 35-83

% Volatile by Weight: N/A

Vapor Pressure (mm Hg/747°C): 2.4

Vapor Density (Air=1): N/A

10. REACTIVITY

Stability: Stable

Incompatibilities: Avoid contact with strong acids. Becomes corrosive to metals when wet.

Decomposition Products: May evolve chlorine gas when in contact with strong acids.

11. TOXICOLOGICAL INFORMATION

Description: Not listed.

12. ECOLOGICAL INFORMATION

Ecotoxicity: Not listed.

Environmental Degradation: Not listed.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method: Follow applicable Federal, state, and local regulations.

14. TRANSPORTATION INFORMATION

D.O.T. Shipping Name: Not listed.

Technical Shipping Name: Not listed.

D.O.T. Hazard Class: Not listed.

U.N./N.A. Number: Not listed.

Product Rq (lbs.): N/A

D.O.T. Label: Not listed.

D.O.T. Placard: N/A

Freight Class Bulk: N/A

Freight Class Package: N/A

Product Label: N/A

15. REGULATORY INFORMATION

OSHA Status: Not listed.

TSCA Status: Listed as non-hazardous.

CERCLA Reportable Quantity SARA Title III
Section 302 Extremely Hazardous Substances: Not listed.

Section 311/312 Hazard Categories: Not listed.

Section 313 Toxic Chemicals: Not listed.

RCRA Status: Not listed.

EINECS Number: 231-598-3

ENCS Number: 1-236

ECL Serial Number: KE-31387

SWISS Number: G-2580

HMIS Rating: 1 0 0 A

State Regulatory Information

Company Name/Cas Number	Concentration	State Code
N/A		

16. OTHER INFORMATION

Reason for Issue: Regulatory compliance.
Prepared By: Steve Karl
Approved By: Dave Merriweather
Title: Technical Director
Approval Date: February 2005
Supersedes Date: September 2002
MSDS Number: ND7

Disclaimer: All statements, technical information and recommendations contained herein are, to the best of our knowledge, reliable and accurate; however, no warranty, either expressed or implied is made with respect thereto, nor will any liability be assumed for damages resultant from the use of the material described.

It is the responsibility of the user to comply with all applicable Federal, state and local laws and regulations. It is also the responsibility of the user to maintain a safe workplace. The user should consider the health hazards and safety information provided herein as a guide and should take the necessary steps to instruct employees, and to develop work practice procedures to ensure a safe work environment.

This information is not intended as a license to operate under, or a recommendation to practice or infringe upon any patent of this Company or others covering any process, composition of matter or use.

Section 1 Chemical Product and Company Identification

PRODUCT NAME: CAIROX® potassium permanganate, $KMnO_4$
SYNONYMS: Permanganic acid potassium salt
Chameleon mineral
Condy's crystals
Permanganate of potash

MANUFACTURER'S NAME: CARUS CHEMICAL COMPANY

MANUFACTURER'S ADDRESS:
Carus Chemical Company
1500 Eighth Street
P. O. Box 1500
LaSalle, IL 61301

TRADE NAME: CAIROX® potassium permanganate

TELEPHONE NUMBER FOR INFORMATION: 815/223-1500

EMERGENCY TELEPHONE NO: 800/435-6856

AFTER HOURS NO. 815/223-1565
5:00 PM-8:00 AM Central Standard Time
Monday-Friday, Weekends and Holidays

CHEMTREC TELEPHONE NO.: 800/424-9300

Section 2 Composition/Information on Ingredients

Material or component	CAS No.	%	Hazard Data	
Potassium permanganate	7722-64-7	97% min. $KMnO_4$	PEL-C	5 mg Mn per cubic meter of air
			TLV-TWA	0.2 mg Mn per cubic meter of air

Section 3 Hazards Identification

1. Eye Contact
   Potassium permanganate is damaging to eye tissue on contact. It may cause severe burns that result in damage to the eye.
2. Skin Contact
   Contact of solutions at room temperature may be irritating to the skin, leaving brown stains. Concentrated solutions at elevated temperature and crystals are damaging to the skin.
3. Inhalation
   Acute inhalation toxicity data are not available. However, airborne concentrations of potassium permanganate in the form of dust or mist may cause damage to the respiratory tract.
4. Ingestion
   Potassium permanganate, if swallowed, may cause severe burns to mucous membranes of the mouth, throat, esophagus, and stomach.

Section 4 First Aid Measures

1. Eyes
   Immediately flush eyes with large amounts of water for at least 15 minutes holding lids apart to ensure flushing of the entire surface. Do not attempt to neutralize chemically. Seek medical attention immediately. Note to physician: Soluble decomposition products are alkaline. Insoluble decomposition product is brown manganese dioxide.

2. Skin
   Immediately wash contaminated areas with large amounts of water. Remove contaminated clothing and footwear. Wash clothing and decontaminate footwear before reuse. Seek medical attention immediately if irritation is severe or persistent.

3. Inhalation
   Remove person from contaminated area to fresh air. If breathing has stopped, resuscitate and administer oxygen if readily available. Seek medical attention immediately.

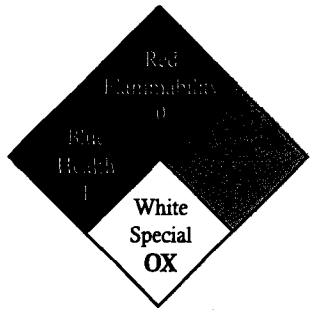
4. Ingestion
   Never give anything by mouth to an unconscious or convulsing person. If person is conscious, give large quantities of water. Seek medical attention immediately.

Section 5 Fire Fighting Measures

NFPA* HAZARD SIGNAL

Health Hazard (less than 1 hour exposure)	1	=	Materials which under fire conditions would give off irritating combustion products. Materials which on the skin could cause irritation.
Flammability Hazard	0	=	Materials that will not burn.
Reactivity Hazard	0	=	Materials which in themselves are normally stable, even under fire exposure conditions, and which are not reactive with water.
Special Hazard	OX	=	Oxidizer

***National Fire Protection Association 704**



FIRST RESPONDERS:

Wear protective gloves, boots, goggles, and respirator. In case of fire, wear positive pressure breathing apparatus. Approach site of incident with caution. Use Emergency Response Guide NAERG 96 (RSPA P5800.7), Guide No. 140.

FLASHPOINT None

FLAMMABLE OR EXPLOSIVE LIMITS Lower: Nonflammable Upper: Nonflammable

EXTINGUISHING MEDIA Use large quantities of water. Water will turn pink to purple if in contact with potassium permanganate. Dike to contain. Do not use dry chemicals, CO_2, Halon® or foams.

SPECIAL FIREFIGHTING PROCEDURES If material is involved in fire, flood with water. Cool all affected containers with large quantities of water. Apply water from as far a distance as possible. Wear self-contained breathing apparatus and full protective clothing.

Section 6 Accidental Release Measures

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED
Clean up spills immediately by sweeping or shoveling up the material. Do not return spilled material to the original container. Transfer to a clean metal drum. EPA banned the land disposal of D001 ignitable waste oxidizers. These wastes must be deactivated by reduction. To clean floors, flush with abundant quantities of water into sewer, if permitted by Federal, State, and Local regulations. If not permitted, collect water and treat chemically (Section 13).

PERSONAL PRECAUTIONS
Personnel should wear protective clothing suitable for the task. Remove all ignition sources and incompatible materials before attempting clean-up.

Section 7 Handling and Storage

WORK/HYGENIC PRACTICES
Wash hands thoroughly with soap and water after handling potassium permanganate, and before eating or smoking. Wear proper protective equipment. Remove contaminated clothing.

VENTILATION REQUIREMENTS
Provide sufficient area or local exhaust to maintain exposure below the TLV-TWA.

CONDITIONS FOR SAFE STORAGE
Store in accordance with NFPA 430 requirements for Class II oxidizers. Protect containers from physical damage. Store in a cool, dry area in closed containers. Segregate from acids, peroxides, formaldehyde, and all combustible, organic or easily oxidizable materials including anti-freeze and hydraulic fluid.

Section 8 Exposure Controls/Personal Protection

RESPIRATORY PROTECTION
In the case where overexposure may exist, the use of an approved NIOSH-MSHA dust respirator or an air supplied respirator is advised. Engineering or administrative controls should be implemented to control dust.

EYE
Faceshield, goggles, or safety glasses with side shields should be worn. Provide eye wash in working area.

GLOVES
Rubber or plastic gloves should be worn.

OTHER PROTECTIVE EQUIPMENT
Normal work clothing covering arms and legs, and rubber or plastic apron should be worn.

Section 9 Physical and Chemical Properties

APPEARANCE AND ODOR	Dark purple solid with a metallic luster, odorless
BOILING POINT, 760 mm Hg	Not applicable
VAPOR PRESSURE (mm Hg)	Not applicable
SOLUBILITY IN WATER % BY SOLUTION	6% at 20°C (68°F), and 20% at 65°C (149°F)
PERCENT VOLATILE BY VOLUME	Not volatile
EVAPORATION RATE (BUTYL ACETATE=1)	Not applicable
MELTING POINT	Starts to decompose with evolution of oxygen (O_2) at temperatures above 150°C (302°F). Once initiated, the decomposition is exothermic and self-sustaining.
OXIDIZING PROPERTIES	Strong oxidizer
SPECIFIC GRAVITY	2.7 @ 20°C (68°F)
VAPOR DENSITY (AIR=1)	Not applicable

Section 10 Stability and Reactivity

STABILITY Under normal conditions, the material is stable.

CONDITIONS TO AVOID Contact with incompatible materials or heat (>150°C/302°F).

INCOMPATIBLE MATERIALS Acids, peroxides, formaldehyde, anti-freeze, hydraulic fluids, and all combustible organic or readily oxidizable inorganic materials including metal powders. With hydrochloric acid, toxic chlorine gas is liberated.

HAZARDOUS DECOMPOSITION PRODUCTS When involved in a fire, potassium permanganate may liberate corrosive fumes.

CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION Material is not known to polymerize.

Section 11 Toxicological Information

Potassium permanganate: Acute oral LD_{50}(rat) = 780 mg/kg Male (14 days); 525 mg/kg Female (14 days)
The fatal adult human dose by ingestion is estimated to be 10 grams. (Ref. Handbook of Poisoning: Prevention, Diagnosis & Treatment, Twelfth Edition)

EFFECTS OF OVEREXPOSURE

1. Acute Overexposure
   Irritating to body tissue with which it comes into contact.

2. Chronic Overexposure
   No known cases of chronic poisoning due to potassium permanganate have been reported. Prolonged exposure, usually over many years, to heavy concentrations of manganese oxides in the form of dust and fumes, may lead to chronic manganese poisoning, chiefly involving the central nervous system.

3. Carcinogenicity
   Potassium permanganate has not been classified as a carcinogen by OSHA, NTP, IARC.

4. Medical Conditions Generally Aggravated by Exposure
   Potassium permanganate will cause further irritation of tissue, open wounds, burns or mucous membranes.

Registry of Toxic Effects of Chemical Substances
RTECS #SD6476000

Section 12 Ecological Information

Entry to the Environment

Potassium Permanganate has a low estimated lifetime in the environment, being readily converted by oxidizable materials to insoluble manganese dioxide (MnO_2).

Bioconcentration Potential

In non-reducing and non-acidic environments manganese dioxide (MnO_2) is insoluble and has a very low bioaccumulative potential.

Aquatic Toxicity

Rainbow trout, 96 hour LC_{50}: 1.8 mg/L
Bluegill sunfish, 96 hour LC_{50}: 2.3 mg/L

Section 13 Disposal Consideration

DEACTIVATION OF D001 IGNITABLE WASTE OXIDIZERS BY CHEMICAL REDUCTION

Reduce potassium permanganate in aqueous solutions with sodium thiosulfate (Hypo), or sodium bisulfite or ferrous salt solution. The thiosulfite or ferrous salt may require some dilute sulfuric acid to promote rapid reduction. If acid was used, neutralize with sodium bicarbonate to neutral pH. Decant or filter, and mix the sludge with sodium carbonate and deposit in an approved landfill. Where permitted, the sludge can be drained into sewer with large quantities of water. Use caution when reacting chemicals. Contact Carus Chemical Company for additional recommendations.

Section 14 Transport Information

U. S. DEPARTMENT OF TRANSPORTATION INFORMATION:

Proper Shipping Name:	49 CFR 172.101	Potassium Permanganate
ID Number:	49 CFR 172.101	UN 1490
Hazard Class:	49 CFR 172.101	Oxidizer
Division:	49 CFR 172.101	5.1
Packing Group:	49 CFR 172.101	II

Section 15 Regulatory Information

TSCA Listed in the TSCA Chemical Substance Inventory

CERCLA Hazardous Substance

Reportable Quantity "RQ" 100 lb. 40 CFR 116.4, 40 CFR 302.4

RCRA Oxidizers such as potassium permanganate meet the criteria of ignitable waste. 40 CFR 261.21

SARA TITLE III Information

Section 302: Extremely hazardous substance: Not listed
Section 311/312: Hazard categories: Fire, acute and chronic toxicity
Section 313: CAIROX® potassium permanganate contains 97% Manganese Compound as part of the chemical structure (manganese compounds CAS Reg. No. N/A) and is subject to the reporting requirements of Section 313 of Title III, Superfund Amendments and Reauthorization Act of 1986 and 40 CFR 372.

Responsible Care®
A Public Commitment

Section 15 Regulatory Information (cont.)

STATE LISTS	Michigan Critical Materials Register:	Not listed
	California Proposition 65:	Not listed
	Massachusetts Substance List:	5 F8
	Pennsylvania Hazard Substance List:	E
FOREIGN LISTS	Canadian Domestic Substances List (DSL)	Listed
	Canadian Ingredient Disclosure List	Listed
	European Inventory of Existing Chemical Substances (EINECS)	2317603

Section 16 Other Information

NIOSH	National Institute for Occupational Safety and Health
MSHA	Mine Safety and Health Administration
OSHA	Occupational Safety and Health Administration
NTP	National Toxicology Program
IARC	International Agency for Research on Cancer
TSCA	Toxic Substances Control Act
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act of 1980
RCRA	Resource Conservation and Recovery Act
SARA	Superfund Amendments and Reauthorization Act of 1986
PEL-C	OSHA Permissible Exposure Limit-OSHA Ceiling Exposure Limit
TLV-TWA	Threshold Limit Value - Time Weighted Average (American Conference of Governmental Industrial Hygienists)

Kenneth Krogulski
May 2000

CARUS

Responsible Care®
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Material Safety Data Sheet

IODINE TINCTURE 7% Page 1 of 2

MATERIAL SAFETY DATA SHEET

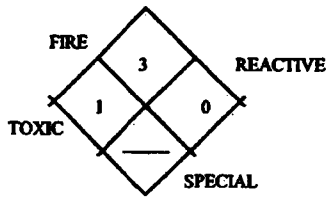
11/01

Tetradyne

P.O. BOX 3135-TURLOCK,CA 95381
1-209-667-4325

HAZARD RATING

4-EXTREME
3-HIGH
2-MODERATE
1-SLIGHT
0-INSIGNIFICANT



24 HOUR EMERGENCY: 1-800-255-3924

MAY BE USED TO COMPLY WITH OSHA'S HAZARD COMMUNICATION STANDARD, 29 CFR 1910.1200

PRODUCT NAME

TETRADYNE IODINE TINCTURE 7%

CHEMICAL FAMILY	FORMULA
IODINE	MIXTURE

Hazardous Components (Specific Chemical Identity: Common Name(s))	OSHA PEL	ACGIH TLV	Other limits Recommended	%
ISOPROPANOL ALCOHOL				85.0
CAS # 67-63-0				
IODINE				7.0
CAS # 7553-56-2				

BOILING POINT(°F)	177 - 212	SPECIFIC GRAVITY (H2O = 1)	.895
VAPOR PRESSURE(mm Hg)	NA	PERCENT, VOLATILE BY VOLUME (%)	85%
VAPOR DENSITY (AIR = 1)	NA	EVAPORATION RATE (WATER = 1)	1.7
SOLUBILITY IN WATER	COMPLETE	MELTING POINT	NA
APPEARANCE	DARK BROWN LIQUID	ODOR IODINE	INTENSITY MILD

FLASH POINT (Method Used)	FLAMMABLE LIMITS	Lel	Uel
61deg F	2.1	—	—

EXTINGUISHING MEDIA

CARBON DIOXIDE, DRY CHEMICAL, ALCOHOL FOAM

SPECIAL FIRE FIGHTING PROCEDURES

WATER MAY BE INEFFECTIVE, BUT MAY BE USED TO COOL CONTAINERS.

UNUSUAL FIRE AND EXPLOSION HAZARDS

KEEP AWAY FROM HEAT, SPARKS, AND OPEN FLAME. EMITS TOXIC FUMES.

EFFECTS OF OVEREXPOSURE
SKIN AND EYE IRRITATION. BREATHING OF VAPORS CAN BE IRRITATING TO NOSE AND THROAT. IN HIGH CONCENTRATION MAY CAUSE NAUSEA, DIZZINESS, HEADACHES, STUPOR. INGESTION IS HARMFUL AND MAY CAUSE SIMILAR EFFECTS.
EMERGENCY AND FIRST AID PROCEDURES
EYES: IMMEDIATELY FLUSH WITH PLENTY OF WATER FOR AT LEAST 15 MINUTES. GET MEDICAL ATTENTION IMMEDIATELY.
SKIN: WASH CONTAMINATED AREA WITH PLENTY OF WATER AND REMOVE CONTAMINATED CLOTHING.
INGESTION: THIN STARCH OR FLOUR PASTE-INDUCED VOMITING. CALL A PHYSICIAN IMMEDIATELY.

	UNSTABLE:		CONDITIONS TO AVOID
STABILITY:			
	STABLE:	X	HEAT, SPARKS, OPEN FLAME
INCOMPATIBILITY(Materials to avoid)			SRTONG OXIDIZERS, ACETALDEHYDE, ALUMINUM, AMMONIA
HAZARDOUS DECOMPOSITION PRODUCTS			
			TOXIC FUMES
	MAY OCCUR		**CONDITIONS TO AVOID**
HAZARDOUS			
POLYMERIZATION	**WILL NOT OCCUR**	X	—

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED
ELIMINATE ALL SOURCES OF IGNITION, AVOID BREATHING VAPORS. VENTILATE AREA. REMOVE WITH INERT ABSORBENT AND NON-SPARKING TOOLS.
WASTE DISPOSAL METHOD
PACKAGE, STORE, TRANSPORT AND DISPOSE OF ALL CLEAN-UP MATERIAL/WASTE IN ACCORDANCE WITH APPLICABLE FEDERAL AND LOCAL REGULATIONS.

RESPIRATORY PROTECTION(*Specify type*)				
FOR EMERGENCY, ORGANIC CANISTER OR SELF CONTAINDED AIR-PACK.				
VENTILATION	**LOCAL EXHAUST**	NONE	**SPECIAL**	NONE
	MECHANICAL(General)	NONE	**OTHER**	NONE
PROTECTIVE GLOVES			**EYE PROTECTION**	
RUBBER GLOVES - SOLVENT RESISTENT			SAFETY GOGGLES.	
OTHER PROTECTIVE EQUIPMENT				
NONE.				

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING
FLAMMABLE. DO NOT EXPOSE TO HEAT OR STORE AT A TEMPERATURE ABOVE 120 deg F. DO NOT USE NEAR AN OPEN FLAME. POISON
OTHER PRECAUTIONS
DO NOT STORE IN MISLABELED CONTAINER AND/OR CONTAINERS WITH NO LABELS.
KEEP AWAY FROM CHILDREN.
CARCINOGENICITY/MUTAGENICITY
NONE KNOWN

Material Safety Data Sheet

Product Name: ADMIRAL LIQUID
Product Code: BUI/ADMIRAL

HMIS Codes: H F R P
1 1 0 X

Section I – Manufacturer Identification

Manufacturer's Name: Becker Underwood, Inc.
Address: P.O. Box 667, 801 Dayton Ave., Ames, IA 50010
Emergency Phone: Chemtrec (800) 424-9300
Information Phone: (515) 232-5907
Prepared By: MSDS Coordinator
Date Revised: May 13, 2002

Section II – Hazardous Ingredients/SARA III Information

Hazardous Components **Occupational Exposure Limits**

Component	CAS Number	OSHA PEL	ACGIH TLV	Weight Percent

No reportable quantities of hazardous ingredients are present
No reportable quantities of toxic chemical(s) subject to the reporting requirements of Section 313 of SARA Title III and of 40 CFR 372 are present

Section III - Physical/Chemical Characteristics

Boiling Point: > 200° F
Specific Gravity: (H_20 = 1): ~ 1.1
Vapor Density: Heavier than air
Evaporation Rate: Slower than ether
Solubility In Water: Soluble
Appearance and Odor: Dark blue liquid, mild odor

Section IV - Fire and Explosion Hazard Data:

Flash Point: > 200° F
Method Used: NA
Flammable Limits in Air by Volume: NA
Lower: NA **Upper:** NA
Extinguishing Media: Foam, alcohol foam, CO2, dry chemical, water fog
Fire Fighting Precautions & Hazards: Fire fighters should wear butyl rubber boots, gloves, and body suit and a NIOSH/MSHA self-contained breathing apparatus.
Unusual Fire and Explosion Hazards: Not a fire or explosion hazard when stored under normal conditions.

Section V – Reactivity Data

Stability: Stable
Conditions to Avoid: Extremes in temperature. High humidity.
Incompatibility (Materials to Avoid): Long term storage in direct contact with reactive metals such as aluminum, zinc, copper, nickel, magnesium, etc. Other materials to avoid include strong oxidizing agents.
Hazardous Decomposition Products: When involved in a fire, burning may evolve noxious fumes which may include carbon monoxide, carbon dioxide, nitrous oxides, acetic acid, or other toxic compounds depending on the chemical composition and combustion conditions. However, all of the water must be driven off first for this to occur.
Hazardous Polymerization: Will not occur.

Section VI - Health Hazard Data

Inhalation Health Risks and Symptoms of Exposure: Prolonged inhalation may lead to respiratory tract irritation.
Skin and Eye Contact Health Risks and Symptoms of Exposure: Prolonged or repeated contact may result in irritation.
Skin Absorption Health risks and Symptoms of Exposure: None expected.
Ingestion Health Risks and Symptoms of Exposure: Ingestion of large quantities may be harmful.
Health Hazards (acute and chronic): None known.
Carcinogenicity NTP? No **IARC Monographs?** No
Existing Medical Conditions Generally Aggravated By Exposure: May provoke asthmatic response in persons with asthma who are sensitive to airway irritants.

Section VI - Health Hazard Data (Continued)

Emergency and First Aid Procedures:

Eyes: Flush with flowing water for at least 15 minutes. Call a physician.

Skin: Wash affected area with soap and water. If irritation develops consult a physician. Remove and launder contaminated clothing before reuse.

Inhalation: If difficulty in breathing occurs, move to fresh air. Get immediate medical attention.

Ingestion: Get immediate medical attention. Unless advised otherwise, dilute with water or milk.

Section VII – Precautions for Safe Handling and Use

Steps to be Taken in Case Material is Released or Spilled: Contain the spill to prevent a large discharge to surface streams or storm sewers. Since landfill operations will not accept liquid waste, allow to dry if possible before collecting for disposal. An absorbent material would aid in cleaning up a liquid spill. If liquid cleanup is necessary, collect in drums, buckets, or other containers.

Waste Disposal Method: The environmental concern is discoloration of land or water. If possible, the product should be dried before disposal. Disposal must be made in accordance with federal, state, and local regulation.

Precautions to be Taken in Handling and Storing: Local exhaust. Do not freeze. Avoid unnecessary skin contact. Do not breathe fumes.

Other Precautions: Eye wash fountains should be easily accessible. As with all chemicals, keep out of the reach of children.

Section VIII - Control Measures

Respiratory: If excessive vapors or mists are generated, wear NIOSH/MSHA approved organic vapor/mist respirator.

Ventilation: Use local exhaust to control excessive vapors/mists. If applicable, proper personal protection is a NIOSH/MSHA approved respirator.

Clothing: Gloves, coveralls, apron, boots as necessary to prevent skin contact as needed.

Eye: Chemical goggles; wear face shield if splashing hazard exists.

Other: Open wounds or skin surface disruptions should be covered with a chemical resistant patch to minimize absorption risks. Clean clothing should be worn daily to avoid possible long-term build up of the product leading to chronic overexposure. . Safety shower, eye wash fountain, and washing facilities should be readily available.

Section IX - Shipping and Labeling Information

D.O.T. Shipping Data: Not regulated.

D.O.T. Hazard Classification NA

D.O.T. Labels Required: NA

D.O.T. Identification NA

Section X - Disclaimer

The opinions expressed herein are those of qualified persons with Becker Underwood, Inc. We believe the information contained here is current as of the date of this Material Safety Data Sheet. Since the use of this product is not within the control of Becker Underwood, Inc., it is the user's obligation to determine a safe end use of this product.

Section 4 – First Aid Measures

ORAL EXPOSURE

If swallowed, wash mouth out with water provided the person is conscious. Follow with with plenty of water. Do not induce vomiting. NEVER GIVE LIQUIDS TO AN UNCONCIOUS PERSON. Call a physician.

INHALATION EXPOSURE

If inhaled, remove to fresh air. If breathing becomes difficult call a physician.

DERMAL EXPOSURE

In case of contact, immediately wash skin with soap and copious amounts of water.

EYE EXPOSURE

In case of contact with eyes, flush with copious amounts of water for at least 15 minutes. Assure adequate flushing by separating the eyelids with fingers. Call a physician.

Section 5 – Firefighting Measures

FLASH POINT

Not / Applicable (N/A)

AUTO-IGNITION

N/A

FLAMMABILITY

N/A

EXTINGUISHING MEDIA

Water Spray, carbon dioxide, dry chemical powder, or appropriate foam.

FIREFIGHTING

Wear self contained breathing apparatus and protective clothing to prevent contact with skin and eyes. Emits toxic fumes under fire conditions.

Section 6 – Accidental Release Measures

PERSONAL PRECAUTION(S)

Exercise appropriate precautions to minimize direct contact with skin or eyes and prevent inhalation of aerosol.

METHODS FOR CLEANING UP

Soak up with appropriate absorbent material, place in a bag, and hold for disposal. Ventilate area and wash spill site after picking up material.

Section 7 – Handling and Storage.

HANDLING

Avoid inhalation, contact with eyes, skin, and clothing. Avoid repeated or prolonged exposure.

STORAGE

Keep container tightly closed.

Section 8 – Exposure Controls/PPE

ENGINEERING CONTROLS

Safety shower and eye bath. Mechanical exhaust required.

PERSONAL PROTECTIVE EQUIPMENT

Where protection from nuisance levels of aerosol is present, use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Respiratory protection is not required. . Use protective gloves, chemical safety goggles, boots, and apron or lab coat.

Section 9 – Physical/Chemical properties

APPEARANCE

Color	Brown.
Physical Form	Liquid
Molecular weight	Not / Applicable
pH	6.0 to 7.0
Odor	faint odor, characteristic
BP/BP Range	130°C
Freezing Point	N/A
Vapor Pressure	N/A
Vapor Density	N/A
Saturated Vapor Density	N/A
SG/Density	approx. 1.03
Bulk Density	N/A
Odor threshold	N/A
Water content	≤ 88%
Solvent content	N/A
Evaporation rate	N/A
Viscosity	N/A
Partition Coefficient	N/A
Decomposition Temperature	N/A
Solubility	N/A

N/A = Not Available

Section 10 – Stability and Reactivity

Stability
Stable.

Materials to Avoid
Strong Oxidizing agents.

Hazardous Polymerization
Will not occur.

Section 11 – Toxicological Information

Skin Irritation:
Rabbit slightly irritating (BASF test)

Eye irritation:
Rabbit severely irritating (OECD Guideline 405)

Section 12 – Ecological Information

Environmental Toxicity.

Section 13 – Disposal Considerations

Appropriate Method of disposal of Substance or Preparation Contain the spill. Do not allow it to flow into water supplies. Absorb any leaked or spilled material. Observe all federal, state, and local regulations when disposing..

Section 14 – Transport Information

DOT
Considered non-hazardous for transport.

IATA
Considered non-hazardous for air transport.

Section 15 – Regulatory Information

US regulatory information
SARA Listed: No

Section 16 – Other Information

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. The burden of safe use of our materials must rest with the user. We cannot assume responsibility for the completeness or accuracy of any information supplied by us concerning the hazards and recommended use of this product.

QUIP LABORATORIES INCORPORATED

QUIP SERVICE SELLS QUIP

MATERIAL SAFETY DATA SHEET

SECTION 1: CHEMICAL PRODUCT AND COMPANY IDENTIFICATION:

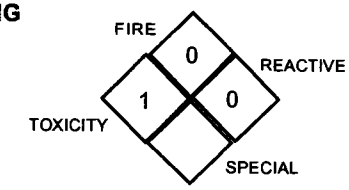
Manufactured by:
Quip Laboratories, Inc.
1500 Eastlawn Avenue
Wilmington, DE 19802
Non-Emergency: (302) 761-2600

CHEMICAL EMERGENCY NUMBER
CHEMTREC
1-800-424-9300

Product Name:	**Iodex AR/18**
Common Name:	Iodine Disinfectant
Chemical Name:	Iodine Solution
Formula:	Iodine/Phosphoric acid Mixture
Product Use:	Cleaner/Disinfectant/Sanitizer

HAZARD RATING

4-EXTREME
3-HIGH
2-MODERATE
1-SLIGHT
0-INSIGNIFICANT



SECTION 2: COMPOSITION / INFORMATION ON INGREDIENTS:

INGREDIENTS:		% / Wt.	TLV/ACGIH
Phosphoric Acid	(C.A.S. # 7664-38-2)	16.00%	1 Mg/M^3
Iodine	(C.A.S. # 7553-56-2)	1.75%	0.1 ppm
Water	(C.A.S. # 7732-18-5)	To qs.	None Established

SECTION 3: PHYSICAL DATA:

APPEARANCE: Dark brown liquid.
SPECIFIC GRAVITY: 1.135
SOLUBILITY IN WATER: Complete
VOLATILE BY VOLUME: N/A
VAPOR DENSITY: N/A
ODOR: Mild iodine odor
pH: 1.5 - 2.0
EVAPORATION RATE: 1 (water=1)
BOILING POINT: N/A
VAPOR PRESSURE: N/A

SECTION 4: FIRE & EXPLOSION DATA:

FLASH POINT: Non-flammable **ESTIMATED EXPLOSIVE LIMIT RANGE: LEL:** 0.00% **UEL:** 0.00%
FLASH POINT METHOD USED: N/A
EXTINGUISHING MEDIA: Water spray, carbon dioxide.
SPECIAL FIRE-FIGHTING PROCEDURES: Use self-contained breathing apparatus.
UNUSUAL FIRE AND EXPLOSION HAZARDS: May emit toxic fumes of iodine and phosphorous oxide with high heat.

SECTION 5: HEALTH HAZARD DATA:

ROUTES OF ENTRY/SIGNS AND SYMPTOMS OF EXPOSURE:
EYES CONTACT: Corrosive to the eyes, may cause severe damage.
SKIN CONTACT: Substance is corrosive. May cause severe skin burns.
INHALATION: Irritating to the nose, throat, and respiratory tract.
INGESTION: Harmful if swallowed. Swallowing product can cause severe burns to the lining of the mouth, throat, and digestive tract.
Signs and Symptoms of Overexposure: Irritation to eye and skin tissue.
Aggravated Medical Conditions: N/A
Supplemental Health Information: Probable mucosal damage may contraindicate the use of gastric lavage. Measures against circulatory shock, respiratory depression, and convulsions may be needed.

SECTION 6: EMERGENCY & FIRST AID PROCEDURES:

EYE CONTACT: Flush immediately with plenty of water for at least 15 minutes. Remove contacts, if worn, after the first 5 minutes, then continue rinsing. Get immediate medical attention.

SKIN CONTACT: Immediately flush with plenty of water for 15 minutes, while removing contaminated clothing and shoes. Get immediate medical attention. Wash contaminated clothing before reuse.

INHALATION: Remove to fresh air. If not breathing, call 911 or an ambulance, then give artificial respiration. If breathing is difficult, give oxygen. Get immediate medical attention.

INGESTION: DO NOT INDUCE VOMITING. Give victim large amounts of milk or water to dilute. Get immediate medical attention. Never give anything by mouth to an unconscious person.

SECTION 7: SPECIAL PROTECTION INFORMATION:

PROTECTIVE GLOVES: Chemically resistant gloves are required.

EYE PROTECTION: Safety glasses with side shields (or goggles) and a face shield.

RESPIRATORY PROTECTION: Recommended. NIOSH/MSHA approved (or equivalent) respirator if mist is generated.

LOCAL EXHAUST: Use only with adequate ventilation.

OTHER EQUIPMENT: Boots, apron, eye bath and safety shower.

Work/Hygiene Practices: Use good personal hygiene when handling this product. Wash hands after use, before smoking, or using the toilet.

SECTION 8 :REACTIVITY DATA:

STABILITY: Stable. Do not store below 25° F or above 100° F for extended periods of time.
CONDITIONS TO AVOID: N/A
INCOMPATIBILITY: Reducing agents, alkalis, strong oxides, and chlorinated products.
HAZARDOUS POLYMERIZATION: Will not occur
HAZARDOUS DECOMPOSITION OR BY PRODUCTS: May give off iodine vapors with high temperatures.

SECTION 9: SPILL OR LEAK PROCEDURES:

SPILL RESPONSE: Neutralize the acid with soda ash or sodium bicarbonate, and the Iodine with Sodium Thiosulfate or Sodium Sulfite, or flood area with large amounts of water. After neutralization with Sodium Sulfite and soda ash, wash to sewer if in accordance with local, state and federal regulations.

WASTE DISPOSAL METHODS: Do not reuse empty container. Rinse container before disposing in a safe manner. Follow all Federal, State, and local regulations.

ENVIRONMENTAL HAZARDS: This product is toxic to fish and aquatic organisms. Do not contaminate water by cleaning of equipment or disposal of waste. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination Systems (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product into sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA.

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING: Do not store product above 100° F for extended periods of time.

OTHER PRECAUTIONS: THOROUGHLY RINSE ALL MEASURING DEVICES AND STORE OUT OF REACH OF CHILDREN. Keep container tightly closed when not in use. Avoid contamination of food or feed.

SECTION 10: REGULATORY INFORMATION:

SHIPPING NAME: Corrosive liquid, acidic, inorganic (Contains Phosphoric acid)
HAZARD CLASS: 8 (Corrosive)
UN NUMBER: UN3264
PACKING GROUP: PG II
DOT CLASS: Corrosive liquid.

REGULATORY INFORMATION: SARA/TITLE III Hazard Categories;
Immediate (Acute) Health: Yes Delayed (Chronic) Health: No Fire Hazard: No
Reactive Hazard: No Sudden Release of Pressure: No
Contains ingredient (s) reportable according to 40 CFR, 302, Table 304.2: (CERCLA) Reportable Quantities (RQ). Environmental releases exceeding reportable quantities must be reported to the National Response Center by calling 800-424-8802 (202-426-2675), as well as state and local authorities.

SECTION 11. SPECIAL INFORMATION:

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING: Keep container tightly closed when not in use. Do not store below 25° F or above 100° F for extended periods of time. Avoid contamination with food or feed.

Container Disposal: Do not reuse empty container. Triple rinse (or equivalent) and dispose of container in a safe manner.

PREPARED BY: D. M. McFadden DATE: 3/4/2004

WESTERN CHEMICAL INC.
Product Purity & Environmental Stewardship

Material Safety Data Sheet

Section 1 – Product and Company Information

Product Name:	**1.75% Iodine**
Company	Western Chemical, Inc.
Street Address	1269 Lattimore Rd. Ferndale, WA 98248 USA
Technical phone:	360-384-5898
Fax:	360-384-0270
Emergency phone (Chemtrec)	**1-800-424-9300**
Date Updated:	September 2007
Reviewed By:	Jim Garnett

Section 2 – Composition/Information on Ingredient

Substance Name	CAS #	% by weight
Iodine	7553-56-2	1.75
Phosphoric acid	7664-38-2	16.0

Section 3 – Hazards Identification

Emergency Overview

Caution: Corrosive to eyes, respiratory system, and skin.

HIMS Rating
- Health: 3
- Flammability: 0
- Reactivity: 0

NFPA Rating
- Health: 3
- Flammability: 0
- Reactivity: 0

For additional information on toxicity, please refer to Section 11.

Section 4 – First Aid Measures

ORAL EXPOSURE

If swallowed, wash mouth out with water provided the person is conscious. Do not induce vomiting. Give large quantities of water and call a physician.

INHALATION EXPOSURE

If inhaled, remove to fresh air. If breathing becomes difficult call a physician.

DERMAL EXPOSURE

In case of contact, immediately flush with copious amounts of water for at least 15 minutes. If irritation persists contact physician.

EYE EXPOSURE

In case of contact with eyes, check for and remove contact lenses, then flush with copious amounts of water for at least 15 minutes. Assure adequate flushing by separating the eyelids with fingers. Call a physician.

Section 5 – Firefighting Measures

FLASH POINT

Not Flammable

AUTO-IGNITION

Not Flammable

FLAMMABILITY

Not Flammable

HAZARDOUS DECOMPOSITION PRODUCTS: Combustion products are fumes of Iodine and Phosphorus Oxide

EXTINGUISHING MEDIA

Water Spray, carbon dioxide, dry chemical powder, or appropriate foam. Do not use water jet.

FIREFIGHTING

Wear self contained breathing apparatus and protective clothing to prevent contact with skin and eyes. Emits toxic fumes under fire conditions.

Section 6 – Accidental Release Measures

PROCEDURE(S) OF PERSONAL PRECAUTION(S)

Exercise appropriate precautions to minimize direct contact with skin or eyes and prevent inhalation of dust.

METHODS FOR CLEANING UP

Carefully neutralize the acid with soda ash or sodium bicarbonate. Neutralize the Iodine with Sodium Thiosulfate or flood area with large quantities of water. Wash to sewer in accordance with local, state, and federal regulations.

Section 7 – Handling and Storage.

HANDLING

Keep the container closed when not in use. Keep away from feed and food products.

STORAGE
Store in a cool dry location away from alkalis and reducing agents

Section 8 – Exposure Controls/PPE

ENGINEERING CONTROLS

Have safety shower and eye bath available. Mechanical exhaust required.

PERSONAL PROTECTIVE EQUIPMENT

Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Where risk assessment shows air-purifying respirators are appropriate, use type N95 (US) or type P1 (EN 143) respirator. Use protective gloves, chemical safety goggles, boots, and apron or lab coat.

Section 9 – Physical/Chemical properties

APPEARANCE

Color	dark brown
Physical Form	liquid
Molecular weight	ND
pH	<3.0
BP/BP Range	N/A
MP/MP Range	N/A
Freezing Point	N/A
Vapor Pressure	N/A
Vapor Density	N/A
Saturated Vapor Density	N/A
SG/Density	1.13
Bulk Density	N/A
Odor threshold	ND
Volatile %	N/A
VOC content	N/A
Water content	N/A
Solvent content	None
Evaporation rate	N/A
Viscosity	N/A
Partition Coefficient	N/A
Decomposition Temperature	N/A
Flash point °F	N/A
Flash point °C	N/A
Explosion limits	N/A
Auto-ignition temperature	N/A
Solubility	highly soluble in water.

N/A = Not Applicable
ND = No Data

Section 10 – Stability and Reactivity

Stability
Stable.

Conditions to Avoid
None Known.

Materials to Avoid
Strong Oxidizing agents. Alkalis, chlorinated products and reducing agents.

Hazardous Polymerization
Will not occur.

Section 11 – Toxicological Information

Route of Exposure
Skin Contact: May cause severe skin burns.
Eye contact: may cause irreversible eye damage.
Inhalation: Inhalation of high concentrations of Iodine may cause severe burns to the respiratory tract.
Ingestion: Harmful if swallowed. Swallowing product will cause severe burns to the throat and stomach.

Toxicity to animals
Unknown

Section 12 – Ecological Information

To the best of our knowledge the toxicity to the environment has not been fully explored yet.

Section 13 – Disposal Considerations

Appropriate Method of Disposal of Substance or Preparation
Do not use empty container. Rinse empty container and dispose of following all local, state, and federal regulations.

Section 14 – Transport Information

DOT
Proper shipping name: disinfectants , Liquid Corrosive, N.O.S. (contains Phosphoric Acid) 8, UN 1903, PG II

Air transport: restricted.

Section 15 – Regulatory Information

US Classification and label text

US Statements required: Corrosive.

Section 16 – Other Information

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. The burden of safe use of our materials must rest with the user. We cannot assume responsibility for the completeness or accuracy of any information supplied by us concerning the hazards and recommended use of this product.

ARGENT CHEMICAL LABS -- ARGENTYNE -- 6810-00N047826

========== Product Identification ==========

Product ID:ARGENTYNE
MSDS Date:10/19/1988
FSC:6810
NIIN:00N047826
MSDS Number: BVBXC
=== Responsible Party ===
Company Name:ARGENT CHEMICAL LABS
Address:8702 152ND AVE N.E.
City:REDMOND
State:WA
ZIP:98052
Country:US
Info Phone Num:206-885-3777
Emergency Phone Num:206-885-3777
CAGE:0LX87
=== Contractor Identification ===
Company Name:ARGENT CHEMICAL LABS
Address:8702 152ND AVE N.E.
Box:City:REDMOND
State:WA
ZIP:98052
Country:US
Phone:206-885-3777
CAGE:0LX87

========== Composition/Information on Ingredients ==========

Ingred Name:POLY (1-(2-OXO-1-PYRROLIDINYL)ETHYLENE) IODINE COMPLEX.
LD50:(ORAL MOUSE) 3400 MG/KG/24HRS
CAS:25655-41-8
RTECS #:TR1579600
OSHA PEL:N/K
ACGIH TLV:N/K

Ingred Name:SODIUM BICARBONATE (1:1). LD50 (ORAL RAT) 4220 MG/KG
CAS:144-55-8
RTECS #:VZ0950000
OSHA PEL:N/K
ACGIH TLV:N/K

========== Hazards Identification ==========

LD50 LC50 Mixture:SEE INGREDIENTS
Routes of Entry: Inhalation:YES Skin:YES Ingestion:YES
Reports of Carcinogenicity:NTP:NO IARC:NO OSHA:NO
Health Hazards Acute and Chronic:DIRECT CONTACT WITH EYES MAY BE IRRITATING. AVOID PROLONGED OR EXCESSIVE CONTACT WITH SKIN. IRRITATION. DO NOT INGEST.
Explanation of Carcinogenicity:NOT RELEVANT.
Effects of Overexposure:IRRITATION OF EYES UPON DIRECT CONTACT. SKIN IRRITATION.
Medical Cond Aggravated by Exposure:NONE KNOWN.

========== First Aid Measures ==========

First Aid:INHAL:REMOVE TO FRESH AIR. SUPPORT BREATHING (GIVE O*2/ARTF RESP) . EYES:FLUSH WITH RUNNING WATER FOR AT LEAST 15 MINUTES. CALL PHYS. SKIN:WASH WITH SOAP AND WATER. INGEST:CALL PHYSICIAN IMMEDIA TELY.

========== Fire Fighting Measures ==========

Flash Point:NON-FLAM SOLN
Extinguishing Media:WATER SPRAY, CO*2, DRY CHEMICAL, FOAM.
Fire Fighting Procedures:USE NIOSH/MSHA APPROVED SCBA & FULL BUNKER GEAR TO MINIMIZE CONTACT WITH SKIN, EYES, AND RESPIRATORY TRACT.
Unusual Fire/Explosion Hazard:NONE KNOWN.

========== Accidental Release Measures ==========

Spill Release Procedures:DIKE UP AND USE ABSORBANTS TO SOAK UP. PLACE ABSORBANTS INTO DOT-APPROVED CONTAINER & HOLD FOR DISPOSAL. WEAR GOGGLES AND GLOVES. SODIUM THIOSULFATE, PENTAHYDRATE MAY BE USED TO REDUCE TO A COLORLESS SODIUM IODATE SOLUTION.
Neutralizing Agent:NONE SPECIFIED BY MANUFACTURER.

========== Handling and Storage ==========

Handling and Storage Precautions:STORE IN A COOL LOCATION. KEEP CONTAINERS TIGHTLY CLOSED WHEN NOT IN USE.
Other Precautions:NONE KNOWN.

========== Exposure Controls/Personal Protection ==========

Respiratory Protection:NIOSH/MSHA APPROVED RESPIRATOR APPROPRIATE FOR EXPOSURE OF CONCERN .
Ventilation:GENERAL.
Protective Gloves:CHEMICAL RESISTANT GLOVES.
Eye Protection:ANSI APPVD CHEM WORK GOGG .
Other Protective Equipment:NONE SPECIFIED BY MANUFACTURER.
Work Hygienic Practices:WASH THOROUGHLY AFTER HANDLING.
Supplemental Safety and Health
NONE SPECIFIED BY MANUFACTURER.

========== Physical/Chemical Properties ==========

HCC:N1
Boiling Pt:B.P. Text:212F,100C
Spec Gravity:1.1 (H*20=1)
Solubility in Water:SOLUBLE
Appearance and Odor:DARK BROWN-RED LIQUID-NO ODOR

========== Stability and Reactivity Data ==========

Stability Indicator/Materials to Avoid:YES
NONE KNOWN.
Stability Condition to Avoid:STORE AWAY FROM HEAT.
Hazardous Decomposition Products:NONE KNOWN.

========== Disposal Considerations ==========

Waste Disposal Methods:DISPOSE OF IN ACCORDANCE WITH ALL APPLICABLE FEDERAL, STATE AND LOCAL LAWS.

Disclaimer (provided with this information by the compiling agencies):

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Responsible Care®
Good Chemistry at Work

MATERIAL SAFETY DATA SHEET

http://www.ekamsds.com

HERCULES

an Akzo Nobel company

1. Chemical Product and Company Identification

Eka Chemicals Inc.
1775 West Oak Commons Court
Marietta, GA 30062
USA

24 Hour Emergency Number
US CHEMTREC 1-800-424-9300
CANADA CANUTEC 1-613-966-6666

Product Name
35% PEROX-AID®

Chemical Name
Inorganic Peroxide, Oxidizer

CAS #
Not Applicable

Synonym(s)
Hydrogen Peroxide 35% by Wt. In aqueous solution.

Chemical Type
Inorganic Peroxide, Oxidizer. CAS Number 7722-84-1.

Intended Use
External microbiocide for control of mortality in freshwater-reared finfish eggs due to saprolegniasis, in freshwater-reared salmonids due to bacterial gill disease, and in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease.

2 Hazards Identification

Emergency Overview
35% PEROX-AID® is a clear colorless liquid with a slightly pungent odor, containing the active ingredient hydrogen peroxide. Harmful if swallowed. Oxidizer: accelerates combustion of organic materials (wood, paper, oil, clothing). Elevated temperatures above 38 C (100F) can increase the decomposition rate of the product. Material will decompose when exposed to heat, metals, alkalis, reducing agents or other impurities and generate oxygen gas, steam, and heat.

Routes of Exposure
Skin and eye contact, ingestion and inhalation

Potential Health Effects

Ingestion
This product is harmful if swallowed. Large exposure may be fatal. Can burn mouth, throat and stomach. Oxygen gas in the esophagus and stomach causes extreme swelling leading to severe injuries.

Skin
Prolonged exposure may cause skin irritation. Prolonged exposure may cause skin irritation or burns.

Eyes
Irritating and may injure eye tissue causing corneal damage and possible blindness.

Inhalation
Irritating to nose, throat, and respiratory tract. Severe overexposure may be fatal.

Target organs
Overexposure may cause lung damage, eye damage and skin damage.

Chronic Effects
Not listed as a possible carcinogenic by OSHA, I ARC or NTP. Mutagenic for bacteria and yeast. No studies were found on the possible teratogenic effects of hydrogen peroxide in humans or experimental animals. No studies were found on the possible developmental or reproductive effects of hydrogen peroxide in humans or experimental animals.

3. Composition / Information on Ingredients

Component	*CAS #*	*% Wt/Wt*
Water	7732-18-5	< 65 %
Hydrogen peroxide	7722-84-1	< 35 %
ACGIH - Threshold Limits Values - Time Weighted Averages (TLV-TWA)	1 ppm TWA	

Specific Gravity	1.132 (Water = 1)
Solubility (H2O)	100 % In water
Coefficient of Water/Oil Distribution	-1.36
Octanol/H2O Coeff	Not applicable
Auto Ignition Temperature	Not flammable.
Decomposition Temperature	Not Available
VOC	< 1 mg/l by EPA Method 8260 for volitile organics by purge and trap GC/MS
Viscosity	1.11 cP at 20C
Percent Volatile	100 % (nearly)

10. Chemical Stability & Reactivity Information

Conditions to Avoid	When placed in an unsuitable container or introduced to other contaminants, elevated temperatures above 38 C (100F) can increase the decomposition rate of the product.
Incompatible Materials	Incompatible with high pH materials, metals, salts, organics, reducing agents, dust and dirt.
Hazardous Decomposition Products	Hydrogen peroxide decomposes on heating to produce oxygen gas, steam and heat.
Possibility of Hazardous Reactions	Stable when stored under suitable storage conditions. Will not occur.

11. Toxicological Information

Toxicological Information	Harmful if swallowed. Large exposure may be fatal.
Component Analysis - LD50	For Hydrogen Peroxide 90%: Oral (LD50): > 2000 mg/kg (mouse). Vapor (LD50): 1437 ppm. 4 hours [rat].
Inhalation Effects	Irritating to nose, throat and respiratory tract. Severe overexposure may be fatal.
Irritation to skin	Prolonged exposure may cause skin irritation or burns.
Irritation to eyes	Irritation and may injure eye tissue causing damage and possible blindness.
Carcinogenicity/mutagenicity & long term effects	Both IARC (Group 3 - not classifiable as to its carcinogenicity to humans) and ACGIH (A3 - confirmed animal carcinogen with unknown relevance to humans) have concluded that the available animal carcinogenicity information from tests of hydrogen peroxide is of unknown relevance to humans.

U.S. - Rhode Island - Hazardous Substance List

Hydrogen peroxide	7722-84-1	Toxic; Flammable

12. Ecological Information

Ecotoxicity

Aquatic toxicity	Harmful to aquatic organisms especially to algae. Fish: 96 hour LD50 Pimephales promelas (fathead minnow) = 16.4 mg/l. Crustaceans: 48 hour LC50 Daphnia pulex (water flea) = 2.4 mg/l. Algae: Freshwater algae are affected by hydrogen peroxide concentrations from 2 - 20 mg/l, while 1 mg/l affects certain marine algae.
Environmental Effects	Hydrogen peroxide occurs naturally as a result of photochemical processes in living organisms. Tropospheric half-life of hydrogen peroxide is normally 10-20 hours. Soil half-life varies between several minutes to 15 hours. Decomposition in soil takes minutes or several hours depending on the mineral content and concentration of micro-organisms. Decomposes into water and oxygen.
Persistance/Degradability	Hydrogen peroxide is decomposed by enzymatic action and does not accumulate in cell systems. BOD5 and COD: Not applicable.

Other Information	JETSIZE® is a registered trademark of Eka Chemicals Inc. in the United States, Canada and several other countries. COMPOZIL® is a registered trademark of Eka Chemicals Inc. in the United States, Canada, Mexico and several other countries. AZCOTE® is a registered trademark of Eka Chemicals Inc. in the United States. BLEACHMARK® is a registered trademark of Eka Chemicals Inc. in the United States. KZCOTE® is a registered trademark of Eka Chemicals Inc. in the United States. MONITROL® is a registered trademark of Eka Chemicals Inc. in the United States. PEROX-AID® is a registered trademark of Eka Chemicals Inc. in the United States and Canada. PEROXY-BLEND® is a registered trademark of Eka Chemicals Inc. in the United States. PEROXYCLEAR® is a registered trademark of Eka Chemicals Inc. in the United States. S-QUAD® is a registered trademark of Eka Chemicals Inc. in the United States. SVP-HP® is a registered trademark of Eka Chemicals Inc. in the United States.
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Issue Date: 21-Feb-2007

MSDS Sections Updated

Chemical Product and Company Identification: Product Synonyms

Date of Approval: January 11, 2007

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-255

35% PEROX-AID

Hydrogen peroxide
Liquid solution

"For the control of mortality in freshwater-reared finfish eggs due to saprolegniasis,

For the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium branchiophilum*,

And

For the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare (Flexibacter columnaris)*."

Sponsored by:

Eka Chemicals, Inc.

TABLE OF CONTENTS

I. GENERAL INFORMATION:

A. File Number: NADA 141-255

B. Sponsor: Eka Chemicals, Inc.
1775 West Oak Commons Ct.
Marietta, GA 30062-2254

Drug Labeler Code: 061088

C. Proprietary Name: 35% PEROX-AID

D. Established Name: Hydrogen peroxide

E. Pharmacological Category: External disinfectant

F. Dosage Form: Liquid solution

G. Amount of Active Ingredient: 35% w/w (weight in water)

H. How Supplied: 5-gallon and 55-gallon containers

I. How Dispensed: Over-the-counter (OTC)

J. Dosages: Freshwater-reared finfish eggs: 500 to 1000 mg/L for 15 minutes in a continuous flow system once per day on consecutive or alternate days until hatch for all coldwater and coolwater species of freshwater-reared finfish eggs or 750 to 1000 mg/L for 15 minutes in a continuous flow system once per day on consecutive or alternate days until hatch for all warmwater species of freshwater-reared finfish eggs.

Freshwater-reared finfish:

Freshwater-reared salmonids: 100 mg/L for 30 minutes or 50 to 100 mg/L for 60 minutes once per day on alternate days for three treatments in a continuous flow water supply or as a static bath.

Coolwater species of freshwater-reared **finfish** (except northern pike & paddlefish) and channel catfish*: 50 to 75 mg/L for 60 minutes once per day on alternate days for three treatments in a

continuous flow water supply or as a static bath. Coolwater species of freshwater-reared **finfish fry** (except northern pike, pallid sturgeon & paddlefish) and channel catfish fry*: 50 mg/L for 60 minutes once per day on alternate days for three treatments in continuous flow water supply or as a static bath.

*Initial bioassay on a small number is recommended before treating the entire group. Use with caution on walleye.

K. Route of Administration: Immersion

L. Species/Classes: Freshwater-reared finfish eggs; and freshwater-reared salmonids, coolwater finfish and channel catfish

M. Indications: For the control of mortality in freshwater-reared finfish eggs due to saprolegniasis, for the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium branchiophilum*, and for the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare (Flexibacter columnaris)*

II. EFFECTIVENESS:

The data summarized in this section are publicly available and contained in Public Master File 005639 and Investigational New Animal Drug File 010023 which were compiled by the U.S. Geological Survey, Upper Midwest Environmental Sciences Center.

A. Dosage Characterization:

The primary effect of hydrogen peroxide results from localized action at the topical site of administration. The concentration of the active drug at the topical site is a function of the administered concentration, exposure period, and water conditions. These three conditions and the sensitivity of the pathogen to the drug are considered the primary determinants of effectiveness. The dosage characterization studies included one non-treated group and different concentrations of hydrogen peroxide in water. The effectiveness of hydrogen peroxide at specific concentrations and exposure times was tested for the control of mortality associated with bacterial gill disease on freshwater-reared finfish and for the control of egg mortality associated with saprolegniasis on all cold- and coolwater species of freshwater-reared finfish.

B. Substantial Evidence for the Control of Mortality in Freshwater-Reared Finfish Eggs Due to Saprolegniasis:

1. Clinical Field Trial- Study No. CAP-00-FUNGUS

Title: Efficacy of Hydrogen Peroxide to Control Mortality Associated with Saprolegniasis in Channel Catfish *(Ictalurus punctatus)* Eggs

Investigator: Tommy Crawford

Study Location: Lost Valley Fish Hatchery
Warsaw, MO

General Design of the Study:

a. Purpose: To evaluate the effectiveness of daily 15-minute treatments with 500 and 750 mg/L hydrogen peroxide over 6 days to control egg mortality associated with saprolegniasis as measured by the probability of egg hatch.

b. Animals: Channel catfish eggs, contained in their natural gelatin matrix and naturally infected with *Saprolegnia parasitica*, were used.

c. Test Article: Hydrogen peroxide (35%) was used in the study.

d. Study Design: Egg masses of 0.79 kg (equivalent to approximately 17,500 non-eyed eggs), in the natural gelatin matrix, were randomly assigned among nine McDonald egg jars to three treatment concentrations: 0 (control), 500, and

750 mg/L. Eggs were treated for 15 minutes daily for 6 days until eggs hatched. Egg samples were collected for disease confirmation; subculture produced zoospores that were identified as *Saprolegnia parasitica*.

e. Variables Measured: Mean percent hatch was the primary variable used to evaluate effectiveness of the treatment. Temperature, dissolved oxygen, and pH were monitored daily. During each treatment, a water sample was collected from each egg jar and analyzed for hydrogen peroxide concentration using a permanganate titration method.

f. Results: Table 1 summarizes the mean percent hatch of channel catfish eggs after hydrogen peroxide treatment.

Table 1. Mean percent hatch of channel catfish eggs after treatment with hydrogen peroxide for 15 minutes daily for 6 days.

Treatment mg/L	**Hatch (%)**
0	44
500	54
750	69

Mean temperature of the hatchery water was 27.8 °C. Total hardness was 150 mg/L; alkalinity was 130 mg/L; and pH ranged from 8.09 to 8.20. Mean dissolved oxygen readings ranged from 7.4 to 10.5 mg/L. Mean hydrogen peroxide concentrations were within +/- 20% of the target concentrations.

Mean hatch rate for eggs treated with 750 mg/L hydrogen peroxide was approximately 1.5 times greater than the mean hatch of the control.

g. Conclusions: This study demonstrates the effectiveness of hydrogen peroxide at 750 mg/L for 15 minutes daily until hatch to control mortality in channel catfish eggs due to saprolegniasis. Hydrogen peroxide is clinically effective in controlling mortality due to *Saprolegnia parasitica* as supported by a numerical increase in hatch rate in channel catfish eggs compared with controls.

2. Study TOX-89-00048

Title: Efficacy of Hydrogen Peroxide Treatments to Control and Prevent Saprolegniasis Infections on Salmonid Eggs

Study Director: Jeffrey J. Rach

Investigators: Jeffrey J. Rach, Theresa M. Schreier, George E. Howe

Study Location: US Geological Survey
Upper Mississippi Science Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the effectiveness of hydrogen peroxide administered at concentrations of 113, 283, 566, and 1132 mg/L (100, 200, 500, and 1000 µL/L) for 15 minutes every other day until hatch to control saprolegniasis on rainbow trout eggs.

b. Animals: Each treatment consisted of three replicates of 500 non-eyed fertilized rainbow trout eggs, 36-hours old, in each of the two trials. Each trial used eggs from a different lot (different parents and different time of year).

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Two trials were conducted. In Trial 1, hydrogen peroxide was administered at 0, 113, 283 or 566 mg/L. In Trial 2, hydrogen peroxide was administered at 0 or 1132 mg/L. Eggs were exposed for 15 minutes every other day until they hatched. Studies in both trials were conducted on groups with induced *Saprolegnia parasitica* infections (10% of eggs visibly infected) at the start of treatment. Eggs were placed in tanks with constant flow for 53 days.

   This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables Measured: Mortality and fungal infection rates were recorded before the first and the last treatment. Fry hatch was assessed after all viable eggs completed the process. Percent hatch was corrected for initial mortality using the formula [(Number of eggs hatched)/(500 eggs-initial mortalities)] x 100. Samples of water were collected for hydrogen peroxide concentration analysis by permanganate titrimetric analysis. Water pH, dissolved oxygen, and temperature were recorded daily.

f. Results: Mean infection rates and mean hatch of rainbow trout eggs infected with *Saprolegnia parasitica* and treated with hydrogen peroxide are summarized in Tables 2 and 3 (Trials 1 and 2).

Table 2. Trial 1: Infection rates of rainbow trout eggs infected with *Saprolegnia parasitica* and mean hatch rates after treatment with hydrogen peroxide for 15 minutes every other day.

Hydrogen peroxide (mg/L)	**Mean Initial Infection (%)**	**Mean Final Infection (%)**	**Mean Hatch (%)**
0	150/1500 (10%)	811/1500 (54%)	727/1453 (50%)
113	151/1500 (10%)	740/1500 (49%)	817/1455 (56%)
283	150/1500 (10%)	577/1500 (38%)	944/1460 (65%)
566	150/1500 (10%)	385/1500 (26%)	1166/1458 (80%)

Table 3. Trial 2: Infection rates of rainbow trout eggs infected with *Saprolegnia parasitica* and mean hatch rates after treatment with hydrogen peroxide for 15 minutes every other day.

Hydrogen peroxide (mg/L)	**Mean Initial Infection (%)**	**Mean Final Infection (%)**	**Mean Hatch (%)**
0	150/1500 (10%)	1019/1500 (68%)	385/1406 (27%)
1132	150/1500 (10%)	435/1500 (29%)	964/1411 (68%)

Measured hydrogen peroxide concentrations ranged from 102.4 to 111.9% of expected values. Water temperature ranged from 11.4 to 14.5 °C; dissolved oxygen ranged from 9.6 to 13.5 mg/L; and pH ranged from 7.66 to 8.46.

g. Substantiating literature: Marking LL, JJ Rach, and TM Schreier. Evaluation of antifungal agents for fish culture. *The Progressive Fish Culturist*. 56: 225-240, 1998. This published article provides additional evidence for the effectiveness of hydrogen peroxide to control mortality of salmonid eggs infected by *Saprolegnia spp.* and supports the conclusion drawn from Study TOX-89-00048.

Conclusions: This study, together with substantiating literature, demonstrates the effectiveness of hydrogen peroxide at 566 and 1132 mg/L for 15 minutes every other day until hatch to control mortality in salmonid eggs due to saprolegniasis. Continuous flow treatments with hydrogen peroxide at 566 mg/L (Trial 1) and 1132 mg/L (Trial 2) for 15 minutes every other day were clinically effective in the control of mortality of rainbow trout eggs associated with *Saprolegnia parasitica* infection.

3. Clinical Field Trial – Study TOX-94-0048-2

Title: Effectiveness of Hydrogen Peroxide to Control Mortality Associated with Saprolegniasis on Walleye *(Stizostedion vitreum)* and White Sucker *(Catostomus commersonii)* Eggs

Study Director: Jeffrey J. Rach

Study Location: US Geological Survey
Upper Midwest Experimental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To determine the effectiveness of hydrogen peroxide to control mortality associated with fungal infections associated with saprolegniasis on walleye and white sucker eggs as measured by the probability of egg hatch.

b. Animals: Non-eyed eggs of walleye and white sucker were used.

c. Test Article: Hydrogen peroxide (35%) was used in the study.

d. Study Design: For each species, 30 mL volumes of non-eyed eggs were assigned to four test groups in egg hatching systems. Approximately 2931 walleye eggs and 639 white sucker eggs (30 mL) were placed in each hatch container. Water flow was monitored and adjusted daily to maintain a flow of 240 +/- 25 mL/minute. Hydrogen peroxide was administered at 0, 283, 565, or 1130 mg/L for 15-minute exposures every other day until eggs hatched. Walleye eggs were treated four times, and white sucker eggs received five treatments. Eggs were incubated at 12 +/- 2 °C.

e. Variables Measured: The primary variable considered was the percent hatched fry after the treatment. Concentrations of hydrogen peroxide were analyzed for each treatment using a permanganate titrimetric method. Temperature, dissolved oxygen, and pH were measured in all containers during the study.

f. Statistical Analysis: Cumulative mortality of non-eyed walleye and white sucker eggs was analyzed using a general linear model ANOVA with binomial

distribution and logit link, using the SAS procedure GENMOD at the 0.05 level of significance.

g. Results: Fungal infections (visible fungus) spread to most of the untreated control eggs whereas the treated eggs had reduced or no visible fungus on the eggs. Effectiveness of hydrogen peroxide treatment on walleye and white sucker eggs is summarized in Table 4. Mean hydrogen peroxide concentrations in the water during the study were within 15% of expected concentrations.

Table 4. Mean percent hatch of walleye and white sucker non-eyed eggs after the treatment with hydrogen peroxide for 15 minutes every other day.

Eggs **Fish Species**	**Hydrogen Peroxide (mg/L)** Mean Hatch (%)			
	0	**283**	**565**	**1130**
Walleye (% hatch)	11	55*	49*	65*
White Sucker (% hatch)	9	23*	47*	69*

*Percent hatch significantly different from control ($p \leq 0.05$).

h. Conclusions: This study supports the effectiveness of hydrogen peroxide in a flow-through system at 283, 565, and 1130 mg/L for 15 minutes every other day until hatch to control mortality associated in walleye and white sucker eggs due to saprolegniasis. Effectiveness in this study is evidenced by increased hatching success.

4. Clinical Field Trial – Study TOX-94-0048-2

Title: Efficacy of Hydrogen Peroxide to Control Mortality Associated with Saprolegniasis Caused by *Saprolegnia parasitica* in Walleye Eggs (*Stizostedion vitreum)*

Investigator: Lynn A. Lee

Study Location: US Geological Survey
Upper Midwest Experimental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the effectiveness of 500 and 750 mg/L hydrogen peroxide administered as a flow-through treatment for 15 minutes on 12 consecutive days to control mortalities from saprolegniasis caused by *Saprolegnia parasitica* on walleye eggs.

b. Animals: Using von Bayer egg counts, an estimated 2.398 million eggs (14.36 kg) were used in this trial. Fertilized eggs were mixed with a solution of Fuller's earth and water.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: There were three treatment groups: 0 (control), 500 and 750 mg/L hydrogen peroxide. There were three jars (replicates) for each of the two treatment groups, and two jars (replicates) for the untreated controls. A partially randomized design was used to assign treatments to the McDonald egg jars. Eggs were randomly distributed to jars; approximately 326,000 eggs were placed in each jar. Hydrogen peroxide was administered as a continuous flow exposure for 15 minutes each day for 12 treatments. Eggs were assumed to have fungal zoospores upon study initiation; during the study a composite sample of eggs with visible fungal growth was collected and submitted to a laboratory for definitive identification.

e. Variables Measured: Survival was estimated by dividing the total number of fry that hatched from each jar by either the initial number of non-eyed eggs or estimated number of eyed eggs from samples removed on Day 8. Water hardness and alkalinity were measured twice during the experiment. Water temperature, dissolved oxygen, and pH were measured in each egg jar during treatment. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Hatching success was analyzed using a generalized linear model employing a binomial distribution and logit link at the 0.05 level of significance.

g. Results: The fungus in the composite egg sample was identified as *Saprolegnia parasitica.*

Effectiveness of hydrogen peroxide treatment on eggs is summarized in Table 5.

Table 5. Mean percent hatch of walleye eggs with saprolegniasis after the treatment with hydrogen peroxide for 15 minutes every day for 12 treatments.

	Hydrogen Peroxide mg/L Mean Hatch (%)		
	0	**451**	**695**
Non-eyed Eggs	48.6	53.1*	49.6
Eyed Eggs	66.0	78.2*	70.0

*Hatch rate differs significantly from controls ($p \leq 0.05$).

Verified mean hydrogen peroxide concentrations were 451 mg/L for the 500 mg/L jars and 695 mg/L for the 750 mg/L jars.

h. Conclusions: This study supports the effectiveness of hydrogen peroxide at 451 mg/L in a flow-through system for 15 minutes daily to control mortality in walleye eggs due to saprolegniasis.

C. Substantial Evidence for the Control of Mortality in Freshwater-Reared Salmonids Due to Bacterial Gill Disease Associated with *Flavobacterium branchiophilum*:

1. Clinical Field Trial - Study No. CAP-97-0048-09

Title: Pivotal Studies to Evaluate the Efficacy of Hydrogen Peroxide to Control Mortalities Associated with External Flavobacter Infections on Cultured Fish at Selected Fish Hatcheries

Study Directors: Jeffrey J. Rach

Investigator: Mark P. Gaikowski

Study Location: US Geological Survey
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the effectiveness of hydrogen peroxide as a static bath at concentrations of 0, 57, 113, and 226 mg/L for 30 minutes (rainbow trout, *Oncorhynchus mykiss*) and 60 minutes (brown trout, *Salmo trutta*, and Chinook salmon, *Oncorhynchus tschawytscha*) every other day for three treatments to control mortality in fish with bacterial gill disease.

b. Animals: Fingerling brown trout (9 g), Chinook salmon (3.5 g), and rainbow trout (10 g) were used in the study.

c. Test article: Hydrogen peroxide (35% w/w) was used on the treated fish.

d. Study Design: All fish were cultured in outdoor raceways and were naturally infected with bacterial gill disease. After microscopic diagnosis of the disease, fish were removed from the source raceway and hand-counted according to random assignment into each test tank (brown trout, $n = 20$; Chinook salmon, $n = 44$; rainbow trout, $n = 28$). Four treatment groups were used for each species: 0 (control), 57, 113, and 226 mg/L. The study was conducted using fish held in three tanks of 20 and 40 L. Water flow was 187 mL/min for Chinook salmon, 1.5 L/min for brown trout, and 1.9 L/min for rainbow trout. Fish were exposed to a static hydrogen peroxide bath once every other day for 3 treatments. Each treatment was replicated three times. Brown trout were observed for mortality for 12 days after the last treatment, while the post-treatment observation period was 14 days for rainbow trout and Chinook salmon.

A clinical diagnosis of bacterial gill disease was made if fish were lethargic, rode high in the water, oriented to water flow, or rejected food. Bacterial gill disease is

a superficial infection of the gill epithelia by filamentous bacteria, *Flavobacterium branchiophilum*, although other opportunistic Gram-negative bacteria have been associated with the disease. Diagnosis was confirmed by microscopic examination of gill swabs and verification of the presence of filamentous bacteria.

This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables measured: Cumulative mortality was recorded daily during the 5-day treatment period and the 12- or 14-day observation period after the last treatment. Dissolved oxygen, temperature, and pH of the water were recorded daily in each test tank. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Cumulative mortality was analyzed using a general linear model analysis of variance (ANOVA) with binomial distribution and logit link using the GENMOD procedure in SAS at the 0.05 level of significance.

g. Results: Cumulative mortality through the end of the post-treatment observation period is summarized in Table 6.

Table 6: Cumulative mean mortality (%) at 12 (a) or 14 (b) days after 30- or 60-minute treatments every other day for three treatments.

H_2O_2 Concentration (mg/L)	**Brown Trout (a) (60-min. bath)**	**Chinook Salmon (b) (60-min. bath)**	**Rainbow Trout (b) (30-min. bath)**
0	11.7^{a}	21.2^{a}	31.0^{a}
57	0.0^{b}	7.6^{a}	25.0^{ab}
113	6.7^{a}	22.0^{a}	14.3^{bc}
226	36.7^{c}	72.0^{b}	7.1^{c}

^{a,b,c} Percentages with different superscripts differ ($p \leq 0.05$)

Hydrogen peroxide concentrations were within +/- 10% of the target concentrations.

h. Conclusions: This study demonstrates the clinical effectiveness of hydrogen peroxide at 57 mg/L for 60 minutes and 113 mg/L for 30 minutes every other day for three treatments to control mortality in freshwater-reared salmonids due to bacterial gill disease. The data in this study show that for brown trout fingerlings, hydrogen peroxide at 57 mg/L administered as a 60-minute static bath significantly reduces mortality associated with bacterial gill disease as compared to the controls. For rainbow trout fingerlings, hydrogen peroxide at 113 mg/L administered as a 30-minute static bath significantly reduces mortality as compared to the controls. Mortality among brown trout and Chinook salmon in

the 226 mg/L groups (1 hour treatment) is significantly higher than among control groups and is consistent with dose-related toxicity.

2. **Supporting Data – Published Literature**

Source: Lumsden JS, VE Ostland, and HW Ferguson. Use of Hydrogen Peroxide to Treat Experimentally Induced Bacterial Gill Disease in Rainbow Trout. *Journal of Aquatic Animal Health*. 10: 230–240, 1998.

Study Location: Fish Pathology Laboratory
University of Guelph
Ontario, Canada

General Design of the Study:

a. Purpose: To determine the efficacy of hydrogen peroxide to control mortality associated with experimentally induced bacterial gill disease in rainbow trout.

b. Animals: Rainbow trout fingerlings weighing 12 to 20 grams were used in the study.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Fingerlings were experimentally infected by challenge in a static tank containing *Flavobacterium branchiophilum* at a concentration of 1×10^5 colony-forming units (CFU) per mL for 1 hour. *F. branchiophilum* challenge concentrations were verified by plate count. Treatments were administered in the same tanks where the fish were infected. Fish were stocked at 100 g/L into experimental tanks. Hydrogen peroxide treatments were administered as a static bath at 0 (control), 25, 75, 100, 125, 175, or 250 mg/L for 60 minutes every other day for two exposures (Experiments 1 and 2) or every day for three exposures (Experiment 3). Treatment was initiated 48 hours post-infection. The disease was diagnosed prior to and after the treatment by identifying the bacteria and associated microscopic lesions.

e. Variables Measured: Cumulative mortality was recorded and analyzed to evaluate effectiveness. Mortality was monitored through the second day after the last death was noted. Hydrogen peroxide concentrations were measured using iodometric titration.

f. Statistical Analysis: Inability to access the underlying data in this publication precluded statistical analysis. Conclusions were drawn based on numerical differences evident in the report.

g. Results: Cumulative mortality in each experiment is summarized in Table 7.

Table 7. Cumulative mortality after treatment with hydrogen peroxide to control bacterial gill disease in rainbow trout.

	Cumulative Mortality (%)		
H_2O_2 (mg/L)	**Exp. #1 (Two treatments EOD)**	**Exp. #2 (Two treatments EOD)**	**Exp. #3 (Three treatments SID)**
0	44.4	61.1	60.0
25	34.1	*	4.2
75	*	*	7.5
100	25.9	21.1	*
125	*	*	13.3
175	*	*	9.2
250	2.2	15.5	24.2

*Not tested

Hydrogen peroxide concentrations were within 10% of the target concentrations.

h. Conclusions: This study supports the effectiveness of hydrogen peroxide at 100 and 250 mg/L for 60 minutes every other day for two treatments to control mortality in rainbow trout due to bacterial gill disease associated with *Flavobacterium branchiophilum.*

D. Substantial Evidence for the Control of Mortality in Freshwater-Reared Coolwater Finfish and Channel Catfish Due to External Columnaris Disease Associated with *Flavobacterium columnare (Flexibacter columnaris)*:

1. Clinical Field Trial – Study No. CAP-00-BACTERIA

Title: Effectiveness of Hydrogen Peroxide to Control Mortality Associated with External Columnaris [*Flavobacterium columnare (Flexibacter columnaris)*] on Channel Catfish *(Ictalurus punctatus)*

Investigators: Alan Johnson, Jeffrey J. Rach

Study Location: Rathbun Fish Hatchery
Moravia, IA

General Design of the Study:

a. Purpose: To evaluate the effectiveness of hydrogen peroxide to control mortality associated with external columnaris on channel catfish fingerlings.

b. Animals: Naturally infected channel catfish fingerlings (2.28 g) from a single production lot were used in the study.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Four treatment groups of fish were included: control (0 mg/L), and treated with hydrogen peroxide at 50, 75, and 100 mg/L. Treatments were administered as a static bath for 60 minutes every other day for three treatments. Each treatment group was replicated three times. After the fish were diagnosed with columnaris, 26 fish were randomly assigned to each of 12 test tanks (312 fish total), and treatments were initiated on the same day without an acclimation period. The last exposure was followed by a 10-day post-treatment observation period. Observation of visual lesions and microscopic examination were used to diagnose the disease.

e. Variables Measured: Mortalities were recorded daily with the initial recording made approximately 24 hours after the first treatment. Dissolved oxygen, temperature and pH were recorded daily in each test tank. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Cumulative survival to post-treatment was analyzed using logistic regression based on the SAS procedure GENMOD. Model fit was based on scaled deviance. Differences between means were determined using least square means at the 0.05 level of significance.

g. Results: Mortality rates after treatment are summarized in Table 8.

Table 8: Percent mortality at the end of the 15-day study (10 days after treating with hydrogen peroxide for 60 minutes every other day for three treatments.)

Treatment Group (mg/L)	% Cumulative Mortality
0	80.8[a]
50	47.4[b]
75	28.2[b]
100	41.0[b]

[a,b] Means with different superscripts differ ($p \leq 0.05$)

Hydrogen peroxide concentrations were within +/- 5% of the target concentrations.

h. Conclusions: This study demonstrates the effectiveness of hydrogen peroxide at or above 50 mg/L for 60 minutes every other day for three treatments to control mortality in channel catfish due to external columnaris disease.

2. Clinical Field Trial- CAP-00-BACTERIA (Rathbun-10-023-Ia-Bacteria-2)

Title: Efficacy of Hydrogen Peroxide to Control Mortality Associated with External Columnaris on Walleye *(Stizostedium vitreum).*

Investigators: Alan Johnson, Jeffrey J. Rach

Study Location: Rathbun Fish Hatchery
Moravia, IA

General Design of the Study:

a. Purpose: To evaluate the effectiveness of hydrogen peroxide to control mortality associated with external columnaris on walleye fingerlings.

b. Animals: A total of 156 walleye fingerlings with mean body weight of 12 g and length ranging from 10 to 13 cm were used in the study.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Fish naturally infected with external columnaris were randomized to treatments with 0 (control), 50, 75, or 100 mg/L hydrogen peroxide administered as a static bath for 60 minutes every other day for three treatments. Each treatment was conducted with three replicate tanks and with 13 fish allocated to each tank. Before testing began, twelve fish were collected from the reference population for disease diagnosis. Observation of visual lesions and microscopic examination were used to diagnose columnaris. Water flow was

suspended during treatment. Aeration was supplied for the duration of the study. Post-treatment mortality data was collected daily for 10 days following the final treatment.

e. Variables Measured: Mortality was recorded and dead fish were removed from the tank daily. Water was analyzed for hardness and alkalinity. Dissolved oxygen, temperature, and pH were recorded daily in each test tank. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Logit transformed cumulative mortality was analyzed using a general linear model ANOVA based on the GENMOD procedure in SAS.

g. Results: Cumulative mortality after the treatment is summarized in Table 9.

Table 9. Mortality rates after hydrogen peroxide treatment of walleye fingerlings infected with external columnaris.

Treatment Group (mg/L)	**% Cumulative Mortality (Days 1-15)**
0	69.2[a]
50	35.9[b]
75	56.4[a]
100	61.5[a]

[a,b] Rates with different superscripts differ ($p \leq 0.05$).

Hydrogen peroxide concentrations were within +/- 12% of the target concentrations. The mean water temperature was 25.3 °C. Water total hardness was 90 mg/L, alkalinity was 75 mg/L, average pH was 7.77, and average dissolved oxygen was 7.9 mg/L.

h. Conclusions: This study demonstrates the effectiveness of hydrogen peroxide at 50 mg/L of water for 60 minutes every other day for three treatments to control mortality in walleye due to external columnaris disease.

3. Supporting Data – Study CAP-97-0048-09

Title: Pivotal Studies to Evaluate the Efficacy of Hydrogen Peroxide to Control Mortalities Associated with External Flavobacter Infections on Cultured Fish at Selected Fish Hatcheries

Study Director: Jeffrey J. Rach

Investigator: Mark P. Gaikowski

Study Location: US Geological Survey
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the effectiveness of hydrogen peroxide at 57 and 113 mg/L for 60 minutes in a static bath every other day for three treatments to control mortality associated with external columnaris disease in yellow perch.

b. Animals: Yellow perch weighing approximately 1 g were used in the study.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Prior to treatment, the fish were experiencing a natural outbreak of columnaris with 50% mortality. Observation of visual lesions and microscopic examination were used to diagnose columnaris. Fish were randomly assigned to 20 L tanks and were exposed to hydrogen peroxide in a static bath at concentrations of 0 (control), 57, or 113 mg/L for 60 minutes every other day for three treatments. There were three replicates per treatment concentration. Aeration was maintained during the study and water flow was suspended during treatment period.

   This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables Measured: Mortality was recorded daily in each tank for 14 days, including 9 days after the last treatment. Water temperature, dissolved oxygen, and pH were measured daily. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Results: Cumulative mean mortality after the treatment is summarized in Table 10.

Table 10. Cumulative mortality in yellow perch fingerlings with external columnaris after treatment with 0, 57, or 113 mg/L hydrogen peroxide as a static bath for 60 minutes every other day for three treatments. Mortality was observed for 14 days, beginning with the first day of treatment.

Treatment Group (mg/L)	**% Cumulative Mortality (Days 1-14)**
0	7.5
57	1.1
113	5.2

The water temperature ranged from 12.0 to 13.3 °C, dissolved oxygen from 8.0 to 10.4 mg/L, and pH from 7.64 to 8.11. Hydrogen peroxide concentrations were within +/- 10% of the target concentrations.

g. Conclusions: This study supports the clinical effectiveness of hydrogen peroxide at 57 mg/L for 60 minutes every other day for three treatments to control mortality in yellow perch associated with external columnaris disease.

III. TARGET ANIMAL SAFETY:

Target animal safety was determined by considering studies summarized in this section as well as data provided in effectiveness trials.

The data summarized in this section are publicly available and contained in Public Master File 005639 and Investigational New Animal Drug File 010023 which were compiled by the U.S. Geological Survey, Upper Midwest Environmental Sciences Center.

A. Toxicity Studies on Freshwater-Reared Finfish Eggs

1. Freshwater Reared Finfish Eggs – Study TOX – 94 -00048 – 3

Title: Safety of Hydrogen Peroxide to Non-Eyed and Eyed Rainbow Trout *Oncorhynchus mykiss* Eggs

Study Director: Jeffrey J. Rach

Study Location: US Geological Survey
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To investigate the toxicity of hydrogen peroxide treatments on rainbow trout non-eyed and eyed eggs at up to ten times the proposed dose (500 to 1000 mg/L) and for up to three times the proposed duration of treatment (15 minutes).

b. Animals: Two lots of fertilized non-eyed and eyed eggs were used in the study. Lot # 9403 was cultured at 12 °C, and lot # 9452 was cultured at 15 °C.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: A 30 mL volume of eggs containing approximately 197 to 312 eggs was randomly assigned to each test jar. Two lots of eggs were used. Hydrogen peroxide was administered at 0, 1130, 3390, 5650, and 11300 mg/L of water (approximately 0X, 1X, 3X, 5X, and 10X the highest proposed label dose) for 15 or 45 minutes (1X and 3X the treatment duration) every other day until the eggs became eyed (non-eyed egg treatments) or until eggs hatched (eyed egg treatments). The details of exposure time, egg lots and temperature of the water are presented in Table 11.

Treatments were terminated 13 days post-fertilization for eggs incubated at 12 °C, and 10 days post-fertilization for eggs incubated at 15 °C.

Table 11. Hydrogen peroxide treatment groups of two lots of rainbow trout fertilized eggs treated at 15 or 45 minutes every other day.

Group #	Egg Lot #	Temperature (+/- 2 °C)	Treatment Duration (Minutes)	# Treatments	Egg Stage at Test Initiation	Egg Age (days)	Final Life Stage
1	9403	12	15	6	Non-eyed	2	Eyed eggs
2	9403	12	45	6	Non-eyed	2	Eyed eggs
3	9452	15	15	4	Non-eyed	2	Eyed eggs
4	9452	15	45	4	Non-eyed	2	Eyed eggs
5	9403	12	15	5	eyed	14	Fry
6	9403	12	45	5	eyed	14	Fry
7	9452	15	15	3	eyed	14	Fry
8	9452	15	45	3	eyed	14	Fry

e. Variables Measured: The total number of dead and live eggs and fry at the termination of each trial was enumerated by direct count. Water flow was monitored daily and was turned off during hydrogen peroxide exposure. Water temperature, dissolved oxygen, pH, alkalinity, and hardness were measured during the study. Hydrogen peroxide concentrations were analyzed using a permanganate titration method.

f. Statistical Analysis: Survival of the non-eyed eggs to eye-up or eyed eggs to hatch was analyzed using a general linear model ANOVA with binomial distribution and logit link at the 0.10 level of significance. Incubation vessels were the experimental unit.

g. Results: Survival of non-eyed eggs to eye-up is illustrated in Table 12, and survival of eyed eggs to hatch is illustrated in Table 13.

Table 12. Mean percent eye-up of two lots of non-eyed rainbow trout eggs treated with hydrogen peroxide every other day for 15 or 45 minutes until eggs reached the eyed-egg stage at incubation temperatures of 12 or 15 +/- 2 °C.

Temperature °C	Time Minutes	Lot #	Treatment Concentration (mg/L)				
			0	1130	3390	5650	11300
			Mean eye-up (%)				
12	15	9403	96	86*	54*	59*	42*
12	45	9403	96	48*	16*	4*	NT
15	15	9452	76	57*	39*	33*	10*
15	45	9452	76	26*	10*	5*	NT

NT: Not tested

* Significantly different from control ($p \leq 0.10$)

Table 13. Mean percent hatch of two lots of eyed rainbow trout eggs treated with hydrogen peroxide every other day for 15 or 45 minutes at incubation temperatures of 12 or 15 +/- 2 °C until hatch.

Temperature °C	Time Minutes	Lot #	Treatment Concentration (mg/L)				
			0	1130	3390	5650	11300
			Mean hatch (%)				
12	15	9403	90	97*	95*	97*	97*
12	45	9403	90	95*	92	95*	NT
15	15	9452	90	88	88	89	85*
15	45	9452	90	86*	85[1]	84*	NT

NT: Not tested

* Significantly different from control ($p \leq 0.10$)

[1] Not significant because of large standard error

Water flow was adjusted to 300 mL/minute between treatments. Temperatures ranged from 12.1 to 12.9 °C and 14.5 to 15.2 °C. Dissolved oxygen ranged from 8.9 to 20.0 mg/L; pH ranged from 7.0 to 8.3; alkalinity ranged from 97 to 102 mg/L; and water hardness ranged from 140 to 142 mg/L. Hydrogen peroxide concentrations in the water were within acceptable ranges (+/- 15% of the target concentrations).

The probability of eye-up was significantly less in the treated non-eyed eggs than in the control eggs. The probability of hatch was significantly less in control eggs than in treated eyed eggs that were incubated at 12 °C, except for the 3X concentration group with 45-minute treatments which showed a numerical difference. The probability of hatch was not significantly different when eyed eggs incubated at 15 °C were treated at doses up to 5X the highest label dose in 15-minute applications compared to untreated controls. When eyed eggs incubated at 15 °C were treated with hydrogen peroxide for 45 minutes every other day, the probability of hatch was always less, sometimes significantly, in the treated groups than in the control.

h. Conclusions: This study demonstrates the safety of hydrogen peroxide at 1000 mg/L for 15 minutes daily until hatch on eyed rainbow trout eggs. An adequate margin of safety exists above 1130 mg/L for hydrogen peroxide treatment of eyed rainbow trout eggs for 15 minutes every other day. Hydrogen peroxide treatment at 1130 mg/L or higher for 15 minutes every other day from egg fertilization to eye-up decreased the probability of egg eye-up. See further investigation in Section III.A.4.

2. Target Animal Safety Study – No. TOX-95-00048-7 (1995 – 1996) – Report No. 2

Title: Safety of Hydrogen Peroxide Treatments on Fish Eggs

Study Director: Jeffrey J. Rach

Study Location: US Geological Survey
Upper Mississippi Science Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the safety of hydrogen peroxide as a 15-minute water treatment at concentrations of 566, 1132, 3396, and 6792 mg/L daily until hatching of fertilized eggs. These concentrations approximate the low end of the label dose range and 1X, 3X, and 6X the high end of the label dose range.

b. Animals: One to three-day old fertilized eggs were used; Table 14 lists the species tested.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study. Hydrogen peroxide was administered in a continuous flow system.

d. Study Design: Each aquarium (for catfish and perch) or jar received 30 mL of eggs. Eggs of walleye (*Stizostedion vitreum*), yellow perch (*Perca flavescens*), white sucker (*Catostomus commersonii*), lake sturgeon (*Acipenser fulvescens*), paddlefish (*Polyodon spathula*), common carp (*Cyprinus carpio*), and channel catfish (*Ictalurus punctatus*) were treated with hydrogen peroxide at 0, 1132, 3396, and 6792 mg/L. Eggs of northern pike (*Esox lucius*) were allocated in the same manner and treated with hydrogen peroxide at 0, 566, 1132, and 3396 mg/L. Treatments were initiated when the eggs were 1 to 3 days old and were administered for 15 minutes once daily (Monday through Friday) until all viable eggs hatched. There were three replicates for each concentration.

   This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables measured: Mean percent hatch and water flow, temperature, dissolved oxygen, pH, and hardness. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Percent hatch was calculated by dividing the number of fry by the initial number of eggs and multiplying by 100.

g. Results: Hatch results are summarized in Table 14.

Water hardness ranged from 142 to 160 mg/L $CaCO_3$; alkalinity ranged from 101 to 138 mg/L $CaCO_3$. Hydrogen peroxide concentrations in the test tanks were within 5% of the target concentrations. Water flow rate was 360 +/- 36 mL/minute in all tanks. Water temperature was 12 +/- 2 °C for eggs of northern pike, walleye, yellow perch and white sucker; 17 +/- 2 °C for lake sturgeon, paddlefish, and carp; and 22 +/- 2 °C for channel catfish. Dissolved oxygen was maintained between 7.4 to 20.0 mg/L. Water pH ranged from 7.89 to 8.72.

Table 14. Mean percent hatch of fish eggs treated with hydrogen peroxide.

	Treatment Groups (mg/L)				
Species	0 mg/L	566 mg/L	1132 mg/L	3396 mg/L	6792 mg/L
Northern pike	32	32	37	34	-[a]
Walleye	0[b]	-[a]	77	61	5
Yellow perch	59[b]	-[a]	100[c]	66	18
White sucker	15[b]	-[a]	61	42	0
Lake sturgeon	51[b]	-[a]	57[c]	61[c]	40
Paddlefish	72[b]	-[a]	82[c]	53	42[d]
Common carp	6[b]	-[a]	59	53	48
Channel catfish	19[b]	-[a]	78	68	0

a. Not tested
b. Fungus observed on eggs
c. One replicate not used due to aquarium overflow (n=2)
d. All fish died after post-hatch treatments

Hydrogen peroxide concentrations were within 5% of the target concentrations.

h. Conclusions: This study demonstrates an adequate margin of safety for hydrogen peroxide above 1132 mg/L for treatments administered for 15 minutes daily on northern pike, lake sturgeon, and common carp. The margin of safety above 1132 mg/L for walleye, yellow perch, white sucker, paddlefish, and channel catfish could not be determined from this study. The effect of treatment was confounded by variable fungal infection of the treated and control eggs in this study.

3. Freshwater-Reared Finfish Eggs – Study TOX – 94 -00048 – 2, Part 1

Title: Hydrogen Peroxide Treatment Toxicity to Rainbow Trout Eggs, Part 1: Safety

Study Director: Jeffrey J. Rach

Study Location: Upper Mississippi Science Center
US Geological Survey
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the safety of hydrogen peroxide at 566, 1132, and 3396 mg/L for 15 minutes daily from fertilization until 5 days after hatch on eggs and fry of rainbow trout and steelhead trout. These concentrations approximate the low end of the label dose range and 1X and 3X the high end of the label dose range.

b. Animals: Five lots of non-eyed 36-hour-old fertilized rainbow trout (*Oncorhynchus mykiss*) eggs were used in the study. Lots 9624, 9653, and 9658 were rainbow trout (75,000 eggs); lot 9604 (5,000 eggs) was rainbow trout steelhead strain Skamania; and lot 9621 was rainbow trout steelhead strain Ganaraska. Control and treated eggs from all lots tested remained free of fungal infection throughout incubation.

c. Test Articles: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: A volume of 30 mL of eggs of each strain was assigned to each experimental group. The suspension included approximately 148 to 273 eggs. Three replicates were included in the study. Hydrogen peroxide was delivered using a peristaltic pump at 0, 566, 1132, and 3396 mg/L for 15 minutes daily (Monday through Friday) from fertilization until 5 days after hatch.

e. Variables: Percent hatch was calculated by dividing the number of fry (live and dead) by the total number of eggs and multiplying by 100. Water flow, temperature, dissolved oxygen, pH, and alkalinity were measured during the study. Hydrogen peroxide concentrations were verified analytically using a permanganate titration method.

f. Statistical Analysis: Percent hatch was calculated by dividing the number of fry (live and dead) by the total number of eggs and multiplying by 100.

g. Results: The percent hatch for each treatment is summarized in Table 15.

Water temperature was 12 +/- 2 °C; dissolved oxygen was 9.0 to 20.0 mg/L; and water pH ranged from 7.88 to 8.13. Hydrogen peroxide exposure concentrations were within +/- 10% of the target concentrations.

Table 15. Mean percent hatch of rainbow trout and steelhead trout eggs after exposure to hydrogen peroxide treatment for 15 minutes daily from fertilization until 5 days after hatch.

	Hydrogen Peroxide mg/L Mean Hatch (%)			
Eggs Lot Number	**0**	**566**	**1132**	**3396**
9614 Rainbow trout	94.1	92.1	86.7	79.0
9653 Rainbow trout	78.4	77.7	71.6	65.2
9658 Rainbow trout	83.1	77.2	67.7	57.8
9604 Skamania steelhead	73.6	49.6	28.7	28.0
9621 Ganaraska steelhead	79.1	72.6	73.5	3.5

h. Conclusions: This study does not demonstrate the safety of hydrogen peroxide on rainbow trout eggs. There is a numerical decrease in mean percent hatch as the concentration of hydrogen peroxide increases. Steelhead trout eggs are more sensitive to treatment than rainbow trout eggs. A statement is needed on the label which recommends that users conduct bioassays on a small number before treating the entire group to discern potential species-specific sensitivities. Further investigations with rainbow trout eggs revealed a sensitive period during incubation between 70 and 140 Daily Thermal Units degrees Celsius; see Sections III.A.4 and III.A.5.

4. Freshwater-Reared Finfish Eggs – Study CAP-96-00048-2, Part 2

Title: Hydrogen Peroxide Treatment Toxicity to Rainbow Trout Eggs, Part 2: Identification of the Sensitive Period During the Exposure of Rainbow Trout Eggs to Hydrogen Peroxide

Study Director: Mark P. Gaikowski

Study Location: US Geological Survey
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To assess the sensitivity of rainbow trout embryos to hydrogen peroxide at 0 (control), 566, 1132, and 3396 mg/L of water for a 15-minute daily treatment from 1 to 3 days post-fertilization (≤ 20 Daily Thermal Units degrees Celsius (DTU °C)) through hatch. These concentrations approximate the low end of the label dosage range and 1X and 3X the high end of the label dosage range.

b. Animals: A total of 75,000 rainbow trout eggs were used in the study. They were obtained from three different geographic locations (Lots 9628, 9653, and 9658). Treatments were initiated when eggs were 1 to 3 days post-fertilization. Eggs remained free of fungus throughout incubation.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Four treatments with three replicates each were established in the study. Hydrogen peroxide was tested at 0, 566, 1132, and 3396 mg/L as an immersion treatment in a continuous flow system for 15 minutes daily every weekday (Monday through Friday) until all eggs hatched. Eggs were added to each tank as a 30 mL volume, containing approximately 203 to 274 eggs.

   This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables Measured: Dead eggs were removed daily from aquaria to calculate the mean daily cumulative percent mortality. The day after all viable eggs hatched, all hatched fry (live and dead) and dead eggs were counted. Water flow rate, temperature, dissolved oxygen, and pH were measured and recorded during the study. Water samples were collected during treatment exposure, and hydrogen peroxide concentrations were analyzed using a permanganate titration method.

f. Statistical Analysis: Mean cumulative daily percent mortality was calculated for non-statistical comparisons between days within treatments. Embryo sensitivity was compared using numbers of live and dead eggs recorded during a given 5-day

5. Freshwater-Reared Finfish Eggs – Study CAP-00-H2O2 – 1

Title: Safety of Hydrogen Peroxide to Paddlefish *Polyodon spathula* and Rainbow Trout *Oncorhynchus mykiss* eggs

Study Director: Jeffrey J. Rach

Study Location: US Geological Survey
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To evaluate the safety of hydrogen peroxide exposure to paddlefish eggs and rainbow trout eyed and non-eyed eggs.

b: Animals: Paddlefish eggs and rainbow trout eggs were used in the study.

c. Test Article: Hydrogen peroxide (35% w/w) was used in the study.

d. Study Design: Hydrogen peroxide was administered as a continuous flow treatment; flow rate was 360 +/- 36 mL/minute. A 30 mL volume of eggs of each fish species was placed in each McDonald jar that was connected to an aquarium. The mean number of eggs per jar was 1,830 for paddlefish and 360 for rainbow trout. Each test had five treatment groups: 0 (control), 1000, 1500, 2000, and 2500 mg/L. These concentrations represent 0X, 1X, 1.5X, 2.0X and 2.5X the high end of the label dosage range, respectively. For paddlefish, there were 3 replicates for each treatment concentration and for rainbow trout, there were 6 replicates for each treatment concentration. Each group was treated for 15 minutes daily starting within 72 hours of fertilization and continuing daily until all viable eggs hatched. Paddlefish eggs were maintained at 17 +/- 2 °C, and rainbow trout eggs were incubated at 12 +/- 2 °C. Jars were protected from direct sun light. The duration of the study was 8 days for paddlefish and 26 to 27 days for rainbow trout.

This study was conducted in accordance with Good Laboratory Practices (21 CFR 58).

e. Variables Measured: At the end of the study, dead and live eggs and fry were counted. Water temperature, water alkalinity, water hardness, dissolved oxygen, and pH were monitored daily. Hydrogen peroxide concentrations in each group were verified analytically using a permanganate titration method.

f. Statistical Analysis: Logit transformed hatch rates were analyzed using a generalized linear model ANOVA based on the SAS procedure GENMOD.

Treatment comparisons were made at the 0.10 level of significance using least-square means.

g. Results: Mean percent hatch of treated eggs is summarized in Table 17.

Table 17. Mean percent hatch of paddlefish and rainbow trout eggs treated with hydrogen peroxide for 15 minutes daily.

	Treatment Groups (mg/L) Hatch (%)				
Species	**0**	**1000**	**1500**	**2000**	**2500**
Rainbow trout	75.7^{a}	52.2^{b}	47.5^{bc}	44.0^{c}	34.5^{d}
Paddlefish	7^{a}	35^{b}	26^{b}	27^{b}	25^{b}

^{a,b,c,d} Means with different superscripts within a species differ at the 0.10 level of significance.

Water temperature ranged from 16.9 to 18.5 °C for paddlefish eggs, and 12.2 to 15.0 °C for rainbow trout eggs. The pH ranged from 7.37 to 8.22 for paddlefish eggs and 7.67 to 8.14 for rainbow trout eggs. Alkalinity ranged from 107 to 138 mg/L (as $CaCO_3$) and hardness from 140 to 162 mg/L (as $CaCO_3$). Dissolved oxygen concentrations ranged from 4.4 (due to one deviation) to greater than 20 mg/L for paddlefish eggs and from 8.0 to 18.0 mg/L for rainbow trout eggs. The mean hydrogen peroxide concentrations for all tests were within 15% of anticipated concentrations.

h. Conclusions: This study demonstrates a margin of safety of hydrogen peroxide above the highest proposed dose, 1000 mg/L for 15 minutes daily until hatch, on paddlefish eggs, because there was no significant decrease in percent hatch of paddlefish eggs between concentrations 1000 and 2500 mg/L. The mortality in rainbow trout eggs in this study is similar to that observed in the study in Section III.A.4, supporting the need for a limitation and caution statement on the label.

B. Toxicity Studies on Freshwater-Reared Finfish:

1. Target Animal Safety Study – No. CAP-97-00048-08

Title: Toxicity Assessment of Hydrogen Peroxide to Cold-, Cool-, and Warmwater Fish

Study Director: Mark P. Gaikowski

Study Locations: U.S. Geological Survey
a. Upper Midwest Environmental Sciences Center
La Crosse, WI
b. Kearneysville, WV

General Design of the Study:

a. Purpose: To determine the species most sensitive to 60- and 180-minute hydrogen peroxide bath treatments by testing fry and/or fingerlings of one or more fish species from each of the major families cultured by public aquaculture (Salmonidae, Esocidae, Percidae, Ictaluridae, Catostomidae, Centrarchidae, Cyprinidae, Percichthyidae, Acipenseridae, and Polyodontidae).

b. Animals/Controls: For all fish species, fingerlings tested were at least one month older at study initiation than the fry tested. The following species were tested: rainbow trout (*Oncorhynchus mykiss*), lake trout (*Salvelinus namaycush*), Atlantic salmon (*Salmo salar*), northern pike (*Esox lucius*), muskellunge (*Esox masquinongy*), walleye (*Stizostedion vitreum*), yellow perch (*Perca flavescens*), channel catfish (*Ictalurus punctatus*), large mouth bass (*Micropterus salmoides*), bluegill (*Lepomis macrochirus*), white sucker (*Catostomus commersonii*), fathead minnow (*Pimephales promelas*), pallid sturgeon (*Scaphirhynchus albus*), and paddlefish (*Polyodon spathula*). Fish were obtained from various state and federal hatcheries. Test fish were maintained at appropriate temperatures and culture conditions for their species and life stage. Test fish were fed a diet appropriate for their species and life stage.

c. Study Design: There were six groups (five treated and one non-treated control) for each species and life stage. The drug concentrations for the 60- and 180-minute exposure times varied depending on the results of an initial range-finding study. Dose ranges were selected to include therapeutic and lethal concentrations. Fish were exposed to a total of three static baths of hydrogen peroxide administered every other day. Each treatment group was replicated 3 times. Fish were observed for mortality for 96 hours after the last exposure. Masking procedures were followed for allocation of fish to tanks, water sampling, dose verification, mortality recording, and gill histology evaluation. Well water was used in all tanks and was kept at 12 +/- 2 °C, 17 +/- 2 °C, or 22 +/- 2 °C

Table 19. Results: Fish species and life stages, mean percent mortality after treatment, hydrogen peroxide concentrations, and exposure times.

Species	Mean Mortality (%) / Hydrogen peroxide Conc. (mg/L)	Exposure time
Atlantic salmon fingerlings	7/0, 7/150, 0/250, 53/417, 100/695, 100/1158	60 minutes
	0/0, 0/49, 0/81, 0/136, 67/226, 100/376	180 minutes
Rainbow trout fry	0/0, 7/212, 67/354, 100/706, 100/1413, 100/2825	60 minutes
	0/0, 20/88, 87/147, 100/244, 100/407, 100/678	180 minutes
Rainbow trout fingerlings	0/0, 4/183, 12/305, 96/509, 100/848, 100/1413	60 minutes
	0/0, 0/92, 58/153, 100/254, 100/424, 100/706	180 minutes
Lake trout fingerlings	0/0, 13/337, 100/562, 100/936, 100/1559, 100/2599	60 minutes
	0/0, 0/46, 0/77, 13/128, 67/212, 100/354	180 minutes
Northern pike fry	30/0, 27/111, 50/185, 93/310, 100/515, 100/859	60 minutes
	17/0, 33/36, 30/61, 62/102, 100/170, 100/283	180 minutes
Northern pike fingerlings	4/0, 37/86, 100/144, 100/238, 100/398, 100/663	60 minutes
	0/0, 12/36, 75/61, 100/102, 100/170, 100/283	180 minutes
Muskellunge fry	4/0, 0/118, 62/195, 71/325, 100/542, 100/904	60 minutes
	0/0, 0/36, 8/61, 88/102, 100/170, 100/283	180 minutes
Muskellunge fingerlings	0/0, 0/118, 25/195, 75/325, 100/542, 100/904	60 minutes
	0/0, 0/53, 0/88, 29/147, 100/244, 100/407	180 minutes
Walleye fry	0/0, 0/29, 0/49, 20/81, 67/136, 100/226	60 minutes
	0/0, 0/18, 0/29, 0/49, 7/81, 100/136	180 minutes
Walleye fingerlings	4/0, 0/24, 0/40, 0/66, 20/108, 93/181	60 minutes
	8/0, 0/11, 4/19, 0/32, 13/53, 80/88	180 minutes
Yellow perch fry	0/0, 13/32, 13/53, 40/88, 100/147, 100/244	60 minutes
	0/0, 7/10, 0/17, 20/28, 7/47, 60/79	180 minutes
Yellow perch fingerlings	0/0, 0/88, 12/147, 71/244, 93/407, 100/678	60 minutes
	0/0, 0/53, 0/88, 50/147, 93/244, 100/407	180 minutes
Channel catfish fry	0/0, 0/53, 7/88, 87/147, 100/244, 100/407	60 minutes
	0/0, 0/19, 0/32, 31/53, 100/88, 100/147	180 minutes
Channel catfish fingerlings	0/0, 0/53, 17/88, 87/147, 100/244, 100/407	60 minutes
	0/0, 0/19, 0/32, 12/53, 100/88, 100/147	180 minutes
Largemouth bass fry	0/0, 0/121, 0/202, 67/337, 100/562, 100/936	60 minutes
	0/0, 0/103, 93/171, 100/285, 100/475, 100/791	180 minutes
Largemouth bass fingerlings	4/0, 0/53, 4/88, 8/147, 87/244, 67/407	60 minutes
	0/0, 0/53, 42/88, 100/147, 100/244, 100/407	180 minutes
Bluegill fry	0/0, 0/53, 0/88, 80/147, 100/244, 100/407	60 minutes
	0/0, 0/32, 0/53, 40/88, 100/147, 100/244	180 minutes
Bluegill fingerlings	0/0, 0/32, 0/53, 12/88, 77/147, 67/244	60 minutes
	0/0, 0/32, 0/53, 87/88, 100/147, 100/244	180 minutes
White sucker fry	7/0, 0/53, 60/88, 100/147, 100/244, 100/407	60 minutes
	7/0, 7/19, 7/32, 33/53, 93/88, 100/147	180 minutes
White sucker fingerlings	0/0, 4/88, 67/147, 100/244, 100/407, 100/678	60 minutes
	0/0, 4/53, 73/88, 100/147, 100/244, 100/407	180 minutes
Fathead minnow fry	0/0, 0/19, 0/32, 0/53, 60/88, 100/147	60 minutes
	0/0, 0/11, 0/19, 0/32, 93/53, 100/88	180 minutes
Fathead minnow fingerlings	0/0, 0/53, 12/88, 96/147, 100/244, 100/407	60 minutes
	0/0, 0/32, 0/53, 96/88, 100/147, 100/244	180 minutes
Pallid sturgeon fry	4/0, 67/129, 67/215, 100/366, 100/610, 100/1017	60 minutes
	0/0, 4/32, 50/53, 100/88, 100/147, 100/244	180 minutes
Pallid sturgeon fingerlings	0/0, 4/105, 42/175, 100/293, 100/488, 100/814	60 minutes
	0/0, 0/32, 0/53, 96/88, 100/147, 100/244	180 minutes
Paddlefish fingerlings	0/0, 73/73, 100/122, 100/203, 100/339, 100/565	60 minutes
	Not tested	180 minutes

g. Conclusions: This study demonstrates an adequate margin of safety for the use of hydrogen peroxide for the following dosing tiers: Up to 100 mg/L for 60 minutes

in a static bath or for 30 minutes in a continuous flow system are safe for freshwater-reared salmonids, largemouth bass, and muskellunge. For fingerlings, static bath treatments up to 75 mg/L for 60 minutes are safe for pallid sturgeon, walleye, white sucker, bluegill, channel catfish, fathead minnow, yellow perch, and all other freshwater-reared finfish (except northern pike and paddlefish). For fry, static bath treatments up to 50 mg/L for 60 minutes are safe for walleye, white sucker, bluegill, channel catfish, fathead minnow, yellow perch, and all other freshwater-reared finfish (except northern pike, paddlefish, and pallid sturgeon). Hydrogen peroxide is not safe for use in pallid sturgeon fry or any non-egg life stages of northern pike or paddlefish. A preliminary bioassay should be done to determine species and life stage sensitivity before treating a large group of fish.

IV. HUMAN FOOD SAFETY:

The human food safety of the use of hydrogen peroxide on all species and life stages of fish, including eggs, has been met by safety evaluations completed by several groups: the Select Committee on Generally Recognized as Safe (GRAS) Substances, FDA (48 FR 52323), and the U.S. Environmental Protection Agency (EPA) (63 FR 24955). Also considered in the human food safety evaluation were the dosing regimes for finfish and finfish eggs, and the fact that hydrogen peroxide is a normal product of aerobic metabolism, decomposing to oxygen and water in the absence of a stabilizing agent.

The Select Committee was chosen by the Life Sciences Research Office of the Federation of American Societies for Experimental Biology (FASEB) for FDA's proposed affirmation that hydrogen peroxide is GRAS, with specific limitations, as a direct human food ingredient. The Select Committee determined that specific uses of hydrogen peroxide are GRAS after a consideration that most of the chemical is destroyed or dissipated during processing and that there is no nutritionally significant destruction of essential nutrients from the use of hydrogen peroxide. In addition, there was no evidence that hydrogen peroxide is carcinogenic, teratogenic, or mutagenic at levels present in foods treated with hydrogen peroxide during processing. Also, none of the oxidation products formed by action of hydrogen peroxide on food constituents were proven to be carcinogenic when given by mouth.

FDA concurred with the conclusion of the Select Committee and conducted its own evaluation of the safety of hydrogen peroxide using all available information on hydrogen peroxide, including information not available to the Select Committee. In addition, FDA determined that there is not sufficient evidence to conclude that hydrogen peroxide is a duodenal carcinogen (memorandum of FDA's Cancer Assessment Committee meetings on this matter is on file under Docket No. 78N-0369).

EPA completed a risk assessment to support an exemption from the requirement of a tolerance for residues of the antimicrobial pesticide hydrogen peroxide up to 120 ppm, in or on raw agricultural commodities, in processed commodities, when such residues result from the use of hydrogen peroxide as an antimicrobial agent on fruits, tree nuts, cereal

grains, herbs, and spices. At the low proposed use concentrations, no residues of toxicological concern were expected on any animal feeds that may be exposed to hydrogen peroxide and no residues of toxicological concern were anticipated either in animals that may consume these feeds, or in associated animal by-products.

The dosing regime for hydrogen peroxide on finfish and their eggs ensures that animals will not remain in contact with hydrogen peroxide indefinitely. Fish and their eggs will be exposed to water containing hydrogen peroxide for a finite period of time. After the treatment period is over, the fish and their eggs will either be removed from the treated water or the treated water will be flushed out and replaced with untreated water.

Any hydrogen peroxide remaining on the finfish or eggs will degrade into oxygen and water which are compounds of no toxicological concern. The small amount of hydrogen peroxide that could be ingested by humans will most likely decompose in the gastrointestinal tract, leaving little intact compound for absorption thereby posing a low risk for the development of hydrogen peroxide resistance and any associated antimicrobial resistance in foodborne pathogens of human health concern, including *Escherichia coli*, *Salmonella* and *Campylobacter*. Any absorbed hydrogen peroxide would be rapidly decomposed by tissue catalase or peroxidase to oxygen and water and would probably not cause any adverse effect on the human intestinal flora.

The human food safety concerns for the use of hydrogen peroxide on all finfish and their eggs are satisfied. Neither an acceptable daily intake (ADI), tolerance, withdrawal time, nor regulatory methods are assigned.

V. USER SAFETY:

User safety was evaluated by reviewing the Material Safety Data Sheet and product fact sheet and incorporating appropriate information on the product label. The product label contains the following information regarding safety to humans handling, administering, or exposed to 35% PEROX-AID:

EMERGENCY FIRST AID:
In case of contact, immediately flush eyes or skin with plenty of water for at least 15 minutes. Call a physician. Remove and wash contaminated clothing and shoes promptly and thoroughly.

If inhaled, move to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

If swallowed, do not induce vomiting. Give large quantities of water. Never give anything by mouth to an unconscious person. Call a physician. NOTE TO PHYSICIAN: If swallowed, large quantities of oxygen may be released quickly. The distension of the stomach or esophagus may be injurious. Insertion of a gastric tube may be advisable.

INHALATION (Breathing):
Avoid breathing vapor or mist; causes irritation of the nose, throat, and lungs; overexposure may be fatal.

INGESTION (Swallowing):
Do not swallow. This product is harmful if swallowed. Large exposures may be fatal. Can burn mouth, throat and stomach.

EYE CONTACT:
Do not get in eyes; causes eye burns and possible blindness; effects may be delayed.

SKIN CONTACT:
Avoid contact with skin; causes irritation or burns.

HUMAN PRECAUTIONS:
Wear chemical safety goggles. Wear neoprene, butyl or vinyl gloves. Keep out of reach of children. Use only in adequate ventilation. Keep containers tightly closed when not in use. Wear suitable protective clothing

VI. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data demonstrate that 35% PEROX-AID, when used according to the label, is safe and effective for the control of mortality in freshwater-reared finfish eggs due to saprolegniasis, for the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium branchiophilum*, and for the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare (Flexibacter columnaris)*. Additionally, data demonstrate that residues in food products derived from finfish treated with 35% PEROX-AID will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons, and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

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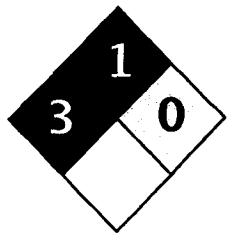

Health	3
Fire	1
Reactivity	0
Personal Protection	J

Material Safety Data Sheet
Benzalkonium chloride MSDS

Section 1: Chemical Product and Company Identification

Product Name: Benzalkonium chloride

Catalog Codes: SLB1921

CAS#: 8001-54-5

RTECS: BO3150000

TSCA: TSCA 8(b) inventory: No products were found.

CI#: Not available.

Synonym: Zephiral, Zephiran chloride, Osvan, Paralkan, Germitol, Germicin, Enuclen, Drapolex, Drapolene, Cequartyl, Benzalkonium A, Benirol, Bayclean, Ammonyx; Alkyl dimethylbenzyl ammonium chloride; Ammonium, Alkyldimethyl(phenylmethyl) Chloride; Alkylbenzyldimethylammonium Chloride; Alkyldimethyl(phenylmethyl)quaternary ammonium chlorides; Quaternary ammonium compounds, alkylbenzyldimethyl, chlorides

Chemical Name: Ammonium, alkyldimethylbenzyl-, chloride

Chemical Formula: Not available.

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call: 1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Benzalkonium chloride	8001-54-5	100

Toxicological Data on Ingredients: Benzalkonium chloride: ORAL (LD50): Acute: 240 mg/kg [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive), of eye contact (corrosive). The amount of tissue damage depends on length of contact. Eye contact can result in corneal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to gastro-intestinal or respiratory tract, characterized by burning, sneezing and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness or death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by

itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available.
MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.
TERATOGENIC EFFECTS: Not available.
DEVELOPMENTAL TOXICITY: Classified Reproductive system/toxin/female, Reproductive system/toxin/male [POSSIBLE].
The substance may be toxic to kidneys, liver, heart, gastrointestinal tract, cardiovascular system, central nervous system (CNS).
Repeated or prolonged exposure to the substance can produce target organs damage. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can produce local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degree of respiratory irritation or lung damage.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used.Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:
Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: OPEN CUP: 250°C (482°F).

Flammable Limits: Not available.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Slightly flammable to flammable in presence of heat.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available.
Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:
SMALL FIRE: Use DRY chemical powder.
LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: As with most organic solids, fire is possible at elevated temperatures

Special Remarks on Explosion Hazards:
Fine dust dispersed in air in sufficient concentrations, and in the presences of an ignition source is a potential dust explosion hazard.

Section 6: Accidental Release Measures

Small Spill: Use appropriate tools to put the spilled solid in a convenient waste disposal container.

Large Spill:
Corrosive solid.
Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Eliminate all ignition sources. Call for assistance on disposal.

Section 7: Handling and Storage

Precautions:
Keep locked up.. Keep container dry. Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Do not ingest. Do not breathe dust. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, moisture.

Storage:
Hygroscopic. Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 23°C (73.4°F).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:
Splash goggles. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Vapor and dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Amorphous solid powder or lumps.)

Odor: Aromatic.

Taste: Bitter. (Strong.)

Molecular Weight: Not available.

Color: White to yellowish.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: Decomposition temperature: >140°C (284°F)

Critical Temperature: Not available.

Specific Gravity: 0.98 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, acetone.

Solubility:
Easily soluble in cold water, hot water.
Soluble in acetone.
Very slightly soluble in diethyl ether.
Very soluble in alcohol.
Soluble in benzene. Solubility in Benzene: 1 g dissolves in 6 ml of benzene.
Solubility in Ether: 1 g dissolves in 100 ml of Ether

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, dust generation, moisture, incompatible materials.

Incompatibility with various substances: Reactive with oxidizing agents.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Hygroscopic. Also incompatible with nitrates, anion detergents

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 240 mg/kg [Rat].

Chronic Effects on Humans:
MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast.
DEVELOPMENTAL TOXICITY: Classified Reproductive system/toxin/female, Reproductive system/toxin/male [POSSIBLE].
May cause damage to the following organs: kidneys, liver, heart, gastrointestinal tract, cardiovascular system, central nervous system (CNS).

Other Toxic Effects on Humans:
Very hazardous in case of skin contact (irritant), of ingestion, .
Hazardous in case of skin contact (corrosive), of eye contact (corrosive), of inhalation (lung corrosive).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans:
May affect genetic material (mutagen) and cause adverse reproductive effects (fetotoxicity, fertility (female)) based on laboratory experiments on animals.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects:
Skin: Causes severe skin irritation and burns.
Eyes: Causes sever eye irritation and burns.
Ingestion: Harmful if swallowed. May cause severe and permanent damage to the digestive tract. Causes gastrointestinal (digestive) tract burns. May affect behavior (central nervous system depression, depression) and metabolism. May produce burning pains in the mouth, throat, and abdomen, profuse salivation, muscle weakness. May also affect the respiratory system and cardiovascular system, liver and kidneys.
Inhalation: May cause severe irritation of the respiratory tract with sore throat, coughing, shortness of breath, and delayed lung edema. Causes chemical burns to the respiratory tract. Causes irritation of the mucous membranes.
Chronic Potential Health Effects: May affect material (mutagenic) and may cause adverse reproductive effects. Prolonged or repeated skin contact may cause dermatitis.
Repeated or prolonged exposure may cause allergic reactions in sensitive individuals. May cause cyanosis of the skin and lips caused by lack of oxygen.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: Not available.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Corrosive Solid, Acid, Organic, n.o.s. (Benzalkonium Chloride) UNNA: 3261 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations: No products were found.

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada):
CLASS D-1B: Material causing immediate and serious toxic effects (TOXIC).
CLASS D-2B: Material causing other toxic effects (TOXIC).
CLASS E: Corrosive solid.

DSCL (EEC):
R21/22- Harmful in contact with skin
and if swallowed.
R34- Causes burns.
R50- Very toxic to aquatic organisms.
S26- In case of contact with eyes, rinse
immediately with plenty of water and seek
medical advice.
S28- After contact with skin, wash immediately
with plenty of water.
S36/37/39- Wear suitable protective clothing,
gloves and eye/face protection.
S45- In case of accident or if you feel unwell,
seek medical advice immediately (show the
label where possible).
S61- Avoid release to the environment. Refer to
special instructions/Safety data sheets.

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 1

Reactivity: 0

Personal Protection: j

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves.

Synthetic apron.
Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.
Splash goggles.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/09/2005 04:19 PM

Last Updated: 10/09/2005 04:19 PM

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Arch Chemicals, Inc.

MATERIAL SAFETY DATA

FOR ANY EMERGENCY, CALL 24 HOURS/7 DAYS:	**1-800-654-6911**
FOR ALL TRANSPORTATION ACCIDENTS, CALL CHEMTREC®:	1-800-424-9300
FOR ALL MSDS QUESTIONS & REQUESTS, CALL MSDS CONTROL:	1-800-511-MSDS

PRODUCT NAME: CALCIUM HYPOCHLORITE

SECTION 1 PRODUCT AND COMPANY IDENTIFICATION

REVISION DATE: 03-04-2004 SUPERCEDES: 10-01-2003
MSDS NO: 00002-0211 - 30518

MANUFACTURER: **Arch Chemicals, Inc. 501 Merritt 7 PO Box 5204 Norwalk, CT 06856-5204**

SYNONYMS: None
CHEMICAL FAMILY: Hypochlorite
FORMULA: Not Applicable/Mixture
DESCRIPTION: Sanitizer and oxidizer
OSHA HAZARD CLASSIFICATION: Oxidizer, toxic by inhalation, corrosive, skin and eye hazard, lung toxin

SECTION 2 COMPONENT DATA

PRODUCT COMPOSITION

CAS or CHEMICAL NAME: Calcium hypochlorite
CAS NUMBER: 7778-54-3
PERCENTAGE RANGE: 60-80%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS: 3 mg/cubic meter (ceiling) as Chlorine:Manufacturer's Internal Exposure Standard

CAS or CHEMICAL NAME: Sodium chloride
CAS NUMBER: 7647-14-5
PERCENTAGE RANGE: 10-20%
HAZARDOUS PER 29 CFR 1910.1200: No
EXPOSURE STANDARDS: None Established

CAS or CHEMICAL NAME: Calcium chlorate
CAS NUMBER: 10137-74-3
PERCENTAGE RANGE: 0-5%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS: None Established

CAS or CHEMICAL NAME: Calcium chloride
CAS NUMBER: 10043-52-4
PERCENTAGE RANGE: 0-5%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS: None Established

CAS or CHEMICAL NAME: Calcium hydroxide
CAS NUMBER: 1305-62-0
PERCENTAGE RANGE: 0-4%

HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:	None			5
CEILING:	None		None	
STEL:	None		None	

CAS or CHEMICAL NAME: Calcium carbonate
CAS NUMBER: 471-34-1
PERCENTAGE RANGE: 0-5%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:		15 (Total Dust) 5 (Respirable fraction)		10
CEILING:	None		None	
STEL:	None		None	

CAS or CHEMICAL NAME: Water
CAS NUMBER: 7732-18-5
PERCENTAGE RANGE: 5.5-10%
HAZARDOUS PER 29 CFR 1910.1200: No
EXPOSURE STANDARDS: None Established

SECTION 3 PRECAUTIONS FOR SAFE HANDLING AND STORAGE

DO NOT TAKE INTERNALLY. AVOID INHALATION OF DUST AND FUMES. AVOID CONTACT WITH EYES, SKIN OR CLOTHING. UPON CONTACT WITH SKIN OR EYES, WASH OFF WITH WATER. REMOVE AND WASH CONTAMINATED CLOTHING BEFORE REUSE.

STORAGE CONDITIONS: Keep product tightly sealed in original containers. Store product in a cool, dry, well-ventilated area. Store away from combustible or flammable products. Keep product packaging clean and free of all contamination, including, e.g., other pool treatment products, acids, organic materials, nitrogen-containing compounds, dry powder fire extinguishers (containing mono-ammonium phosphate), oxidizers, all corrosive liquids, flammable or combustible materials, etc.

DO NOT STORE AT TEMPERATURES ABOVE: 52 Deg.C (125 Deg.F)
Storage above this temperature may result in rapid decomposition, evolution of chlorine gas and heat sufficient to ignite combustible products.

PRODUCT STABILITY AND COMPATIBILITY

SHELF LIFE LIMITATIONS: Shelf life (that is, the period of time before the product goes below stated label strength) is determined by storage time and temperatures. Do not store product at temperatures above 52 Deg.C (125 Deg.F). When stored under moderate temperature conditions, product will maintain stated label strength for approximately two years. Prolonged storage at 35 Deg.C (95 Deg.F) or above will significantly shorten the shelf life. Storage in a climate-controlled storage area or building is recommended in those areas where extremes of high temperature occur.

INCOMPATIBLE MATERIALS FOR PACKAGING: Product packaging must be clean and free of contamination by other materials, including, e.g., other pool treatment products, acids, organic materials, nitrogen-containing compounds, dry powder fire extinguishers (containing mono-ammonium phosphate), oxidizers, all corrosive liquids, flammable or combustible materials, etc.

INCOMPATIBLE MATERIALS FOR STORAGE OR TRANSPORT: Do not allow product to come in contact with other materials, including, e.g., other pool treatment products, acids, organic materials, nitrogen-containing compounds, dry powder fire extinguishers (containing mono-ammonium phosphate), oxidizers, all corrosive liquids, flammable or combustible materials, etc.

SECTION 4 PHYSICAL DATA

APPEARANCE: White, free flowing powder
FREEZING POINT: Not Applicable
BOILING POINT: Not Applicable
DECOMPOSITION TEMPERATURE: Onset - Approximately 170-180 Deg.C (338-356 Deg.F)
SPECIFIC GRAVITY: Not Applicable
BULK DENSITY: 0.8 g/cc, loose
pH @ 25 DEG.C: 10.4-10.8 (1% solution)
VAPOR PRESSURE @ 25 DEG.C: Not Applicable
SOLUBILITY IN WATER: Approximately 18% @ 25 Deg.C (Product also contains calcium hydroxide and calcium carbonate which will leave a residue.)
VOLATILES, PERCENT BY VOLUME: Not Applicable
EVAPORATION RATE: Not Applicable
VAPOR DENSITY: Not Applicable
MOLECULAR WEIGHT: 143 (Active ingredient)
ODOR: Chlorine-like
COEFFICIENT OF OIL/WATER DISTRIBUTION: Not Applicable

SECTION 5 PERSONAL PROTECTIVE EQUIPMENT REQUIREMENTS

PERSONAL PROTECTION FOR ROUTINE USE OF PRODUCT:
RESPIRATORY PROTECTION: Wear NIOSH approved respirator if dusts are created.
VENTILATION: Use local exhaust ventilation to minimize dust and chlorine levels where industrial use occurs. Otherwise, ensure good general ventilation.
SKIN AND EYE PROTECTIVE EQUIPMENT: Wear gloves, and safety glasses to avoid skin and eye contact. Where industrial use occurs, chemical goggles or full impermeable suit may be required.

EQUIPMENT SPECIFICATIONS (WHEN APPLICABLE):
RESPIRATOR TYPE: NIOSH approved full face-piece respirator with chlorine cartridges and dust/mist prefilter.
PROTECTIVE CLOTHING TYPE: Neoprene (This includes: gloves, boots, apron, protective suit)

SECTION 6 FIRE AND EXPLOSION HAZARD INFORMATION

This product is chemically reactive with many substances. Any contamination of the product with other substances by spill or otherwise may result in a chemical reaction and fire. This product is a strong oxidizer which is capable of intensifying a fire once started.

FLAMMABILITY DATA:
FLAMMABLE: No
COMBUSTIBLE: No
PYROPHORIC: No
FLASH POINT: Not Applicable
AUTOIGNITION TEMPERATURE: Not Applicable
FLAMMABLE LIMITS AT NORMAL ATMOSPHERIC TEMPERATURE AND PRESSURE (PERCENT VOLUME IN AIR): UEL - Not Applicable LEL - Not Applicable

NFPA RATINGS:
  Health: 3
  Flammability: 0
  Reactivity: 1
  Special Hazard Warning: OX (OXIDIZER)

HMIS RATINGS:
  Health: 3
  Flammability: 0
  Reactivity: 1

EXTINGUISHING MEDIA:
  Water only

FIRE FIGHTING TECHNIQUES AND COMMENTS:
  Use water to cool containers exposed to fire. Also see Section 11.

  OTHER: Do not use dry extinguishers containing ammonium compounds

SECTION 7 REACTIVITY INFORMATION

CONDITIONS UNDER WHICH THIS PRODUCT MAY BE UNSTABLE:
  TEMPERATURES ABOVE: 170 Deg.C (338 Deg.F)
  MECHANICAL SHOCK OR IMPACT: No
  ELECTRICAL (STATIC) DISCHARGE: No
  HAZARDOUS POLYMERIZATION: Will not occur
  INCOMPATIBLE MATERIALS: This product is chemically reactive with many substances, including, e.g., other pool treatment products, acids, organics, nitrogen-containing compounds, dry powder fire extinguishers (containing mono-ammonium phosphate), oxidizers, corrosive, flammable or combustible materials.
  HAZARDOUS DECOMPOSITION PRODUCTS: Chlorine gas
  OTHER CONDITIONS TO AVOID: Storage at temperatures >125 Deg.F (52 Deg.C) Prevent ingress of humidity and moisture into container or package. Always close the lid.

SUMMARY OF REACTIVITY: (See also Section 6)
  OXIDIZER: Yes
  PYROPHORIC: No
  ORGANIC PEROXIDE: No
  WATER REACTIVE: No
  OTHER: Arch calcium hypochlorite products meet the specifications of ASTM method E-487-74 as set forth in 49 C. F. R. Sec. 173.21, Title 49-Code of Federal Regs.(DOT Regs.)

SECTION 8 FIRST AID

EYES: Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Call a physician at once.

SKIN: Immediately flush with water for at least 15 minutes. Call a physician. If clothing comes in contact with the product, it should be removed immediately and laundered before reuse.

INGESTION: Immediately drink large quantities of water. DO NOT induce vomiting. Call a physician at once. DO NOT give anything by mouth if the person is unconscious or if having convulsions.

INHALATION: Remove victim to fresh air. Support respiration if needed. Call a physician.

SECTION 9 TOXICOLOGY AND HEALTH INFORMATION

ROUTES OF ABSORPTION
Inhalation, skin and eye contact, ingestion

WARNING STATEMENT AND WARNING PROPERTIES
MAY BE FATAL IF SWALLOWED. AVOID BREATHING DUST OR FUMES. HARMFUL IF PRODUCT IS INHALED IN HIGH CONCENTRATIONS. CAUSES SKIN, EYE, DIGESTIVE TRACT AND RESPIRATORY TRACT BURNS.

HUMAN RESPONSE DATA
ODOR THRESHOLD: Approximately 1.4 mg/cubic-meter, based on odor threshold of chlorine.
IRRITATION THRESHOLD: Approximately 13-22 mg/cubic meter, based on the irritation threshold of chlorine.
IMMEDIATELY DANGEROUS TO LIFE OR HEALTH: Approximately 45 mg/cubic-meter, based on IDLH concentration of chlorine.

SIGNS, SYMPTOMS, AND EFFECTS OF EXPOSURE
INHALATION
ACUTE:
Inhalation of dust or vapor from this product can be irritating to the nose, mouth, throat and lungs. In confined areas, mechanical agitation can result in high levels of dust, and reaction with incompatible materials (as listed in Section VII) can result in high concentrations of chlorine vapor, either of which may result in burns to the respiratory tract, producing lung edema, shortness of breath, wheezing, choking, chest pains, impairment of lung function and possible permanent lung damage.
CHRONIC:
Chronic (repeated) inhalation exposure may cause impairment of lung function and permanent lung damage.

EYE
Severe irritation and/or burns can occur following eye exposure. Contact may cause impairment of vision and corneal damage.

SKIN
ACUTE:
Dermal exposure can cause severe irritation and/or burns characterized by redness, swelling and scab formation. Prolonged skin exposure may cause permanent damage.
CHRONIC:
Effects from chronic skin exposure would be similar to those from single exposure except for effects secondary to tissue destruction.

INGESTION
ACUTE:
Irritation and/or burns can occur to the entire gastrointestinal tract, including the stomach and intestines, characterized by nausea, vomiting, diarrhea, abdominal pain, bleeding and/or tissue ulceration. Due to the corrosive nature of this product, ingestion may be fatal.
CHRONIC:
There are no known or reported effects from chronic exposure except for effects similar to those experienced from single exposure.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE
Asthma, respiratory and cardiovascular disease

INTERACTIONS WITH OTHER CHEMICALS WHICH ENHANCE TOXICITY
None known or reported

ANIMAL TOXICOLOGY

ACUTE TOXICITY:

Inhalation LC 50: Approximately 1300 mg/cubic-meter (1 hr., rat) - based on acute inhalation toxicity for chlorine

Oral LD 50: 850 mg/kg. (rat)

Dermal LD 50: > 2 g/kg. (rabbit)

Causes burns to eyes and skin

CHRONIC TOXICITY:

There are no known or reported effects from repeated exposure.

REPRODUCTIVE TOXICITY:

Calcium hypochlorite has been tested for teratogenicity in laboratory animals. Results of this study have shown that calcium hypochlorite is not a teratogen.

CARCINOGENICITY:

This product is not known or reported to be carcinogenic by any reference source, including: IARC, OSHA, NTP or EPA.
One hundred mice were exposed dermally 3 times a week for 18 months to a solution of calcium hypochlorite. Histopathological examination failed to show an increased incidence of tumors.

IARC (International Agency for Research on Cancer) reviewed studies conducted with several hypochlorite salts. IARC has classified hypochlorite salts as having inadequate evidence for carcinogenicity to humans and animals. IARC therefore considers hypochlorite salts to be not classifiable as to their carcinogenicity to humans.

MUTAGENICITY:

Calcium hypochlorite has been tested in the Dominant lethal assay in male mice, and it did not induce a dominant lethal response.
Calcium hypochlorite has been reported to produce mutagenic activity in two in vitro assays. It has, however, been shown to lack the capability to produce mutations in animals based on results from the micronucleus assay. In vitro assays frequently are inappropriate to judge the mutagenic potential of bactericidal chemicals due to a high degree of cellular toxicity. The concentration which produces mutations in these in vitro assays is significantly greater than the concentrations used for disinfection. Based on high cellular toxicity in in vitro assays and the lack of mutagenicity in animals, the risk of genetic damage to humans is judged not significant.

AQUATIC TOXICITY:

Bluegill, 96 hr. LC50: 0.088 mg/l (nominal, static)
Rainbow trout, 96 hr. LC50: 0.16 mg/l (nominal, static)
Daphnia magna, 48 hr. LC50: 0.11 mg/l (nominal, static)

TOXICITY TO WILDLIFE:

Bobwhite quail, dietary LC50: > 5,000 ppm
Mallard ducklings, dietary LC50: > 5,000 ppm
Bobwhite quail, oral LD50: 3474 mg/kg.

SECTION 10 TRANSPORTATION INFORMATION

THIS MATERIAL IS REGULATED AS A DOT HAZARDOUS MATERIAL.

DOT DESCRIPTION FROM THE HAZARDOUS MATERIALS TABLE 49 CFR 172.101:
LAND (U.S. DOT): CALCIUM HYPOCHLORITE, HYDRATED MIXTURES, 5.1, UN 2880, PG II

WATER (IMO): SAME AS ABOVE

AIR (IATA/ICAO): SAME AS ABOVE

HAZARD LABEL/PLACARD: OXIDIZER
REPORTABLE QUANTITY: 10 lbs. (Per 49 CFR 172.101, Appendix)
EMERGENCY GUIDE NO: 140
SPECIAL COMMENT: Under specific circumstances, this product can ship under two transport exceptions, Limited Quantity or Consumer Commodity. See Bill of Lading for proper shipping description.

SECTION 11 SPILL AND LEAKAGE PROCEDURES

FOR ALL TRANSPORTATION ACCIDENTS, CALL CHEMTREC AT 800-424-9300.

REPORTABLE QUANTITY: 10 lbs. (as Calcium hypochlorite) Per 40 CFR 302.4

SPILL MITIGATION PROCEDURES:
Hazardous concentrations in air may be found in local spill area and immediately downwind. Remove all sources of ignition. Stop source of spill as soon as possible and notify appropriate personnel.

AIR RELEASE: Vapors may be suppressed by the use of a water fog. All water utilized to assist in fume suppression, decontamination or fire suppression may be contaminated and must be contained before disposal and/or treatment.

WATER RELEASE: This material is heavier than water. This material is soluble in water. Monitor all exit water for available chlorine and pH. Advise local authorities of any contaminated water release.

LAND SPILL: Contact at 1-800-654-6911 immediately.
DANGER: All spills of this product should be treated as contaminated. Contaminated product may initiate a chemical reaction which may spontaneously ignite any combustible material present, resulting in a fire of great intensity. In case of a spill, separate all spilled product from packaging, debris and other material. Using a clean broom or shovel, place all spilled product into plastic bags, and place those bags into a clean, dry disposal container, properly marked and labelled. Disposal containers made of plastic or metal are recommended. Do not seal disposal containers tightly. Immediately remove all product in disposal containers to an isolated area outdoors. Place all damaged packaging material in a disposal container of water to assure decontamination (i.e. removal of all product) before disposal. Place all undamaged packaging in a clean, dry container properly marked and labelled. Call for disposal procedures.

SPILL RESIDUES:
Dispose of per guidelines under Section 12, WASTE DISPOSAL.

This material may be neutralized for disposal; you are requested to contact at 800-654-6911 before beginning any such operation.

PERSONAL PROTECTION FOR EMERGENCY SPILL AND FIRE-FIGHTING SITUATIONS:
Response to a large quantity spill (100 pounds or greater) or when dusting or decomposition gas exposure could occur requires the use of a positive pressure full face supplied air respirator or self contained breathing

apparatus (SCBA), chemical resistant gloves, coveralls and boots. In case of fire, this personal protective equipment should be used in addition to normal fire fighter equipment.

SECTION 12 WASTE DISPOSAL

If this product becomes a waste, it meets the criteria of a hazardous waste as defined under 40 CFR 261 and would have the following EPA hazardous waste number: D001.

If this product becomes a waste, it will be a hazardous waste which is subject to the Land Disposal Restrictions under 40 CFR 268 and must be managed accordingly.

As a hazardous solid waste, it must be disposed of in accordance with local, state, and federal regulations in a permitted hazardous waste treatment, storage and disposal facility by treatment.

CARE MUST BE TAKEN TO PREVENT ENVIRONMENTAL CONTAMINATION FROM THE USE OF THIS MATERIAL. THE USER OF THIS MATERIAL HAS THE RESPONSIBILITY TO DISPOSE OF UNUSED MATERIAL, RESIDUES AND CONTAINERS IN COMPLIANCE WITH ALL RELEVANT LOCAL, STATE AND FEDERAL LAWS AND REGULATIONS REGARDING TREATMENT, STORAGE AND DISPOSAL FOR HAZARDOUS AND NONHAZARDOUS WASTES.

SECTION 13 ADDITIONAL REGULATORY STATUS INFORMATION

TOXIC SUBSTANCES CONTROL ACT:
This substance is listed on the Toxic Substances Control Act inventory.

NSF LIMITS: NSF Maximum Drinking Water Use Concentration - 15 mg/l
as calcium hypochlorite product

SUPERFUND AMENDMENT AND REAUTHORIZATION ACT TITLE 3:
HAZARD CATEGORIES, PER 40 CFR 370.2:
HEALTH:
Immediate (Acute)
PHYSICAL:
Fire and Reactivity

EMERGENCY PLANNING AND COMMUNITY RIGHT TO KNOW, PER 40 CFR 355, APP.A:
EXTREME HAZARDOUS SUBSTANCE - THRESHOLD PLANNING QUANTITY:
None Established
SUPPLIER NOTIFICATION REQUIREMENTS, PER 40 CFR 372.45:
None Established

SECTION 14 ADDITIONAL INFORMATION

REGULATED UNDER FIFRA, USDA & FDA

MSDS REVISION STATUS: Revision to Section 11

SECTION 15 MAJOR REFERENCES

1. Ishidate, M. et al. (1984). Primary mutagenicity screening of food additives currently used in Japan. Fd. Chem. Toxicol. 22:623-636.
2. Hayashi, M. et al. (1988). Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals. Fd. Chem. Toxicol. 26:487-500.
3. Report on the Acute Inhalation in Rats, Acute Oral LD50 in Rats, Eye Irritation in Rabbits, Dermal Irritation in Rabbits, and Acute Dermal Toxicity in Rabbits of HTH. Biometric Testing Laboratories, Inc., Whippany, NJ. Experiment Reference #A-1490 (RC-30406), February 9, 1975.

4. Report on the Teratogenic Study with Calcium Hypochlorite in Albino Rats. Industrial Bio-Test Laboratories, Inc., Northbrook, IL. IBT #B758b, April 18, 1972.
5. Report on the Mutagenic Study with Monosodium Cyanurate and Calcium Hypochlorite (HTH) in Albino Mice. Industrial Bio-Test Laboratories, Inc., Northbrook, IL. IBT #E756. April 18, 1972.
6. Chemical Hazard Summary No. 20: Calcium Hypochlorite. Canadian Centre for Occupational Health and Safety, Hamilton, Ontario, Canada L8N 1H6. December 1986.
7. Report on 18-Month Dermal Carcinogenicity Study with Monosodium Cyanuric Acid and HTH in Swiss White Mice. Industrial Bio-Test Laboratories,Inc., Northbrook, IL, IBT #651-00751, April 9, 1974.
8. Report to PPG Industries, Inc. on the Acute Toxicity Studies with PITTCHLOR (Granular Calcium Hypochlorite). Industrial Bio-Test Laboratories, Inc., Northbrook, IL, IBT #601-06659, May 7, 1975.
9. Report on the Acute Toxicity of HTH to Bluegill, Rainbow Trout and the Water Flea. E G & G, Bionomics Aquatic Toxicology Laboratory, Wareham, MA, July 1977.
10. Report on the 8-Day Dietary LD50 Study with HTH in Mallard Ducklings. Industrial Bio-Test Laboratories, Inc., Northbrook, IL, IBT #651-06184, May 15, 1975.
11. Report on the 8-Day Dietary LC50 with HTH in Bobwhite Quail.Industrial Bio-Test Laboratories, Inc., Northbrook, IL, IBT #651-06183.
12. Final Report on the Acute Oral LD50 of Calcium Hypochlorite in Bobwhite Quail. Wildlife International, LTD., Easton, MD, Project #133-107, July 15, 1977.
13. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 52: Chlorinated Drinking Water; Chlorination By-Products; Some Other Halogenated Compounds; Cobalt and Cobalt Compounds. World Health Organization, International Agency for Research on Cancer (IARC), Lyon, France, 1991.
14. Sittig, Marshall, Handbook of Toxic and Hazardous Chemicals and Carcinogens, 2nd Ed., Noyes Publications, Park Ridge, NJ, 1985.
15. Chemical Hazard Response Information System (CHRIS), Vol. II, U.S. Coast Guard, Washington, D.C., 1984.
16. Chlorine and Your Health. The Chlorine Institute, Inc., Washington, D.C., August 1988.
17. ACGIH Documentation of the Threshold Limit Values and Biological Exposure Indices, Sixth Edition, 1991. American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH.
18. Amoore, John E. and Earl Hautala, Odor as an Aid to Chemical Safety: Odor Thresholds Compared with Threshold Limit Values and Volatiles for 214 Industrial Chemicals in Air and Water Dilution. Journal of Applied Toxicology, Vol. 3, No. 6, pp. 272-290, 1983.
19. Forsberg, K., and S.Z. Mansdorf, Quick Selection Guide to Chemical Protective Clothing, Second Edition, Van Nostrand Reinhold, N.Y., 1993.

Additional references are available upon request

Arch Chemicals, Inc.
MSDS Control
501 Merritt 7
PO Box 5204
Norwalk, CT 06856-5204

Univar USA Inc.
6100 Carillon Point
Kirkland, WA 98033
(425) 889-3400

For Emergency Assistance involving chemicals call - CHEMTREC (800) 424-9300

The Version Date for this MSDS is : 02/09/2004

****
PRODUCT IDENTIFICATION
****

PRODUCT NAME: ACCU-TAB CALCIUM HYPOCHLORITE TABLETS

MSDS#: 39151

DATE ISSUED: 01/02/04

SUPERSEDES: 08/11/03

ISSUED BY: 008812

MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME: Accu-Tab(R) SI Calcium Hypochlorite Tablets
PRODUCT ID: 59422
SYNONYMS: Calcium Hypochlorite Tablets; Cal Hypo Tablets; Ca(OCI)2;
MSDS No. 0122
ISSUE DATE: 01/02/2004
EDITION NO.: 10

PPG Industries, Inc.
One PPG Place, Pittsburgh, PA 15272, USA
24-hour Emergency Telephone Number: 1-304-843-1300
For Product Information (8am-5pm Eastern time):
1-800-245-2974 (Cal Hypo)

PREPARER: Product Safety, Chemicals

2. COMPOSITION/INFORMATION ON INGREDIENTS

Material/CAS Number	Percent
Calcium Hypochlorite	>65
7778-54-3	
Calcium Chlorate	<2

Drench with large quantities of water only. Do not use dry chemicals or foams. Product supplies own oxygen, therefore attempts to smother fire with a wet blanket, carbon dioxide, dry chemical extinguisher or other means are not effective.

SPECIAL FIREFIGHTING PROCEDURES:
Product decomposes at approximately 338-356 F (170-180 C) releasing oxygen gas. Container may rupture. Fire-fighters must wear NIOSH approved, pressure demand, self-contained breathing apparatus with full face piece for possible exposure to hazardous gases. Emits toxic fumes under fire conditions.

6. ACCIDENTAL RELEASE MEASURES

ACTION TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED:
Use extreme caution in handling spilled material. Do not mix with any other chemicals. Contamination with moisture, acids, organics or other easily combustible materials such as petroleum, paint products, wood or paper may cause fire or violent decomposition. If fire or decomposition occurs in area of spill, immediately douse with plenty of water. Otherwise, sweep up all visible material using a clean (new, if possible), dry shovel and broom and dissolve material in water. Spilled material that has been swept up and dissolved in water should be used immediately in the normal application for which this product is being consumed.

7. HANDLING AND STORAGE

PRECAUTIONS TO BE TAKEN DURING HANDLING AND STORAGE:
Store in a cool, dry, well-ventilated place. Keep in original container. Keep container closed when not in use. Keep away from heat, sparks, flames, direct sunlight, and other sources of heat, including lighted tobacco products. Use only a clean (new, if possible), dry scoop made of metal or plastic each time product is taken from the container. Do not add this product to any dispensing device containing remnants of any other product. Such use may cause violent reaction leading to fire or explosion. Add this product only to water. Never add water to product. Always add the product to large quantities of water. May cause fire or explosion if mixed with other chemicals. Fire may result if contaminated with acids, organic materials and other easily combustible materials such as oil, kerosene, gasoline, paint products wood and paper. Do not reuse container. Residual material remaining in empty container can react to cause fire. Thoroughly flush empty container with water then destroy by placing in trash collection. Do not contaminate water, food, or feed by storage or disposal of this product.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Limits:
8-hour Time Weighted Average (TWA); 15-minute Short-Term Exposure Limit (STEL)

OSHA:
The OSHA exposure limit(s) for Calcium hydroxide: 5 Mg/M3 TWA. Calcium carbonate: 15 Mg/M3 (total dust) 5 mg/m3 (respirable dust)

ACGIH:
The ACGIH exposure limit(s) for Calcium hydroxide: 5 Mg/M3 TWA Calcium carbonate: 10 Mg/M3 (total dust) 3 mg/m3 (respirable nuisance particulate) TWA.

PPG (IPEL): Calcium hypochlorite: 1 mg/ms TWA. 2 mg/m3 STEL.

RESPIRATORY PROTECTION:
Where the potential for exposure to dust exists, use the appropriate regulatory compliant full facepiece air-purifying respirator with acid gas cartridge and particulate prefilter. Carefully read and follow the respirator manufacturer's instructions and information.

VENTILATION:
Use local exhaust or general room/dilution ventilation sufficient to maintain employee exposure below permissible exposure limits.

EYE AND FACE PROTECTION:
Splash proof goggles and faceshield.

PROTECTIVE GLOVES:
Butyl rubber. Neoprene. Nitrile.

OTHER PROTECTIVE EQUIPMENT:
Boots, aprons, or chemical suits should be used when necessary to prevent skin contact.

9. PHYSICAL AND CHEMICAL PROPERTIES

BOILING POINT:	Decomposes at approximately 338-356 F (170-180 C)
VAPOR DENSITY (Air=1):	NA
SPECIFIC GRAVITY (Water-1):	NA
pH:	Alkaline
FREEZING/MELTING POINT:	NA
SOLUBILITY (wt.% in water):	217 g/l @ 27 C
BULK DENSITY:	67-71 lbs./cu.ft.
VOLUME % VOLATILE:	NA
VAPOR PRESSURE:	NA
EVAPORATION RATE:	NA
HEAT OF SOLUTION:	Slightly exothermic
PHYSICAL STATE:	Tablets
ODOR:	Slight chlorine
COLOR:	White

10. STABILITY AND REACTIVITY

STABILITY:
Unstable above 338 F (170 C).

HAZARDOUS POLYMERIZATION:
Will not occur.

INCOMPATIBILITY (CONDITIONS/MATERIALS TO AVOID):
Contamination. Excessive heat above 338 F (170 C). Moisture. Acids. Reducing agents. Organics. Combustible materials. Petroleum products. Paint products. Wood and paper.

HAZARDOUS THERMAL DECOMPOSITION/COMBUSTION PRODUCTS:
Acid or ammonia contamination will release toxic gases. Excessive heat will cause decomposition resulting in the release of oxygen and chlorine gas.

11. TOXICOLOGICAL INFORMATION

ACUTE INHALATION LC50:
No mortality at 3.5 mg/l (rat) (1 hour). Slight to very low toxicity.

ACUTE DERMAL LD50: >1000 mg/kg. (rabbit) Slight to very low toxicity.

SKIN IRRITATION: Corrosive.
EYE IRRITATION: Corrosive.
ACUTE ORAL LD50: .50 mg/kg. (rat) Moderate toxicity.

CARCINOGENICITY STATUS:
This product is NOT listed as a carcinogen or suspected carcinogen by NTP, IARC, ACGIH, or OSHA.

MEDICAL CONDITIONS AGGRAVATED:
None known.

EFFECTS OF OVEREXPOSURE:

ACUTE:
Inhalation: Inhalation of calcium hypochlorite dust and deposition of particles in the respiratory tract can lead to irritation of the tissue and cause a variety of effects. These effects are dependent on concentration and include: upper respiratory tract irritation, nasal congestion, coughing, sore throat, laryngitis and shortness of breath. In operations where there are high concentrations of respirable particulates, pulmonary edema (fluid in the lung) may be produced. If not treated immediately, pulmonary edema can be life threatening. Since this product is in granular or tablet form, particles of respirable size are not generally encountered.

Eye/Skin:
Calcium hypochlorite is corrosive to the eyes. Contact of calcium hypochlorite dust with the eyes, even a minute amount for a short duration, can cause severe irritation and even blindness. Contact with the skin may cause severe irritation, burns, or tissue destruction. In studies utilizing rabbits, the skin irritation score was 8/8 and the eye irritation score was 98.5/110.

Ingestion:
Calcium hypochiorite, if swallowed, causes severe burns to the digestive tract and can be fatal.

CHRONIC:

Genotoxicity:
Calcium hypochlorite produced positive responses in in-vitro assays using bacterial systems (the Ames test) and chromosomal aberrations in Chinese hamster fibroblasts. In a whole animal experiment (mouse micronucleus test), exposures ranging from 20 to 160 mg/kg produced no compound related chromosomal abnormalities.

Carcinogenisis:
Although no study has been conducted with calcium hypochlorite, the carcinogenic potential of sodium hypochlorite was studied in F344 rats. After 104 weeks of drinking water containing up to 2000 ppm sodium hypochlorite, there was no evidence that this chemical produced any carcinogenic response. In addition, this exposure did not result in any adverse effects

12. ECOLOGICAL INFORMATION

ECOTOXICOLOGICAL INFORMATION:
0.088 mg/l (Bluegill) 96-hour LC50. Extreme toxicity.

13. DISPOSAL CONSIDERATIONS

DISPOSAL METHOD:

CERCLA Hazardous Substance:
The following materials are listed as CERCLA Hazardous Substances in Table 302.4 of 40 CFR Part 302: Calcium Hypochlorite (7778-54-3)
RQ = 10 lbs./4.54 kg.

CANADA REGULATIONS (WHMIS): Class C - Oxidizing material.

FIFRA:
This product is registered with EPA as a pesticide.

16. OTHER INFORMATION

Other Information:
NSF Drinking Water Treatment Chemicals Listing - PPG calcium hypochlorite is certified for maximum use at 15 mg/L under NSF/ANSI Standard 60.

The following has been revised since the last issue of this MSDS:
Date. Edition. Section 1 has been updated. Section 5 has been updated. Section 8 has been updated. Section 9 has been updated. Section 11 has been updated. Section 12 has been updated.

Section 16 has been updated.

Previous revision date: 08/11/2003
Previous edition number: 009

NA = Not Available

For Additional Information:
Contact: MSDS Coordinator - Univar USA
During business hours, Pacific Time - (425) 889-3400

NOTICE
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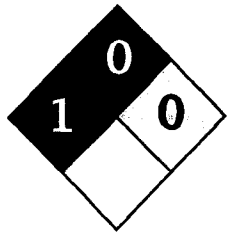

Health	1
Fire	0
Reactivity	0
Personal Protection	A

Material Safety Data Sheet
Sodium Thiosulfate, 1.0N MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium Thiosulfate, 1.0N

Catalog Codes: SLS3877

CAS#: Mixture.

RTECS: Not applicable.

TSCA: TSCA 8(b) inventory: Sodium thiosulfate anhydrous; Sodium carbonate; Water

CI#: Not available.

Synonym:

Chemical Name: Not applicable.

Chemical Formula: Not applicable.

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium thiosulfate anhydrous	7772-98-7	15.8
Sodium carbonate	497-19-8	0.2
Water	7732-18-5	84

Toxicological Data on Ingredients:

Section 3: Hazards Identification

Potential Acute Health Effects:
Slightly hazardous in case of skin contact (irritant, permeator), of eye contact (irritant), of ingestion, of inhalation. Non-sensitizer for skin.

Potential Chronic Health Effects:
Non-corrosive for skin. Non-irritant for skin. Non-sensitizer for skin. Non-permeator by skin. Non-irritating to the eyes. Non-hazardous in case of ingestion. Non-hazardous in case of inhalation.
CARCINOGENIC EFFECTS: Not available.
MUTAGENIC EFFECTS: Not available.
TERATOGENIC EFFECTS: Not available.
DEVELOPMENTAL TOXICITY: Not available.

The substance is toxic to lungs, mucous membranes.
Repeated or prolonged exposure to the substance can produce target organs damage.

Section 4: First Aid Measures

Eye Contact: Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used.

Skin Contact:
After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cold water may be used. Cover the irritated skin with an emollient. If irritation persists, seek medical attention.

Serious Skin Contact: Not available.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:
Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available.
Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:
Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:
Absorb with an inert material and put the spilled material in an appropriate waste disposal. Finish cleaning by

Solubility: Easily soluble in cold water, hot water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Slightly reactive to reactive with acids.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Not available.

Toxicity to Animals:
LD50: Not available.
LC50: Not available.

Chronic Effects on Humans: The substance is toxic to lungs, mucous membranes.

Other Toxic Effects on Humans:
Slightly hazardous in case of skin contact (irritant, permeator), of ingestion, of inhalation.
Non-sensitizer for skin.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: Sodium thiosulfate anhydrous; Sodium carbonate; Water

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC): R36- Irritating to eyes.

HMIS (U.S.A.):

Health Hazard: 1

Fire Hazard: 0

Reactivity: 0

Personal Protection: a

National Fire Protection Association (U.S.A.):

Health: 1

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:
Not applicable.
Lab coat.
Wear appropriate respirator when
ventilation is inadequate.
Safety glasses.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

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Last Updated: 01/11/2006 03:14 PM

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WESTERN CHEMICAL INC.
Product Purity & Environmental Stewardship

Material Safety Data Sheet

Section 1 – Product and Company Information

Product Name:	**Sodium Thiosulfate**
Brand	
Company	Western Chemical, Inc.
Street Address	1269 Lattimore Rd. Ferndale, WA 98248 USA
Technical phone:	360-384-5898
Fax:	360-384-0270
Emergency phone (Chemtrec)	**1-800-424-9300**
Date Updated:	June 2006
Reviewed By:	Jim Garnett

Section 2 – Composition/Information on Ingredient

Substance Name	CAS #	SARA 313
Sodium Thiosulfate	7772-98-7	No

Formula $Na_2S_2O_3$

Section 3 – Hazards Identification

Emergency Overview

CAUTION! MAY BE HARMFUL IF SWALLOWED OR INHALED. MAY CAUSE IRRITATION TO SKIN, EYES, AND RESPIRATORY TRACT.

HIMS Rating
- Health: 1
- Flammability: 0
- Reactivity: 1

NFPA Rating
- Health: 1
- Flammability: 0
- Reactivity: 0

Lab Protective Equipment: Goggles; Lab Coat; Proper Gloves

Potential Health Effects

Inhalation:
May cause irritation to the respiratory tract. Symptoms may include coughing and shortness of breath.

Ingestion:
Low level of toxicity by ingestion. Diarrhea may occur by ingestion of large quantities.

Skin Contact:
Irritation may occur from prolonged skin contact.

Eye Contact:
Contact may cause mechanical irritation.
Chronic Exposure:
Chronic exposure may cause skin effects.
Aggravation of Pre-existing Conditions:
No information found.

For additional information on toxicity, please refer to Section 11.

Section 4 – First Aid Measures

Inhalation:
Remove to fresh air. Get medical attention for any breathing difficulty.
Ingestion:
Induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person. Get medical attention.
Skin Contact:
Wash exposed area with soap and water. Get medical advice if irritation develops.
Eye Contact:
Wash thoroughly with running water. Get medical advice if irritation develops.

Section 5 – Firefighting Measures

Fire:
Not considered to be a fire hazard.
Explosion:
Not considered to be an explosion hazard.
Fire Extinguishing Media:
Use any means suitable for extinguishing surrounding fire.
Special Information:
Use protective clothing and breathing equipment appropriate for the surrounding fire.

Section 6 – Accidental Release Measures

Ventilate area of leak or spill. Wear appropriate personal protective equipment as specified in Section 8. Spills: Sweep up and containerize for reclamation or disposal. Vacuuming or wet sweeping may be used to avoid dust dispersal.

Section 7 – Handling and Storage.

Keep in a tightly closed container, stored in a cool, dry, ventilated area. Protect against physical damage. Isolate from incompatible substances. Containers of this material may be hazardous when empty since they retain product residues (dust, solids); observe all warnings and precautions listed for the product.

Section 8 – Exposure Controls/PPE

ENGINEERING CONTROLS

In general, dilution ventilation is a satisfactory health hazard control for this substance. However, if conditions of use create discomfort to the worker, a local exhaust system should be considered.

PERSONAL PROTECTIVE EQUIPMENT

For conditions of use where exposure to dust or mist is apparent and engineering controls are not feasible, a particulate respirator (NIOSH type N95 or better filters) may be worn. If oil particles (e.g. lubricants, cutting fluids, glycerine, etc.) are present, use a NIOSH type R or P filter. For emergencies or instances where the exposure levels are not known, use a full-face positive-pressure, air-supplied respirator. WARNING: Air-purifying respirators do not protect workers in oxygen-deficient atmospheres.

Skin Protection:

Wear protective gloves and clean body-covering clothing.

Eye Protection:

Safety glasses. Maintain eye wash fountain and quick-drench facilities in work area.

Section 9 – Physical/Chemical properties

Appearance:

Monoclinic, colorless crystals.

Odor:

Odorless.

Solubility:

79g/100 ml water @ 4C (39F)

Density:

1.75

pH:

No information found.

% Volatiles by volume @ 21C (70F):

0

Boiling Point:

> 100C (> 212F)

Melting Point:

48C (118F) Loses water @ 100C (212F)

Vapor Density (Air=1):

No information found.

Vapor Pressure (mm Hg):

No information found.

Evaporation Rate (BuAc=1):

No information found.

Section 10 – Stability and Reactivity

Stability:
Stable under ordinary conditions of use and storage. Stability limited in solution.
Hazardous Decomposition Products:
Oxides of sulfur and hydrogen sulfide.
Hazardous Polymerization:
Will not occur.
Incompatibilities:
Sodium nitrate, halogens, and oxidizing agents. Reacts with acids to release sulfur dioxide.
Conditions to Avoid:
Incompatibles.

Section 11 – Toxicological Information

No LD50/LC50 information found relating to normal routes of occupational exposure.

--------\Cancer Lists\----------

Ingredient	Known	---NTP Carcinogen--- Anticipated	IARC Category
Sodium Thiosulfate (7772-98-7)	No	No	None

Section 12 – Ecological Information

No data available.

Section 13 – Disposal Considerations

Whatever cannot be saved for recovery or recycling should be managed in an appropriate and approved waste disposal facility. Processing, use or contamination of this product may change the waste management options. State and local disposal regulations may differ from federal disposal regulations. Dispose of container and unused contents in accordance with federal, state and local requirements.

Section 14 – Transport Information

DOT

Proper shipping name: None
Considered non-hazardous for transport.

IATA

Considered non-hazardous for air transport.

Section 15 – Regulatory Information

--------\Chemical Inventory Status - Part 1\----------

Ingredient	TSCA	EC	Japan	Australia
Sodium Thiosulfate (7772-98-7)	Yes	Yes	Yes	Yes

--------\Chemical Inventory Status - Part 2\----------

Ingredient	Korea	--Canada-- DSL	NDSL	Phil.
Sodium Thiosulfate (7772-98-7)	Yes	Yes	No	Yes

--------\Federal, State & International Regulations - Part 1\--------

Ingredient	-SARA 302- RQ	TPQ	------SARA 313------ List	Chemical Catg.
Sodium Thiosulfate (7772-98-7)	No	No	No	No

--------\Federal, State & International Regulations - Part 2\--------

Ingredient	CERCLA	-RCRA- 261.33	-TSCA- 8(d)
Sodium Thiosulfate (7772-98-7)	No	No	No

Chemical Weapons Convention: No TSCA 12(b): No CDTA: No
SARA 311/312: Acute: Yes Chronic: No Fire: No Pressure: No
Reactivity: No (Pure / Solid)

Section 16 – Other Information

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. The burden of safe use of our materials must rest with the user. We cannot assume responsibility for the completeness or accuracy of any information supplied by us concerning the hazards and recommended use of this product.

TRICAINE-S

Brand of Tricaine Methanesulfonate
For Anesthesia and Tranquilization of Fishes and
Other Cold-Blooded Animals
KEEP TIGHTLY CLOSED.
USE ONLY FRESH SOLUTION.
CAUTION: It is imperative to read accompanying descriptive literature before using this drug.
Store at room temperature
(Approximately 25°C)
KEEP OUT OF REACH OF CHILDREN

TRICAINE-S is intended for the temporary immobilization of fish, amphibians, and other aquatic, cold-blooded animals. It has long been recognized as a valuable tool for the proper handling of these animals during manual spawning (fish stripping), weighing, measuring, marking, surgical operations, transport, photography, and research.

WARNINGS

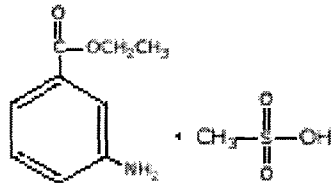
Do not use within 21 days of harvesting fish for food.

When used in food fish, use should be restricted to Ictaluridae, Salmonidae, Esocidae, and Percidae and water temperature should exceed 10°C. (50°F.).

In other fish and other cold-blooded animals (poikilotherms), TRICAINE-S should be limited to hatchery or laboratory use.

CHEMISTRY

TRICAINE-S is the methanesulfonate of meta-amino benzoic acid ethylester, or simply ethyl m-amino benzoate. It is thus an isomer of benzocaine having the formula $C_9H_{11}O_2N + CH_3SO_3H$ and the following structure:



TRICAINE-S is a fine white crystalline powder. Its molecular weight is 261.3. Soluble to 11%, it forms clear, colorless acid solutions in water.

TOXICOLOGY

Comparative toxicological studies carried out on fish and frogs gave the following results:

FISH TOXICITY STUDIES - The toxicity 1 of TRICAINE-S was measured by standard methods in laboratory bioassays with rainbow trout, brown trout, brook trout, lake trout, northern pike, channel catfish, bluegill, largemouth bass, and walleye. The 24, 48, and 96 hour LC50 (lethal concentration for 50 per cent of the animals) values for trout ranged from 52 to 31 mg/liter; for northern pike, from 56 to 48 mg/liter; for catfish, from 66 to 50 mg/liter; for bluegill and largemouth bass, from 61 to 39 mg/liter; for the walleye, the values were 49 to 46 mg/liter.

Safety index: The safety indices for TRICAINE-S refer to the margin between concentrations which cause anesthesia and mortality. They expressed by the quotient of the lethal concentration for 50 per cent of the fish (LC50) and the effective concentration for 50 per cent of the fish (EC50).

Safety Indices for Rainbow Trout and Channel Catfish at 12℃ (54℉)

Species	Exposure Minutes	LC_{50} (mg./liter)	EC_{50} (mg./liter)	Index
Rainbow trout[2]	15	65	32	2.0
"	30	57	32	1.8
"	60	56	29	1.9
Channel catfish[2]	15	139	47	3.0
"	30	118	45	2.6
"	60	110	46	2.4

FROG TOXICITY STUDIES[3] - Frogs were put into various concentrations of TRICAINE-S for 30 minutes and then transferred to tap water in order to determine the LC50. The LC50 was 6.2 per cent TRICAINE-S. Therefore, the anesthetic must be used in very high concentration before it is fatal to frogs.

I. DIRECTIONS FOR USE ON FISH

CONCENTRATIONS

TRICAINE-S is effective and safe for the anesthesia of fish when used as directed. Its use is governed by, and can be tailored to, the needs of individual fishery personnel. Sedation and various rates of anesthetization are controlled by the concentration. The versatility of TRICAINE-S is demonstrated by the fact that it has been used in fisheries at levels ranging from 10 to 1,000 mg/liter[3]. The action of the anesthetic is slowed at cooler temperatures, in extremely soft water (approximately 10 mg/liter of $CaCO_3$, or less), and in larger fish[4]. Also, efficacy may vary with species[4]. **Thus, it is imperative that preliminary tests of anesthetic to determines the desired rates of anesthesia and exposure times for the specific lots of fish under prevailing conditions.**

The following tables may be used as guidelines in selecting concentrations of TRICAINE-S for the anesthetization of various fishes:

Table 1: Concentration Required for Rapid Anesthesia
(Induction time less than 2-5 minutes; used in spawning, marking, measuring, and some surgical operations)

Fish	Temperature	Concentration (mg./liter)	Max. tolerated exposure time* min.)	Recovery time in fresh water (min.)
Salmonidae[4] (Pacific and Atlantic salmon;trout;chars;etc)	7-17° C (45-63° F)	80-135	4-12	3-19
Esocidae[3] (Northern pike; muskellunge)	8-12° C (46-54° F)	150	8-28	8-31
Cyprinidae[2] (Carp; goldfish)	16° C (61° F)	150-200		
Ictaluridae[4] (Channel catfish)	7-27°C (45-81° F)	140-270	4-11	3-24
Centrarchidae[5] (Bluegill;largemouth bass)	10-27° C (50-81° F)	260-330	3-5	7-11
Percidae[5] (Walleye)	10-16° C (50-61° F)	100-120	7-18	5-40
Pet and Tropical[7] Live bearers Egg layers	24-27° C (75-81° F) 24-27° C (75-81° F)	85 75	12 hrs. 12 hrs.	

Table 2: Concentration Required for Moderately Rapid Anesthesia
(Induction time less than 15-20 minutes; used in surgical operations and in spawning and marking where longer exposures are more important than rapid immobilization)

Fish	Temperature	Concentration (mg/liter)	Max. tolerated exposure time* (min.)	Recovery time in fresh water (min.)
Salmonidae[4] (Pacific and Atlantic salmon;trout;chars;etc..)	7-17° C (45-63° F)	50-60	30 or >	2-20
Ictaluridae[4] (Channel catfish)	7-27°C (45-81° F)	70	30 or >	1-10

*Maximum tolerated exposure time (in minutes) of fish to TRICAINE-S olution.

Table 3: Concentration MS-222 Required for Sedation
(Induction within 15 minutes; used in fish transport)

Fish	Temperature	Concentration (mg/liter)	Maintenance of sedation (hr.)
Salmonidae[4] (Pacific and Atlantic salmon;trout;chars;etc..)	7-17° C (45-63° F)	15-30	6
Esocidae[3] (Chain pickerel)	8-12° C (46-54° F)	40	
Ictaluridae[2] (Channel catfish)	7-27°C (45-81° F)	20-40	6
Centrarchidae[5] (Bluegills)	10-27° C (50-81° F)	25	8-13
Pet and Tropical[6] [Bettas, Piranhas, etc. (uncrowded)	24-27° C (75-81° F)	66	48
Goldfish]	24-27° C (75-81° F)	37	48

IMPORTANT: Since, in many cases, relatively rapid rates of anesthesia can be achieved only by exceeding the lethal concentration of TRICAINE-S, it is necessary to return anesthetized fish to fresh water before they are overexposed. Excessive exposures are avoided by bserving the following sensory and motor responses of the fish which characterize progressively deeper levels of anesthesia.

Sedation - Decreased reactivity to visual and vibrational stimuli; opercular activity reduced.

Total loss of equilibrium - Fish turns over; locomotion increases; fish swims or extends fins in response to pressure on caudal fin or peduncle.

Total loss of reflex - No response to pressure on caudal fin or peduncle; opercular rate slow and erratic.

Medullary collapse - Opercular activity ceases.

Laboratory and field investigations[3,9], have shown that the action of TRICAINE-S is readily reversed when the fish are transferred to fresh water before opercular activity ceases. *Additional exposure following medullary collapse may result in mortality.* A rough estimate of the safe total exposure can be made by multiplying the time required for anesthesia by a factor of 2 or 3.

WATER
Since TRICAINE-S is very soluble (1:9) in water, it dissolves with equal readiness in spring water, tap water, or seawater. *Do not use distilled or deionized water, or water containing chlorine, heavy metals (copper, zinc, etc.), or other toxic contaminants.* The anesthetic solution should be well oxygenated, and its temperature should be similar to that of the water from which fish are taken. In the field, many water quality problems are eliminated by using natural water to which the fish are acclimated, provided the water does not possess high chemical or biologic oxygen demand.

METHODS OF APPLICATION

1. General anesthesia: - For most situations where rapid or moderately rapid anesthesia is required, TRICAINE-S may be applied in a bath, i.e., the fish are immersed in the anesthetic solution. Containers may be of glass, plastic, steel, aluminum, or other suitable material. *However, do not use galvanized or brass containers unless treated or sealed to prevent dissolution of zinc.* Size of container is determined by individual needs, but t he fish should not be overcrowded. Discard anesthetic solutions when a loss in potency is noted, or when the solutions become fouled with mucus or excrement.

2. For surgery and certain physiologic studies, the fish may be anesthetized to loss of reflex, removed from the anesthetic, and then positioned so that the gills are bathed in a sedating concentration of TRICAINE-S. Some investigators have developed flowing, recirculating systems for bathing the gills with anesthetic during surgery.

Large fishes such as sharks and rays are anesthetized within minutes by spraying the gills with a 1g./liter solution of TRICAINE-S[10] . The application is made by means of a water pistol, bulb syringe, hand pump, etc.

3. Transport - TRICAINE-S has been used to sedate fish during transport. It is more successful in cold than in warm water, and it is instrumental in reducing injuries because of hyperactivity. Fish are usually transported by means of distribution units (tank trucks), or by air in plastic bags[11,12]. In either case, the fish should be fasted before-hand to reduce metabolic wastes. Also, some workers suggest pre-transport sedation for several hours to lower metabolism. With distribution units, the fish may be fasted and sedated prior to loading. The anesthetic solution is prepared in the distribution unit and oxygenated. Then, the fish are added and temperature acclimated.

In air shipments, the anesthetic solution is placed in a suitable plastic bag, the sedated fish are added, the bag inflated with oxygen, tied securely, and placed in a second bag. This bag is also tied, and then placed on ice in an insulated container[13]. A modification of this method involves complete anesthesia of the fish, and placing them in water bags which contain no anesthetic. In any case, upon arrival, the fish should be acclimated slowly to new environmental temperatures.

PREPARATION OF TRICAINE-S® SOLUTIONS

Prior to use, TRICAINE-S may be weighed out into amounts which are convenient for the volume of water to be used. A handy unit is 2 g. since this quantity in 5 gallons of water yields a concentration of about 100 mg/liter. For rough approximations, one level teaspoonful contains 2.0 to 2.5 g. Thus a level teaspoonful of anesthetic in 5 gallons gives a concentration of about 120 mg/liter.

To convert mg/liter into g/gal.: multiply number of mg. by 0.00378

e.g. 80 mg/liter = 80 x 0.00378 = .0302 g./gal.

To convert mg/liter into a ratio of TRICAINE-S to water: divide 1,000,000 by the number of mg.

e.g. 80 mg/liter = 1,000,000 / 80 = 1:12,500

LIMITATIONS IN USE

Since TRICAINE-S is taken up into the blood of fish, residues of the drug may occur in edible tissues. However, the residues dissipate rapidly after the fish are placed in fresh water[14]. Thus, *treated fish which may be used for food must be held in fresh water above 10℃. (50℉.) for a perio d of 21 days.*

Withdrawal in fresh water is unnecessary for non food fishes such as goldfish, bait fish, and ornamentals. Also, withdrawal is unnecessary for sublegal sizes of the following species of fish because they are not used as food immediately following anesthesia (Table 4).

Table 4 - Sublegal Sizes of Fish Species not used as Food Immediately after Anesthesia 15

Species	Size (in.)	Species	Size (in.)
Pink salmon	6	Lake trout	5
Chum salmon	6	Splake trout	6
Coho Salmon	6	Grayling	6
Sockeye salmon	6	Northern pike	12
Chinook Salmon	6	Muskellunge	12
Cutthroat trout	6	Channel catfish	6
Steelhead trout	8	Flathead catfish	6
Rainbow trout	6	Bluegill	3
Atlantic salmon	10	Redear sunfish	3
Brown trout	6	Smallmouth bass	5
Brook trout	6	Largemouth bass	5
		Walleye	6

PRECAUTIONS

1. Avoid inhaling TRICAINE-S or getting it into the eyes.
2. Always conduct preliminary tests with TRICAINE-S to determine desired rates of anesthesia and optimal length of exposure.
3. Do not overexpose fish to lethal levels of TRICAINE-S.
4. Do not anesthetize more fish than can be handled effectively.
5. Do not contaminate eggs or sperm with TRICAINE-S when stripping fish.
6. Do note use water containing chlorine, or other toxic agents.
7. Insure adequate oxygen in anesthetic solution.
8. Discard anesthetic solutions when fouled with mucus or metabolic wastes.
9. Do not discard TRICAINE-S solutions into water supplies of natural waters.
10. Store TRICAINE-S solutions in a cool place away from light.*
11. Discard stock solutions of TRICAINE-S after several days.*
12. Treated fish destined for food must be held in fresh water above 10℃. (50℉.) For 21 days before use.

*The color of TRICAINE-S solutions may change rapidly to yellow or brown when exposed to light. This does not affect activity in any significant way. However, for best results use freshly prepared solutions. A 10 per cent solution stored at room temperature shows no significant loss of potency after three days, but after 10 days, a brownish color and an activity decrease of about 5 per cent is observed.

II. GUIDELINES FOR USE ON AMPHIBIANS

Table 5. Effects of Varying Concentrations of TRICAINE-S on Salamanders

Salamander	Concentration*	Duration of Anesthesia *	Remarks
EMBRYOS	1:10,000 (3b)	2 days	No adverse effects
Ambystoma opacum	1:3,000 (3c)	To 30 min.	"
LARVAE	1:1,0000 (3b)	2 days	"
	1:12,000(3f)	10-15 min.	
	1:20,000(3f)	10-15 min.	"
Ambystoma opacum	1:3,000 (3c)	To 30 min.	"
ADULTS	1:1,000 (3b)	Few min.	"
	1:3,000 (3b)	3 day	"
Newts	1:1,000 (3b)	Few min.	"
	1:10,000 (3b)	2 days	"
Triturus sp.	1:1,000 (3k)	20 min.	"
Triturus viridescens	1:3,000 (3g)	1 hour	"
Mole salamanders *Ambystoma opacum*	1:3,000 (3c)	To 30 min.	"
Ambystoma tigrinum	1:2,000 (3j)		"
Ambystoma punctatum	1:2,000 (3j)	15-30 min.	"
Mud-puppy *Necturus maculosus*	1:1,500 (3i)	To 6 hours	Maintenance does, 0.1 of induction concentration. At exposure to induction concentration of more than 20-30 min., renal circulation becomes sluggish or stops.

*When an individual of any of the species listed is exposed at the designated concentration, the data available suggest that the animal may be safely maintained under anesthesia for the time noted. Prolonging exposure to the anesthetic beyond the time indicated may cause deaths. See PRECAUTIONS.

Table 6 - Effects of Varying Concentrations of TRICAINE-S on Frogs

Frog	Concentration*	Duration of Anesthesia *	Remarks
EMBRYOS	1:1,000 (3b)	few min.	No adverse effects
	1:10,000 (3b)	2 days	"
	1:15,0000 (3h)	3 days	"
TADPOLES	1:1,000(3j)	30 min.	No adverse effects
	1:3,000(3f)	10-15 min.	"
	1:10,000 (3b)	2 days	"
	1:15,000 (3h)	3 days	"
Rana sp.	1:5,000 (3k)	5 hours	No adverse effects
Rana pipiens	1:1,000 (3j)	15-30 min.	"
	1:3,333 (3a)	2 min.	"
	variable (3d)	1 hour	"
ADULTS	1:1,000 (3c)	30 min.	No adverse effects
Leopard frog *Rana pipiens*	1:3,000 (3c)	to 30 min.	No adverse effects
Eastern wood frog *Rana sylvatica*	1:8,000 (3j)	5-10 min.	Only slightly under anesthesia.

* When an individual of any of the species listed is exposed at the designated concentration, the data available suggest that the animal may be safely maintained under anesthesia for the time noted. Prolonging exposure to the anesthetic beyond the time indicated may cause deaths. See PRECAUTIONS.

AVAILABILITY OF TRICAINE-S

Bottles of Net Wt. 3.5 oz. (100 grams), and Net Wt. 2.2 lb. (1000 grams)

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REFERENCES

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3. Personal communications:
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    b. Butler, E.G., Princeton University, Dept. of Biology, Princeton, N.J.
    c. Dalton, H.D., and Charipper, H.A., Washington Square College, Dept. Of Biology, New York, N.Y.
    d. Etkin, W., City College, Dept. Of Biology, New York, N.Y.
    e. Goss, R.J., Brown University, Providence, R.I.
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    h. Rose, S.M., University of Illinois, Urbana, Ill.
    i. Schatzmann, J.H., Harvard Medical School, Boston, Mass.
    j. Taylor, A.C., Rockefeller Institute of Medical Research, New York, N.Y.

k. Thornton, C.S., Kenyon College, Dept. of Biology, Gambier, Ohio.
l. Van Stone, J.M., Trinity College, Dept. of Biology, Hartford, Conn.
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Manufactured by:

WESTERN CHEMICAL
Product Purity & Environmental Stewardship

Western Chemical Inc.
1269 Lattimore Road
Ferndale, WA 98248
(800) 283-5292
(360) 384-5898
FAX (360) 384-0270

DERMAL EXPOSURE

In case of contact, immediately wash skin with soap and copious amounts of water.

EYE EXPOSURE

In case of contact with eyes, check for and remove contact lenses, then flush with copious amounts of water for at least 15 minutes. Assure adequate flushing by separating the eyelids with fingers. Call a physician.

Section 5 – Firefighting Measures

FLASH POINT

N/A

AUTO-IGNITION

N/A

FLAMMABILITY

N/A

HAZARDOUS DECOMPOSITION PRODUCTS: Combustion products are carbon oxides (CO, CO_2), nitrogen oxides (NO, NO_2....), and sulfur oxides (SO_2, SO3,...).

EXTINGUISHING MEDIA

Water Spray, carbon dioxide, dry chemical powder, or appropriate foam. Do not use water jet.

FIREFIGHTING

Wear self contained breathing apparatus and protective clothing to prevent contact with skin and eyes. Emits toxic fumes under fire conditions.

Section 6 – Accidental Release Measures

PROCEDURE(S) OF PERSONAL PRECAUTION(S)

Exercise appropriate precautions to minimize direct contact with skin or eyes and prevent inhalation of dust.

METHODS FOR CLEANING UP

Sweep up, place in a bag, and hold for disposal. Avoid breathing dust. Ventilate area and wash spill site after picking up material.

Section 7 – Handling and Storage.

HANDLING

Avoid inhalation, contact with eyes, skin, and clothing. Avoid repeated or prolonged exposure.

STORAGE

Keep container tightly closed. Keep away from heat, open flame, and strong oxidizing agents. Ground all storage and handling equipment.

Section 8 – Exposure Controls/PPE

ENGINEERING CONTROLS

Have safety shower and eye bath available. Mechanical exhaust required.

PERSONAL PROTECTIVE EQUIPMENT

Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Where risk assessment shows air-purifying respirators are appropriate, use type N95 (US) or type P1 (EN 143) respirator. Use protective gloves, chemical safety goggles, boots, and apron or lab coat.

Section 9 – Physical/Chemical properties

APPEARANCE

Color	white
Physical Form	Crystalline powder
Molecular weight	261.29 AMU
pH	N/A
BP/BP Range	N/A
MP/MP Range	147 – 150 °C
Freezing Point	N/A
Vapor Pressure	N/A
Vapor Density	N/A
Saturated Vapor Density	N/A
SG/Density	N/A
Bulk Density	N/A
Odor threshold	N/A
Volatile %	N/A
VOC content	N/A
Water content	<0.1%
Solvent content	N/A
Evaporation rate	N/A
Viscosity	N/A
Partition Coefficient	N/A
Decomposition Temperature	N/A
Flash point °F	N/A
Flash point °C	N/A
Explosion limits	N/A
Auto-ignition temperature	N/A
Solubility	highly soluble in water.

N/A = Not Available

Section 10 – Stability and Reactivity

Stability

Stable.

Conditions to Avoid

Excessive heat or open flame.

Materials to Avoid

Strong Oxidizing agents.

Hazardous Polymerization

Will not occur.

Section 11 – Toxicological Information

Route of Exposure

Skin Contact: May cause skin irritation.
Skin Absorption: May be harmful if absorbed through the skin.
Eye contact: may cause eye irritation.
Inhalation: Dust may be irritating to the mucous membranes and upper respiratory tract. May be harmful if inhaled.
Ingestion: may be harmful if swallowed.

Signs and symptoms of exposure

To the best of our knowledge, the chemical, physical, and toxological properties have not been thoroughly investigated.

Toxicity to animals

Intravenous
Mouse
180 mg/Kg
LD50

Section 12 – Ecological Information

To the best of our knowledge the toxicity to the environment has not been fully explored yet.

Section 13 – Disposal Considerations

Appropriate Method of Disposal of Substance or Preparation

Contact a licensed professional disposal service to dispose of this material. Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. Observe all federal, state, and local regulations.

Section 14 – Transport Information

DOT

Proper shipping name: None
Considered non-hazardous for transport.

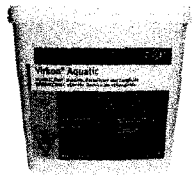
NADA 200-226Approval Date: November 21, 1997
Freedom of Information Summary
NADA 200-226
I. GENERAL INFORMATION:
NADA200-226
Sponsor: Western Chemical, Inc.
Western Chemical, Inc.
1269 Lattimore Road
Ferndale, WA 98248
Generic Name:tricaine methanesulfonate
Trade Name:Tricaine-S
Marketing Status:Over the Counter (OTC)

2. Indications for Use:
TRICAINE-S is intended for the temporary immobilization of fish, amphibians, and other aquatic, cold-blooded animals. It has been recognized as a valuable tool for the proper handling of these animals during manual spawning (fish stripping), weighing, measuring, marking, surgical operations, transport, photography, and research.
3. Dosage Form(s), Route(s) of Administration and Recommended Dosages and Contraindications:
a. Dosage Form:
The product is available in the form of a crystalline powder to be mixed in water for immersion of the animal.
b. Route(s) of Administration and Recommended Dosage:
The route of administration is immersion of the animal at levels ranging from 10 to 1,000 mg/liter .
4. Effectiveness and Bioequivalency:
Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act, (53 FR 50460, December 15, 1988, First GADPTRA Policy Letter) an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety data, drug effectiveness data, and human food safety data (other than tissue residue data) are not required for approval of an ANADA. Instead, the ANADA sponsor must show that the generic product is bioequivalent to the pioneer. For certain dosage forms, the agency will grant a waiver from conducting an in vivo bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, April 1996).
Based on the formulation characteristics of the generic product (single pure active ingredient), Western Chemical, Inc. was granted a waiver from the requirement of an in vivo bioequivalence study for the generic product TRICAINE-S (tricaine methanesulfonate). The generic product is administered as an solution and contains the same active ingredients in the same concentration as the pioneer product.
5. Animal Safety:
Since this drug is a generic copy of the brand name drug whose safety has been established, no safety studies have been required for this application.
6. HUMAN FOOD SAFETY
Withdrawal Time
When a waiver from the requirement of an in vivo bioequivalence study is

granted, the withdrawal times established for the pioneer product apply to the generic product.
Do not use within 21 days of harvesting fish for food.
When used in food fish, use should be restricted to Ictaluridae, salmonidae, Esocidas, and Percidae and water temperature should not exceed 10°C (50°F).
Expiry Time: 24 months.

7. AGENCY CONCLUSIONS
This ANADA submitted under section 512(b) of the Federal Food, Drug, And Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that TRICAINE-S, when used under its proposed conditions of use, is safe and effective for the labeled indications.
Attachments:
Facsimile labeling for generic TRICAINE-S:
3.5 oz (100 grams) and 2.2 lb. (1 kilogram)
Approved pioneer labels and package insert for FINQUEL® sponsored by Argent Chemical, Inc.
3.5 oz (100 grams) and 2.2 lb. (1000 grams)
Copies of applicable labels may be obtained by writing to the:
Freedom of Information Office
Center for Veterinary Medicine, FDA
7500 Standish Place
Rockville, MD 20855

Virkon® Aquatic



Virkon® Aquatic - Directions for General Use

A 1% Virkon® Aquatic solution is recommended for cleaning and disinfection of surfaces associated with aquaculture including: vehicles, boats, nets, boots, waders, dive suits, & other equipment.

Mix the Virkon® Aquatic powder with clean water according to the dilution instructions in the following table.

For heavily soiled surfaces, it is recommended to clean with an appropriate detergent prior to disinfection.

Dilution Instructions

	% Dilution Required		
	0.5% (1:200)	**1.0% (1:100)**	**2.0% (1:50)**
Final Disinfectant Solution Required	Quantity of Virkon® Aquatic Powder Required		
1 Quart	**0.15 ounces**	**0.3 ounces**	**0.7 ounces**
1 Gallon	**0.65 ounces**	**1.3 ounces ***	**2.7 ounces**
10 Gallons	**6.7 ounces**	**13.4 ounces**	**26.7 ounces**
50 Gallons	**33.4 ounces**	**66.8 ounces**	**133.5 ounces**

1. Do not apply Virkon® Aquatic powder directly on surfaces you are trying to disinfect, always mix with water first.
2. Always make your solution in a clean container of known volume.
3. Measure the correct amount of Virkon® Aquatic powder using the measuring scoop provided.
   - * The scoop holds approximately 1.3 ounces of Virkon® Aquatic powder, which when added to 1 gallon of water will make a 1.0% disinfectant solution.
4. Stir the mixture to dissolve the Virkon® Aquatic powder.
5. Apply the solution to the surfaces to be disinfected, wait for the recommended contact time, and follow with a clean water rinse.
   - One gallon of solution is sufficient to disinfect approximately 135 sq ft.
6. Virkon® Aquatic solutions are stable for up to 7 days. Test strips are available to determine the mixed solution's strength.

Virkon® Aquatic is US EPA (Reg. No. 71654-6) and Health Canada (DIN # 02276356) approved and is available in 10 lb. (4.53 kg) plastic tubs in the US and in 22 lb (10 kg) plastic tubs in Canada

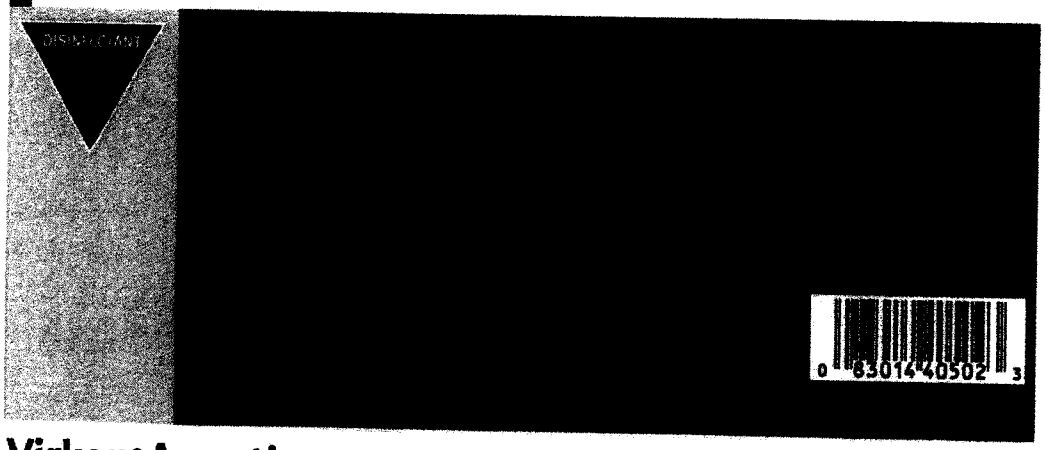
The
AQUATIC LIFE SCIENCES
Companies

Available in Canada from
Syndel Laboratories Ltd
(800) 663-2282
www.syndel.com

Available in the USA from
Western Chemical Inc
(800) 283-5292
www.wchemical.com

Virkon® Aquatic

DISINFECTANT AND VIRUCIDE



Virkon® Aquatic

DISINFECTANT AND VIRUCIDE

VIRKON® AQUATIC DISINFECTANT AND VIRUCIDE DILUTION CHART

Fill container with desired amount of water and add Virkon® Aquatic Disinfectant and Virucide to achieve recommended solution concentration.

Solutions are stable for 7 days. Do not soak metal objects in Virkon® Aquatic Disinfectant and Virucide for long periods - 10 minutes is maximum necessary contact time. One gallon of solution is sufficient to treat 135 sq. ft.

Measuring cup provided.

Quantity of Water	0.5% Solution*	1% Solution	2% Solution
1 Quart	0.15 ounces*	0.3 ounces	0.7 ounces
1 Gallon	0.65 ounces*	1.3 ounces	2.7 ounces
10 Gallons	6.7 ounces*	13.4 ounces	26.7 ounces
50 Gallons	33.4 ounces*	66.8 ounces	133.5 ounces

**The 0.5% solution currently is not approved for use in California.*

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

AQUACULTURE

Not approved for this use in California Virkon® Aquatic Disinfectant and Virucide is intended to disinfect inanimate environmental surfaces associated with aquaculture including vehicles, nets, boots, waders, dive suits, hoses, brushes and other similar equipment. Virkon® Aquatic Disinfectant and Virucide may also be used in foot dips.

Virkon® Aquatic Disinfectant and Virucide must not be applied directly to water.

Equipment used in separate sites, tanks, ponds in aquacultural settings should be disinfected before each new use by soaking for 20-30 minutes in a 1% Virkon® Aquatic Disinfectant and Virucide solution followed by a water rinse.

EFFECTIVE AGAINST THE FOLLOWING PATHOGENS:
ANIMAL AND ZOONOTIC PATHOGENS

BACTERIA
- *Actinobacillus pleuropneumoniae*
- *Klebsiella pneumoniae*
- *Streptococcus pyogenes*
- *Mycobacterium bovis*
- *Mycoplasma mycoides*
- *Pseudomonas aeruginosa*
- *Escherichia coli*
- *Staphylococcus aureus*
- *Salmonella typhimurium*
- *Listeria monocytogenes*

VIRUSES
- *Infectious Pancreatic Necrosis Virus*
- *Snakehead rhabdovirus*
- *Infectious Salmon Anaemia Virus*

FUNGI
- *Aspergillus fumigatus*

Manufactured for:
E. I. du Pont de Nemours and Company
DuPont Animal Health Solutions
PO Box 80023
Wilmington, DE 19880-0023 USA
www.aha.dupont.com

Questions? Call 1-800-441-7515
Outside the US, contact: 1-302-774-1000

CCL-03
New 10/20/06

Virkon® Aquatic

DISINFECTANT AND VIRUCIDE

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER. Powder is Corrosive. Causes irreversible eye damage or skin burns. Harmful if swallowed or absorbed through the skin. Do not get in eyes, on skin or on clothing. Wear goggles (or face shield). Wear protective clothing (long sleeve shirt and long pants, socks plus shoes and chemical resistant gloves such as water proof gloves). Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

Corrosive statement refers to powder only not in use solution.

STORAGE AND DISPOSAL

Store in a cool, dry place in a tightly closed container away from children. Always replace lid after use.

Wash empty container thoroughly and dispose in trash. Do not mix this chemical with other chemicals.

ENVIRONMENTAL HAZARDS:

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

BROAD SPECTRUM DISINFECTANT:

Virkon® Aquatic Disinfectant and Virucide is effective against numerous microorganisms: viruses, gram positive and gram negative bacteria, fungi (molds and yeasts) and mycoplasma. Efficacy of the 1% solution against bacteria and viruses was determined in the presence of 400 ppm AOAC hard water and 5% organic material in most cases.

The exceptions are noted with qualifiers, e.g., "no hard water," "no soil load," and "use 2% solution."

The MSDS format adheres to the standards and regulatory requirements of the United States and may not meet regulatory requirements in other countries.

Virkon(R) Aquatic
ANTEC055 Revised 6-DEC-2006

CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Product Use

Animal Premises' Disinfectant and Cleaner

Tradenames and Synonyms

"Virkon" is a registered trademark of Antec(tm) Int'l Ltd.

Company Identification

MANUFACTURER/DISTRIBUTOR
DuPont Chemical Solutions Enterprise
1007 Market Street
Wilmington, DE 19898

PHONE NUMBERS
Product Information : 1-800-441-7515 (outside the U.S. 302-774-1000)
Transport Emergency : CHEMTREC 1-800-424-9300(outside U.S. 703-527-3887)
Medical Emergency : 1-800-441-3637 (outside the U.S. 302-774-1000)

COMPOSITION/INFORMATION ON INGREDIENTS

Components

Material	CAS Number	%
Potassium Peroxymonosulfate	70693-62-8	
Sulfamic Acid	5329-14-6	
Sodium Chloride	7647-14-5	

Unique Label Statements

KEEP OUT OF REACH OF CHILDREN **********

HAZARDS IDENTIFICATION

Potential Health Effects

Skin contact with product diluted in water according to package directions (1% solution) is not a skin irritant. Skin contact with dry powder may cause skin burns or ulceration. In rare cases, skin contact with dry powder may cause an allergic skin reaction in sensitive individuals.

Eye contact with product diluted in water according to

(HAZARDS IDENTIFICATION - Continued)

package directions (1% solution) is not an eye irritant. Eye contact with dry powder may cause eye corrosion or ulceration. Severe eye damage may result if not immediately treated.

Inhalation of this product may cause nose bleed or irritation of the upper respiratory passages, with coughing, sneezing, runny nose and sore throat. Gross overexposure may cause ulceration of mucous membranes.

Ingestion of this product may cause gastritis, with stomach pain, nausea, vomiting, diarrhea, headache or weakness; possibly progressing to necrosis or hemorrhage with gross overexposure.

Carcinogenicity Information

None of the components present in this material at concentrations equal to or greater than 0.1% are listed by IARC, NTP, OSHA or ACGIH as a carcinogen.

FIRST AID MEASURES

First Aid

IF ON SKIN: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a Poison Control Center or doctor for further treatment advice.

IF IN EYES: Hold eye open & rinse slowly & gently with water for 15-20 minutes. Remove contact lenses, if present after 5 minutes, then continue rinsing eye. Call a Poison Control Center or doctor for further treatment advice.

IF INHALED: Move person to fresh air. If person in not breathing call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth, if possible. Call a Poison Control Center or doctor for further treatment advice.

IF SWALLOWED: Call Poison Control Center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.

FIRE FIGHTING MEASURES

Extinguishing Media

Dry Powder (Sand or Met-L-X), CO2.

Fire Fighting Instructions

Evacuate personnel to a safe area. Wear self-contained breathing apparatus (SCBA) and full protective equipment.

ACCIDENTAL RELEASE MEASURES

Safeguards (Personnel)

NOTE: Review FIRE FIGHTING MEASURES and HANDLING (PERSONNEL) sections before proceeding with clean-up. Use appropriate PERSONAL PROTECTIVE EQUIPMENT during clean-up.

Spill Clean Up

Sweep, shovel, vacuum or scoop up into suitable containers for disposal. Prevent powder from becoming moist while awaiting disposal. Moist product must be kept away from combustible material and stored in a manner that allows suitable ventilation of the waste.

HANDLING AND STORAGE

Handling (Personnel)

Do not get in eyes, on skin or clothing. Avoid breathing dust. Wash thoroughly after handling. Wash contaminated clothing prior to reuse.

Storage

Store in a cool, dry place.

Keep containers tightly sealed and avoid coming into contact with moisture.

EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Use only with adequate ventilation.

Personal Protective Equipment

EYE/FACE PROTECTION

(EXPOSURE CONTROLS/PERSONAL PROTECTION - Continued)

Wear coverall chemical splash goggles. Additionally, wear a face shield where the possibility exists for face contact due to splashing or spraying of material.

RESPIRATORS Wear NIOSH approved respiratory protection as appropriate.

PROTECTIVE CLOTHING

Where there is potential for skin contact have available and wear as appropriate impervious gloves, apron, pants, jacket, hood and boots.

Exposure Guidelines

Applicable Exposure Limits

Potassium Peroxymonosulfate

PEL	(OSHA)	: None Established
TLV	(ACGIH)	: None Established
AEL *	(DuPont)	: 1 mg/m3, 8 & 12 Hr. TWA

Sulfamic Acid

PEL	(OSHA)	: None Established
TLV	(ACGIH)	: None Established
AEL *	(DuPont)	: 0.5 mg/m3, 8 & 12 Hr. TWA 1.5 mg/m3, 15 minute TWA

* AEL is DuPont's Acceptable Exposure Limit. Where governmentally imposed occupational exposure limits which are lower than the AEL are in effect, such limits shall take precedence.

PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Boiling Point: Decomposes on heating
Solubility in Water: 65 g/litre (8.2 oz/gallon) at 20 C/68 F
Form: Free flowing powder
Color: Yellow
Odor: Faint lemon
Specific Gravity: ~1.07

STABILITY AND REACTIVITY

Chemical Stability

Stable at normal temperatures and storage conditions.

(STABILITY AND REACTIVITY - Continued)

Incompatibility with Other Materials

Incompatiblity with strong alkalies and moisture. When wet reacts slowly in solution to make small amount of hypochlorous acid or hypochlorite, depending on pH.

Decomposition

Hazardous decomposition products are: sulfur dioxide and chlorine under extreme conditions if powder is allowed to become damp through incorrect storage or long exposure to the atmosphere.

Polymerization

Polymerization will not occur.

DISPOSAL CONSIDERATIONS

Waste Disposal

Treatment, storage, transportation, and disposal must be in accordance with applicable Federal, State/Provincial, and Local regulations.

TRANSPORTATION INFORMATION

Shipping Information

Not Regulated as a hazardous material by DOT, IMO, or IATA.

REGULATORY INFORMATION

U.S. Federal Regulations

TSCA Inventory Status : Listed.

OTHER INFORMATION

Additional Information

Antec(tm) International Ltd.
A DuPont Company
Windham Road
Chilton Industrial Estates
Sudbury, Suffolk, United Kingdom CO10 2XD

Telephone: 44-(0)-1787-377305

(Continued)

EPA Reg. No. 71654-6

The data in this Material Safety Data Sheet relates only to the specific material designated herein and does not relate to use in combination with any other material or in any process.

Responsible for MSDS : MSDS Coordinator
> : DuPont Chemical Solutions Enterprise
Address : Wilmington, DE 19898
Telephone : (800) 441-7515

This information is based upon technical information believed to be reliable. It is subject to revision as additional knowledge and experience is gained.

End of MSDS

Back to Chloramine T Trihydrate (Reagent)

Material Safety Data Sheet
Chloramine T Trihydrate

ACC# 45371

Section 1 - Chemical Product and Company Identification

MSDS Name: Chloramine T Trihydrate
Catalog Numbers: NC9483232, NES6100-250, O1779 250, O1779-250, O1779250
Synonyms: Benzenesulfonamide, N-Chloro-4-Methyl-, Sodium Salt, Trihydrate; Sodium, (N-Chloro-p-toluenesulfonamido)-, Trihydrate; Tosylchlora
Company Identification:
Fisher Scientific
1 Reagent Lane
Fairlawn, NJ 07410
For information, call: 201-796-7100
Emergency Number: 201-796-7100
For CHEMTREC assistance, call: 800-424-9300
For International CHEMTREC assistance, call: 703-527-3887

Section 2 - Composition, Information on Ingredients

CAS#	Chemical Name	Percent	EINECS/ELINCS
7080-50-4	Chloramine T Trihydrate	ca. 100	unlisted

Hazard Symbols: XI
Risk Phrases: 36/37/38

Section 3 - Hazards Identification

EMERGENCY OVERVIEW

Appearance: white to yellow. Caution! Methemoglobin forming agent. May causeeye and skin irritation. May cause respiratory and digestive tractirritation. Skin sensitizer.
Target Organs: Blood, skin.

Potential Health Effects

Eye: May cause eye irritation.
Skin: May cause skin sensitization, an allergic reaction, which becomes evident upon re-exposure to this material.
May cause severe skin irritation with possible burns, especially if skin is wet or moist.
Ingestion: May cause gastrointestinal irritation with nausea, vomiting and diarrhea. Methemoglobinemia is characterized by dizziness, drowsiness, headache, breath shortness, cyanosis with bluish skin, rapid heart rate
and chocolate-brown colored blood. Overexposure may cause methemoglobinemia.

Inhalation: May cause irritation of the respiratory tract with burning pain in the nose and throat, coughing, wheezing, shortness of breath and pulmonary edema.
Chronic: May cause methemoglobinemia, which is characterized by chocolate-brown colored blood, headache,
weakness, dizziness, breath shortness, cyanosis, rapid heart rate, unconsciousness and possible death.

Section 4 - First Aid Measures

Eyes: Flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower lids. Get
medical aid immediately.
Skin: Get medical aid immediately. Flush skin with plenty of soap and water.
Ingestion: If victim is conscious and alert, give 2-4 cupfuls of milk or water. Never give anything by mouth to an
unconscious person. Get medical aid immediately.
Inhalation: Get medical aid immediately. Remove from exposure to fresh air immediately. If not breathing, give
artificial respiration. If breathing is difficult, give oxygen.
Notes to Physician: Absorption of this product into the body may cause cyanosis. Moderate degrees of cyanosis
need to be treated only by supportive measures: bed rest and oxygen inhalation. For methemoglobinemia, administer oxygen alone or with Methylene blue depending on the methemoglobinemia concentration in the blood.
Cleansing of the entire contaminated area of the body is of utmost importance.

Section 5 - Firefighting Measures

General Information: As in any fire, wear a self-contained breathing apparatus in pressure-demand, MSHA/NIOSH (approved or equivalent), and full protective gear.
Extinguishing Media: Use alcohol foam, carbon dioxide, or water spray when fighting fires involving this material.
Autoignition Temperature: Not available.
Flash Point: 278 deg F (136.67 deg C)
NFPA Rating: Not published. Explosion Limits, Lower: Not available. Upper: Not available.

Section 6 - Accidental Release Measures

General Information: Use proper personal protective equipment as indicated in Section 8.
Spills/Leaks: Clean up spills immediately, observing precautions in the Protective Equipment section. Sweep up or
absorb material, then place into a suitable clean, dry, closed container for disposal. Flush spill area with water.

Section 7 - Handling and Storage

Handling: Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Use with
adequate ventilation. Avoid contact with skin and eyes. Avoid ingestion and inhalation.

Hazardous Decomposition Products: Sulfur dioxide, carbon monoxide, oxides of nitrogen, carbon dioxide, chloride fumes.
Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

RTECS#:
CAS# 7080-50-4 unlisted.
LD50/LC50:
Not available.

Carcinogenicity:
CAS# 7080-50-4: Not listed by ACGIH, IARC, NIOSH, NTP, or OSHA.
Epidemiology: No data available.
Other Studies: No data available.

Section 12 - Ecological Information

Environmental Fate: Not available.

Section 13 - Disposal Considerations

Dispose of in a manner consistent with federal, state, and local regulations.
RCRA D-Series Maximum Concentration ofContaminants: None listed.
RCRA D-Series Chronic Toxicity ReferenceLevels: None listed.
RCRA F-Series: None listed.
RCRA P-Series: None listed.
RCRA U-Series: None listed.

Section 14 - Transport Information

	US DOT	IATA	RID/ADR	IMO	Canada TDG
Shipping Name:	No information available.	No information available.	No information available.	No information available.	No information available.
Hazard Class:					
UN Number:					
Packing Group:					

Section 15 - Regulatory Information

US FEDERAL

TSCA
CAS# 7080-50-4 is not listed on the TSCA inventory. It is for research and development use only.
Health & Safety Reporting List
None of the chemicals are on the Health & Safety Reporting List.
Chemical Test Rules
None of the chemicals in this product are under a Chemical Test Rule.
Section 12b
None of the chemicals are listed under TSCA Section 12b.
TSCA Significant New Use Rule
None of the chemicals in this material have a SNUR under TSCA.
SARA

Section 302 (RQ)
None of the chemicals in this material have an RQ.
Section 302 (TPQ)
None of the chemicals in this product have a TPQ.
Section 313
No chemicals are reportable under Section 313.
Clean Air Act:
This material does not contain any hazardous air pollutants. This material does not contain any Class 1 Ozone
depletors. This material does not contain any Class 2 Ozone depletors.
Clean Water Act:
None of the chemicals in this product are listed as Hazardous Substances under the CWA. None of the chemicals
in this product are listed as Priority Pollutants under the CWA. None of the chemicals in this product are listed as
Toxic Pollutants under the CWA.
OSHA:
None of the chemicals in this product are considered highly hazardous by OSHA.
STATE
CAS# 7080-50-4 is not present on state lists from CA, PA, MN, MA, FL, or NJ.
California No Significant Risk Level: None of the chemicals in this product are listed.
European/International
Regulations
European Labeling in Accordance with EC Directives
Hazard Symbols:
XI
Risk Phrases:
R 36/37/38 Irritating to eyes, respiratory system and skin.
Safety Phrases:
S 15 Keep away from heat. S 2 Keep out of reach of children. S 7 Keep container tightly closed.
WGK (Water Danger/Protection)
CAS# 7080-50-4: No information available.
Canada

None of the chemicals in this product are listed on the DSL/NDSL list. This product has a WHMIS classification of
D2B.

CAS# 7080-50-4 is not listed on Canada's Ingredient Disclosure List.
Exposure Limits

Section 16 - Additional Information

MSDS Creation Date: 6/13/1995
Revision #6 Date: 5/12/1998
The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of
merchantability or any other warranty, express or implied, with respect to such information, and we assume no liability resulting from its use.
Users should make their own investigations to determine the suitability of the information for their particular purposes. In no way shall Fisher be
liable for any claims, losses, or damages of any third party or for lost profits or any special, indirect, incidental, consequential or exemplary
damages, howsoever arising, even if Fisher has been advised of the possibility of such damages.

MEDICAL CONDITIONS GENERALLY AGGRAVATED BY EXPOSURE: None known

SECTION 4: FIRST AID MEASURES

EYES: Remove any contact lenses and immediately flush eyes with water for at least 15 minutes. If irritation develops or persists, seek medical attention.

SKIN: Remove any contaminated clothing and immidiatly flush with water for at least 15 minutes.If irritation develops or persists, seek medical attention. Wash contaminated clothing before reuse.

INHALATION: If inhaled, remove victim to fresh air, if not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

INGESTION: If ingested and conscious, give several glasses of water. Never give anything by mouth to an unconscious person. Do not induce vomiting. Seek medical advice immediately.

NOTES TO PHYSICIANS OR FIRST AID PROVIDERS: No further data known

SECTION 5: FIRE-FIGHTING MEASURES

FIRE AND EXPLOSIVE PROPERTIES:

FLAMMABLE LIMITS IN AIR, UPPER: None
(% BY VOLUME) LOWER: None

FLASH POINT: 378 °F/192 °C
FLAMMABLE LIMITS: None

AUTOIGNITION TEMPERATURE: None Known

NFPA HAZARD CLASSIFICATION
HEALTH: NA **FLAMMABILITY:** NA **REACTIVITY:** NA **OTHER:** NA

HMIS HAZARD CLASSIFICATION
HEALTH: 2 **FLAMMABILITY:** 0 **REACTIVITY:** 1 **PROTECTION:** NA

EXTINGUISHING MEDIA: Water, Dry Chemical, CO_2, Foam

SPECIAL FIRE FIGHTING PROCEDURES: Wear full protective equipment including self-contained breathing apparatus (eye, body, respiratory).

UNUSUAL FIRE AND EXPLOSION HAZARDS: Product may decompose rapidly if heated above 130 °C.

HAZARDOUS DECOMPOSITION PRODUCTS: Chlorine, Sulfur, Nitrogen and oxides of carbon.

SECTION 6: ACCIDENTAL RELEASE MEASURES

CLEAN-UP MEASURES: : Shut off any ignition sources. Wear full protective clothing including, approved safety eyewear, gloves and dust mask. Sweep up and place in a closed container for disposal. Avoid getting on clothing. Wash clothing after handling.

SECTION 7: HANDLING AND STORAGE

HANDLING: Utilize protective rubber gloves dust mask and apron. Use in adequately ventilated area. Utilize sufficient general or local exhaust to control dust below levels of 10 milligrams per cubic meter. Use a NIOSH approved respirator for dust. These protective measures should be considered the minimum protection when handling this product. Additional protection may be advisable depending upon conditions of use.

Empty containers may contain product residue. All safety precautions taken when handling this product should also be taken when handling empty drums and containers. Keep containers closed when not in use.

STORAGE: Keep this material stored in a cool, dry area away from reducing materials, acids, ammonia and ammonium salts, direct sunlight, moisture and excessive heat.

OTHER PRECAUTIONS: For Industrial & Institutional use only.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

ENGINEERING CONTROLS: Utilize sufficient general or local exhaust to control dust below levels of 10 milligrams per cubic meter. The user may wish to refer to 29 CFR 1910.1000(d)(2) and the ACGIH "Threshold Limit Values for Chemical Substances and Physical Agents Biological Exposure Indicies" (Appendix C) for the determination of exposure limits of mixtures.

RESPIRATORY PROTECTION: Use a NIOSH approved respirator for dust.

EYE PROTECTION: Wear protective eyewear recommended by OSHA to prevent accidental exposure Wear eye protection appropriate to prevent eye exposure. Chemical goggles or full face shield is recommended.

SKIN PROTECTION: Utilize protective rubber gloves and apron.

OTHER PERSONAL PROTECTIVE EQUIPMENT: Selection of personal protective equipment should be based upon the anticipated exposure and made in accordance with OSHA's Personal Protective Equipment Standard found in 29 CFR 1910 Subpart I. The following information may be used to assist in PPE selection.

HYGIENIC PRACTICES: Wash hands after use. Keep containers closed when not in use.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE:	White Powder
ODOR:	NA
PHYSICAL STATE:	Solid
pH AS SUPPLIED:	NA
pH (Other):	7 – 9 (1 gram in 400 grams water)
BOILING POINT:	NA
MELTING POINT:	167 – 169 °C (decomposes)
FREEZING POINT:	NA
VAPOR PRESSURE (mmHg):	NA
VAPOR DENSITY (AIR = 1):	NA
SPECIFIC GRAVITY (H2O = 1):	1.43
EVAPORATION RATE:	NA
BASIS (=1):	NA
SOLUBILITY IN WATER: 7.5%	15% @ 25 °C. Insoluble in benzene, chloroform, and most ethers, soluble in 95% alcohol @ 20C (with decomposition).
PERCENT SOLIDS BY WEIGHT:	NA
PERCENT VOLATILE: BY WT/ BY VOL @	Nil
MOLECULAR WEIGHT:	281.69

LABEL STATEMENT:	NA
WATER TRANSPORTATION	
PROPER SHIPPING NAME:	Corrosive Solid, Basic, Organic N.O.S. (Sodium p-Toluenesulfonchloramide)
HAZARD CLASS:	8
ID NUMBER:	UN3263
PACKING GROUP:	PG III
AIR TRANSPORTATION	
PROPER SHIPPING NAME:	Corrosive Solid, Basic, Organic N.O.S. (Sodium p-Toluenesulfonchloramide)
HAZARD CLASS:	8
ID NUMBER:	UN3263
PACKING GROUP:	PG III
OTHER AGENCIES:	Not regulated

SECTION 15: REGULATORY INFORMATION

U.S. FEDERAL REGULATIONS

SARA 313: This product contains none of the substances subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR Part 372.

CLEAN WATER ACT / OIL POLLUTION ACT: This product contains none of the chemicals subject to regulation by Section 311 of the Clean Water Act and the Oil Pollution Act. Releases of the product into or leading to surface waters must be reported to the National Response Center at 1-800-424-8802.

CERCLA REPORTABLE QUANTITY: Any components listed below have been assigned a reportable quantity (RQ) by the Federal EPA. Release of the product into the environment that exceed the RQ for a particular component must be reported to the National Response Center at 1-800-424-8802.

COMPONENT: None

TOXIC SUBSTANCES CONTROL ACT: The components of this product are listed on the TSCA Inventory.

OZONE DEPLETING SUBSTANCES: This product contains no ozone depleting substances as defined by the Clean Air Act.

HAZARDOUS AIR POLLUTANTS: Any components listed below are defined by the Federal EPA as hazardous air pollutants. **COMPONENT:** None

STATE REGULATIONS: Check with the appropriate state agency to determine whether regulations exists.

INTERNATIONAL REGULATIONS: NA

SECTION 16: OTHER INFORMATION

DATE OF ISSUE: 05/18/07 **DATE OF LAST REVISION:** 9/2006

PREPARED BY: **ChemTel Inc.**
1305 North Florida Avenue
Tampa, Florida 33602

We believe the information given is accurate. It is offered in good faith, but without guarantee. Since conditions are beyond our control, user assumes all responsibility and risk.

MATERIAL SAFETY DATA SHEET

AB Aquashade OA

11. Toxicological Information - Continued

Chronic/Carcinogenicity

Dye Acid Blue 9: Lifetime feeding studies in rats and mice indicate that Acid Blue 9 is not carcinogenic. The no-observed-adverse-effect levels (NOAEL) in these studies were highest dose tested in male rats (1072 mg/kg/day) and both sexes of mice (7354-8966 mg/kg/day); the NOAEL in female rats was 631 mg/kg/day based on decrements in terminal body weight and survival.

Reproductive Effects

Acid Blue 9: No reproductive or developmental effects have been observed in rats or rabbits.

12. Ecological Information

Ecotoxicological Information

Acid Blue 9: %BOD after 7 days = 77
12 days = 84
20 days = 88

13. Disposal Considerations

Dispose in accordance with applicable federal, state and local government regulations.

14. Transport Information

Proper Shipping Name
Not regulated

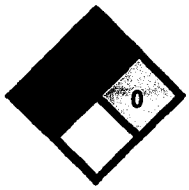
Hazard Class
None assigned

DOT Identification Number
NONE

15. Regulatory Information

No Data Available...

NFPA



HMIS

	1
	0
REACTIVITY	0
PERSONAL PROTECTION	B

16. Other Information

Revision/Preparer Information
MSDS Preparer: JHW
This MSDS Superceeds A Previous MSDS Dated: 10/24/2006

Disclaimer

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitablility of this information for the user's intended purposes or for the consequences of its use. Each individual should make a determination as to the suitability of the information for their particular purposes(s).

Applied Biochemists (WI)

Protective Clothing (Pictograms)

8. Exposure Controls/Personal Protection

Engineering Controls
Local exhaust acceptable. Special exhaust normally not required

Eye/Face Protection
Safety glasses with side shields or goggles.

Skin Protection
Chemical resistant gloves

Respiratory Protection
Not normally required.

9. Physical And Chemical Properties

Appearance
Blue liquid

Odor
None

Chemical Type: Mixture
Physical State: Liquid
Melting Point: NA °F
Boiling Point: 212 °F 100 °C
Specific Gravity: 0.998 (Water = 1)
Percent Volitales: Not determined
Vapor Pressure: Not determined
pH Factor: 4.2-4.7
Solubility: Miscible in water
Evaporation Rate: Not determined

10. Stability And Reactivity

Stability: Stable
Hazardous Polymerization: Does not occur

Conditions To Avoid (Stability)
Keep away from intense heat and open flame.

Incompatible Materials
None known

Hazardous Decomposition Products
None known

Conditions To Avoid (Polymerization)
None

11. Toxicological Information

Acute Oral Effects
C.I. Acid Blue 9, Disodium Salt: Oral, Rat, adult: LD50 > 2000 mg/kg

4. First Aid Measures

Eye
Flush with large amounts of water for at least 15 minutes. Contact a physician if irritation occurs.

Skin
Wash the area with large amounts of soap and water for at least 15 minutes. Wash clothes thoroughly before reuse.

Ingestion
Induce vomiting. Call a physician.

Inhalation
Remove to fresh air.

Fire Fighting (Pictograms)

5. Fire Fighting Measures

Flash Point: NA °F
Flammability Class: Non-flammable

Fire And Explosion Hazards
None known.

Extinguishing Media
Water, carbon dioxide, or foam

Fire Fighting Instructions
Cool area to prevent product containers from bursting or melting. Firefighters should be equipped with self-contained breathing apparatus.

6. Accidental Release Measures

Contain spill. Soak up with absorbant. Place in a suitable container for disposal. Wash area with soap and water. Care should be taken when handling this product as it can stain. Wear appropriate personal protective equipment. Do not flush liquid into public sewer, water systems, or surface waters.

Handling & Storage (Pictograms)

7. Handling And Storage

Handling And Storage Precautions
Keep away from intense heat and open flame.

Handling Precautions
Avoid eye contact. Avoid repeated or prolonged skin contact. Avoid drinking, tasting, swallowing or ingesting this product. Was thoroughly after handling this product. Always wash before eating, smoking, or using the facilities. Use under well-ventilated conditions.

Storage Precautions
Keep container closed when not in use. Do not store in open, unlabeled or mislabeled containers.

SECTION 3 - HAZARDS IDENTIFICATION continued

Ingestion

Short term effects	Ingestion of this material may cause effects similar to those generally seen in clinical use of antibiotics including gastrointestinal irritation, vomiting, transient diarrhea, nausea, and abdominal pain. Persons sensitive to this material or other materials in its chemical class may develop allergic reactions.
Long term effects	Symptoms of chronic exposure to tetracyclines include redness and swelling of the skin, rash, chills, yellowing of the skin and eyes, tooth discoloration, nausea, vomiting, diarrhea, stomach pain, and chest pain. Wheezing, asthma, low or high blood pressure, dizziness, lung congestion, blood changes (leukocytosis, atypical lymphocytes, toxic granulation of granulocytes and thrombocytopenia purpura), convulsion or shock may also occur.

SECTION 4 - FIRST AID MEASURES

Eyes	Immediately flush eyes with plenty of water. If irritation occurs or persists, get medical attention.
Skin	Wash skin with soap and plenty of water. Remove contaminated clothing and shoes. Wash clothing and thoroughly clean shoes before reuse. If irritation occurs or persists, get medical attention.
Inhalation	Remove to fresh air. If discomfort persists, get medical attention.
Ingestion	If swallowed, get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

SECTION 5 - FIRE FIGHTING MEASURES

General hazard	Toxic or corrosive emissions may be given off in a fire. See Hazardous combustion products, below, and Hazardous decomposition products in Section 10 - STABILITY AND REACTIVITY.
Fire fighting instructions	Wear approved positive pressure, self contained breathing apparatus and full protective turn out gear. Use caution in approaching fire.
Extinguisher to use	Use carbon dioxide, dry chemical, or water spray.
Hazardous combustion products	Emits toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen, hydrogen chloride and other chlorine-containing compounds.
Flash point	Not applicable
Autoignition	Not applicable
Minimum explosive concentration for dust/vapor	Not known
Flammability limits	Not applicable

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Occupational spill	Contain the source of spill or leak. Scoop spilled material into a labeled container for disposal. Avoid creating airborne dust. Clean spill area thoroughly with detergent and water.
Clean up - large spill	Review Section 3, 8 and 12 before proceeding with clean up. Use appropriate containment to avoid environmental contamination. Scoop or shovel spilled material into a labeled container for disposal. Avoid creating airborne dust. Close container and move it to a secure holding area.

SECTION 6 - ACCIDENTAL RELEASE MEASURES continued

SECTION 7 - HANDLING AND STORAGE

General handling	Do not generate airborne dust or expose to ignition sources. Ground and bond all bulk transfer equipment. Keep away from heat. Use with adequate ventilation. Avoid contact with eyes, skin and clothing. Avoid breathing dust. When handling, use proper personal protective equipment specified in Section 8.
Storage	Keep container tightly closed when not in use. Store out of direct sunlight in a well ventilated area at ambient temperature.
Temperature range	15 - 30 °C

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure limits

Hazardous Ingredient	OEL	Type	Value
Betaine hydrochloride	Pfizer	TWA-8	Not established
Oxytetracycline hydrochloride	Pfizer	TWA-8	0.5 mg/m³
Sucrose	ACGIH	TWA-8	10 mg/m³
	OSHA	TWA-8	15 mg/m³ (total dust)
	OSHA	TWA-8	5 mg/m³ (respirable fraction)

Exposure information	See exposure limits for components listed above.
Measurement method	Oxytetracycline: CAM-KAS-99-003 (contact Pfizer for additional details).
Ventilation	Keep airborne contamination levels below the Exposure Limits listed above in this section. General room ventilation is adequate unless the process generates dust or fumes. Do not use in a confined space.
Eye protection	Safety glasses or goggles.
Skin protection	Use protective clothing (uniforms, lab coats, disposable coveralls, etc.) in both production and laboratory areas.
Hand protection	Rubber gloves are recommended if there is a potential for contact.
Respiratory protection	If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Physical form	Powder
Color	Yellow
Molecular weight	Not applicable
Molecular formula	Not applicable
pH	Not applicable
Melting point	Not applicable
Pour point	Not applicable
Vapor pressure	Not applicable
Water solubility	No data available
Solvent solubility	No data available

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES continued

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	Stable
Conditions to avoid	Contact with moist air causes darkening of this material. Avoid direct sunlight, excessive heat, sparks or open flame
Incompatibilities	Alkalies
Hazardous decomposition products	Exposure to high temperatures may cause decomposition of the active ingredient.
Hazardous polymerization	Will not occur
Oxidizing properties	No data available
Explosive properties	Possible dust explosion hazard (has not been evaluated)

SECTION 11 - TOXICOLOGY INFORMATION

Acute toxicity

Type	Route	Species	Dosage
LD50	Oral	Mouse	6696 mg/kg
LD50	SC	Mouse	600 mg/kg
LD50	SC	Rat	800 mg/kg

Eye No data available, see Section 3 - HAZARD IDENTIFICATION, above.

Skin No data available, see Section 3 - HAZARD IDENTIFICATION, above.

Inhalation No data available, see Section 3 - HAZARD IDENTIFICATION, above.

Ingestion Acute oral LD50s for the active ingredient(s) are listed above in the table. While this formulation has not been tested as a whole, it would not be expected to be acutely toxic by ingestion based on the amount of the active ingredient(s) in the mixture.

Mutagenicity No evidence of mutagenicity was observed in the Ames test using Salmonella typhimurium strains in the presence or absence of metabolic activation. Oxytetracycline hydrochloride was mutagenic in mouse lymphoma cells L5178Y/TK in the presence but not in the absence of metabolic activation. It was weakly positive in inducing sister chromatid exchanges in cultured Chinese hamster ovary cells with and without metabolic activation but did not induce chromosomal aberrations.

Subchronic effects Subacute and subchronic toxicity studies of oxytetracycline hydrochloride were performed in mice and rats for 14 days and 13 weeks. In the 14-day studies, no compound-related gross pathologic effects were seen in mice or rats given up to 100,000 ppm in their feed. In the 13-week studies, no compound-related gross or histopathologic effects were observed in male or female mice or in female rats given up 50,000 ppm in their diet. In male rats, fatty metamorphosis of minimal severity was observed in the liver in all treated animals.

Chronic toxicity See Chronic effects/Carcinogenicity below.

Chronic effects/ Carcinogenicity Long-term oral chronic and carcinogenicity studies of oxytetracycline hydrochloride toxicity were conducted by the US National Toxicology Program (NTP) in mice at dose levels of 650 or 1400 mg/kg/day and in rats at dose levels of 1000 or 2000 mg/kg/day for 2 years. In mice, no compound-related increases in nonneoplastic or neoplastic lesions were observed in males or females. In rats, increased incidences of pheochromocytomas of the adrenal gland in males and adenomas of the pituitary gland in females were observed.
Under the conditions of these 2-year studies, the US National Toxicology Program concluded that there was equivocal evidence of carcinogenicity in male

SECTION 11 - TOXICOLOGY INFORMATION continued

	and female rats but no evidence of carcinogenicity in male or female mice.
OSHA carcinogen	No
NTP carcinogen	Not classified
IARC carcinogen	Not classified
Reproductive effects	Effects on fertility (litter size) and embryo- or fetotoxicity were observed in rats at subcutaneous dose of oxytetracycline at 1000 mg/kg, rabbits at intramuscular dose of 789 mg/kg, and dogs (643 mg/kg) (no other details reported). Tetracyclines as a class are capable of crossing the placenta and causing staining of the primary teeth.
Teratogenicity	No increase in congenital defects was found in mice and rats treated with oxytetracycline at oral doses of 1500 and 2100 mg/kg on days 6 - 15 of gestation, respectively. In rabbits, oxytetracycline was administered intramuscularly at 41.5 mg/kg/day from days 10 to 28 of gestation. The number and percentage of partial and total resorptions were significantly increased; no effects on fetal body weight were observed. No abnormalities were found at necropsy.
At increased risk from exposure	Individuals who have shown hypersensitivity to this material or other materials in its chemical class and individuals with liver and/or kidney dysfunction or impairment may be more susceptible to toxicity in cases of overexposure. Individuals with alcoholic liver disease and also individuals with hyperlipidemia, especially hypertriglyceridemia, may be more likely to exhibit fatty changes from tetracycline.
Additional data	PREGNANCY RISK CATEGORY D. Results of animal studies indicate that tetracyclines as a class cross the placenta, are found in fetal tissues, and can have toxic effects on the developing fetus (retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy. Tetracyclines as a class are also known to cause tooth discoloration in young children and children exposed to the drug in utero.

SECTION 12 - ECOLOGICAL INFORMATION

Environmental overview See Aquatic toxicity data of the active ingredient below:

Aquatic toxicity

Type	Species	Dosage
LC50/96h	Lake trout	< 200 mg/L

SECTION 13 - DISPOSAL INFORMATION

Disposal procedure Incineration is the recommended means of disposal for this material. This material may also be disposed in landfills. Federal, State and Local environmental regulations and Site conditions may affect proper disposal options.

SECTION 14 - TRANSPORTATION INFORMATION

Proper shipping name	TERRAMYCIN-343® soluble powder blend
General shipping instructions	Non-regulated

SECTION 15 - REGULATORY INFORMATION

EEC Classification/Labelling	
	TOXIC; T Substance Toxic to Reproduction; Category 1 (T)
Risk phrases	R61 - May cause harm to the unborn child.
Safety phrases	S53 - Avoid exposure - obtain special instructions before use.
TSCA status	No
SARA section 302	No
SARA section 313	No
California proposition 65	Y (see below)

SECTION 16 - OTHER

Summary	THIS PRODUCT IS OR CONTAINS CHEMICAL(S) KNOWN TO THE STATE OF CALIFORNIA TO CAUSE DEVELOPMENTAL TOXICITY.
Disclaimer	**Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without a warranty of any kind, expressed or implied.**

Date of Approval: September 15, 2004

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-247

OXYTETRACYCLINE HCL SOLUBLE POWDER-343

oxytetracycline hydrochloride

To add a claim for the skeletal marking of finfish fry and fingerlings

Sponsored by:

Phoenix Scientific, Inc.

1. *GENERAL INFORMATION*

a. File Number:	ANADA 200-247
b. Sponsor:	Phoenix Scientific, Inc. 3915 South 48th St. Terrace St. Joseph, MO 64503 Drug Labeler Code: 059130
c. Established Name:	Oxytetracycline hydrochloride
d. Proprietary Name:	OXYTETRACYCLINE HCL SOLUBLE POWDER-343
e. Dosage Form:	Soluble powder
f. How Supplied:	135.5 g (4.78 oz) and 272.2 g (9.6 oz.) foil pouches
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	272.2 g packet contains 204.8 g oxytetracycline HCl; 135.5 g packet contains 102.4 g oxytetracycline HCl
i. Route of Administration:	Immersion
j. Species/Class:	Finfish/fry and fingerling
j. Recommended Dosage:	200 to 700 mg oxytetracycline/L of water for 2-6 hrs
l. Pharmacological Category:	Antimicrobial
m. Indications:	For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.
n. Effect of Supplement:	To provide a new indication for the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.

2. *EFFECTIVENESS:*

A combination of data from many different fish species reared in different temperatures and management systems were used to support the determination of effectiveness in all teleost (bony) fish, consistent with the *Guidance for Industry: FDA Approval of Animal Drugs for Minor Uses and for Minor Species* (FDA/CVM January 1999). The data summarized in this section are publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special uses. The range of oxytetracycline concentrations, 200 to 700 mg OTC/L of water, is supported by the studies summarized in this section, as well as the literature references at the end of this section.

a. Dosage Characterization:

Reports of successful marking of bony structures of fish, especially the otoliths, have been published for decades. There is a significant body of evidence that tetracyclines stain bony tissues in a wide range of species. The process of marking bony structures with tetracyclines was described in the literature as early as 1962. The literature reflects the widespread use of oxytetracycline by various routes and demonstrates the breadth and number of available publications on marking. This literature provided information to demonstrate the safety and effectiveness of oxytetracycline marking of finfish.

The otolith was selected for evaluation of marking success because otoliths are the first permanent calcified structures present in the earliest life stages of fish and are, effectively, biological internal tags. Once deposited, calcium in the otolith was mobilized little if at all.

Immersion was chosen as the route of administration because immersion marking allows fish to be mass marked with minimal handling. The doses selected were based on the doses found in the published literature.

b. Substantial Evidence:

1. Field Study

   Type of Study: Clinical Field Trial

   Name and Address of Investigator: W. Jenkins
   South Carolina Department of Natural Resources
   Charleston, SC

   General Design of the Study:

   a. Purpose of the Study: To evaluate the effectiveness of using oxytetracycline (OTC) to mark red drum fingerlings for later identification as stocked fish in wild populations.

b. Test Animals: Red drum fingerlings *(Sciaenops ocellatus)*

c. Treatment Groups: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosage Used: 500 mg oxytetracycline/L of water for 4 hours

g. Test Duration: 30 days (treatment to examination)

h. Variables: Examination of otoliths to identify marks and mortality associated with OTC immersion marking

Methods: Red drum were harvested from 5 ponds in the fall of 1996 and 4 ponds in the spring of 1997 for immersion treatment. Fish were placed in a holding tank and acclimated to 15 ppt salinity water. OTC was added to the tank to provide a 500 mg/L OTC concentration. Fish were held for 4 hours. Fish were then transferred to a hauling trailer filled with 15 ppt salinity water. Fish were restocked in a pond at the culture facility and held for 7 days. The salinity in the pond was raised to the concentration of the area to be stocked during the 7-day holding period. Fish were harvested and transported to stocking sites for release. A subsample of each group of marked fish was retained for 30 days to confirm mark effectiveness.

Results: Visible marks could be detected on otoliths in all batches of treated fish. Samples of fish from the wild population indicated that up to 40% of stocked age one year fish had OTC otolith marks.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith is a four-hour immersion at 500 mg/L oxytetracycline hydrochloride.

2. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: M. L. Hendricks
Pennsylvania Fish & Boat Commission
State College, PA

General Design of the Study:

a. Purpose of the Study: To apply unique multiple marks needed to discriminate between groups of fish from different egg source rivers, fish released as fry or fingerlings, and fish released at different sites.

b. Test Animals: American shad fry *(Alosa sapidissima)*, 3-15 days old

c. Treatment Groups: Six different single and multiple marks were applied. A total of 8,500,000 fry were produced with all except 13,500 stocked in the Susquehanna River and its tributaries, or the Lehigh River. Fry were marked in 1200 L rearing tanks (40 total), each containing up to 500,000 fry.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosage Used: 256 mg oxytetracycline (buffered)/L of water for 4 hours

g. Variable: Fry from 6 tanks and raceways were sampled for otolith mark retention.

Results: Retention of immersion marks for American shad fry was 100% for all production groups in 1996. Refer to the following table.

Table 2.1. Oxytetracycline mark retention for American shad reared in 1996.

Tank/ Raceway	Mark Applied (day)	Marks Visualized (day)	Number Examined	Number Marked	Number stocked
Race F1	9,12,15	9,12,15	19	19	171,700
Race F3	3,9,12,15	3,9,12,15	19	19	277,100
Race E1	3,6,9	3,6,9	18	18	42,900
Race F2	3,9,12	3,9,12	19	19	561,100
Race F4	3,6,9,12	3,6,9,12	19	19	682,500
Not Sampled	3	3	-	-	5,730,200
Tank J4*	3	3	17	17	Not stocked

*Sampled at 28 days of age.

All fry produced received marks.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith is a four-hour immersion at 256 mg/L oxytetracycline hydrochloride.

3. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

General Design of the Investigation:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of fry and fingerling fish of different species.

b. Test Animals and Treatment Groups: Largemouth bass (*Micropterus salmoides*) fingerlings, walleye (*Stizostedion vitreum*) fry and fingerlings, and sauger (*Stizostedion canadense*) fry and fingerlings.

c. Treatment Groups: The fish were assigned to either treatment (500 mg/L for 6 hours) or smaller control groups.

Table 2.2. Number of each fish species treated during 1997.

Species	Treated	Control
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 30 to 45 days (from treatment to sampling)

h. Variables: Clinical observations and examination of otoliths to identify marks (50 fish from each treated group, and 50 from each control group).

Methods:

Fry – Groups of 100,000 fry were placed in a 500 mg/L concentration of oxytetracycline in 3 gallons of water within a plastic fish hauling bag for six hours. To ascertain mark retention, 100,000 of the marked and control fry were placed into separate rearing ponds. At the end of the rearing period (45 days for walleye and 60 days for sauger), samples of 50 fish per group were collected at harvest and checked for mark effectiveness.

Fingerlings – Fish were immersed in a 500 mg/L concentration of oxytetracycline for six hours. Marked and control fish were retained for 30 days post-treatment and then harvested for examination. Samples of at least 50 fish from each group were checked for mark effectiveness.

Results: Results are shown in the following table.

Table 2.3. Results of otolith marking field effectiveness trials in 1997.

Species	Treatment	Number Examined	Number Marked	Percent Marked
Walleye fry	OTC Immersion	50	50	100
	Control	50	7	14
Walleye fingerlings	OTC Immersion	50	100	100
	Control	50	0	0
Sauger fingerlings	OTC Immersion	50	50	100
	Control	50	0	0
Sauger fry	OTC Immersion	50	50	100
	Control	50	0	0
Largemouth bass fingerlings	OTC Immersion	50	50	100
	Control	50	0	0

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otoliths of walleye fry and fingerlings, sauger fry and fingerlings, and largemouth bass fingerlings is a six-hour immersion in 500 mg/L oxytetracycline hydrochloride.

4. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: D. O. Lucchesi
South Dakota Department of Game, Fish, and Parks
Pierre, South Dakota

General Design of the Study:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of walleye fry and fingerlings.

b. Test Animals: Walleye (*Stizostedion vitreum*) fry and fingerlings.

Table 2.4. Fish treated during a field study.

Species	Number of Fish
Walleye fry	12,000,000
Walleye fingerlings	150,000

c. Treatment Groups: Natural rearing ponds were stocked with either 500 mg/L or 700 mg/L marked fry, or 500 mg/L marked fingerlings. Two ponds were stocked with 500 mg/L marked fry and two ponds were stocked with 700 mg/L marked fry. Equal numbers of marked and unmarked fry were stocked into 0.8 ha hatchery ponds to compare survival.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride.

e. Route of Administration: Immersion (bath).

f. Dosages Used: Walleye fry were marked at either 500 mg/L or 700 mg/L. Walleye fingerlings were marked at 500 mg/L. Immersion was for 6 hours.

g. Test Duration: 30 days to 3 months (from treatment to sampling).

h. Variables: Examination of otoliths to identify marks and mortality associated with OTC immersion marking

Methods:

To produce the marking bath, an OTC slurry was mixed in a 20 L plastic bucket and was then buffered to a neutral pH using sodium phosphate (dibasic, Na_2HPO_4). Walleye fry were immersed for 6 hours in 683 liter fiberglass raceways containing either 500 or 700 mg OTC/L. Density of fry did not exceed 2,000 fry per liter. Pond-reared fingerlings were marked by immersion for 6 hours in a 500 mg OTC/L water solution in 632 liter fiberglass transfer tanks. Fingerling densities did not exceed 50 fish per liter.

To evaluate marking effectiveness and mark retention, OTC-marked fry and fingerlings were stocked into natural rearing ponds that had complete fish kills the previous winter. These test ponds contained marked individuals from one of three test groups: fry immersed in 500 mg OTC/L or 700 mg OTC/L, or fingerlings immersed in 500 mg/L. Test ponds were electrofished in early fall (approximately 3 months after marking) to recover walleye for evaluation of the mark quality.

To evaluate mortality associated with OTC immersion marking, the 0.8 ha ponds were seined approximately 30-40 days after stocking. A sample of 100 fingerlings per pond was examined for OTC otolith marks.

Results: Results are shown in the following table.

Table 2.5. Visibility of walleye otolith marks 3 months after marking as fry.

OTC Concentration (mg/L)	Mark Intensity 0	1	2	3
500[a]	50%	40%	10%	0
700[a]	0	0	18%	82%
700[b]	0	0	2%	98%

[a]1996 [b]1997

These findings suggest that better quality marks are obtained when fish are immersed in a bath containing 700 mg/L OTC. Problems with OTC precipitating out of solution typically occurred at a pH of higher than 8.0. Therefore, the pH of the bath was maintained at 7.0 to 7.6, even when hatchery water pH exceeded that range.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith of walleye fry is a six-hour immersion at 700 mg/L OTC.

SUPPORTING LITERATURE

The following published articles were submitted to support the effectiveness of oxytetracycline for the marking of otoliths in bony fish:

1. Brooks, R.C., R.C. Heidinger, and C.C. Kohler. Mass-Marking Otoliths of Larval and Juvenile Walleyes by Immersion in Oxytetracycline, Calcein, or Calcein Blue. North American Journal of Fisheries Management 14: 43-150, 1994.

2. Hendricks, M.L., T.R. Bender, and V.A. Mudrak. Multiple Marking of American Shad Otoliths with Tetracycline Antibiotics. North American Journal of Fisheries Management, 11:212-219, 1991.

3. Secor, D.H., M.G White, and J.M Dean. Immersion Marking of Larval and Juvenile Hatchery-Produced Striped Bass with Oxytetracycline. Transactions of the American Fisheries Society, 120:261-266, 1991.

4. Thomas, L.M. Chemical Mark Application in Red Drum (*Sciaenops ocellatus*). Thesis for Master of Science at Corpus Christi State University, Corpus Christi, Texas. 44 pages, 1993.

5. Younk, J.A. and M.F. Cook. Fluorescent Chemical Marking of Walleye Larvae with a Selected Literature Review of Similar Investigations. Minnesota Department of Natural Resources Investigational Report 408. 18 pages, 1991.

2. ***TARGET ANIMAL SAFETY:***

The data summarized in this section is publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special used.

a. "Toxicity of Oxytetracycline and Calcein to Juvenile Striped Bass."

1. Type of Study: Target animal safety

2. Name and Address of Investigators: B.W. Bumguardner and T.L. King
Texas Parks and Wildlife Department
Palacios, Texas

3. General Design of the Study:

a. Purpose of the Study: The study was designed to identify adverse effects of exposing fish to a geometric sequence of oxytetracycline by immersion.

b. Test Animals: Juvenile striped bass (*Morone saxatilis*), approximately 48 mm total length and 2.2 g.

c. Treatment Groups: Three replicates per concentration were tested with ten fish per replicate. The first set of tests included 6 different OTC concentrations. The second set of tests included 3 higher concentrations.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: Concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg/L; second set of tests: 893, 1786, and 3572 mg/L. 6-hour immersion exposure.

g. Test Duration: 26 days (from set up to final observations)

h. Variables: Survival and behavior at 1 hour intervals during the 6-hour treatment and for 6 hours after treatment were observered. Mortality was monitored daily for the next 4 days. Water conditions were also monitored for temperature, salinity, pH, and total hardness.

4. Methods:

After a 22-day acclimation period in a recirculating raceway, the fish were transferred to the test chambers. The test chambers were 4.5 liter aquaria containing salt water (enough to make the total volume 2 liters after addition of OTC solution). OTC HCl unbuffered solution was added to provide concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg/L. Since no deaths were seen, the 893 mg/L concentration was repeated and 1786 and 3572 mg/L concentrations were added. Fish were immersed for 6 hours. Fish were then

placed in a beaker while the aquaria were rinsed. Fish were then placed back into aquaria. Water was exchanged every 24 hrs for 4 days.

5. Results:

   a. Water conditions: Water conditions are included in the following table.

   Table 3.1. Water conditions during a study to evaluate the safety of oxytetracycline solutions with juvenile striped bass.

Condition	Pre Treatment	During Treatment
Temperature	26°C	26°C
Salinity	5 ± 1.9%	7%
pH	8.3	3.25-8.56*
Total hardness		33.4 mg/L (as CaCO3)

*pH varied depending on OTC concentration

   A white precipitate was observed in the higher OTC concentration test chambers.

   b. Mean Mortality: Percent mean mortality results are included in the following table.

   Table 3.2. Mean mortality (%) results of a study to evaluate the safety of calcein and oxytetracycline solutions with juvenile striped bass.

Concentration	During Treatment	After Treatment	Total (and range)
0 (control)	0	6.7	6.7 (0-10)
55.8 mg/L	0	0	0
111.6 mg/L	0	0	0
223.3 mg/L	0	0	0
446.5 mg/L	0	30	30 (10-60)
893 mg/L	0	81.7	81.7 (60-100)
1786 mg/L	23.3	73.3	96.7 (90-100)
3572 mg/L	100	-	100

   Stressed behavior (rapid swimming at the water's surface) was reported in concentrations of OTC 446.5 mg/L and higher.

6. Conclusion: The pH of the immersion solution may have caused or contributed to the death of the fish in the highest dose groups. The mean pH of test aquaria water after addition of OTC solution began to decrease significantly at 893 mg OTC/L. At 1786 mg/L, the pH was more than 1.5 units lower than that of the control group; at 3572 mg/L, the pH was more than 5 units lower than that of the control group.

Water quality, especially pH, must be monitored and controlled when using higher concentrations of OTC for immersion of fish. Buffering of the water can be done to maintain a healthy pH when OTC is used.

b. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: W. Jenkins
South Carolina Department of Natural Resources
Charleston, SC

3. General Design of the Study:

a. Purpose of the Study: This study was primarily designed to demonstrate effectiveness. During the fall of 1996 and spring of 1997, fish were stocked in hatchery ponds following treatment. The ponds were harvested approximately one week later to evaluate post-treatment mortality.

b. Test Animals: Red drum *(Scianenops ocellatus)* fingerlings.

c. Treatment Group: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 500 mg oxytetracycline/L for 4 hours

g. Test Duration: Approximately one week (treatment to harvest)

h. Variables: Mortality occurring one week following treatment was recorded.

4. Methods: Red drum fingerlings were placed in a holding tank on a trailer and acclimated to approximately 15 ppt salinity. Adequate OTC was added to provide a 500 mg/L concentration. Fish were held for 4 hours and then transferred to a hauling trailer. Fish were stocked in a pond at the culture facility and held for one week. During that week pond salinity was slowly raised to the same concentration as the area to be stocked (29-30 ppt). Fish were then harvested and transported to stocking sites for release.

5. Results: Results are included in the following table.

Table 3.3. Mean size and survival of red drum fingerlings treated from 9/96-5/97 with OTC at a concentration of 500 mg/L for 4 hours.

Treatment Date	Mean Length (mm)	Mean Weight (g)	Number of Fish Treated	Survival (%)	Number Harvested
9/16	39	0.59	37,047	72.2	26,746
10/15	37	0.67	63,898	43.1	28,061[a]
10/16	25	0.21	381,028	66.6	253,637
10/22	37	0.68	43,332	71.1	30,801
11/7	13	0.10	265,593	86.4	229,712[b]
5/15	33	0.36	65,810	82.8	54,474
5/22	28	0.25	114,423	80.7	92,395
5/27	29	0.24	470,611	86.8	408,653
5/29	34	0.31	143,589	93.9	134,900

[a]This pond had a dense growth of macrophytic algae. Fish got stranded in the algal mat during harvest.
[b]A salinity acclimation error during post-treatment resulted in 20% mortality during harvest and release, therefore only 183,770 fish were released alive.

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a four-hour immersion in 500 mg/L oxytetracycline, is safe to red drum fingerlings.

c. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

3. General Design of the Study:

a. Purpose of the Study: The studies were primarily designed to demonstrate effectiveness. The studies involved the treatment of many species and large numbers of fish. The studies demonstrate several issues related to target animal safety.

b. Test Animals: Largemouth bass (*Micropterus salmoides*) fingerlings, walleye (*Stizostedion vitreum*) fry and fingerlings, and sauger (*Stizostedion canadense*) fry and fingerlings.

c. Treatment Groups: The fish were assigned to either treatment (500 mg/L for 6 hours) or smaller control groups according to the following table.

Table 3.4. Treatment groups for a marking study conducted in 1997.

Species	Treatment (number)	Control (Number)
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 1 day (fish stocked the day of treatment)

h. Variables: Mortality and adverse reactions were recorded.

4. Methods:

Fry - Groups of 100,000 fry were placed in a 500 mg/L concentration of oxytetracycline in 3 gallons of water within a plastic fish hauling bag for six hours.

Fingerlings - Fish were immersed in a 500 mg/L concentration of oxytetracycline for six hours.

5. Results: Results are included in the following table.

Table 3.5. Mortality and adverse reactions observed in 1997 at Jake Wolf, Little Grassy and LaSalle Hatcheries in Illinois.

Species	Number Treated	Mortalities	Adverse Reactions
Largemouth bass fingerlings	25,000	0	None
Walleye fry	5,824,080	0	None
Walleye fingerlings	138,626	0	None
Sauger fry	22,000,000	0	None
Sauger fingerlings	166,934	0	None

No adverse reactions or mortality occurred in control groups in any of the species treated.

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a six-hour immersion at 500 mg/L, is safe to fry and fingerlings

d. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: R. T. Colesante
New York State Department of Environmental Conservation
Constantia, NY

3. General Design of the Study:

a. Purpose of the Study: Evaluate the survival of walleye fry after oxytetracycline (OTC) marking and stocking in earthen ponds.

b. Test Animals: Walleye (*Stizostedion vitreum*) fry

c. Treatment Groups: Oxytetracycline-treated and untreated fry

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 45-55 days (treatment to harvest)

h. Variable: Survival was recorded.

4. Methods: In 1994, fry were immersed in a 500 mg/L oxytetracycline static bath for 6 hours or left untreated. Six ponds were stocked with marked fry and an additional six ponds were stocked with unmarked fry. Each pond was stocked with 20,000 fry. Ponds were harvested after 45-55 days.

5. Results: Survival results from each pond are shown in the following table.

Table 3.6. Survival results following otolith marking with oxytetracycline.

Pond No.	Treatment Group	Fry Stocked	Fingerling Return	
			Unmarked	Marked
1	OTC	20,000	-	22,728
2	OTC	20,000	-	15,557
3	OTC	20,000	-	11,347
4	Control	20,000	5,360	-
5	Control	20,000	12,964	-
6	OTC	20,000	-	14,118
7	Control	20,000	18,184	-
8	OTC	20,000	-	13,432
9	Control	20,000	12,367	-
10	Control	20,000	12,727	-
11	Control	20,000	13,457	-
12	OTC	20,000	-	11,697
Mean Survival			**62.5 %**	**74.1 %**

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a six-hour immersion at 500 mg/L, is safe to walleye fry.

4. HUMAN SAFETY:

- **Toxicity:** An acceptable daily intake (ADI) of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline) (21 CFR 556.500).

- **Residue Depletion Studies:** Residue depletion data for fish marked with oxytetracycline have been summarized in PMF 5667 (67 FR 46527 dated July 15, 2002). The data are from PMF 3265 and the public literature. A discussion on the long inherent withdrawal period which occurs between treatment of the fish and possible consumption by humans also appears in PMF 5667. The data in PMF 5667 and the public literature, and the long inherent withdrawal period support the human food safety of the use of oxytetracycline to mark finfish fry and fingerlings.

- **Tolerance and Withdrawal Time:** A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish (21 CFR 556.500). A withdrawal time beyond the grow-out period is not needed.

- **Microbial Food Safety:** The potential human health impact of the microbial effects associated with the use of oxytetracycline HCl to mark skeletal tissue, most often the otoliths, of finfish fry or fingerlings for subsequent identification, was assessed pursuant to CVM's Guidance for Industry #78 titled *Consideration of the Human Health Impact of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals.* The Agency has determined that use of oxytetracycline HCl as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline HCl.

- **Regulatory Method for Residues:** The analytical method for detection of residues of oxytetracycline is a microbiological assay using *Bacillus cereus* var. *mycoides*. This method may be found in "Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports, and Protocols" (revised October 1968, reprinted December 1974), National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204). The method is on file at the Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855.

5. *AGENCY CONCLUSIONS:*

The data submitted in support of this ANADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that OXYTETRACYCLINE HCL SOLUBLE POWDER-343, when administered by immersion at concentrations of 200 to 700 mg oxytetracycline hydrochloride/liter of water for 2 to 6 hours, is safe and effective to mark skeletal tissues of finfish fry and fingerlings as an aid in identification.

OXYTETRACYCLINE HCL SOLUBLE POWDER-343 for use in food-producing animals is currently marketed as an over-the-counter product. Adequate directions for safe and effective use by the layperson have been provided. Therefore, the Agency has concluded that this product may retain over-the-counter marketing status.

A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish. A withdrawal time beyond the grow-out period is not needed. An ADI of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline). The potential human health impact of the microbial effects associated with the use of oxytetracycline hydrochloride to mark skeletal tissues of finfish as described in this document was assessed. The Agency has determined that use of oxytetracycline hydrochloride as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline hydrochloride.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food-producing animals does not qualify for marketing exclusivity.

In accordance with 21 CFR 514.106(b)(2)(vii), this is a Category II change involving the addition of a species and a new claim. The safety and effectiveness data in the parent application did not need to be reevaluated.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

OXYTETRACYCLINE HCL SOLUBLE POWDER-343 135.5 g (4.78 oz)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 25 x 135.5 g (4.78 oz)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 272.2 g (9.6 oz)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 25 x 272.2 g (9.6 oz)

Date of Approval: June 13, 2005

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 008-622

TERRAMYCIN-343 (oxytetracycline HCl) Soluble Powder

To add a claim for the skeletal marking of finfish fry and fingerlings

Sponsored by:

Pfizer, Inc.

1. *GENERAL INFORMATION*

a. File Number:	NADA 008-622
b. Sponsor:	Pfizer, Inc. 235 East 42d St. New York, NY 10017 Drug Labeler Code: 000069
c. Established Name:	Oxytetracycline HCl
d. Proprietary Name:	TERRAMYCIN-343 Soluble Powder
e. Dosage Form:	Soluble powder
f. How Supplied:	4.78 oz (135.5 g) and 9.55 oz. (270.7 g) packets and 4.5 lb (2041.2 g) tub
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	4.78 oz packet contains 102.4 g oxytetracycline HCl; 9.55 oz packet contains 204.8 g oxytetracycline HCl; 4.5 lb tub contains 1543.5 g oxytetracycline HCl
i. Route of Administration:	Immersion
j. Species/Class:	Finfish/fry and fingerlings
j. Recommended Dosage:	200 to 700 mg oxytetracycline HCl/L of water for 2-6 hrs
l. Pharmacological Category:	Antimicrobial
m. Indications:	For the marking of skeletal tissues in finfish fry and fingerlings.
n. Effect of Supplement:	To provide a new indication for the marking of skeletal tissues in finfish fry and fingerlings.

2. *EFFECTIVENESS:*

A combination of data from many different fish species reared in different temperatures and management systems were used to support the determination of effectiveness in all teleost (bony) fish, consistent with the *Guidance for Industry: FDA Approval of Animal Drugs for Minor Uses and for Minor Species* (FDA/CVM January 1999). The data summarized in this section are publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special uses. The range of oxytetracycline concentrations, 200 to 700 mg oxytetracycline HCl/L of water, is supported by the studies summarized in this section, as well as the literature references at the end of this section.

a. Dosage Characterization:

Reports of successful marking of bony structures of fish, especially the otoliths, have been published for decades. There is a significant body of evidence that tetracyclines stain bony tissues in a wide range of species. The process of marking bony structures with tetracyclines was described in the literature as early as 1962. The literature reflects the widespread use of oxytetracycline by various routes and demonstrates the breadth and number of available publications on marking. This literature provided information to demonstrate the safety and effectiveness of oxytetracycline marking of finfish.

The otolith was selected for evaluation of marking success because otoliths are the first permanent calcified structures present in the earliest life stages of fish and are, effectively, biological internal tags. Once deposited, calcium in the otolith was mobilized little if at all.

Immersion was chosen as the route of administration because immersion marking allows fish to be mass marked with minimal handling. The doses selected were based on the doses found in the published literature.

b. Substantial Evidence:

1. Field Study

   Type of Study: Clinical Field Trial

   Name and Address of Investigator: W. Jenkins
   South Carolina Department of Natural Resources
   Charleston, SC

   General Design of the Study:

   a. Purpose of the Study: To evaluate the effectiveness of using oxytetracycline HCl to mark red drum fingerlings for later identification as stocked fish in wild populations.

b. Test Animals: Red drum fingerlings *(Sciaenops ocellatus)*

c. Treatment Groups: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosage Used: 500 mg oxytetracycline HCl/L of water for 4 hours

g. Test Duration: 30 days (treatment to examination)

h. Variables: Examination of otoliths to identify marks and mortality

Methods: Red drum were harvested from 5 ponds in the fall of 1996 and 4 ponds in the spring of 1997 for immersion treatment. Fish were placed in a holding tank and acclimated to 15 ppt salinity water. Oxtetracycline HCl was added to the tank to provide a 500 mg oxytetracycline HCl/L of water concentration. Fish were held for 4 hours. Fish were then transferred to a hauling trailer filled with 15 ppt salinity water. Fish were restocked in a pond at the culture facility and held for 7 days. The salinity in the pond was raised to the concentration of the area to be stocked during the 7-day holding period. Fish were harvested and transported to stocking sites for release. A subsample of each group of marked fish was retained for 30 days to confirm mark effectiveness.

Results: Visible marks could be detected on otoliths in all batches of treated fish. Samples of fish from the wild population indicated that up to 40% of stocked age one year fish had otolith marks.

Conclusion: Based on this study, the recommended dose to achieve a fluorescent mark on the otolith is a four-hour immersion at 500 mg oxytetracycline HCl/L of water.

2. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: M. L. Hendricks
Pennsylvania Fish & Boat Commission
State College, PA

General Design of the Study:

a. Purpose of the Study: To apply unique multiple marks needed to discriminate between groups of fish from different egg source rivers, fish released as fry or fingerlings, and fish released at different sites.

b. Test Animals: American shad fry *(Alosa sapidissima)*, 3-15 days old

c. Treatment Groups: Six different single and multiple marks were applied. A

total of 8,500,000 fry were produced with all except 13,500 stocked in the Susquehanna River and its tributaries, or the Lehigh River. Fry were marked in 1200 L rearing tanks (40 total), each containing up to 500,000 fry.

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosage Used: 256 mg oxytetracycline HCl/L of water for 4 hours

g. Variable: Fry from 6 tanks and raceways were sampled for otolith mark retention.

Results: Retention of immersion marks for American shad fry was 100% for all production groups in 1996. Refer to the following table.

Table 2.1. Oxytetracycline mark retention for American shad reared in 1996.

Tank/ Raceway	Mark Applied (day)	Marks Visualized (day)	Number Examined	Number Marked	Number stocked
Race F1	9,12,15	9,12,15	19	19	171,700
Race F3	3,9,12,15	3,9,12,15	19	19	277,100
Race E1	3,6,9	3,6,9	18	18	42,900
Race F2	3,9,12	3,9,12	19	19	561,100
Race F4	3,6,9,12	3,6,9,12	19	19	682,500
Not Sampled	3	3	-	-	5,730,200
Tank J4*	3	3	17	17	Not stocked

*Sampled at 28 days of age.

All fry produced received marks.

Conclusion: Based on this study, the recommended dose to achieve a fluorescent mark on the otolith is a four-hour immersion at 256 mg oxytetracycline HCl/L of water.

3. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

General Design of the Investigation:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of fry and fingerling fish of different species.

b. Test Animals and Treatment Groups: Largemouth bass (*Micropterus*

salmoides) fingerlings, walleye (*Stizostedion vitreum*) fry and fingerlings, and sauger (*Stizostedion canadense*) fry and fingerlings.

c. Treatment Groups: The fish were assigned to either treatment (500 mg/L for 6 hours) or smaller control groups.

Table 2.2. Number of each fish species treated during 1997.

Species	Treated	Control
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline HCl/L of water for 6 hours

g. Test Duration: 30 to 45 days (from treatment to sampling)

h. Variables: Clinical observations and examination of otoliths to identify marks (50 fish from each treated group, and 50 from each control group).

Methods:

Fry – Groups of 100,000 fry were placed in a 500 mg oxytetracycline HCl/L of water concentration in 3 gallons of water within a plastic fish hauling bag for six hours. To ascertain mark retention, 100,000 of the marked and control fry were placed into separate rearing ponds. At the end of the rearing period (45 days for walleye and 60 days for sauger), samples of 50 fish per group were collected at harvest and checked for mark effectiveness.

Fingerlings – Fish were immersed in a 500 mg oxytetracycline HCl/L of water concentration for six hours. Marked and control fish were retained for 30 days post-treatment and then harvested for examination. Samples of at least 50 fish from each group were checked for mark effectiveness.

Results: Results are shown in the following table.

Table 2.3. Results of otolith marking field effectiveness trials in 1997.

Species	Treatment	Number Examined	Number Marked	Percent Marked
Walleye fry	OTC Immersion	50	50	100
	Control	50	7	14
Walleye fingerlings	OTC Immersion	50	100	100
	Control	50	0	0
Sauger fingerlings	OTC Immersion	50	50	100
	Control	50	0	0
Sauger fry	OTC Immersion	50	50	100
	Control	50	0	0
Largemouth bass fingerlings	OTC Immersion	50	50	100
	Control	50	0	0

Conclusion: Based on this study, the recommended dose to achieve a fluorescent mark on the otoliths of walleye fry and fingerlings, sauger fry and fingerlings, and largemouth bass fingerlings is a six-hour immersion in 500 mg oxytetracycline HCl/L of water.

4. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: D. O. Lucchesi
South Dakota Department of Game, Fish, and Parks
Pierre, South Dakota

General Design of the Study:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of walleye fry and fingerlings.

b. Test Animals: Walleye (*Stizostedion vitreum*) fry and fingerlings.

Table 2.4. Fish treated during a field study.

Species	Number of Fish
Walleye fry	12,000,000
Walleye fingerlings	150,000

c. Treatment Groups: Natural rearing ponds were stocked with either 500 mg oxytetracycline HCl/L of water or 700 mg oxytetracycline HCl/L of water marked fry, or 500 mg oxytetracycline HCl/L of water marked fingerlings. Two ponds were stocked with 500 mg oxytetracycline HCl/L of water marked fry and two ponds were stocked with 700 mg oxytetracycline HCl/L of water marked fry. Equal numbers of marked and unmarked fry were stocked into 0.8 ha hatchery ponds to compare survival.

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath).

f. Dosages Used: Walleye fry were marked at either 500 mg oxytetracycline HCl/L of water or 700 mg oxytetracycline HCl/L of water. Walleye fingerlings were marked at 500 mg oxytetracycline HCl/L of water. Immersion was for 6 hours.

g. Test Duration: 30 days to 3 months (from treatment to sampling).

h. Variables: Examination of otoliths to identify marks and mortality associated with oxytetracycline HCl immersion marking

Methods:

To produce the marking bath, a slurry was mixed in a 20 L plastic bucket and was then buffered to a neutral pH using sodium phosphate (dibasic, Na_2HPO_4). Walleye fry were immersed for 6 hours in 683 liter fiberglass raceways containing either 500 or 700 mg oxytetrcycline HCl/L of water. Density of fry did not exceed 2,000 fry per liter. Pond-reared fingerlings were marked by immersion for 6 hours in a 500 mg oxytetracycline HCl/L of water solution in 632 liter fiberglass transfer tanks. Fingerling densities did not exceed 50 fish per liter.

To evaluate marking effectiveness and mark retention, marked fry and fingerlings were stocked into natural rearing ponds that had complete fish kills the previous winter. These test ponds contained marked individuals from one of three test groups: fry immersed in 500 mg oxyteracycline HCl/L of water or 700 mg oxytetracycline HCl/L of water, or fingerlings immersed in 500 mg oxytetracycline HCl/L of water. Test ponds were electrofished in early fall (approximately 3 months after marking) to recover walleye for evaluation of the mark quality.

To evaluate mortality associated with immersion marking, the 0.8 ha ponds were seined approximately 30-40 days after stocking. A sample of 100 fingerlings per pond was examined for otolith marks.

Results: Results are shown in the following table.

Table 2.5. Visibility of walleye otolith marks 3 months after marking as fry.

OTC Concentration (mg/L)	Mark Intensity			
	0	1	2	3
500[a]	50%	40%	10%	0
700[a]	0	0	18%	82%
700[b]	0	0	2%	98%

[a]1996 [b]1997

The survival of marked fry was not significantly lower than for unmarked fry and differences in survival of fry marked at 500 mg oxytetracycline HCl/L of water and 700 mg oxytetracycline HCl/L of water were also insignificant. Percent return rates are shown in the following table.

Table E.2. Percent return of walleye fingerlings marked as fry by immersion in oxytetracycline HCl one month after stocking into hatchery ponds

	1996		1997
	500 mg/L n=100	700 mg/L n=200	700 mg/L n=190
Marked	54 %	48 %	53 %
Unmarked	46 %	52 %	47 %

These findings suggest that better quality marks are obtained when fish are immersed in a bath containing 700 mg oxytetracycline HCl/L of water. Problems with oxytetracycline HCl precipitating out of solution typically occurred at a pH of higher than 8.0. Therefore, the pH of the bath was maintained at 7.0 to 7.6, even when hatchery water pH exceeded that range.

Conclusion: Based on this study, the recommended dose to achieve a fluorescent mark on the otolith of walleye fry is a six-hour immersion at 700 mg oxytetracycline HCl/L of water.

SUPPORTING LITERATURE

The following published articles were submitted to support the effectiveness of oxytetracycline for the marking of otoliths in bony fish:

1. Brooks, R.C., R.C. Heidinger, and C.C. Kohler. Mass-Marking Otoliths of Larval and Juvenile Walleyes by Immersion in Oxytetracycline, Calcein, or Calcein Blue. North American Journal of Fisheries Management 14: 43-150, 1994.

2. Hendricks, M.L., T.R. Bender, and V.A. Mudrak. Multiple Marking of American Shad Otoliths with Tetracycline Antibiotics. North American Journal of Fisheries Management, 11:212-219, 1991.

3. Secor, D.H., M.G White, and J.M Dean. Immersion Marking of Larval and Juvenile Hatchery-Produced Striped Bass with Oxytetracycline. Transactions of the American Fisheries Society, 120:261-266, 1991.

4. Thomas, L.M. Chemical Mark Application in Red Drum (*Sciaenops ocellatus*). Thesis for Master of Science at Corpus Christi State University, Corpus Christi, Texas. 44 pages, 1993.

5. Younk, J.A. and M.F. Cook. Fluorescent Chemical Marking of Walleye Larvae with a Selected Literature Review of Similar Investigations. Minnesota Department of Natural Resources Investigational Report 408. 18 pages, 1991.

3. *TARGET ANIMAL SAFETY:*

The data summarized in this section are publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special uses.

a. "Toxicity of Oxytetracycline and Calcein to Juvenile Striped Bass."

1. Type of Study: Target animal safety

2. Name and Address of Investigators: B.W. Bumguardner and T.L. King
Texas Parks and Wildlife Department
Palacios, Texas

3. General Design of the Study:

a. Purpose of the Study: The study was designed to identify adverse effects of exposing fish to a geometric sequence of oxytetracycline by immersion.

b. Test Animals: Juvenile striped bass (*Morone saxatilis*), approximately 48 mm total length and 2.2 g.

c. Treatment Groups: Three replicates per concentration were tested with ten fish per replicate. The first set of tests included 6 different oxytetracycline HCl concentrations. The second set of tests included 3 higher concentrations.

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosages Used: Concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg oxytetracycline HCl/L of water; second set of tests: 893, 1786, and 3572 mg oxytetracycline HCl/L of water. 6-hour immersion exposure.

g. Test Duration: 26 days (from set up to final observations)

h. Variables: Survival and behavior at 1 hour intervals during the 6-hour treatment and for 6 hours after treatment were observered. Mortality was monitored daily for the next 4 days. Water conditions were also monitored for temperature, salinity, pH, and total hardness.

4. Methods:

After a 22-day acclimation period in a recirculating raceway, the fish were transferred to the test chambers. The test chambers were 4.5 liter aquaria containing salt water (enough to make the total volume 2 liters after addition of oxytetracycline HCl solution). Oxytetracycline HCl unbuffered solution was added to provide concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg oxytetracycline HCl/L of water. Since no deaths were seen, the 893 mg oxytetracycline HCl/L of water

concentration was repeated and 1786 and 3572 mg oxytetracycline HCl/L of water concentrations were added. Fish were immersed for 6 hours. Fish were then placed in a beaker while the aquaria were rinsed. Fish were then placed back into aquaria. Water was exchanged every 24 hrs for 4 days.

5. Results:

   a. Water conditions: Water conditions are included in the following table.

   Table 3.1. Water conditions during a study to evaluate the safety of oxytetracycline solutions with juvenile striped bass.

Condition	Pre Treatment	During Treatment
Temperature	26°C	26°C
Salinity	5 ± 1.9%	7%
pH	8.3	3.25-8.56*
Total hardness		33.4 mg/L (as CaCO3)

*pH varied depending on oxytetracycline HCl concentration

   A white precipitate was observed in the higher oxytetracycline HCl concentration test chambers.

   b. Mean Mortality: Percent mean mortality results are included in the following table.

   Table 3.2. Mean mortality (%) results of a study to evaluate the safety of oxytetracycline HCl solutions with juvenile striped bass.

Concentration	During Treatment	After Treatment	Total (and range)
0 (control)	0	6.7	6.7 (0-10)
55.8 mg/L	0	0	0
111.6 mg/L	0	0	0
223.3 mg/L	0	0	0
446.5 mg/L	0	30	30 (10-60)
893 mg/L	0	81.7	81.7 (60-100)
1786 mg/L	23.3	73.3	96.7 (90-100)
3572 mg/L	100	-	100

   Stressed behavior (rapid swimming at the water's surface) was reported in concentrations of 446.5 mg oxytetracycline HCl/L of water and higher.

6. Conclusion: The pH of the immersion solution may have caused or contributed to the death of the fish in the highest dose groups. The mean pH of test aquaria water after addition of oxytetracycline HCl solution began to decrease significantly at 893 mg oxytetracycline HCl/L of water. At 1786 mg oxytetracycline HCl/L of water, the pH was more than 1.5 units lower than that of the control group; at 3572 mg oxytetracycline HCl/L of water, the pH was more than 5 units lower than that of the

control group.

Water quality, especially pH, must be monitored and controlled when using higher concentrations of oxytetracycline HCl for immersion of fish. Buffering of the water can be done to maintain a healthy pH when oxytetracycline HCl is used.

b. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: W. Jenkins
South Carolina Department of Natural Resources
Charleston, SC

3. General Design of the Study:

a. Purpose of the Study: This study was primarily designed to demonstrate effectiveness. During the fall of 1996 and spring of 1997, fish were stocked in hatchery ponds following treatment. The ponds were harvested approximately one week later to evaluate post-treatment mortality.

b. Test Animals: Red drum *(Scianenops ocellatus)* fingerlings.

c. Treatment Group: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosages Used: 500 mg oxytetracycline HCl/L of water for 4 hours

g. Test Duration: Approximately one week (treatment to harvest)

h. Variables: Mortality occurring one week following treatment was recorded.

4. Methods: Red drum fingerlings were placed in a holding tank on a trailer and acclimated to approximately 15 ppt salinity. Adequate oxytetracycline HCl was added to provide a 500 mg oxytetracycline HCl/L of water concentration. Fish were held for 4 hours and then transferred to a hauling trailer. Fish were stocked in a pond at the culture facility and held for one week. During that week pond salinity was slowly raised to the same concentration as the area to be stocked (29-30 ppt). Fish were then harvested and transported to stocking sites for release.

5. Results: Results are included in the following table.

Table 3.3. Mean size and survival of red drum fingerlings treated from 9/96-5/97 at a concentration of 500 mg oxytetracycline HCl/L of water for 4 hours.

Treatment Date	Mean Length (mm)	Mean Weight (g)	Number of Fish Treated	Survival (%)	Number Harvested
9/16	39	0.59	37,047	72.2	26,746
10/15	37	0.67	63,898	43.1	28,061[a]
10/16	25	0.21	381,028	66.6	253,637
10/22	37	0.68	43,332	71.1	30,801
11/7	13	0.10	265,593	86.4	229,712[b]
5/15	33	0.36	65,810	82.8	54,474
5/22	28	0.25	114,423	80.7	92,395
5/27	29	0.24	470,611	86.8	408,653
5/29	34	0.31	143,589	93.9	134,900

[a]This pond had a dense growth of macrophytic algae. Fish got stranded in the algal mat during harvest.
[b]A salinity acclimation error during post-treatment resulted in 20% mortality during harvest and release, therefore only 183,770 fish were released alive.

6. Conclusion: Based on this study, a four-hour immersion at the recommended dose of 500 mg oxytetracycline HCl/L of water is safe to red drum fingerlings.

c. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

3. General Design of the Study:

a. Purpose of the Study: The studies were primarily designed to demonstrate effectiveness. The studies involved the treatment of many species and large numbers of fish. The studies demonstrate several issues related to target animal safety.

b. Test Animals: Largemouth bass (*Micropterus salmoides*) fingerlings, walleye (*Stizostedion vitreum*) fry and fingerlings, and sauger (*Stizostedion canadense*) fry and fingerlings.

c. Treatment Groups: The fish were assigned to either treatment (500 mg oxytetracycline HCl/L of water for 6 hours) or smaller control groups according to the following table.

Table 3.4. Treatment groups for a marking study conducted in 1997.

Species	Treatment (number)	Control (Number)
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline HCl/L of water for 6 hours

g. Test Duration: 1 day (fish stocked the day of treatment)

h. Variables: Mortality and adverse reactions were recorded.

4. Methods:

Fry - Groups of 100,000 fry were placed in a 500 mg oxytetracycline HCL/L of water concentration in 3 gallons of water within a plastic fish hauling bag for six hours.

Fingerlings - Fish were immersed in a 500 mg oxytetracycline HCl/L of water concentration for six hours.

5. Results: Results are included in the following table.

Table 3.5. Mortality and adverse reactions observed in 1997 at Jake Wolf, Little Grassy and LaSalle Hatcheries in Illinois.

Species	Number Treated	Mortalities	Adverse Reactions
Largemouth bass fingerlings	25,000	0	None
Walleye fry	5,824,080	0	None
Walleye fingerlings	138,626	0	None
Sauger fry	22,000,000	0	None
Sauger fingerlings	166,934	0	None

No adverse reactions or mortality occurred in control groups in any of the species treated.

6. Conclusion: Based on this study, the recommended dose of oxytetracycline HCl, a six-hour immersion at 500 mg oxytetracycline HCl/L of water, is safe to walleye and sauger fry, and largemouth bass, walleye, and sauger fingerlings.

d. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: R. T. Colesante
New York State Department of Environmental Conservation
Constantia, NY

3. General Design of the Study:

a. Purpose of the Study: Evaluate the survival of walleye fry after oxytetracycline HCl marking and stocking in earthen ponds.

b. Test Animals: Walleye (*Stizostedion vitreum*) fry

c. Treatment Groups: Oxytetracycline-treated and untreated fry

d. Dosage Form: Water-soluble oxytetracycline HCl

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline HCl/L of water for 6 hours

g. Test Duration: 45-55 days (treatment to harvest)

h. Variable: Survival was recorded.

4. Methods: In 1994, fry were immersed in a 500 mg oxytetracycline HCl/L of water static bath for 6 hours or left untreated. Six ponds were stocked with marked fry and an additional six ponds were stocked with unmarked fry. Each pond was stocked with 20,000 fry. Ponds were harvested after 45-55 days.

5. Results: Survival results from each pond are shown in the following table.

Table 3.6. Survival results following otolith marking with oxytetracycline HCl (OTC).

Pond No.	Treatment Group	Fry Stocked	Fingerling Return	
			Unmarked	Marked
1	OTC	20,000	-	22,728
2	OTC	20,000	-	15,557
3	OTC	20,000	-	11,347
4	Control	20,000	5,360	-
5	Control	20,000	12,964	-
6	OTC	20,000	-	14,118
7	Control	20,000	18,184	-
8	OTC	20,000	-	13,432
9	Control	20,000	12,367	-
10	Control	20,000	12,727	-
11	Control	20,000	13,457	-
12	OTC	20,000	-	11,697
Mean Survival			**62.5 %**	**74.1 %**

6. Conclusion: Based on this study, the recommended dose, a six-hour immersion at 500 mg oxytetracycline HCl/L of water, is safe to walleye fry.

4. HUMAN SAFETY:

- **Toxicity:** An acceptable daily intake (ADI) of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline) (21 CFR 556.500).

- **Residue Depletion Studies:** Residue depletion data for fish marked with oxytetracycline HCl have been summarized in PMF 5667 (67 FR 46527 dated July 15, 2002). The data are from PMF 3265 and the public literature. A discussion on the long inherent withdrawal period which occurs between treatment of the fish and possible consumption by humans also appears in PMF 5667. The data in PMF 5667 and the public literature, and the long inherent withdrawal period support the human food safety of the use of oxytetracycline HCl to mark finfish fry and fingerlings.

- **Tolerance and Withdrawal Time:** A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish (21 CFR 556.500). A withdrawal time beyond the grow-out period is not needed.

- **Microbial Food Safety:** The potential human health impact of the microbial effects associated with the use of oxytetracycline HCl to mark skeletal tissue, most often the otoliths, of finfish fry or fingerlings for subsequent identification, was assessed pursuant to CVM's Guidance for Industry #78 titled *Consideration of the Human Health Impact of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals*. The Agency has determined that use of oxytetracycline HCl as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline HCl.

- **Regulatory Method for Residues:** The analytical method for detection of residues of oxytetracycline is a microbiological assay using *Bacillus cereus* var. *mycoides*. This method may be found in "Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports, and Protocols" (revised October 1968, reprinted December 1974), National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204). The method is on file at the Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855.

5. *AGENCY CONCLUSIONS:*

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that TERRAMYCIN-343, when administered by immersion at concentrations of 200 to 700 mg oxytetracycline HCl/L of water for 2 to 6 hours, is safe and effective to mark skeletal tissues of finfish fry and fingerlings.

TERRAMYCIN-343 for use in food-producing animals is currently marketed as an over-the-counter product. Adequate directions for safe and effective use by the layperson have been provided. Therefore, the Agency has concluded that this product may retain over-the-counter marketing status.

A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish. A withdrawal time beyond the grow-out period is not needed. An ADI of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline). The potential human health impact of the microbial effects associated with the use of oxytetracycline HCl to mark skeletal tissues of finfish as described in this document was assessed. The Agency has determined that use of oxytetracycline HCl as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline HCl.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food-producing animals does not qualify for marketing exclusivity.

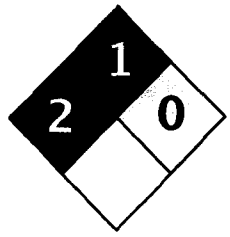
In accordance with 21 CFR 514.106(b)(2)(vii), this is a Category II change involving the addition of a species and a new claim. The safety and effectiveness data in the parent application did not need to be reevaluated.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

TERRAMYCIN-343 4.78 oz (135.5 g)
TERRAMYCIN-343 14.9 lb (6.7 kg) (50 x 4.78 oz unit packages)
TERRAMYCIN-343 9.55 oz (270.7 g)
TERRAMYCIN-343 4.5 lb (2041.2 g)

ScienceLab.com
Chemicals & Laboratory Equipment



Health	2
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet
Erythromycin MSDS

Section 1: Chemical Product and Company Identification

Product Name: Erythromycin

Catalog Codes: SLE1798

CAS#: 114-07-8

RTECS: KF4375000

TSCA: TSCA 8(b) inventory: No products were found.

CI#: Not available.

Synonym:

Chemical Name: Not available.

Chemical Formula: C37H67NO13

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Erythromycin	114-07-8	100

Toxicological Data on Ingredients: Erythromycin LD50: Not available. LC50: Not available.

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of ingestion. Hazardous in case of eye contact (irritant), of inhalation. Slightly hazardous in case of skin contact (irritant, permeator).

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available.
MUTAGENIC EFFECTS: Not available.
TERATOGENIC EFFECTS: Not available.
DEVELOPMENTAL TOXICITY: Not available.
The substance is toxic to blood, kidneys, lungs, liver, mucous membranes.
Repeated or prolonged exposure to the substance can produce target organs damage.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used. Do not use an eye ointment. Seek medical attention.

Skin Contact:
After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.

Serious Skin Contact: Not available.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation: Not available.

Ingestion:
Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO2), nitrogen oxides (NO, NO2...).

Fire Hazards in Presence of Various Substances: Not available.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available.
Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:
SMALL FIRE: Use DRY chemical powder.
LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:
Use appropriate tools to put the spilled solid in a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and dispose of according to local and regional authority requirements.

Large Spill:
Use a shovel to put the material into a convenient waste disposal container. Finish cleaning by spreading water on the contaminated surface and allow to evacuate through the sanitary system.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: Not available.

Solubility: Very slightly soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Eye contact. Inhalation. Ingestion.

Toxicity to Animals:
LD50: Not available.
LC50: Not available.

Chronic Effects on Humans: The substance is toxic to blood, kidneys, lungs, liver, mucous membranes.

Other Toxic Effects on Humans:
Very hazardous in case of ingestion.
Hazardous in case of inhalation.
Slightly hazardous in case of skin contact (irritant, permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Human: passes through the placenta, excreted in maternal milk.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States).

Identification: Not applicable.

Special Provisions for Transport: Not applicable.

Section 15: Other Regulatory Information

Federal and State Regulations: TSCA 8(b) inventory: No products were found.

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC): R36- Irritating to eyes.

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves.
Lab coat.
Dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.
Splash goggles.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/11/2005 11:53 AM

Last Updated: 10/11/2005 11:53 AM

Schering-Plough

Schering Canada Inc.
3535 Trans-Canada
Pointe Claire, Quebec
Canada H9R 1B4

MATERIAL SAFETY DATA SHEET

Schering-Plough urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

MSDS NAME: **Florfenicol Powders**

SYNONYM(S): Aquaflor Medicated Premix for Salmon
Florocol
Aquacol VET Medicated Premix for Salmon

MSDS NUMBER: SP000956

EMERGENCY NUMBER(S): Schering-Plough Security Control Center (908) 820-6921 (24 Hours)

Transportation Emergencies -
CANUTEC: (613) 996-6666 (Canada)

INFORMATION: Animal Health Technical Services:
(888) 306-0069 (Canada)

SCHERING-PLOUGH MSDS HELPLINE: (800) 770-8878 (US and Canada)
(908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Aquaculture product

CHEMICAL FORMULA: Mixture.

The formulations for these products are proprietary information. These formulations have the same hazardous profile; however, the presence of hazardous ingredients may vary by formulation. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 3.

HAZARDOUS COMPONENTS

CHEMICAL NAME	CAS NUMBER	PERCENT
Florfenicol	76639-94-6	50-60
Lactose	63-42-3	40-50
Povidone	9003-39-8	1-10

ADDITIONAL INFORMATION: This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

White
Powder
Odor unknown

May cause allergic reactions in susceptible individuals.

May cause effects to:
- gastrointestinal tract
- male reproductive system

May cause impaired fertility.
May cause developmental effects.

Toxic to fish and aquatic organisms.
May cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS:

The following summary is based upon available information about the individual ingredients of the mixture, or of the expected properties of the mixture.

This product is not for use in humans. Clinical effects in humans have not been determined.

Florfenicol, the active ingredient in this product, is a broad spectrum antibiotioc used in veterinary products. Florfenicol may cause allergic reactions in susceptible individuals. Based on animal studies, florfenicol may cause slight eye irritation, constipation, changes in blood cell counts, changes in stool, or liver effects. It may also cause developmental effects or effects to male reproductive organs.

Lactose is not expected to produce significant toxicity with workplace exposure. Lactose may cause irritation to the eyes, skin, and mucous membranes from mechanical action. Lactose may cause abdominal pain, bloating and diarrhea if ingested in large amounts or in lactose-intolerant individuals. Lactose may cause allergic reactions in sensitive individuals.

Povidone is not-irritating, not-sensitizing and practically not-toxic. Because povidone is not absorbed from the gastrointestinal tract, at high concentrations povidone can cause increased bowel activity, flatulence (gas), and severe constipation. These effects are not expected with occupational handling of the material.

LISTED CARCINOGENS

CHEMICAL NAME	CAS NUMBER	OSHA	IARC	NTP	ACGIH
Povidone	9003-39-8		Not classifiable.		

SECTION 4. FIRST AID MEASURES

INHALATION: Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.

SKIN CONTACT: In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.

EYE CONTACT: In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.

INGESTION: Rinse mouth and drink a glass of water. Do not induce vomiting. If symptoms persist, consult a physician.

NOTE TO PHYSICIAN: This product contains florfenicol, a broad spectrum antibiotic which may cause allergic reactions in susceptible individuals.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

FLASH POINT: Not determined (liquids) or not applicable (solids).

OTHER EXPLOSION HAZARDS:
Under normal conditions of use, this material does not present a significant fire or explosion hazard. However, like most organic compounds, this material may present a dust deflagration hazard if sufficient quantities are suspended in air. This hazard may exist where sufficient quantities of finely divided material are (or may become) suspended in air during typical process operations. An assessment of each operation should be conducted and suitable deflagration prevention and protection techniques employed.

The sensitivity of this material to ignition by electrostatic discharges has not been determined. In the absence of testing data, all conductive plant items and operations personnel handling this material should be suitably grounded.

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing and self-contained breathing apparatus (SCBA).

SUITABLE EXTINGUISHING MEDIA:
Carbon dioxide (CO_2), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:
Keep personnel away from the clean-up area. Wear appropriate personal protective equipment as specified in Section 8. Avoid generation of dust during clean-up.

SPILL RESPONSE / CLEANUP:
All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

ENVIRONMENTAL PRECAUTIONS:
This product is toxic to fish and/or aquatic organisms. Do not allow product to reach ground water, water course, sewage or drainage systems.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7. HANDLING AND STORAGE

HANDLING:
Avoid dust generation. Keep containers adequately sealed during material transfer, transport, or when not in use.

Appropriate handling of this material is dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:
Store in a cool, dry, well ventilated area.

See Section 8 for exposure controls and additional safe handling information.

SECTION 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

The following guidance applies to the handling of the active ingredient in this formulation.

S-P OCCUPATIONAL EXPOSURE GUIDELINE (OEG): Schering-Plough Corporation has established an Occupational Exposure Guideline (OEG) of 180 mcg/m^3 (8-hr TWA) for Florfenicol. Consult your site safety professional for additional guidance.

EXPOSURE CONTROLS:
The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, substitution of approved materials or appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. However, PPE should not be used as a method of permanent or long-term exposure control. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection:	Respirators are not normally required; however, appropriate respiratory protection may be required in situations where exposure (e.g. spills, process upsets, or non-routine maintenance) may exceed any available recommended exposure limit. Consult your site safety staff for guidance.
Skin Protection:	Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.
Eye Protection:	Safety glasses with side shields. Use of goggles or full face protection may be required if there is potential for contact with this material. Consult your site safety staff for guidance.
Body Protection:	In small scale or laboratory operations, lab coats or other equivalent protective clothing is required. In large-scale or manufacturing operations, lab coats or other equivalent protective clothing is required.

EXPOSURE LIMIT VALUES

See Schering-Plough occupational exposure guideline (OEG) listed above.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

FORM: Powder
COLOR: White
ODOR: Odor unknown
SOLUBILITY:

Water:	Florfenicol: 1.32 mg/mL at pH7
Acetone:	Florfenicol: Very soluble

See Section 5 for flammability/explosivity information.

SECTION 10: STABILITY AND REACTIVITY

STABILITY/ REACTIVITY:
Stable under normal conditions.

INCOMPATIBLE MATERIALS / CONDITIONS TO AVOID:
Open flames and high temperatures.

HAZARDOUS DECOMPOSITION PRODUCTS / REACTIONS:
Carbon oxides (COx).

SECTION 11: TOXICOLOGICAL INFORMATION

The toxicological properties of this mixture have not been fully characterized in humans or animals. The information presented below pertains to the following individual ingredients, and not to the mixture.

ACUTE TOXICITY DATA

INHALATION:
Rats exposed to florfenicol for 4 hours showed dry rales, anogenital staining, secretory discharge, soft stool, and decreased body weights. These effects were seen immediately or up to one-week post exposure. Some effects did not resolve by study termination. The inhalation LC50 (4 hr) was >0.28 mg/L in rats.

SKIN:
Florfenicol was not irritating to rabbit skin (PII = 0) Povidone did not produce primary dermal irritation in a human repeated insult patch test.

EYE:
Florfenicol was slightly irritating to the eyes of rabbits. Povidone did not produce ocular irritation in rabbits.

ORAL:
Florfenicol: Oral LD50: >2000 mg/kg (rat, mouse).
Dogs (one animal/sex) were administered successive oral doses of florfenicol that ranged from 160 to 1280 mg/kg. No clinical effects occurred at doses as high as 640 mg/kg. At 640 mg/kg, the only female died from inhalation of vomitus. Vomiting or soft stool occurred at 640 to 1280 mg/kg.

Lactose: Oral LD50: > 10g/kg (rat)
Povidone: (LD50 values vary based on molecular weight):
Rat (Oral) LD50: >100 g/kg (PVP K-30, molecular weight 40,000)
Rat (Oral) LD50: 8.25 g/kg (unspecified molecular weight)

SENSITIZATION:
Florfenicol was not a skin sensitizer in guinea pigs.
Povidone did not produce sensitization in a human repeated insult patch test.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:
Florfenicol was administered orally to dogs, rats, and mice at dosages as high as 100 to 400 mg/kg/day for up to 13 weeks. Effects including decreased body weight, changes in liver weight or liver enzyme levels, changes in testicular weight, testicular atrophy, decreased white blood cell counts, and decreased hemoglobin levels were observed at high dosages. Cellular changes in the liver or lymph nodes of rats and mice, and histopathologic changes in the brain and spinal cord of dogs were also noted at these high dosages. Although some effects were reversible after a 4-week withdrawal from treatment, testicular effects in rats persisted. Intramuscular injections of 45 mg/kg of florfenicol in swine produced diarrhea, injection site lesions, decreased body weight, decreased food and water consumption, changes in serum electrolytes and proteins, decreased red blood cell and white blood cell counts, decreased spleen weight, and decreased kidney weight.

In 52-week oral toxicity studies in dogs and rats, high dosages of florfenicol (12 and 48 mg/kg/day, respectively) increased liver weight and produced cellular changes in the gall bladder of dogs. In rats, florfenicol at the high dosage reduced body weight gain, reduced testicular weight, induced changes in hematologic and clinical chemistry parameters, and increased the incidence of testicular tubular atrophy. In two-year chronic studies in mice and rats, florfenicol caused similar effects as those observed in other long-term studies including reduced body weight gain, reduced red blood cell count, reduced hemoglobin levels, and testicular effects such as small testes, tubular atrophy and aspermatogenesis in both the high dosage rats (48 mg/kg/day) and mice (200 mg/kg/day).

Povidone fed to rats and dogs at 10% in the diet for 90 or 28 days, respectively, had no effect in rats; in dogs it increased spleen weight and accumulated in the mesenteric lymph nodes.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:
In a two-generation reproductive study, oral administration as high as 12 mg/kg/day of florfenicol reduced epididymal weights, decreased pup survival, and reduced lactation index in rats [NOAEL: 3 mg/kg/day].

There was no evidence of teratogenicity in rats administered florfenicol at dosages of 4, 12 or 40 mg/kg/day. Slight maternal toxicity, evidenced by decreased food and water consumption, was observed above 4 mg/kg/day. At 40 mg/kg/day, an increased incidence of delayed ossification and decreased fetal weight occurred. The NOAEL for maternal and fetal toxicity in rats was determined to be 4 mg florfenicol/kg/day.

Two teratogenicity studies were performed in mice. In the first study, the mice were administered florfenicol at dosages of 40, 120, or 400 mg/kg by gavage on days 6-15 of gestation. Florfenicol produced embryolethality at the 400 mg/kg/day dose level, which was evidenced by the high incidence of intrauterine deaths. Significant decreases in mean fetal body weight, soft tissue defects, and retarded skeletal ossification were also observed at 400 mg/kg/day. Skeletal ossification was less pronounced, in a dose-related fashion, at the lower doses tested (40 and 120 mg/kg/day). A developmental NOAEL could not be determined for these data [NOAEL for maternal: 120 mg/kg]. In the second teratogenicity study, florfenicol was retested at lower administered dosages of 1, 3, or 60 mg/kg/day. Maternal effects were limited to a slight increase in water consumption at the 60 mg/kg/day dose. There was no evidence of any adverse effects on the embryo/fetus at doses as high as 60 mg/kg/day in this study. However, based upon the retarded skeletal ossification effects observed in the first study at 40 mg/kg/day the NOAEL for the two studies combined was determined to be between 3 and 40 mg/kg/day.

Pregnancy rate and fetal parameters were unaffected in rabbits given povidone at 1250 mg/kg/day (IV), and in rats fed 10% povidone in the diet.

MUTAGENICITY / GENOTOXICITY:
Florfenicol was negative in a bacterial mutagenicity study (Ames), a mammalian mutagenicity study (mouse lymphoma), a bone marrow micronucleus assay, an in vitro chromosomal aberration assay in CHO cells, a cytogenetics assay in bone marrow, and an unscheduled DNA synthesis assay in rat hepatocytes.

Povidone was negative in a bacterial mutagenicity study (Ames), mammalian mutagenicity study (mouse lymphoma), mouse dominant lethal assay, chromosomal aberration assay, and BALB/C3T3 transformation assay.

CARCINOGENICITY:
This material has not been evaluated for carcinogenicity.

Florfenicol was not carcinogenic in a 2-year study in rats administered dosages up to 48 mg/kg/day for 5 days a week or in mice at dosages up to 200 mg/kg/day for 5 days per week.

In combined chronic toxicity and oncogenicity studies conducted in dogs and rats, there was no evidence of carcinogenicity when povidone was given at 10% concentration in the diet.

SECTION 12: ECOLOGICAL INFORMATION

This information presented below pertains to the following ingredient(s) and does not apply to the final product or its formulation(s).

ECOTOXICITY DATA

INGREDIENT ECOTOXICITY

Florfenicol: 96-hr LC50 (bluegill): >830 mg/L
Florfenicol: 96-hr LC50 (trout): >780 mg/L
Florfenicol: 48-hr EC50 (daphnid): >330 mg/L
Florfenicol: Algae maximum cell density: MIC = 1.5 mg/L
Florfenicol: Algae maximum growth rate: MIC >2.9 mg/L

ENVIRONMENTAL DATA

OTHER INGREDIENT ENVIRONMENTAL DATA:

Florfenicol is not readily biodegradable but there is evidence of inherent biodegradability.

SECTION 13: DISPOSAL CONSIDERATIONS

MATERIAL WASTE:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the ECG or OEG.

PACKAGING AND CONTAINERS:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SPECIAL ENVIRONMENTAL HANDLING PROCEDURES:
This product contains materials that are harmful to the environment. Do not allow product to reach ground water, water courses, sewage or drainage system.

SECTION 14: TRANSPORT INFORMATION

This material is not subject to the transportation regulations of DOT, ICAO, IMO, and the ADR.

SECTION 15: REGULATORY INFORMATION

TSCA LISTING

CHEMICAL NAME	TSCA
Lactose	Listed
Povidone	Listed

WHMIS CLASSIFICATIONS:

This product has been classified in accordance with the hazard criteria on the Controlled Products Regulations and the MSDS contains all the information required by the Controlled Products Regulations.

The final packaged product is not subject to WHMIS classification. The following classification applies to the bulk formulation handled in the workplace.

Controlled Product Class: D2A: Very Toxic

SECTION 16. OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

DEPARTMENT ISSUING MSDS:

Global Safety and Environmental Affairs
Occupational and Environmental Toxicology
Schering-Plough Corporation
1095 Morris Avenue
Union, NJ 07083 USA

SCHERING-PLOUGH MSDS HELPLINE:

(800) 770-8878 (US and Canada)
(908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

MSDS CREATION DATE: 12-Nov-1992
SUPERSEDES DATE: 05-Dec-2003

Date of Approval: October 24, 2005

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-246

AQUAFLOR Type A Medicated Article (florfenicol),
An Antibiotic

For the control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*.

Sponsored by:

Schering-Plough Animal Health Corporation

1. GENERAL INFORMATION

a. File Number:	NADA 141-246
b. Sponsor:	Schering-Plough Animal Health Corporation 1095 Morris Ave. Union, NJ 07083 Drug Labeler Code: 000061
c. Established Name:	Florfenicol
d. Proprietary Name:	AQUAFLOR Type A Medicated Article (florfenicol), An Antibiotic
e. Dosage Form:	Medicated feed
f. How Supplied:	2-kg foil laminate foil pouches (12 x 16 inches) 16-kg fiber board drum (8 x 2-kg pouches)
g. How Dispensed:	Veterinary Feed Directive
h. Amount of Active Ingredients:	500 g of florfenicol per kg
i. Route of Administration:	Oral via feed
j. Species/Class:	Catfish
k. Recommended Dosage:	10 mg of florfenicol per kg of body weight for 10 consecutive days
l. Pharmacological Category:	Antimicrobial
m. Indications:	For the control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri.*

2. *EFFECTIVENESS:*

a. *Dosage Characterization:*

The effectiveness of florfenicol was evaluated for the control of mortality associated with enteric septicemia of catfish (ESC) during a range-finding and dose titration study. The florfenicol formulation used was the commercial formulation and was administered in feed. For both studies, the ESC infection was induced by immersion challenge with *Edwardsiella ictaluri*, the pathogen associated with ESC.

The range-finding study included five treatment groups: 1) not challenged with *E. ictaluri* and fed unmedicated feed, 2) challenged with *E. ictaluri* and fed unmedicated feed, 3) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 10 mg/kg/day for 5 days, 4) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 20 mg/kg/day for 5 days, 5) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 40 mg/kg/day for 5 days. Each treatment group included four tanks with 20 fish per tank (400 total fish). The fish were challenged on Day 0, florfenicol was administered on Days 1 through 5, and monitored for 17 days following treatment. Morbidity and mortality were monitored during the treatment and post-treatment period. Following the post-treatment period all surviving fish were euthanized, examined by gross necropsy and histopathology, and evaluated for the presence of *E. ictaluri*.

A 5-day regimen of 10, 20, or 40 mg florfenicol/kg body weight/day resulted in 0, 1.25, and 1.25% cumulative mortality, respectively. The cumulative mortality for untreated, challenged fish was 57.5% and for untreated, unchallenged fish was 2.5%.

The dose titration study included five treatment groups: 1) not challenged with *E. ictaluri* and fed unmedicated feed, 2) challenged with *E. ictaluri* and fed unmedicated feed, 3) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 5 mg/kg/day for 10 days, 4) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 10 mg/kg/day for 10 days, 5) challenged with *E. ictaluri* and fed medicated feed at a dose rate of 15 mg/kg/day for 10 days. Each treatment group included six tanks with 20 fish per tank (600 total fish). The fish were challenged on Day 0, florfenicol was administered on Days 1 through 10, and monitored for 14 days following treatment. Morbidity and mortality were monitored during the treatment and post-treatment period. All dead fish were assessed microbiologically for the presence of *E. ictaluri*. Following the post-treatment period all surviving fish were euthanized, examined by gross necropsy and histopathology, and evaluated for the presence of *E. ictaluri*.

A 10-day regimen of 5, 10, or 15 mg florfenicol/kg body weight/day resulted in 4.2, 0.8, and 2.5% cumulative mortality, respectively. The unchallenged, untreated group had no mortalities and the challenged, untreated group had 60.0% mortalities.

A dose rate of 10 mg/kg/day administered for 10 consecutive days was selected for the dose confirmation study due to anticipated variability in individual fish responses under field conditions and the potential that fish infected with *E. ictaluri* may not consume medicated feed as readily as required to deliver an effective dosage of florfenicol.

b. ***Substantial Evidence***

1. Dose Confirmation Study, Study No. X00-088-01, Report No. 39963

Title: Florfenicol use in channel catfish (*Ictalurus punctatus*) for treatment of *Edwardsiella ictaluri*: a dose confirmation study

Study Director: Patricia A. Gaunt, D.V.M., Ph.D.

Study Location: Mississippi State University
Thad Cochran National Warmwater Aquaculture Center
Stoneville, MS

General Design of the Study:

a. Purpose: To confirm the appropriate dose rate and duration of administration of florfenicol for the control of mortality associated with enteric septicemia of catfish caused by *E. ictaluri* in channel catfish.

b. Animals: Channel catfish, *Ictalurus punctatus,* fingerlings that ranged in weight from 6.0 to 10.6 g and in age from 150 to 180 days were used. A total of 600 fingerlings were stocked into 30 fish tanks (20 fish/tank). Tanks were supplied with freshwater from wells at temperatures ranging from 25 to 28 °C. Water temperature, pH, chloride, nitrite, ammonia, hardness, and alkalinity levels were recorded.

c. Test article/controls: Florfenicol was incorporated into catfish feed pellets. The test rations were prepared to contain 0 and 400 milligrams florfenicol per kg of basal diet to supply 0 and 10 mg/kg body weight daily respectively when fed at 2.5% of body weight.

d. Study Design: The dose confirmation study was conducted with laboratory-reared channel catfish fingerlings held in 80 L tanks. Fish were evaluated by a modified agglutination assay to determine their immunological status relative to *E. ictaluri* prior to inclusion in the study. Fifteen (15) tanks of fish were assigned to each of the two treatment groups: 1) challenged with *E. ictaluri* and treated with florfenicol or 2) challenged with *E. ictaluri* and not treated. After a 21-day acclimation period, fish were exposed to *E. ictaluri* in water on Day 0 and fed unmedicated feed through Day 1. Starting on Day 2, treated fish received florfenicol-medicated feed for 10 consecutive days (Days 2-11), and untreated fish received unmedicated feed. All fish were monitored for morbidity/mortality during acclimation, during the 10-day dose administration period, and during the 14-day post-

treatment observation period. After the observation period, all surviving fish were euthanized, examined by gross necropsy, and evaluated for the presence of *E. ictaluri* by bacterial culture (isolation and determination of the minimum inhibitory concentration). One florfenicol-treated tank was excluded from the study and the statistical analysis due to inadequate evidence of infection by *E. ictaluri* as the cause of mortality.

e. Parameters measured: Mortality, feeding activity, and water quality parameters were noted throughout the trial. All dead fish were assessed microbiologically for the presence of *E. ictaluri.*

Results: Mortality results are included in the following table.

Table 1. Cumulative mortality for the 10-day treatment period and 14-day post-treatment period for a dose confirmation study in channel catfish.

Florfenicol Dose (mg/kg)	Cumulative Mortality	Mean Tank Percent Cumulative Mortality
0	262	87.3
10	27	9.5

The MIC (minimum inhibitory concentration) of florfenicol for this strain of *E. ictaluri* was 0.25 μg/mL in all 26 fish that were assayed. The mean Kirby-Bauer zone of inhibition for 285 of the 286 isolates was 34.5 mm (range: 32 to 41 mm) from all fish from which *E. ictaluri* was isolated.

Statistical Analysis: Data were analyzed by Logistic Regression using a General Linear Mixed Model with fish nested within tank and tank nested within treatment. The mortality in the dose group treated with florfenicol was significantly ($p<0.001$) lower than the control group.

Conclusion: Florfenicol administered to channel catfish, *Ictalurus punctatus*, at a dose of 10 mg/kg body weight per day for 10 consecutive days is effective for the control of mortality due to enteric septicemia of catfish associated with *E. ictaluri.*

2. Clinical Field Effectiveness Trial, Study No. X01-027-01, Report No. 40128

Title: Florfenicol use in channel catfish (*Ictalurus punctatus*) for control of mortality associated with *Edwardsiella ictaluri*: a pond study

Study Director: Patricia A. Gaunt, D.V.M., Ph.D.

Study Location: Mississippi State University
Thad Cochran National Warmwater Aquaculture Center
Stoneville, MS

General Design:

a. Purpose: To confirm the appropriate dose rate and duration of

administration of florfenicol for the control of mortality associated with enteric septicemia of catfish caused by *E. ictaluri* in channel catfish under field conditions in small ponds.

b. Animals: Approximately 154,000 channel catfish fingerlings 150 to 180 days of age that weighed 6.6 to 7.8 g were used in the study. Fish were allocated to each of fourteen 0.1-acre ponds at the rate of approximately 11,000 fish/pond.

c. Test article: Florfenicol was incorporated into catfish feed pellets. The two trial rations were prepared to contain 0 and 400 milligrams florfenicol per kg of basal diet to supply 0 and 10 mg/kg body weight daily respectively when fed at 2.5% of body weight.

d. Study Design: The pond study was conducted with channel catfish fingerlings held in ponds. Fish were from an ESC-free facility. Ponds were assigned to 2 treatment groups, one group received florfenicol-medicated feed and one group received unmedicated feed. The ponds were challenged with *E. ictaluri* either naturally or by exposure to fish challenged with *E. ictaluri* cultured from a naturally occurring outbreak added to the water. Ponds were observed until the cumulative morbidity/mortality rate attributable to ESC based on clinical signs and/or lesions reached 0.3% per pond. Ponds received the assigned test ration for 10 consecutive days and were monitored for morbidity/mortality. Throughout the study moribund fish were counted as mortalities. After the treatment period, ponds were observed for a 14-day post-treatment observation period during which dead and/or moribund fish were collected, examined by gross necropsy and the presence of *E. ictaluri* was determined microbiologically. A maximum of 5 moribund/dead fish that were not degraded by autolysis which could interfere with bacterial isolation were cultured per week from each pond for isolation of *E. ictaluri*. At the end of the post-treatment observation period, the ponds were harvested, the fish harvested were counted and euthanized, and 20 fish from each pond were examined by gross necropsy and evaluated for the presence of *E. ictaluri* by bacterial culture. MICs were determined on a maximum of 15 fish from each pond. Two of the florfenicol-treated ponds were excluded from the study because florfenicol-medicated feed was administered following the 10-day treatment period.

e. Parameters Measured: Mortality, feed consumption, and microbiological assessments to confirm the presence of *E. ictaluri* in morbid/dead fish and the sensitivity of *E. ictaluri* isolates to florfenicol. Water quality parameters were monitored.

Results: Mortality and harvest results are included in the following table.

Table 2. Cumulative mortality and harvest results for the 10-day treatment period and 14-day post-treatment period for a field study in channel catfish.

Florfenicol Dose-mg/kg (Number of Ponds)	Percent Cumulative Mortality* (Cumulative Mortality)	Percent Recovery at Harvest* (Number)	Percent Missing after Harvest* (Number)
0 (7)	3.0 (2300)	59.4 (45,579)	37.6 (28,891)
10 (5)	2.3 (1256)	64.9 (35,563)	32.8 (17,996)

*Based on the number of fish allocated minus pre-treatment mortality to the ponds.

The missing fish can be attributed to deaths due to handling during stocking, bird parasitism, autolysis, and cannibalism.

The MIC (minimum inhibitory concentration) of florfenicol for this strain of *E. ictaluri* was 0.25 µg/mL in all fish that were assayed. The mean Kirby-Bauer zone of inhibition was 36.8 mm (range: 32 to 50 mm) from all fish from which *E. ictaluri* was isolated.

Conclusion: Florfenicol administered to channel catfish, *Ictalurus punctatus*, at a dose of 10 mg/kg/day for 10 consecutive days is effective for the control of mortality due to enteric septicemia of catfish associated with *E. ictaluri*.

c. ***Microbiology***

1. Dose Selection Study, Study No. 97-049, Report No. 44210

Title: Preliminary Assessment of Florfenicol for Use in Channel Catfish (*Ictalurus punctatus*) for Treatment of *Edwardsiella ictaluri*: a Range Finding Study

Study Director: Patricia A. Gaunt, D.V.M., Ph.D.

Study Location: Mississippi State University
Thad Cochran National Warmwater Aquaculture Center
Stoneville, MS

General Design of the Study:

a. Purpose: To determine the *in vitro* minimum inhibitory concentration (MIC) of florfenicol against *E. ictaluri* and to determine the susceptibility of *E. ictaluri* to florfenicol by the Kirby-Bauer technique using florfenicol impregnated discs.

b. Procedures: Twelve isolates of *E. ictaluri* obtained from infected channel catfish in Mississippi (1994, 1996, and 1997) were characterized to determine susceptibility to florfenicol in terms of the minimum inhibitory concentration and the zone of inhibition by the Kirby-Bauer method.

Minimum Inhibitory Concentration: Florfenicol was serially diluted in agar at concentrations of 0, 0.002, 0.004, 0.008, 0.016, 0.03, 0.06, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, and 64 µg/mL and poured into two plates at each concentration. Plates were inoculated with an *E. ictaluri* strain, cultured at 27 °C for 2 days and observed to determine which concentration completely inhibited growth of *E. ictaluri*.

Zone of Inhibition (Kirby Bauer technique): Plates containing Mueller-Hinton medium with 5% sheep blood were inoculated with *E. ictaluri*. A disc impregnated with 30 µg florfenicol was placed on each plate. Plates were cultured for 2 days at 27 °C and the zone of bacterial growth inhibition was measured (mm) in accordance with the current NCCLS guidelines.

Results: The MIC of florfenicol for 12 isolates of *E. ictaluri* was 0.25 µg/mL. The mean zone of inhibition for the 12 *E. ictaluri* isolates by the Kirby-Bauer technique was 46.8 mm (range: 41 to 51 mm).

Conclusion: The 12 field isolates of *E. ictaluri* obtained from channel catfish in Mississippi during 1994, 1996, and 1997 appear to be susceptible to florfenicol *in vitro*.

2. Minimum Inhibitory Concentrations (MIC) Data

In vitro investigations of certain bacterial fish pathogens have demonstrated florfenicol's activity range. These findings are summarized in **Table 3**.

Table 3. Minimum inhibitory concentrations of florfenicol against selected fish pathogens

Organism	No. of Isolates	MIC (µg/mL)	Year
Edwardsiella ictaluri	12	0.25	1998
Edwardsiella ictaluri	1	0.25	1998
Edwardsiella ictaluri	16	0.25	2000
Edwardsiella ictaluri	26	0.25	2000
Edwardsiella ictaluri	40	0.25	2001

3. TARGET ANIMAL SAFETY:

a. Study No. 97-049, Report No. 44211

This non-GLP study was conducted to determine the appropriate dose rate of florfenicol administered in feed to catfish for the control of mortality associated with enteric septicemia caused by infection with *E. ictaluri*. As part of the study all fish were necropsied at the end of the study and findings from gross pathological and histopathological examinations were recorded. The study methods are summarized in the effectiveness section of this document.

The fish had external and internal lesions compatible with published lesions for enteric septicemia. No lesions indicative of any concurrent diseases were observed. An increased degree of inflammatory cell infiltrate occurred in the liver, heart, gills, anterior kidney, and spleen of the untreated/challenged fish compared to the unchallenged and florfenicol-treated fish.

No significant changes attributable to treatment with florfenicol were observed upon gross necropsy of the skin, fins, mouth, gills, eyes, and viscera. No significant changes attributable to treatment with florfenicol were observed upon histopathological examination of the anterior kidney, posterior kidney, brain, gill, heart, liver, or spleen.

Conclusions: Florfenicol administered in feed to channel catfish, *Ictalurus punctatus*, at dose rates of 10, 20, and 40 mg/kg/day for 5 consecutive days caused no significant histopathological changes in the anterior kidney, posterior kidney, brain, gill, heart, liver, or spleen attributable to treatment.

b. Tolerance Study in Catfish, Study No. 97-049, Report No. 44214

Title: Preliminary Assessment of Florfenicol for Use in Channel Catfish (*Ictalurus punctatus*) for Treatment of *Edwardsiella ictaluri*: A Tolerance Study.

Study Director: Patricia A. Gaunt, D.V.M., Ph.D.

Study Location: Mississippi State University
Thad Cochran National Warmwater Aquaculture Center
Stoneville, MS

General Design of the Study:

a. Purpose: To determine the tolerance of channel catfish for florfenicol when assessed by toxicological and histological methods.

b. Animals: Channel catfish fingerlings in the weight range of 36.9 to 48.5 g were used. A total of 400 fingerlings were stocked into 20 tanks (20 fish/tank). Tanks were supplied with fresh water from wells at temperatures ranging from 21 to 27 °C. Water temperature, pH, chloride, nitrite, ammonia, hardness, and alkalinity levels were recorded.

c. Test article/controls: Florfenicol was incorporated into catfish feed pellets. Trial rations were prepared to contain 0, 400, 800, 1,600, and 4,000 milligrams florfenicol per kg of basal diet to supply 0, 10, 20, 40, and 100 mg/kg body weight daily respectively when fed at 2.5% of body weight.

d. Study Design: The study was conducted with laboratory-reared channel catfish fingerlings held in 120 L tanks. Four tanks were assigned to each of five treatment groups: 1) fed unmedicated feed, 2) fed 10 mg florfenicol/kg body weight (bw), 3) fed 20 mg florfenicol/kg bw, 4) fed 40 mg florfenicol/kg bw, and 5) fed 100 mg florfenicol/kg bw. After the acclimation period, fish

were fed either unmedicated feed or medicated feed for 10 consecutive days. All fish were monitored for feeding activity, mortality, and morbidity for the 10-day treatment period. After the treatment period, all surviving fish were euthanized, necropsied and examined by histopathology.

e. Parameters Measured: Mortality and feeding activity were noted throughout the trial as were water quality parameters. In addition, all fish were necropsied at the end of the study and findings from gross pathological and histopathological examinations were recorded.

GLP Compliant: No

Results: No mortality occurred during the study. The feeding activity of the control fish was vigorous throughout the study. The feeding activity of the treated groups was slightly decreased during the first three days of the treatment period, but was vigorous for the remainder of the treatment period. A 10-day regimen of 0, 10, 20, 40, or 100 mg florfenicol/kg body weight/day resulted in a 16.25%, 15.25%, 20.0%, 14.0%, and 14.5% weight gain respectively. No significant changes attributable to treatment with florfenicol were observed upon gross necropsy of the skin, fins, mouth, gills, eyes, and viscera. No significant changes attributable to treatment with florfenicol were observed upon histopathological examination of the anterior kidney, posterior kidney, brain, gill, heart, liver, or spleen.

Conclusions: No significant changes attributable to treatment with florfenicol were observed upon gross necropsy or histopathological examination of the experimental fish.

c. Safety Study in Catfish, Study No. X00-242-01, Report No. 45485

Title: Target Animal Safety Study of Aquaflor (50% Type A Medicated Article), Florfenicol – SCH25298, Administered in Feed to Channel Catfish, *Ictalurus punctatus*.

Study Director: Mark P. Gaikowski, M.A.

Study Location: U.S.G.S. Biological Resources Division
Upper Midwest Environmental Sciences Center
La Crosse, WI

General Design of the Study:

a. Purpose: To determine the safety of Aquaflor (50% Type A Medicated Article), administered in feed to channel catfish, *Ictalurus punctatus*, at doses of 1X, 3X, and 5X the recommended dose rate of 10 mg/kg body weight for twice the recommended treatment duration of 10 consecutive days.

b. Animals: Channel catfish fingerlings with a mean fish weight per tank of 19.1 to 22.3 g were used. A total of 240 fingerlings were stocked into 12 tanks (20 fish/tank). Tanks were supplied with fresh water from wells at temperatures ranging from 26.3 to 29 °C.

c. Test article/controls: Florfenicol was incorporated into catfish feed pellets. Trial rations were prepared to contain 0, 500, 1,500, and 2,500 mg florfenicol per kg of basal diet to supply 0, 10, 30, and 50 mg/kg body weight daily respectively when fed at 2.0% of body weight.

d. Study Design: The study was conducted with laboratory-reared channel catfish fingerlings held in 80 L tanks. Three tanks were assigned to each of four treatment groups: 1) fed unmedicated feed, 2) fed 10 mg florfenicol/kg (body weight) bw, 3) fed 30 mg florfenicol/kg bw, and 4) fed 50 mg florfenicol/kg bw. After the acclimation period, fish were fed either unmedicated feed or medicated feed for 20 consecutive days. Fish were monitored for feeding activity, mortality, and morbidity. After the treatment period, fish were necropsied and examined histopathologically.

e. Parameters Measured: Mortality, feeding activity, and water quality parameters were noted throughout the trial. In addition, all fish were necropsied at the end of the study and findings from gross pathological and histopathological examinations were recorded.

GLP Compliant: Yes

Statistical Methods: No fish died during treatment, and no fish morbidity was observed during the treatment period. No analysis of mortality or morbidity was conducted. For the histopathological results, the proportion of fish in a tank with a particular pathological lesion was analyzed by logistic regression in a general linear mixed model, using fish (observation unit) nested within tank (experimental unit). Block and tank were random variables.

Results: No mortality or signs of morbidity were observed over the course of the study. No clinically observable changes were detected in fish behavior among the treated fish relative to the controls. Although feed consumption significantly declined through the latter part of the dosing period at the 30 and 50 mg/kg dose rates, there were no significant differences in the fish size at the end of the study. The gross pathology findings during the study were determined to be due to confinement, such as blunted fins and punctate, epidermal erosions. A microscopically evident minimal to mild dose-dependent decrease in hematopoietic/lymphopoietic tissue was observed within the anterior kidneys, posterior kidneys, and spleens of fish that received florfenicol. The incidence of H/L decrease in each organ in each dose group is included in the following table.

Table 4. Incidence and severity of decreased hematopoietic/lymphopoietic tissue in florfenicol-treated channel catfish

Dose Group	Number of Tissues Examined	Tissue*	Decreased Hematopoietic/Lymphopoietic Tissue		
			Minimal	Mild	Total**
Control	30	AK	3	0	3
	30	PK	2	0	2
	30	SP	1	0	1
10 mg/kg	30	AK	9	0	9 (p=0.0685)
	30	PK	8	3	11(p=0.0130)
	30	SP	11	1	12 (p=0.0163)
30 mg/kg	30	AK	14	4	18 (p=0.0004)
	30	PK	12	12	24 (p<0.0001)
	30	SP	13	9	22 (p=0.0009)
50 mg/kg	30	AK	15	8	23 (p<0.0001)
	31	PK	14	12	26 (p<0.0001)
	28	SP	11	8	19 (p=0.0013)

*AK=anterior kidney PK=posterior kidney SP=spleen
**p<0.10 significant

No other histopathological changes were noted in the muscle, skin, brain, gill, heart, or liver.

Conclusions: No significant changes attributable to treatment with florfenicol were observed upon gross necropsy and minor dose-related histopathological changes were observed in the kidney and spleen of fish that received florfenicol. Since the duration of treatment in this study was twice the 10-day recommended treatment duration, florfenicol is safe to administer to catfish at a dose of 10 mg/kg body weight/day for 10 consecutive days.

4. HUMAN FOOD SAFETY:

a. Toxicology:

Summaries of toxicology studies supporting the human food safety of AQUAFLOR 50% Type A Medicated Article are contained in the FOI Summary dated May 31, 1996, for the original approval of NADA 141-063, NUFLOR injectable solution for cattle. For the current approval, an assessment was presented on the effects of florfenicol residues present in edible tissues of catfish on human intestinal flora. It was concluded that the amount of active florfenicol residues reaching the human colon following a 12-day withdrawal period for catfish is probably too low to produce any adverse effect on the human intestinal flora.

The ADI for florfenicol is 10 micrograms per kilogram body weight per day. The safe concentration of total drug-related residues is 2 ppm in catfish muscle.

b. Residue Chemistry

1. Summary of Residue Chemistry Studies

a. Total Residue and Metabolism Study

SCH 25298 (Florfenicol): Total residue depletion of ^{14}C-SCH25298 following a multiple (10-day) oral dose regimen in Atlantic salmon (*Salmo salar)* maintained at 5 °C

Study No. 93702

In-Life Facility – Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, Prince Edward Island

Analytical Labs – Total residue and metabolism work was conducted at Schering-Plough Research Institute, Lafayette, New Jersey. The determinative assay was performed at Hazelton Wisconsin, Inc., Madison, Wisconsin.

The study was conducted according to Good Laboratory Practices (21 CFR 58). Fifty-eight Atlantic salmon (25 months of age, weight range 488 to 793 grams) were used. Fifty-four fish (30 male, 24 female) were test fish. Four fish (2 male, 2 female) were controls. The fish were acclimated for two weeks in 5 $\pm$ 0.5 °C seawater. The test fish were fed feed containing 2.7 g florfenicol/kg of feed to obtain an approximate dose of 10 mg florfenicol/kg body weight/day for 9 consecutive days. On Day 10, the test fish were dosed once by oral gavage with 10 mg ^{14}C-florfenicol/kg body weight. Control fish received nonmedicated feed throughout the study. Six fish were sampled at 3 hours, 12 hours, 1 day, 3 days, 7 days, 15 days, 30 days, 45 days, and 60 days post-dose. Liver, plasma, kidney, muscle, skin, bone, bile, and retained gut contents were collected from each fish. Tissues were analyzed for total radioactivity by combustion and liquid scintillation counting. The radioactive components of pooled samples of plasma, bile, liver, kidneys, muscle, and skin were extracted and characterized by HPLC. Liver, muscle, and skin samples were analyzed using the determinative method for florfenicol amine.

Table 5. Total radioactive residues (μg ^{14}C-florfenicol equivalents/g) in muscle and in skin of Atlantic salmon maintained at 5 °C and dosed first for 9 days with medicated feed containing 10 mg florfenicol/kg body weight/day and then for 1 day by oral gavage with 10 mg ^{14}C-florfenicol/kg body weight.

Withdrawal Time	Muscle (mean ± standard deviation)	Skin (mean ± standard deviation)
3 hours	0.327 ± 0.3254	0.453 ± 0.4797
12 hours	0.414 ± 1.507	4.20 ± 1.801
1 day	5.85 ± 3.074	5.51 ± 2.843
3 days	1.17 ± 0.321	1.65 ± 0.527
7 days	0.097 ± 0.0155	0.506 ± 0.0736
15 days	0.027 ± 0.0134	0.217 ± 0.1272
30 days	0.016 ± 0.0118	0.156 ± 0.1395
45 days	0.030 ± 0.0216	0.247 ± 0.1603
60 days	0.008 ± 0.0071	0.090 ± 0.067

Table 6. Florfenicol amine residues (μg florfenicol equivalents/g) in muscle and in skin of Atlantic salmon maintained at 5 °C and dosed first for 9 days with medicated feed containing 10 mg florfenicol/kg body weight/day and then for 1 day by oral gavage with 10 mg ^{14}C-florfenicol/kg body weight.

Withdrawal Time	Muscle (mean ± standard deviation)	Skin (mean ± standard deviation)
3 hours	12.5 ± 2.42	10.7 ± 3.48
12 hours	16.6 ± 6.33	15.9 ± 3.10
1 day	14.8 ± 5.06	17.2 ± 6.51
3 days	4.22 ± 1.57	6.91 ± 3.90
7 days	0.436 ± 0.066	1.37 ± 0.485
15 days	<0.3	1.19 ± 0.461
30 days	<0.3	0.416 ± 0.106
45 days	<0.3	0.534 ± 0.156
60 days	<0.3	0.371 ± 0.024

Table 7. Total radioactive residues (µg ^{14}C-florfenicol equivalents/g) and florfenicol amine (µg florfenicol amine/g) concentrations in muscle/skin of Atlantic salmon maintained at 5 °C and dosed first for 9 days with medicated feed containing 10 mg florfenicol/kg body weight/day and then for 1 day by oral gavage with 10 mg ^{14}C-florfenicol/kg body weight. Muscle/skin concentrations were calculated using values of 90% muscle and 10% skin as an edible portion.

Withdrawal Time	Total Residues (ppm)	Florfenicol Amine (ppm)
3 hours	0.339	12.34
12 hours	0.793	16.54
1 day	5.816	15.02
3 days	1.22	4.46
7 days	0.138	0.52
15 days	0.046	0.38
30 days	0.03	0.31
45 days	0.052	0.32
60 days	0.016	0.30

Table 8. Percent distribution of ^{14}C-SCH 25298 metabolites in Atlantic salmon muscle and skin salmon maintained at 5°C and dosed first for 9 days with medicated feed containing 10 mg florfenicol/kg body weight/day and then for 1 day by oral gavage with 10 mg ^{14}C-florfenicol/kg body weight.

^{14}C-component	3 hour		12 hour		1 day		3 day		7 day		15 day		30 day	
	muscle	skin	muscle	skin	muscle	skin	muscle	skin	muscle	skin	muscle	skin	muscle	skin
florfenicol amine	9.84	14.51	15.74	NA	36.51	NA	60.77	NA	44.67	37.32	25.63	NA	17.80	14.66
unknown 1	---	---	1.34	NA	1.15	NA	---	NA	2.18	---	---	NA	---	---
florfenicol oxamic acid	0.14	1.19	---	NA	1.25	NA	2.25	NA	1.04	8.36	26.65	NA	20.76	3.08
unknown 2	---	---	---	NA	---	NA	---	NA	---	---	---	NA	---	---
florfenicol alcohol	1.07	2.33	1.14	NA	3.11	NA	8.14	NA	7.67	8.40	---	NA	---	1.79
unknown 3	---	---	---	NA	---	NA	---	NA	1.04	---	---	NA	---	---
unknown 4	---	---	---	NA	---	NA	---	NA	---	---	---	NA	---	---
other unknown(s)	---	---	---	NA	---	NA	---	NA	2.24	---	---	NA	---	---
monochloro-florfenicol	---	---	---	NA	---	NA	---	NA	---	---	1.80	NA	0.65	---
florfenicol	76.41	70.23	70.24	NA	45.10	NA	14.30	NA	1.42	2.84	2.29	NA	0.59	0.38

NA = not analyzed

b. Comparative Metabolism Study

Comparative metabolism of florfenicol in the rat (the animal used in the toxicity tests) and in salmon has been satisfactorily demonstrated by data in NADA 141-063 (florfenicol in cattle) and in studies conducted with florfenicol in salmon, Study No. 93702. All of the major metabolites of florfenicol seen in salmon tissues were also seen in rat tissues or excreta. Individual unknown metabolites in salmon were not greater than 2% of tissue total radioactivity. A metabolism study in catfish was not completed since the metabolism of florfenicol in catfish is anticipated to be similar to that in salmon. Also, the determinative assay for residues uses an acid-catalyzed hydrolysis step to convert parent florfenicol and florfenicol metabolites to a common marker, florfenicol amine.

c. Residue Depletion Study

SCH 25298 (Florfenicol): A Final Residue Depletion Study in Channel Catfish Following Administration in Feed

Study No. 00214, Report No. 00214

Study Director: Christopher L. Wrzesinski, Schering-Plough Research Institute, Lafayette, NJ

Investigator: Patricia S. Gaunt, Thad Cochran National Warmwater Aquaculture Center, Stoneville, MS

In-Life Testing Facility: Delta Western Research Center, Indianola, MS

Tissue Collection Facility: Thad Cochran National Warmwater Aquaculture Center, Stoneville, MS

Analytical Facility: Schering-Plough Research Institute, Lafayette, NJ

The in-life portion of the study was conducted in a non-GLP facility. Deviations from GLP were provided. The analytical phase of the study was conducted following GLPs (21 CFR 58).

Male and female catfish (2 pounds average bodyweight at the beginning of acclimation) were used. The fish were held in a 0.1 acre pond with a stocking density of 7,000 fish/acre. Water temperature remained <25 °C at all times over the course of medication and withdrawal with an average daily high and low water temperature during treatment of 21.9 °C and 19.4 °C, respectively and an average daily high and low water temperature during withdrawal of 19.1 °C and 16.6 °C, respectively. The fish were acclimated for 44 days prior to dosing. Control fish were collected during acclimation and prior to dosing. The test fish were fed medicated pelleted fish feed for 12 days at a target dose of 10 mg florfenicol/kg

bodyweight/day. The average dose over the 12-day dosing period was 8.1 mg florfenicol/kg bodyweight/day. Groups of twenty-five fish were sampled at 1, 2, 4, 7, 14, and 21 days after treatment ended. Residues of florfenicol were measured in muscle of twenty fish per time point using the determinative HPLC method for the marker residue, florfenicol amine.

Table 9. Mean florfenicol amine residues in muscle of catfish fed 8.1 mg florfenicol/kg body weight/day for 12 days.

Withdrawal Time (days)	Mean (ppm) ± standard deviation
1	5.378 ± 7.014
2	2.303± 2.959
4	0.876 ± 0.537
7	0.232 ± 0.109
14	0.157 ± 0.059
21	0.169 ± 0.050

Individual values below the lowest point on the standard curve (0.075 ppm) were not used to calculate the means.

2. Target Tissue and Marker Residue Assignment

For fish, the target tissue is muscle with adhering skin except for species such as catfish where the skin is not typically consumed by humans. Therefore, the target tissue for catfish is muscle.

Florfenicol amine is assigned as the marker residue because the determinative method converts parent and all metabolites to that compound.

3. Tolerance Assignment

Data were not available on the portion of total residues measured by the marker, florfenicol amine, in catfish muscle. The level of marker residues could not be determined when the total residues are 2 ppm (the safe concentration). Therefore, data from a major species were used to establish a tolerance of 1 ppm for florfenicol measured as florfenicol amine in catfish muscle.

4. Withdrawal Times

A 12-day withdrawal time was calculated using 99% statistical tolerance and 95% confidence with the residue depletion data in Study No. 00214 and a tolerance of 1 ppm.

c. Microbial Food Safety

CVM evaluated microbial food safety information for florfenicol for the control of mortality in channel catfish associated with infection by *Edwardsiella ictaluri* using a qualitative risk assessment procedure. This risk assessment procedure

involved conducting 1) a release assessment to describe the probability that the antimicrobial new animal drug and its use in animals will result in the emergence and dissemination of resistant bacteria or resistant determinants in the food animal under proposed conditions of use, 2) an exposure assessment to describe the likelihood of human exposure to the resistant bacteria or resistance determinants through consumption of edible products from treated animals, and 3) a consequence assessment to describe the potential human health consequences of exposure to the defined resistant bacteria or resistance determinants by considering the human medical importance of florfenicol in the treatment of human infectious disease.

The outcome of the release assessment was determined to be **medium**. The outcome of the exposure assessment was determined to be **low,** and the outcome of the consequence assessment was determined to be **medium**. These outcomes were integrated into an overall risk estimation of **medium** for florfenicol under the proposed conditions of use (10 mg/kg body weight per day in feed for 10 consecutive days) in catfish. Risk management strategies associated with an overall risk estimation of **medium** are compatible with the proposed use of florfenicol in catfish.

d. Analytical Method for Residues:

1. Determinative Method

The HPLC determinative procedure approved under NADA 141-063 for bovine tissues was successfully validated according to the Agency's guidelines for the quantitation of florfenicol amine (marker residue) residues in the edible tissues of catfish (muscle) receiving AQUAFLOR Type A Medicated Article, An Antibiotic.

The determinative assay for the marker residue, florfenicol amine, in the edible tissues, is a high performance liquid chromatography (HPLC) method that provides acceptable sensitivity, specificity, accuracy and precision for the routine monitoring of florfenicol residues in catfish. Florfenicol residues (and those of related metabolites) are converted to the marker residue, florfenicol amine, by acid-catalyzed hydrolysis. The determinative procedure was successfully validated at 1 ppm in an independent laboratory.

2. Confirmatory Method

The summary for the confirmatory method for AQUAFLOR Type A Medicated Article, An Antibiotic is contained in NADA 141-063.

3. Availability of Method

The validated regulatory method for detection and confirmation of residues of florfenicol is available from the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

5. *USER SAFETY:*

Human warnings are provided on the product labeling as follows:

> "Avoid inhalation, oral exposure, and direct contact with skin or eyes. Operators mixing and handling Aquaflor should use protective clothing, gloves, goggles and NIOSH-approved dust mask. Wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse thoroughly with water. If irritation persists, seek medical attention. Not for human consumption. Keep out to reach of children. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. For more information or to report adverse effects, call 1-800-224-5318. For customer service, call 1-800-521-5767. For a copy of the MSDS sheet, call 1-800-770-8878."

6. *AGENCY CONCLUSIONS:*

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that AQUAFLOR Type A Medicated Article (florfenicol), An Antibiotic when administered at a dose of 10 mg florfenicol/kg of body weight daily for 10 consecutive days, is safe and effective for the control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*.

Labeling restricts this drug to use by or on order of a licensed veterinarian. This decision was based on the following factors: (a) adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this product, (b) restricting this drug to use by or on order of a licensed veterinarian should help prevent indiscriminate use which could result in violative tissue residues, and (c) the rate of emergence of florfenicol-resistant organisms may be reduced by the involvement of veterinarians in product use. Because the drug will be administered in feed, the drug will be marketed as a Veterinary Feed Directive drug.

A tolerance of 1 ppm in muscle tissue in catfish was established using data from a major species. A 12-day withdrawal time was calculated. Microbial food safety (generation or selection of antimicrobial-resistant bacteria of public health concern and subsequent impact on human therapy) associated with the use of florfenicol in catfish as described in this document was assessed. An overall risk estimation for florfenicol in catfish under the proposed conditions (10 mg/kg body weight per day in feed for 10 consecutive days) was determined to be medium. Risk management strategies associated with the proposed conditions of use of florfenicol in catfish are compatible with an overall risk estimation of medium.

Under section 573(c) of the Federal Food, Drug, and Cosmetic Act (the Act), this approval qualifies for SEVEN years of exclusive marketing rights beginning on the date of approval because the new animal drug has been declared a designated new animal drug by FDA under section 573(a) of the Act.

7. ATTACHMENTS:

Facsimile labeling is attached as indicated below.

AQUAFLOR Type A Medicated Article (florfenicol), An Antibiotic Label 2 kg
AQUAFLOR Type A Medicated Article (florfenicol), An Antibiotic Label 8 x 2 kg
AQUAFLOR Type C Catfish Medicated Feed Label
AQUAFLOR Type A Medicated Article (florfenicol), An Antibiotic VFD Form