HFA-305

FINDING OF NO SIGNIFICANT IMPACT
and
Environmental Assessments

PARASITE-S for Use in Finfish, Finfish Eggs and Shrimp

NADA 140-989 C0018

Western Chemical Inc.
Ferndale, WA

FOR PUBLIC DISPLAY

FINDING OF NO SIGNIFICANT IMPACT

PARASITE-S for Use in Finfish, Finfish Eggs and Shrimp

NADA 140-989 C0018

Western Chemical Inc.
Ferndale, WA

The Center for Veterinary Medicine has considered the potential environmental impact of this action and has concluded that this action will not have a significant impact on the quality of the human environment and that, therefore, an environmental impact statement will not be prepared.

Western Chemical Inc. has submitted a supplement to the approved new animal drug application for PARASITE-S (formalin, an aqueous formaldehyde solution). The supplement provides for the use of the product in all species of finfish and finfish eggs to treat protozoan, parasites and fungi. The product is currently approved in the treatment of specified species of finfish, finfish eggs and penaeid shrimp. The drug is administered as a bath at dosages up to 250 ppm for finfish, 100 ppm for penaeid shrimp and 2000 ppm for finfish eggs. In support of the application, Western Chemical Inc. has referenced an Environmental Assessment (EA) dated January 1995, that was prepared by the National Research Support Project No. 7.

The January 1995 EA provides information on the potential environmental effects from the use of the product in all species of finfish. An amendment to the EA, dated September 6, 1995, was prepared by the Environmental Staff of the Center for Veterinary Medicine to analyze the potential for environmental impacts from the use of formal in to treat fungus on the eggs of all species of finfish. The amendment also refers to the original July 29, 1981, EA for the use of formalin in specified finfish species. Copies of these three documents are attached.

The January 1995 EA requires additional clarification not provided in the September 6, 1995, amendment to the EA, as follows:

(1) The EAs and the amendment refer to the use of formalin on fish and fish eggs. The terms "fish" and "finfish" are normally considered synonymous but the labeling of the product and other components of the NADA contain the term "finfish," which is considered the more specific term.

(2) The January 1995 EA stipulates that the treatment water should be discharged in such a manner that the concentration in the mixing zone of the receiving water is no greater than 1.00 ppm to avoid damage to sensitive aquatic species. This stipulation is too restrictive because 1.00 ppm and greater levels of formalin can occur in the mixing zone of a stream for a short period without causing significant damage to sensitive aquatic species. Data in the EAs indicate that the most sensitive organisms tested were ostracods. The LC50 for these organisms is 1.15 ppm. However, this resulted from exposure to formalin for 24 hours. Exposure in a recieving stream are expected to be much more transient then 24 hours and are expected to be for no more then minutes (e.g., see Case Situation 1 in the Janaury 1995 EA). Exposure to 1 ppm of formalin for several minutes is not expected to cause significant adverse effects.

Instead of stipulating a limitation on the concentration of formal in in the recieving water, the Center is requiring a 10-fold dilution of the finfish and penaeid shrimp treatment water, and 100-fold dilution of finfish egg treatment water. Dilution of the treatment water will result in a concentration of formal in at the point of introduction into the aquatic environment of no greater than 25 ppm. This concentration will further dilute in the receiving stream, These dilutions, the periodic use of the product and the rapid environmental degradation of formalin are expected to reduced the environmental concentration below a level that causes significant effects on aquatic organisms.

The January 1995 EA, the September 6, 1995, amendment to the EA and the July 29, 1981, EA provide adequate information to determine that the use of PARASITE-S, following the approved labeling, is not expected to cause a significant impact on the environment.

3/19/98
Date

for Director, Office of New Animal Drug Evaluation, HFV-100

Attachments: January 1995 EA, September 6, 1995 EA amendment and PARASITE-S labeling

Environmental Impact Assessment for the Use of Formalin in the Control of External Parasites on Fish

January 1995

Proposed Use of Formalin

Formalin, an aqueous solution of formaldehyde gas, containing not less than 37% by weight of formaldehyde gas per weight of water and 6- 13% (12%) methanol, is recommended for the control and prevention of external protozoan parasites on fish. Formalin solution is recommended for use at a concentration of 250 ppm for a contact period of up to one hour for the control of external parasites on fish. Formalin controls the protozoan parasites: Ichthyophthirius spp., Costia spp., Epistylis spp., Chilodonella spp., Scyphidia sp., Trichodina spp.; monogenetic trematodes, including Cleidodiscus spp., Gyrodaclgyrus spp. and Dactylogyrus spp. The treatment should not be used when the water temperature is above 27°C or when the dissolved oxygen drops below 3 to 4 mg/L. The contents of the treatment tanks must be diluted in such a fashion that the formaldehyde concentration in the mixing zone of the receiving waters does not exceed 1 ppm to avoid darnage to formaldehyde-sensitive aquatic species.

Chemical and Physical Properties of Formalin

1. Usually a 37-40% solution, by weight, with 10-15% added methanol which prevents polymerization and the formation of paraldehyde, which is toxic to fish.
2. Molecular Weight of Formaldehyde, 30.03. Contains 30.99% C; 6.73% H; and 53.29% O.
3. Volubility- miscible with water, alcohol, acetone.
4. pH of Solution: 2.8-4.0
5. d 25/25 1.081-1.085
6. ^{20}1.3746
7. Boiling Point 760 mm 96°C
8. Flash Point 60°C

Common Chemical Environmental Reactions of Formaldehyde

$$H_2C=O + H_2O \longrightarrow H_2C(OH)_2$$

Formaldehyde water Formalin or Formaldehyde hydrate

$$2H_2C=O + O_2 \longrightarrow 2\ HCOOH$$

Formaldehyde oxygen Formic Acid

$$HCOOH + O2 \longrightarrow CO_2 + H_2O$$

Formic acid oxygen Carbon dioxide water

After application of the formaldehyde gas to the water containing 10 to 15% methanol, formaldehyde hydrate or formalin is formed. The formalin or formaldehyde will undergo oxidation to formic acid which will undergo metabolic oxidation by microorganisms to form carbon dioxide and water. The reactions of the active ingredients indicate the eventual impact on the environment will be minimal, since the active ingredients will be mineralized to carbon dioxide and water. The environmental concern is the immediate toxic effects of formaldehyde upon sensitive aquatic species.

Introduction into the Environment

Formalin is to be used for the control of external protozoan parasites such as Ichthyophthirius spp., Costia spp., Chilodonella spp., Epistylis spp., Scyphidia spp., Trichodina spp.; monogenetic trematodes such as Cleidodiscus spp., Gyrodactylus spp., and Dactylogyrus spp. at a concentration no greater than 250 ppm formalin for no more than one hour. The treatment water should be discharged in such a manner that the concentration in the mixing zone of the receiving water is no greater than 1.0 ppm to avoid damage to sensitive aquatic species.

The following concentration of formalin is recommended for the control of external parasites on fish.

Concentration of Formalin (ppm)

Tanks and Raceways (up to one hour)	Earthen Ponds (indefinitely)
up to 250	15-25[1]

[1]Use the **lower concentration when the pond is heavily loaded with fish or** phytoplankton.

Methods of Application

Tanks and Raceways - After the water supply has been turned off, apply the appropriate amount of formalin, assuring equal distribution. Provide aeration to the tank or raceway. Allow for a contact or treatment time of up to one hour. Drain the tank or raceway and refill with fresh, well-aerated water. If needed, aeration should be provided to preclude oxygen depletion. Treatment in tanks should not exceed 1 hour, even if fish show no sign of distress.

Ponds - The greatly diluted formalin is applied to the pond using a pump, sprayer, boat bailer or other devices to assure an even distribution. The treatment is allowed to dissipate naturally. Single treatments usually control most parasites, but treatment should be repeated in five to ten days, if needed. If the infective agent is Ichthyophthirius sp., repeat treatments should occur at two-day intervals until control is achieved.

In normal practice, formalin would be added to the ponds at an initial concentration of 15-25 ppm; the concentration declines within 30-36 h. The flow through the ponds would be minimal until the formalin is dissipated. At worst, there would be a minimal discharge of formalin to a stream; at best this form of treatment allows a normal dissipation of the formalin (half-life 36 h).

Discharge of Treatment Water

It is recommended that the contents of treatment tanks or raceways be discharged such that the concentration, as diluted into the stream, should be no greater than 1 ppm.

Assessment of Impact of Formalin in the Environment

The rate of discharge of the formalin-containing treatment water, is a function of the size of the treatment tank or raceway and the receiving body of water.

For the purpose of this assessment, the following assumptions will be made:

1. The model treatment tank/raceway used for this assessment will have a dimension of 50 ft. long x 10 ft. wide x 2 ft. deep and have a volume of 1000 $ft.^3$ or 7,480 gallons.
2. The water in the tank will be exchanged essentially completely after the treatment period and the water completely replaced.
3. The concentration in the treatment tank will be 250 ppm, the maximum use treatment level for parasite infected fish.
4. Unlike the pond systems of growing fish, in the treatment tank or raceway there will be no dissipation of the formalin because of the short time period associated with the treatment period, one hour.
5. The half-life of formalin in water is estimated at 36 hr.

Calculation of Case Situations

Case Situation 1

Assume the disposal would be a direct discharge into an adjacent stream that is 20 ft wide with an average depth of 4 ft and a flow of 2 ft/second. This size stream is not considered excessive, since most fish hatcheries need a stream or water source of significant size to obtain sufficient water for operation without impairing the flow the stream significantly. If the volume of the treatment tank/raceway was 50 ft x 10 ft x 2 ft, the tank/raceway would have a volume of 1000 ft^3 or 7,480 gallons. If the contents of the tank/raceway were pumped directly into a stream using a pump with a capacity of 600 gallon/min (a velocity well within the realm of pumps in most fish hatcheries), 12.46 min would be required to empty the tank and have the tank refilled with fresh stream water. Assuming minimal diffusion between the replacement water and the formalin-containing treatment water, the flow from the treatment tank would be diluted giving the following concentration:

600 gallons/minute pump flow x 250 ppm formalin ÷ [20 ft wide stream x 4 ft average depth x 2 ft/sec flow x 60 seconds x 7.48 $gallons/ft^3$ + 600 gallon pump volume = 2.07 ppm formalin in river water (plug flow).

The concentration of the formalin "plug" would cause exposure of non-target organisms to 2.07 ppm formalin for 12.5 rnin before the plug would pass and dilution would occur. This concentration is above the 24-h LC_{50} for Ostracods. Dilution of the discharge concentration in the mixing zone 10-fold in a stream would not be considered as an unreasonable diminution of concentration. The longer the flow down the stream, the greater the dilution.

Case Situation 2

Because of the desire to maintain the treatment time as close to 1 has possible and not extend the exposure time of the fish to formalin, albeit decreasing levels, by pumping the treatment tank/raceway at a slower rate directly into the stream, it is possible to pump the contents of the treatment tank into a holding tank or holding pond of suitable volume and pumping directly into the stream. Assume the treatment volume of the treatment tank/raceway is pumped into a holding tank/pond and an additional equal volume from a second flush of the treatment tank/raceway was added to the holding tank/pond. The total volume would be 2000 ft^3 or 14,960 gallon. The concentration of formalin in the holding tank/pond would change from 250 to 125 ppm formalin. By pumping into the same stream at 600 gallons/min, the concentration of formalin in the flow "plug" would be 1.035 ppm, very close to the idealized discharge concentration goal of 1.0 ppm. Considering the high probability of further dilution in the stream, this level should not impact adversely upon aquatic species.

Case Situation 3

This situation closely parallels case situation 1. The treatment tank/raceway contents are pumped into a holding tank/pond of suitable volume. The pumping rate was 600 gallons/min and the treatment tank/raceway is emptied by 12.46 min. The pumping rate into the hypothetical stream would be 300 gallons/rein, which would yield the target discharge concentration in the stream of 1 ppm formalin. This model approach offers the operator the ability to vary the discharge rate as a function of the stream flow, and meet the proposed 1.0 ppm mixing zone concentration.

Stability of Formalin in W ater

The calculated half-life of formalin in water is estimated at 36 hr. At that rate of hydrolysis and oxidation, the 1.0 ppm concentration of formalin would drop, in a static situation, to 0.06 ppm within 144 h or 6 days. Considering the further dilution of the discharge in the stream by factors of at least 10, the 1,0 ppm concentration in the mixing zone discharge should be decreased in the stream to very low levels and dissipated well before 7 days.

Environmental Effects of Formalin in the Environment

Toxicity to Non-Target Species

. The following table summarizes the toxicity of formalin to other aquatic species, the non-target species that could be encountered in the aquatic environment.

Toxicity of Formalin to Aquatic Species uL/L or PPM formalin

Species	LC_{50}	Safe Cone.	Hours	T°C
Striped Bass	15-35	---	72	21
Rainbow Trout	125-300	44.5	72	12
Lake Trout	141	---	--	12
Atlantic Salmon	389			
Chinook Salmon	---	---	--	--
Golden Shiner	62	45	72	21
Tilapia	100	100	72	21
Leopard frog Tadpole	21	---	72	21
Bullfrog Tadpole	47	---	--	21
Toad tadpole	45	---	--	21
Daphnia magna	54	13.5	--	--
Ostracods	1.15	---	--	16
Freshwater clam Corbicula SD.	800	---	--	16
Freshwater prawn Paleomonetes kadiakinesis	1105	---	--	16
Backswimmer Notonecta	4500	---	--	16
Spirogyra	---	---	--	--
Sirogonium	---	---	--	--
Stigeoclonium	---	---		--
Rhizoclonium	---	>100	168	--
Oscillatoria	---	>100	168	--
Ankistrodesmusfalcatus	.-	-2.7	46 days	--

From the above data, it can be seen that there is little permanent or even transitory effect that can be expected from the use of formalin in the treatment of fish. Only if and when the dilutions in the mixing zone of the stream exceed the recommended 1.0 ppm could there be an effect upon the non-target species, such as the formaldehyde-sensitive ostracods. The combination of dilution and the

rather rapid degradation of formaldehyde in the aquatic environment should provide a substantial safety factor to all species.

There is little likelihood that the biological oxidation of the formaldehyde in stream water will result in the depletion of oxygen. Since the dilutions of the treatment waters containing formaldehyde are so great, the overall concentration of formaldehyde in the stream low and the organic load provided by the formaldehyde so minimal, there should be no diminution in the dissolved oxygen of the stream, even if the temperature of the stream is warmer than the classical 21°C of many of the toxicological studies.

General Overview

The conditions required for the economic production of fish is such that it would be expected that rearing/growing facilities would be located where sufficient flowing water of reasonably high quality is available for husbandry. Usually, such aquatic systems are ecologically productive and have a large diversity of aquatic life.

There should be little or no effects upon the aquatic environment as the result of the proposed use of formalin in the control of external parasites on stripped bass. The inherent dilutions of the treatment water containing formaldehyde coupled with the relatively rapid degradation of formaldehyde in water preclude any minimal or significant effects on the environment.

Examination of case situation 3 infers that this is the best system to ensure that damage to a receiving stream will not occur. Regardless of the calculations developed, the case situation 3 model allows the greatest versatility. It allows for a storage tank/pond that permits discharge flows to be varied in respect to the flows of the receiving stream. This will allow the facility operators the flexibility to meet the idealized standard of discharge, the 1.0 ppm formalin level. As long as this target level is adhered to, there should be no damage to the non-target organisms in the receiving aquatic biosphere.

Preparation of the Environmental Assessment

This environmental assessment was prepared by Dr. Stanley E. Katz, Professor of Microbiology, Department of Biochemistry and Microbiology, Cook College/NJAES, Rutgers University, New Brunswick, NJ 08903-0231.

References

Kitchens, J. F., R.E. Casner, W.E. Harwood III, B.J. Macri and G.S. Edwards. Investigations of selected potential environmental contaminants: formaldehyde. OTS-USEPA Washington, D.C. 204 pp.

Matheson, J.C. 1981. FONSI and environmental assessment of Formalin-F as a parasiticide and fungicide in fish culture. (NADA 137-687 and MF 3543).

AMENDMENT TO ENVIRONMENTAL ASSESSMENT TITLED "ENVIRONMENTAL IMPACT ASSESSMENT FOR THE USE OF FORMALIN IN THE CONTROL OF EXTERNAL PARASITES ON FISH" (DATED JANUARY 1995)

September 6, 1995

The information provided in this amendment provides supplementary information to that provided in the EA and some clarification of information in the EA.

I. CLARIFICATIONS AND ADDITIONS TO SPECIFIC PARTS OF THE EA:

Proposed Use of Formalin

Add the following:

The proposed extension of the claim for formalin includes not only the control and prevention of external protozoan parasites on all fish, as stated in the EA, but also the use as fungicide on eggs of all fish. The proposed concentrations for treatment would be 1000 to 2000 uL/L (ppm) formalin. This concentration would be added to egg treatment containers for 15 minutes and maybe repeated.

Chemical and Physical Properties of Formalin

Explanation of abbreviations (from The Merck Index, 11th Edition):

a) $d_{25/25}$ specific gravity at 25°C referred to water at 25°C

b) n^{20} index of refraction for 20°C and sodium light. The abbreviation should be n_D^{20}.

Introduction into the Environment

Add the following:

Formalin will also be used as a fungicide on eggs of all fish, at concentrations of 1000 to 2000 uL/L.

Methods of Abdication

Add the following:

a) Eggs are usually kept in jars or trays in relatively small volumes of water. Formalin is added to the constant flow water supply in these containers for approximately 15 minutes. The water is then flushed from the containers. The treatment maybe repeated as often as five times a week (personal communication, FWS personnel, 1995).

b) The decline in concentration of formalin probably varies, depending upon conditions in the treatment facility and receiving water bodies (Helms, 1967; Kitchens, et al., 1976; Mopper and Stahovec, 1986; Hazardous Substances Data Bank, 1995).

Assessment of Impact of Formalin in the Environment

Clarification:

The assumption of a half-life of formalin as 36 hours is approximate and may apply only under certain conditions, such as the parasiticide use in fish ponds and at concentrations in the range of 20-35 uL/L of formalin (see Appendix 1 and Helms, 1967). It is reasonable to assume, however, that formalin degrades within a few days.

Additional information:

See also EA in Appendix I, under the heading, "Introduction into the Environment," for a calculation of concentrations resulting from tank treatments of 250 ppm.

Stability of Formalin in Water

Additional information:

The rate of degradation of formalin in water varies, depending upon factors such as temperature, oxygen levels, and presence of degrading microbes. For example,

a) In nutrient-enriched seawater, a lag period of approximately 40 hours precedes measurable loss of formaldehyde (Mopper and Stahovec, 1986).

b) When known quantities of formaldehyde were added to samples of water from a stagnant lake in Japan, the formaldehyde decomposed in approximately 30 hours at 20°C under aerobic conditions and under anaerobic conditions, in approximately 48 hours (Kitchens, et al., 1976). In the same study, formaldehyde added to sterilized lake water did not decompose.

c) Anecdotal evidence from FWS (see EA in Appendix I) and indirect evidence (Helms, 1967) indicates that at 20 ppm concentrations in ponds, formalin concentrations begin to decline within 30-36 hours (see EA in Appendix I).

It is reasonable to conclude that formalin biodegrades within a few days in most natural aquatic environments.

Environmental Effects of Formalin in the Environment

The following explanations concern the table titled "Toxicity of Formalin to Aquatic Species uL/L or PPM Formalin":

a) For more detailed information concerning toxicity data, including citations, and for additional toxicity data, see "Table 1. Summary of acute toxicity data for formalin in aquatic organisms" in the EA dated July 29, 1981, found in Appendix I.

b) The column labeled "Safe Cone." provides maximum safe concentrations, as determined by studies in which limited or no effects occurred to the organisms at the concentrations and for the time periods listed.

General Overview

Add the following information:

a) There should be no significant impacts from the proposed use of formalin in the control of external parasites on any finfish or from the proposed use of formalin as a fungicide in fish eggs.

b) See also discussion under heading, "Effects of Formalin in the Environment," in EA in Appendix I.

References

The complete citation for the Kitchens paper is provided below under the heading "Literature Cited."

II. ADDITIONAL HEADING:

MITIGATION:

See EA in Appendix I, under the heading, "Mitigation of Possible Adverse Effects." The label will require lOOX dilution for contents of egg treatment tanks, rather than 75X dilution.

LITERATURE CITED

Hazardous Substances Data Bank. 1995. In Micromedex Tomes Plus, Vol. 26. Databank #164.

Helms, D.R. 1967. Use of formalin for selective control of tadpoles in the presence of fishes. Prog. Fish. Cult. 29(l): 43-47.

Kitchens, J.F., R. E. Casner, W.E. Harwood, III, B.J. Macri, and G.S. Edwards. 1976. Investigation of selected potential environmental contaminants: formaldehyde, USEPA 560/2-76-009.

Mopper K. And Stahovec, W.L. 1986. Marine Chemistry 19:305-21.

Environmental Assessment

Use of Formalin in Fish Culture
as a Parasiticide and Fungicide

The information submitted to Master File 3543 by the Fish"and Wildlife Service, Department of Interior has been evaluated. Based on the analysis of that data, we have determined that the use of formalin in accordance with the proposed action will not have any significant effects on the environment and, therefore, will not require the preparation of an environmental impact statement. Information on the environmental impacts of the manufacture of formalin must be submitted by petitioners using this Master File to support a New Animal Drug Application(s) and will be evaluated for potential significant environmental impacts at that time.

7/29/91
Date

John C. Matheson, III
Preparer and Chief
Environmental Impact Staff (HFV-31O)
Bureau of Veterinary Medicine

Environmental Assessment for the Use of Formalin in Fish Culture as a Parasiticide and Fungicide

The U.S. Department of Interior, Fish and Wildlife Service, is preparing supporting information to be used by industry petitioners in a new animal drug application (NADA) which permits the use of formalin (aqueous solution of 37% formaldehyde) in food and non-food fish and fish eggs while in culture in hatcheries and ponds. Representatives of the Fish and Wildlife Service (FWS) have presented information addressing the potential for environmental impacts due to the use of formalin according to the proposed claims to be approved by FDA. The impacts due to the manufacture of formalin must be covered by those petitioners who wish to use the FWS data and this environmental assessment to support an NADA for treatment of fish. The approval of NADA's for this use is not excluded from environmental consideration under 21 CFR 25.1. The generic information supplied by FWS and FDA's environmental assessment of the use of this product reduces the information to be submitted by petitioners, as they may reference these documents in the environmental assessments which accompany their NADA's.

Description of the Proposed Action

The claims which are requested for the use of formalin in fish involve the treatment of fish eggs for fungal growth and the treatment of fish of many species in all life stages for various external parasites. The chemical would be sold over-the-counter to anyone involved in raising these fish, primarily Federal and State hatcheries and private hatcheries and fish farms. Treatment of fish would occur either in baths at high levels (up to 250 ppm formalin = 92.5 ppm formaldehyde) for short periods of time or in ponds at low levels (about 20 ppm formalin = 7.4 ppm formaldehyde) for longer periods. Egg treatments would be small volume, continuous flow treatments at 1000-2000 ppm formalin for 15 minutes. Approval of these claims would standardize and legitimize the long-standing practice of using varying concentrations of formal in' in fish culture.

Introduction Into the Environment

This assessment addresses only the impacts due to environmental introductions resulting from the use of formalin according to the proposed claims. Environmental releases of formalin due to manufacture must be addressed by petitioners seeking to utilize the supplemental information in preparing an NADA.

Formalin entering the environment as a result of pond treatments: Since ponds receiving formalin treatment are managed animal-raising facilities, similar to cattle feedlots, the impact of

formalin treatments on the fish being raised in those ponds is the subject of the FDA's efficacy evaluation of the FWS's submission. While other organisms present in these ponds may be of concern from an environmental standpoint (e.g. populations of amphibians), they are also subject to other management strategies aired at controlling or reducing their numbers (Helms, 1967). Therefore, the primary area of the environment where impacts of formalin releases are of concern is at the site of discharge of treated ponds. These receiving waters contain amphibians, phytoplankton, zooplankton, aquatic plants, crustaceans, and native fish populations which all constitute important parts of the natural aquatic food web.

What concentrations of formalin enter these receiving waters from treated ponds? Under normal conditions, formalin is added to ponds in a static treatment at an initial 20 ppm concentration. This concentration is not maintained and, therefore, begins to decline within 30-36 hours (Environmental Effects of Formalin Use in Fish Culture-, Fred P. Meyer, hereinafter referred to as the "FWS report.") Since the fish manager would normally wish to slow" this decline in treatment concentration in order to obtain maximum benefits from the money he spent on formal in, flow of water through treatment ponds would be minimized. Normally, minimal water would flow through the pond until the formalin was dissipated. Development of a low dissolved oxygen situation, either from the biodegradation of the formal in, decay of plankton killed by formal in, weather conditions, or from confining too ❑ any fish in too small a volume of water would necessitate flushing untreated water into the treatment pond and might result in formalin discharge of less than 20 ppm concentration into receiving streams. This low dissolved oxygen situation would be particularly likely to happen when the water temperature is high, since oxygen volubility in water is lowest at that time. The pond owner would seek to avoid this situation due to the unnecessary stress it would place on the fish. The techniques of (1) lowering the pond level before treatment and adding water to dilute the formalin as the oxygen demand *is* exerted, (2) the addition of potassium permanganate to chemically degrade the formalin after the desired treatment period, and (3) cessation of use in hot weather, are used to maintain acceptable dissolved oxygen levels and result in no discharges from the treatment area. Therefore, any discharges would be much less than the 20 ppm initial formalin concentration and of small volume from pond treatments under normal conditions (FWS report). The concentrations of formalin used are safe for the fish being treated for long periods (Burress, 1978).

Formalin entering the environment as a result of tank and egg treatments: It will be assumed that fish treatment represents a worse case than the low volume, short duration egg treatments. Therefore, estimated concentrations in the environment will be developed for fish tank treatment only.

The FWS report describes the conditions of a typical tank treatment for fish where 424.5 milliliters of formalin is added to a 450 gallon tank to result in a 250 ppm formalin concentration. The report states that most fish farms and hatcheries of economically viable size will have at least a ,600 gallon per minute continuous discharge. If the tank contents were dumped within the space of 1 minute, then effluent concentration of formalin in the 1050 gallons discharged would be

$$\frac{450}{450 + 600} \times 250 \text{ ppm} = 108 \text{ ppm formalin in discharge.}$$

If the stream receiving effluent from the hatchery was small enough that it received a significant portion of its flow from the hatchery, what formalin concentrations would result? Assume that the stream averages 4 feet in width and 2 feet in depth and receives half its flow from the hatchery, 600 gallons per minute. Then:

$4 \times 2 = 8$ ft^2 cross-sectional area of stream at the point of the discharge

600 gallons per minute stream flow above discharge point
+1050 gallons per minute hatchery discharge for 1st minute
1650 gpm flow

$$\frac{\frac{1650 \text{ gallons}}{1 \text{ minute}} \times \frac{1 \text{ ft}^3}{7.48 \text{ gallons}}}{8 \text{ ft}^2 \text{ x-sectional area}} = \frac{221}{8} = 28 \frac{\text{ft}}{\text{minute}}$$

stream velocity for 1st minute after formalin release

$$\frac{\frac{1200 \text{ gallons}}{1 \text{ minute}} \times \frac{1 \text{ ft}^3}{7.48 \text{ gallons}}}{8 \text{ ft}^2 \text{ x-sectional area}} = 20 \text{ ft/minute}$$

stream velocity for following minutes

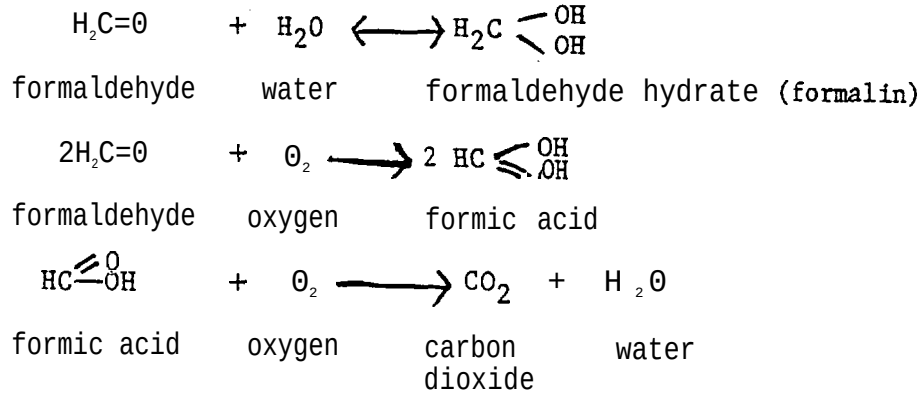
108 ppm formalin in discharge x $\frac{1050}{1650}$ = 69 ppm in receiving water.

Assuming "plug flow," e.g. no mixing or further dilution in the stream, no additional volume inputs (e.g. from tributaries), and no degradation or adsorption of formalin, a plug of formalin-treated water 69 ppm in concentration and 28 feet in length would move downstream. Benthic organisms, attached to rocks or in sediments, would be exposed to this concentration for 1.4 minutes. One could not expect these plug flow conditions to be maintained for more than a few minutes. Notice also that the assumption of 8 ft^2 cross-sectional area for the stream only affects the length of the "plug" of treated water in the stream: the greater the length of stream containing treated water, the longer period of time the plug flow assumption will be met. Plug flow becomes less likely to occur as the stream cross-sectional

area increases because there is much greater opportunity for mixing with adjacent untreated water. Smaller treatment tank volume such as is the case for egg treatments; longer release times from the treatment tank: greater hatchery discharge volume; and greater stream flow; would all decrease the initial concentration of formalin occurring at the discharge point into the receiving stream.

Fate of Formalin in the Environment

Formalin combines with oxygen to yield formic acid which, in turn, combines with oxygen to yield carbon dioxide and water (FWS report).



(An excellent discussion of the chemical properties, industrial uses and production of formalin is contained in Kitchens, et al. (1976).)

This degradation process is mediated by bacterial metabolism (Gellman, 1952). Sills and Allen (manuscript in press, attached) showed that formalin applications of 35 ppm (13 mg/l formaldehyde) to a plastic pool containing water, mud, algae, channel catfish and largemouth bass decreased to 24 ppm formalin (8.9 mg/l formaldehyde) 24 hours after treatment and that no formalin was detectable 72 hours after treatment. The investigators found no free formaldehyde retained in the tissues of the exposed fish.

Formalin oxidation may result in the depression of dissolved oxygen concentrations when the oxygen used by bacteria in the formalin oxidation process is used at a faster rate than the water is reaerated. This condition is most likely in still or slow-moving water at high temperatures because (1) bacterial metabolic activity increases with water temperature and (2) dissolved oxygen saturation level (oxygen storage capacity) and oxygen reaeration rates decrease with increased water temperature. Helms (1967) discusses this oxygen depression effect

using data from aquaria (figures 1 and 2). From the figures it can be seen that the oxygen demand frcm formalin begins to be exerted about 24 hours after formalin application and that anaerobic conditions are more likely to occur in warmer water.

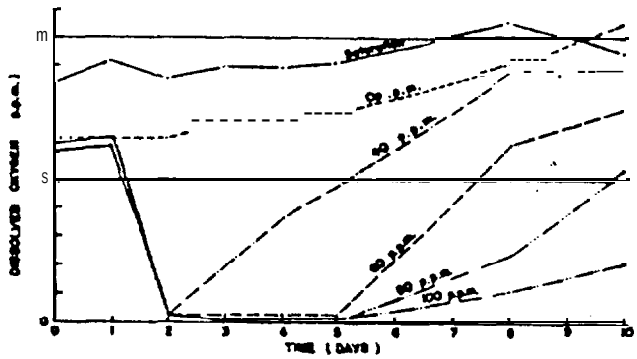


FIGURE 1.--**Effect of concentration of formalin on dissolved oxygen in aquaria with water temperature of 70° F.**

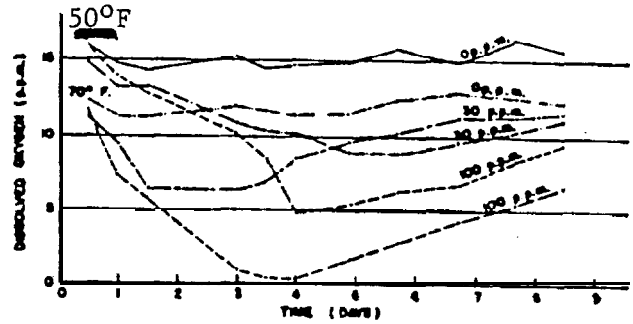


FIGURE 2.-- **Effect of temperature on. reduction of dissolved oxygen by two concentrations of formalin.**

Greater than 30-40 ppm concentrations of formalin in a 70"F body of water for about two days will result in low dissolved oxygen concentrations sufficient to kill fish and other aquatic life. Based on the expected concentrations of formalin in receiving waters at the point of discharge that would result from pond and tank treatments and the 1-2 day period for dilution to occur, it is doubtful that these formalin discharges would result in low dissolved oxygen conditions by themselves or significantly exacerbate existing decreased dissolved oxygen situations.

Effects of Formalin in the Environment

Given the expected concentrations of formalin that would result in receiving waters from the discharge of water frcm formalin tank and pond treatment and the expected rapid bacterial degradation of these formalin residues, acute toxicity to aquatic life would appear to be the most probable environmental effect to be observed.

The potential for acute toxicity effects to occur may be estimated by comparing laboratory data with expected environmental concentrations. Table 1 shows some of the acute toxicity data available from the literature. The limited shorter term toxicity tests available are for fish and indicate that for most fish, except striped bass, formalin concentrations of greater than 400-500 ppm are necessary to cause 50% mortality in 1 hour (Schnick, 1973). Of course, it would be expected that toxic formalin levels would be above the levels used therapeutically in fish.

Table 1. Summary of acute toxicity data for formalin in aquatic organisms.

	conc. of 37% formalin (µℓ/ℓ = ppm) causing 50% mortality			maximum "safe" 37% formalin concentration		conc. of 37% formalin (µℓ/ℓ ppm) causing				
	24 hr	48 hr	72 hr.	conc.	time	conc.	time	°C	°F	
Fish										
Black Bullhead catfish	70+	49	45	35	3 days	--	--	21	70	Helms, 1967
	173	--	--	--	--	--	--	12	54	Bills, Marking and Chandler, 1977
Channel catfish	86.5	67.6	67.6	48.6	1-3 days	--	--	--	--	McKee and Wolf, 963
	87	69	69	50	1-4 days	126	1 day	25	77	Clemens and Sneed, 1958
	122	--	--	--	--	--	--	12	54	Bills, Marking and Chandler, 1977
Bluegill	--	100+	80	45	3 days	--	-	21	70	Helms, 1967
	211	--	--	--	--	--	--	12	54	Bills, Marking and Chandler, 1977
Green sunfish	323	--	--	--	--	--	--	12	54	" "
	--	--	90+	70	3 days	--	--	21	70	Helms, 967
Largemouth bass	--	--	100+	75	3 days	--	--	21	70	" "
	283	--	--	--	--	--	--	12	54	Bills, Marking and Chandler, 1977
Smallmouth bass	222	--	--	--	--	--	--	12	54	" "

Table 1 continued.

Species	cone. of 37% formalin (µl/l = ppm) causing 50% mortality			maximum "safe" 37% formalin concentration (µl/l = ppm)		conc. of 37% formalin (µl/l = ppm) causing 100% mortality		Temperature		Reference
	24 hr.	48 hr.	72 hr.	conc.	time	cone.	time	°C	°F	
Striped bass	15-35	15	15	--	--	35-40	1 day	21	70	Schnick, 1973
	--	--	--	--	--	25-30	-4 days	--	--	--
Rainbow trout	--	<125	--	44.5	3 days	141	3 days	--	--	Holland et al., 1960
	300	--	--	--	--	--	--	12	54	Bills, Marking and Chandler, 1977
Lake trout	141	--	--	--	--	--	--	12	54	" "
Atlantic salmon	389	—	--	--	--	--	--	12	54	" "
Chinook salmon	--	--	--	--	--	125	3 days	--	--	Holland et al., 1960
Golden shiner	87	67	62	45	3 days	--	--	21	70	Helms, 1967
Carp	--	--	70+	70	3 days	--	--	21	70	" "
Tilapia	--	--	100+	100	3 days	--	--	21	70	" "
Amphibians										
Leopard frog tadpole	22	21	21	--	--	30	--	21	70	" "
Toad tadpole	--	--	45	--	--	50	--	21	70	" "
Bullfrog tadpole	53	47	47	—	--	80	--	21	70	" "

Table 1 continued.

Species	conc. of 37% formalin (µl/l = ppm) causing 50% mortality			maximum "safe" 37% formalin concentration (µl/l = ppm)		conc. of 37% formalin (µl/l = ppm) causing 100% mortality		Temperature		Reference
	24 hr	48 hr	72 hr	conc.	time	conc.	time	°C	°F	
Invertebrates										
Daphnia magna	54	--	--	< 13.5	23 days	54 135	3 days 19 hours	--	--	Nazarenko, 96°
ostracods	1.15	--	--	--	--	--	--	16	61	Bells, Marking and Chandler, 1977
freshwater clam Corbicula sp.	800	--	--	--	--	--	--	6	61	" "
Snail Helisoma sp.	710	--	--	--	--	--	--	6	61	" "
Freshwater prawn Paleomonetes kadiakinensis	1105	--	--	--	--	--	--	16	61	" "
backswimmer Notonecta	4500	--	--	--	--	--	--	6	61	" "
Algae and Aquatic Plants										
Spyrogyra	--	--	--	--	--	20	7 days	-	--	Helms, 1964
Sirogonium	--	--	--	--	--	20	7 days	-	--	" "
Scenedesmus	--	--	--	--	--	25	7 days	--	--	" "
Stigeoclonium	--	--	--	--	--	40	7 days	--	--	" "
Rhizoclonium	--	--	--	>100	7 days	--	--	--	--	" "

Table 1 continued.

Species	cone. of 37% formalin (µl/l - ppm) causing 50% mortality			maximum "safe" 37% formalin concentration (µl/l = ppm)		cone. of 37% formalin (µl/l = ppm causing 100% mortality		Temperature		Reference
	24 hr.	48 hr.	72 hr.	cone.	time	cone.	time	°C	°F	
Oscillatoria	--	--	--	>100	7 days	--	--	--	--	Helms, 1964
Aphanothece	--	--	--	>100	7 days					" "
Ankistrodesmus falcatus	--	--	--	~2.7	6 days	-54	46 days	--	--	" "
Ceratophyllum demersum (hornwort)				<2.7	5 days	--	--	--	*-	Nazarenko, 1960

The most sensitive fish appear to be striped bass and channel catfish. Sane organisms which serve as natural food for fish appear to be sensitive to formal in: daphnia (water fleas) and ostracods (seed shrimp) were comparable to or more sensitive than striped bass. Other aquatic invertebrates were less sensitive than fish, for example snails, clams, and backswimmers. Hornwort , a floating aquatic plant, was affected by long-term, low-level exposure to formalin, as were sane but not all algae. Based on the variable sensitivity of the test species, it can be concluded that partial kills of phytoplankton and zooplankton are probable when formalin concentrations of about 10-20 ppm are maintained for greater than 24 hours. Ostracods could be expected to be killed when formalin concentrations around one part per million were maintained for 24 hours or more.

Given the proposed conditions of use, the periodic nature of the use, the rapid degradation of formalin in aquatic environments at the levels discharged, and the limited time needed for dilution of formalin to very low levels in receiving waters, it is safe to conclude that the use of formalin according to the proposed claims in the treatment of fish and fish eggs will not create significant adverse environmental effects. However, in rare circumstances, such as when effluent from fish treatment tanks or egg treatments are released into small, slow flowing or stagnant water bodies, these releases would temporarily inhibit or kill phytoplankton and zooplankton populations and, as a consequence of their decay, result in lowered dissolved oxygen concentrations. Any inhibition or damage to phytoplankton or zooplankton populations would be short-term and followed by rapid recovery. -

Adherence to the cautionary instructions included on the product label (see below, Mitigating Measures) should' reduce any adverse environmental impacts that might result from lack of knowledge of potential adverse effects of effluents containing formalin.

Utilization of Natural Resources and Energy

The formalin which would be used as a result of the proposed actions represents a small percentage of the total U.S. formalin use. Formalin is one of the most widely used industrial compounds, with over 50% of the annual production used to manufacture resins, which are in turn used to manufacture plastics, adhesives, compounds used in laminating, etc. (Kitchens, et al., 1976). Furthermore, the proposed actions do not significantly change, only legitimize, the present use of formalin as a fish chemotherapeutant, since the use of this chemical in fish culture was not recognized until recently as requiring FDA approval.

Mitigation of Possible Adverse Effects

The following cautions are placed on the formalin label:

1. Do not use formalin which has been subjected to temperatures below 40°F or allowed to freeze. Cold or freezing causes the formation of paraformaldehyde, a substance which is toxic to fish.

2. Tolerances to formalin may vary with strains and species of fish. While the indicated concentrations are considered safe for most fishes, a small number of each lot to be treated should be used to check for any unusual sensitivity to formalin before proceeding. Striped bass (Morone saxatilis) are known to be highly sensitive to formalin so pond treatments are not appropriate for this species.

3. Under some conditions, fish may be stressed by normal treatment concentrations. Heavily parasitized or diseased fish often have a greatly reduced tolerance to formalin. Such fish do not tolerate the normal tank treatment regimen the first time they are treated, and the time or dosage may need to be reduced. If the fish 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. Treatments in tanks should never exceed 1 hour even if the fish show no sign of stress.

4. Do not apply formalin to ponds 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). Formalin 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.

5. *Do* not discharge the contents of fish or egg treatment tanks into natural streams or ponds without thorough dilution (greater than or equal to 10x for fish treatment, 75x for egg treatment). This will avoid damage to formalin-sensitive phytoplankton, zooplankton, and fish populations and avoid depletion of dissolved oxygen.

The last two conditions, 4 and 5, serve to prevent environmental damage by helping assure that formalin will not be used in ponds under conditions that might require a rapid release of formalin-treated water into receiving streams and providing instructions for diluting effluent from formalin tank treatments with hatchery effluent before discharge to receiving waters.

Alternatives to the Proposed Action

With the mitigating measure above, there should be no potential adverse environmental effects resulting from the use of formalin as proposed. Therefore no alternative actions will be considered . While there are no readily available substitute materials for the proposed formalin uses, it would be difficult to obtain a broad spectrum therapeutic agent with more desirable environmental fate properties: (1) simple molecule that degrades rapidly to water and carbon dioxide, (2) little bioaccumulation potential probably due to high water volubility, (3) periodic rather than continuous treatment pattern, and (4) use at facilities that would usually discharge large quantities of formalin-free effluent simultaneously with much lower quantities of the formalin-treated water.

List of Preparers

Author:

John C. Matheson, III, has served as an environmental scientist for over four years with the FDA. He received a Master of Science in Public Health in the area of Environmental Sciences and Engineering (1975) and a Bachelor of Science in Biology (1973) from the University of North Carolina, Chapel Hill, N.C. His areas of special expertise include aquatic ecology, microcosms and environmental testing standards.

Contributor:

Fred P. Meyer, Ph.D., Director, National Fishery Research Laboratory, LaCrosse, Wisconsin is the author of many articles on the use of chemotherapeutants in fish culture. He assembled the attached collection of references on the environmental impact of formalin and prepared the report 'environmental effects of formalin use in fish culture" which together served as the basis for this environmental assessment.

References

1. Burress, R. M. 1978. Effects of parasiticidal applications of formalin on nontarget organisms in ponds. U.S. Fish and Wildlife Service, Southeastern Fish Control Laboratory, Warm Springs, Georgia, Special Report. 18 pp.

2. Clemens, H. P., and K. E. Sneed. 1958. The chemical control of sane diseases and parasites of channel catfish. The Progressive, Fish-Culturist 20:8-15.

3. Gellman, I. 1952. Studies on biochemical oxidation of sewage, industrial wastes, and organiccompounds. Thesis, Rutgers Univesity, 260 pp.

4. Helms, D. R. 1967. Use of formalin for the selective control of tadpoles in the presence of fishes. The Progressive Fish-Culturist 29(1):43-47.

5. Helms, D. R. 1964. The use of formalin to control tadpoles in hatchery ponds. M.S. Thesis, Southeastern Illinois University, Carbondale. 29 pp.

6. Holland, G. A., J. E. Lasater, E. D. Neumann, and W. E. Eldridge. 1960. Toxicity effects of organic and inorganic pollutants on young salmon and trout. State of Washington, Department of Fisheries Research Bulletin No. 5. 264 pp.

7. Kitchens, J. F., R. E. Casner, W. E. Harward, III, B.J. Macri, and G. S. Edwards. Investigation of selected potential environmental contaminants: formaldehyde. Office of Toxic Substances, U.S. Environmental Protection Agency, Washington, D.C. 204 pp. Available from National Technical Information Service, Springfield, Virginia.

8. Nazarenko, I. V. 1960. Effect of formaldehyde on aquatic organisms. Transactions of the All Union Hydrobiological Society (Trudy Vsesoyuznogo Gidrobiologicheskogo Obshchestrva) 10:170-174).

9. Schnick, R. A. 1973. Formalin as a therapeutant in fish culture. Fish Control Laboratory, Bureau of Sport Fisheries and Wildlife, Fish and Wildlife Service Publication. FWS-LR-74-09.

10. Sills, J. B., and J. L. Allen. 1979. Residues of formaldehyde undetected in fish exposed to formalin. The Progressive Fish-Culturist. (In press).

HFV-305 (DOCKETS MANAGEMENT BRANCH)

JUN 18 1998

2912 '98 JUL 15 A11:37

FREEDOM OF INFORMATION SUMMARY

Supplement to NADA 140-989

PARASITE-S
(formaldehyde solution)

"for the control of ectoparasites of all finfish and penaeid shrimp, and fungi on the eggs of all finfish"

Sponsored by:

WESTERN CHEMICAL INC.

TABLE OF CONTENTS

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

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

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. Therefore, these studies are considered adequate to demonstrate that use of the drug in all finfish and on all finfish eggs at the recommended concentration will not result in the accumulation of formaldehyde above naturally occurring levels in their edible tissue.

VIII. ENVIRONMENTAL SAFETY

The Center for Veterinary Medicine has considered the potential environmental impact of this action and has concluded that this action will not have a significant impact on the quality of the human environment and that, therefore, an environmental impact statement will not be prepared.

The EA provides information on the potential environmental effects from the use of the product in all species of finfish. An amendment to the EA dated September 6, 1995, was prepared by the Environmental Staff of the Center for Veterinary Medicine to analyze the potential for environmental impacts from the use of formaldehyde to treat fungus on the eggs of all species of finfish.

The EA and the amendment to the EA, indicate that no environmental impact are expected provided that the finfish and penaeid shrimp treatment water is diluted 10-fold and the finfish egg

treatment water is diluted 100-fold. These directions for the dilution of treatment water and additional environmental precautions are contained on the labeling of the product.

The EA, the amendment to the EA and the labeling provides adequate information to determine that the use of PARASITE-S is not expected to cause a significant impact on the environment.

IX. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfies the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The sponsor of this NADA has referenced PMF 5228, PMF 3543, and publicly-disclosable INAD file 8886 to support the addition of the new claims to their existing NADA. The data demonstrate that formalin, 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, and for the control of fungi of the family Saprolegniaceae on the eggs of all finfish.

According to the Center's supplemental approval policy, 21 CFR 514.106(b)(2)(vii) and (ix), 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.

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 (140-989) which was filed for the expansion of the use of formalin as a parasiticide in all finfish, and as a fungicide on the eggs of all finfish.

Additional efficacy studies in other species of finfish were not necessary because interspecies extrapolation is appropriate to demonstrate the efficacy of formalin on all finfish for the control of the same ectoparasites on a select group of finfish for which the drug is currently approved (see 21 CFR 529.1030). Similarly, additional efficacy studies were not needed to demonstrate efficacy of formalin on the eggs of all finfish for the control of the same fungi (Saprolegniaceae) found on the eggs of the previously approved finfish species (see 21 CFR 529.1030).

Additional target safety studies on other finfish species were not needed because interspecies extrapolation is appropriate to demonstrate the safety of formalin on all finfish for the control of the same ectoparasites on a select group of finfish for which the drug is currently approved (see 29 CFR 529.1030) and demonstrated to be safe for use in striped bass, as reported in PMF 5228. Similarly, additional target safety studies on the eggs of other finfish species were not needed, because interspecies extrapolation is appropriate to demonstrate its control of the same fungi (Saprolegniaceae) found on the eggs of the previously approved finfish species (see

21 CFR 529.1030) and demonstrated to be safe for use on the eggs of finfish species, as reported in publicly-disclosable INAD file 8886.

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.

The agency has carefully considered the potential environmental effects of this action. and has concluded that the action will not have a significant impact on the human environment and that an environmental impact statement is not required. The agency's finding of no significant impact (FONSI) has been prepared, which, along with the evidence supporting that finding contained within an environmental assessment, will be placed on display in the Dockets Management Branch (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.

cc:
Courtesy copy for Western Chemical, Inc.
HFV-199/NADA 140-989 C0018, S0028 & S0029
HFV-2 (Special Mailing List)
HFV-12 (FOI Staff)
HFV-102 (GADQC Reserve Copy)
HFV-102 Green Book (NTurner)
HFV-130 (Bell)
HFV-145 (Environmental Assessment Team)
HFA-305 (Dockets Management Branch)
HFR-PA350 (SEA-DO)

HFV-130:TABell:4June98:594-1649
Freedom of Information Summary

ec: CVM Records\ONADE\\N0140989\C0018foi.rev

FOR USE ON CULTURED FINFISH, PENAEID SHRIMP AND FINFISH EGGS

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 Saprolegniacaae.

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 of 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 sensitive 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.

WESTERN chemical inc.

PARASITE-S

PARASITICIDE FOR CULTURED FISH, PENAEID SHRIMP AND FUNGICIDE FOR FINFISH EGGS

ACTIVE DRUG INGREDIENT
FORMALIN (Aqueous solution of formaldehyde)

GUARANTEED ANALYSIS

Formaldehyde (CH_2O)	37%
Methanol	6-14%
Water and inert ingredients	49-57%
	100%

Read entire Package Insert Before Using This Product
Keep out of Reach of Children
Net Contents 208.2 Litres [55 U.S.) GALLONS]

NADA 140-989, Approved by FDA

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

FORMALDEHYDE SOLUTIONS,
8, UN2209, III
CORROSIVE

LOT #_____ Exp.Date_____

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, the-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 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)

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 37grams 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 $HO(CH_2O)H$. Its molecular weight is 30.93. 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 100 µL/L (455 to 37 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 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