44. A Review of Literature on TFM (3-trifluormethyl-4-nitrophenol) as a Lamprey Larvicide
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By Rosalie A. Schnick
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A REVIEW OF LITERATURE ON TFM  
(3-trifluormethyl-4-nitrophenol)  
AS A LAMPREY LARVICIDE

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Abstract. --The search for a selective toxicant to control the sea lamprey, scourge of Great Lakes fisheries, culminated in the discovery of TFM (3-trifluormethyl-4-nitrophenol) in the late 1950's. The research, however, had only begun on its chemical and physical properties, efficacy, toxicity to non-target and target species, residues, and methods. Federal, State, university, and industrial agencies contributed much in the effort to determine the effect of TFM on the environment and other organisms; however, much still remains to be done if TFM is to gain continued clearance by the Environmental Protection Agency for use as a larval lampreyicide in the aquatic environment.

HISTORY OF LAMPRICIDE DEVELOPMENT

The United States Congress directed the Fish and Wildlife Service in 1946 to develop measures for the control of the exotic sea lamprey in the Great Lakes (Van Oosten, 1949a). A master plan was prepared, and a Sea Lamprey Committee was organized by Dr. John Van Oosten, Chief of the Great Lakes Fishery Investigations. One objective of the plan was a study of sea lamprey physiology to determine what agents, including chemicals, might be used to kill the lamprey in any life stage (Van Oosten, 1949b).

Congress appropriated funds for research in 1949 (U. S. Committee on Merchant Marine and Fisheries, 1951). The Fish and Wildlife Service in 1950 took over the U. S. Coast Guard Station at Hammond Bay, Michigan, on the northwest coast of Lake Huron, and renovated the facilities for research on mechanical, electrical, and chemical controls for the sea lamprey (Moffett, 1950).

The initial studies to find toxicants selective to the sea lamprey were assigned to Philip J. Sawyer, a doctoral candidate at the University of Michigan on a Fish and Wildlife Service Research Fellowship (Applegate, 1950; U. S. Branch of Fishery Biology, 1952). Sawyer experimented with 179 compounds at the University before his project was terminated in 1952 (Applegate et al., 1952). Six of the compounds that were selectively toxic to larval lampreys had nitro groups and through hydrolysis yielded a nitrophenol (Sawyer, 1956). Significantly, the chemical group later considered effective against lamprey were the mononitrophenols of which TFM is a member. In the meantime, the Michigan Conservation Department had determined that rotenone was not effective on sea lamprey larvae in streams (U. S. Committee on Merchant Marine and Fisheries, 1952).

Following its early emphasis on mechanical and electrical controls for the sea
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lamprey, the Hammond Bay Laboratory began screening up to 50 chemicals a day in 1953 (Applegate, 1953; U. S. Branch of Fishery Biology, 1953). Over 4,000 selected compounds tested under a military contract at the Fish and Wildlife Service's Microbiological Laboratory at Leetown, West Virginia, were transferred to Hammond Bay for trials against lampreys (Applegate et al., 1957; U. S. Branch of Fishery Biology, 1953). These compounds had been bioassayed against four species of fish and separated into three groups of very toxic, moderately toxic, and negative compounds (Woods, 1953; Lennon, 1954). An additional 2,000 chemicals were obtained from universities, industries, and private individuals (McVeigh, 1958). The results of tests on compounds obtained from the National Academy of Sciences-National Research Council were reported in Summary Tables of Biological Tests (U. S. Fish and Wildlife Service, 1956a and 1956b).

While the U. S. Fish and Wildlife Service was looking for a selective larvicide, investigators in Canada attempted to find a general toxicant that would kill lamprey without too much harm to other fish populations, and would be inexpensive, available, easy to use and handle, and nontoxic to warm-blooded animals (Kerr, 1954). Although they found that toxaphene killed 70 percent of the lamprey larvae, it was too toxic to other fish and warm-blooded animals (Johnson and Tibbles, 1962).

Throughout 1954 and 1955 efforts at Hammond Bay centered almost exclusively on testing a large number of compounds (Applegate, 1954 and 1955). Finally, in 1955, of the eight compounds selectively toxic to sea lamprey, two proved to be promising (Applegate, 1955). One was Compound No. 174, 3-bromo-4-nitrophenol, originally from the Chemical-Biological Coordination Center and the Leetown testing program (Applegate, 1955; Wood, 1953). The other was Compound No. 3579. The restricted Compound No. 3579 and a Pennsalt chemical, O-ethyl-S-pentachlorophenyl thiolcarbonate, may be one and the same for various reasons. A patent for lampricidal use of O-ethyl-S-pentachlorophenyl thiolcarbonate was applied for as early as December 29, 1955 (Neumoyer, 1960). Both compounds at 1 to 3 ppm (parts per million) at 55° F caused 100 percent mortalities among sea lamprey without affecting other fish (Applegate, 1955, 1958, and 1963). Both compounds were difficult to formulate and apply (Applegate, 1955; Howell, 1966). Raceway tests were still made on O-ethyl-S-pentachlorophenyl thiolcarbonate in 1957, but the compound was dropped from the program shortly thereafter (U. S. Bureau of Commercial Fisheries, 1957a; Howell, 1966).

Applegate and Howell (1960) applied for a patent on Compound No. 174, 3-bromo-4-nitrophenol, on March 29, 1956. Whereas 3-bromo-4-nitrophenol was soluble enough in water for larvicidal use, it was hard to synthesize and too expensive to use (Willeford, 1956; McVeigh, 1958; Moffett, 1958a; Howell, 1966). Thus in 1956, the investigators at Hammond Bay turned their attention to other nitrophenols.

In response to a request, at least six companies supplied many nitrophenols (Applegate, Howell, and Smith, 1958). Of the six most promising compounds tested during 1956, five were nitrophenols and one was NP-1458, a Pennsalt chemical (U. S. Fish and Wildlife Service, 1956c and 1956d; Applegate et al., 1957). By April 11, 1957, six mononitrophenols showed enough promise that Applegate and Howell (1965) applied for a United States patent on control of the sea lamprey with mononitrophenols. On March 18, 1958, Applegate and Howell (1964) applied for a Canadian patent on the same compounds. Pyne (1962) later applied for a British patent on one of the mononitrophenols, 2,5-dichloro-4-nitrophenol. Testing in the field demonstrated that
nitrophenols are stable, measurable by a colorimeter, usable under various water quality conditions, harmless to domestic animals and wildlife at the concentrations used, not too toxic to other fish and invertebrates, and inexpensive enough to warrant further research (Moffett, 1958a).

Among nine compounds suggested by Dr. Clarence L. Moyle of Dow Chemical Corporation was one, 3, 4, 6-trichloro-2-nitrophenol, that showed promise (McVeigh, 1958). It was tested against lamprey larvae in raceways, for acute oral and dermal toxicity to mammals, and in drinking water for deer and dairy cows (U.S. Bureau of Commercial Fisheries, 1957a and 1957b). Finally, the compound was tested in the field against larval sea lampreys. On October 29 to 30, 1957, Dowlap 30 (30 percent stock solution of 3, 4, 6-trichloro-2-nitrophenol as a sodium salt), was applied to Little Billies Creek (Elliot Creek), Michigan, resulting in a 96.6 percent kill of lampreys and little harm to other fauna (Moffett, 1958a and 1958b; Westerman, 1958; U.S. Bureau of Commercial Fisheries, 1957a and 1957b). Further testing was done in 1958 on Carp Creek, (Black Mallard Creek), Michigan, with Dowlap 20 (20 ppm of 3, 4, 6-trichloro-2-nitrophenol), but the results disclosed that Dowlap 20 or 30 had to be used in relatively high concentrations (13 ppm) and did not have a high differential in selectivity (Anonymous, 1959; Keller, 1966; U.S. Bureau of Commercial Fisheries, 1958a and 1958b).

The search continued, and promising compounds were tested both in the laboratory and raceways (Moffett, 1958a; U.S. Bureau of Commercial Fisheries, 1957a). A compound more effective at lower concentrations than Dowlap 30 was found - TFM (Moffett, 1958a).\footnote{3-trifluormethyl-4-nitrophenol. See Appendix A for other names and technical data for TFM.} It was formulated as a sodium salt, dissolved in an acceptable solvent, and sold to the Fish and Wildlife Service as Lamprecid 2770 by the Progressive Color and Chemical Company of New York" (Moffett, 1958a). Another source listed TFM as originally produced by Farbwerke Hoechst of Germany as a dye intermediate and supplied by the U.S. outlet, Hoechst Chemical, under the name of Lamprecid 2770 (Anonymous, 1959). When the U.S. Bureau of Commercial Fisheries originally began dealing with Farbwerke Hoechst of Germany, the American outlet was the Progressive Color and Chemical Company and later the Hoechst Chemical Company. Farbwerke Hoechst Aktiengesellschaft later succeeded in obtaining patents on TFM for lampricidal use in the United States, Great Britain, Germany, and Canada (Scherer, Frensch, and Stähler, 1960, 1962, and 1964). Because TFM killed lamprey at 2 ppm, it was easier and cheaper to transport than Dowlap 30 (Keller, 1966; Johnson, 1961). Therefore, the U.S. Government purchased 10,000 pounds of TFM from Dow Chemical Company in 1958, 25,000 pounds from Maumee Chemical Company in 1959, and 25,000 pounds for use in 1960 from Dow Chemical Company (Anonymous, 1959; U.S. Bureau of Commercial Fisheries, 1959b). The Canadian unit obtained the amine salt of TFM through the Maumee Chemical Company for use in 1960 and 1961 treatments (Tibbles et al., 1961). The first field testing of TFM was done on the Mosquito River, Michigan, May 14, 1958, and on the Silver River, Michigan, June 11, 1958 (Moffett, 1958a). The trials were successful, and they marked the end of research efforts in the field. Control crews treated eight streams with two formulations in 1958. One compound contained 45 percent active ingredient (Lamprecid 2770), and the other contained 30 percent active ingredient (Dowlap F40) (U.S. Bureau of Commercial Fisheries, 1958b).
experimental field work on the Canadian side was completed on the Pancake River, Ontario, August 26 to 27, 1958, and on the West Davignon River, Ontario, November 5, 1958 (Johnson and Tibbles, 1962; Johnson, 1959; Fisheries Research Board of Canada, 1958). Checks were made on the effects of TFM on invertebrates and fish. In all these tests, TFM performed well enough to cause the Great Lakes Fishery Commission to authorize treatment of streams for control of sea lamprey (Moffett, 1958a).

PHYSICAL AND CHEMICAL PROPERTIES

The identification of TFM was accomplished in 1930. In the preparation and isolation of nitrotrifluoracetanilide, DeBrouwer (1930) obtained a substance which he identified as 1,3,6-nitrotrifluorocresol, or TFM. He determined the melting point (76°), molecular weight (207), position of the NO₂ grouping, resistance of the radical CF₃, the constant of ionization (4.4 x 10⁻⁷), and the preparation of its barium salt.

Applegate et al. (1961) listed several properties of TFM including its form at room temperature, color, solubility, stability, detoxification, and properties in different formulations. Smith, Applegate, and Johnson (1960) determined that TFM is a fairly strong acid (pK 6.07 ± 0.03), that its color is at its height at pH 8.0 or above, and that it has a molar absorbance of 13,130 at 395 nm (nanometer). They also determined its ultraviolet, infrared, and visible spectra, and potentiometric titrations (Smith, Applegate, and Johnson, 1961). Daniels et al. (1965) mentioned the molecular weight, melting point of the free phenol and the impurities of TFM. Rogers and Watson (1965) studied the electron spin resonance (esr) spectra of the anion radicals of TFM.

In an attempt to determine the reason for the selectivity of mononitrophenols, especially TFM, Applegate, Johnson, and Smith (1966) tested phenols with nitro groups in the para position and the halogen in the meta position and discovered that they are generally more toxic to lampreys. Other related compounds were studied for possible selective properties, but none was found. A condensed version of the preceding report appeared a year later (Applegate, Smith, and Willeford, 1967).

Observations at present seem to indicate that the toxicity of TFM is related to the amount of free phenol present. When TFM is exposed to low pH (6.8), it exists as a free phenol, but when exposed to high pH, most of the TFM exists as a phenolate ion (Lennon, 1971).

Information on the degradation and residues appears in the section of this report entitled, Residues.

Several methods for preparing TFM are known. Maumee Chemical Company used benzotrifluoride as a starting point (Anonymous, 1959). In the preparation of 2,5-dihydroxybenzotrifluoride, Whalley (1949) found one of the derivatives to be 2-nitro-5-hydroxybenzotrifluoride (C₇H₄F₃NO₂) or TFM. The preliminary laboratory tests were done with a sample recrystallized from benzene-petroleum ether (Applegate et al., 1961). Using 3-(trifluormethyl)-4-nitro-aniline, a diazonium was formed which was then hydrolyzed in a series of steps to yield TFM (U. S. Rubber Company, 1963). None of the various methods has produced a very pure compound. Farbw erke Hoechst produced a technical-grade preparation (91 percent pure) of TFM, which was used in raceway tests and all experimental stream treatments (Johnson, 1959 and Applegate et al., 1961). Lech (1971) discussed methods for crystallizing TFM, and for preparing reduced TFM.
(RTFM) and tritiated TFM and RTFM. Synthesis of C\textsuperscript{14} ring-labeled TFM was accomplished by the Mallinckrodt Chemical Works (1971).

**EFFICACY**

In preliminary laboratory tests at 55±1°F, a 2 ppm concentration of TFM with both free phenol and sodium salts was effective on sea lamprey larvae (Applegate, Howell, and Smith, 1958). In preliminary field tests, an application of 5.5 ppm of TFM for 9 hours killed all lamprey larvae within 7-3/4 hours in the Mosquito River, Michigan, and a concentration of 2.8 ppm applied for 13-1/2 hours killed all lamprey larvae in the Silver River, Michigan (U. S. Bureau of Commercial Fisheries, 1958b). A range of 3 to 10 ppm was established for lamprey control in laboratory tests by 1962 (Applegate and King, 1962). Taking various water chemistries into account, concentrations of 1 to 17 ppm are lethal to lamprey larvae (Dykstra and Lennon, 1966).

**Life stages**

Applegate, Howell, and Smith (1958) found that TFM was effective against sea lamprey in the 2- to 5-year classes at 2 ppm. Later, Applegate et al. (1961) exposed larval, recently transformed, and adult lampreys to 1.5 to 13 ppm of TFM in raceway tests at 45 to 55°F. The mortality of larvae was 100 percent at concentrations as low as 3 ppm. At 1.5 ppm, 91.5 percent of the larvae died. Adults and recently transformed lampreys died at concentrations as low as 3 ppm. Thus, treatment of streams when the adults are spawning in spring, or when the recently transformed lampreys are moving downstream in fall or winter could destroy some of the migrants. Dustin and Higginson (1967) observed that larvae in late stages of transformation (mid-summer) seem to be more resistant to a mixture of TFM and Bayluscide\textsuperscript{10}(a synergist used to reduce the amount of TFM needed).

Piavis (1962) undertook a study in 1956 to determine whether certain selective larvicides would have any effect upon the developing embryos, prolarvae (larvae still bearing a yolk), and young larvae. He found that all Stage 18 larvae (larvae with gut instead of yolk) exposed to 10 ppm of TFM died in 1 or 2 hours. It seemed to Piavis that chemical treatment of earlier stages (blastula through hatching) delayed development and led to death, but that prolarvae could survive until they become larvae. He suggested, therefore, that control of the sea lamprey would be most effective if conducted at least 40 days after all spawning so that larvae would have reached Stage 18 in their development.

In 1962, investigators at Hammond Bay exposed sea lamprey at all stages of embryonic development to 10 ppm of TFM for 24 hours. After exposure, eggs and larvae were washed and placed in fresh water. The exposure of Stages 1 through pre-hatching Stage 13 resulted in disintegration of the embryo before it reached Stage 18. All embryos exposed during prolarval stages, 14 to 17, died during or immediately following exposure. All Stage 18 larvae died within hours after exposure (Erkkila, 1962).

**Temperature**

Preliminary work on the effects of temperature on the efficacy of TFM was done in the laboratory. Lamprey larvae from 3.5 to 5 inches long were exposed to TFM in water from Hammond Bay of Lake Huron at 35, 45, and 55°F. The results indicated little difference in the activity of TFM at these temperatures. The MLC (minimum lethal concentration - the concentration killing 100 percent of the larvae within 24 hours) for larvae was 2 ppm, and the death rate slowed as the temperature decreased. The selectivity in toxicity between fish and
lamprey increased when the temperature dropped near 32° F (Applegate et al., 1961; Keller, 1966).

When the use of TFM was extended to include warm-water streams, a graduate student at the University of Michigan tested American brook lamprey from 3.5 to 7.5 inches long at 55, 60, and 65° F in Huron River water, and at 35 to 75° F (10-degree intervals from 35 to 55°, and 5-degree intervals from 55 to 75°) in city water (Cooper, 1965). In both waters the time required for effective exposure increased at colder temperatures. He found that the minimum lethal concentration was 5 ppm at 55°, 4 ppm at 60°, but at 65° F it was again 5 ppm. Cooper suggested that: 1) results may differ if pre-control bioassays are done in water warmer than the stream; 2) less chemical is needed if treatments were postponed until streams warm up; and 3) large streams should not be treated in late fall, winter, or early spring. He concluded that lower temperatures slow the death of lamprey, and added that no data are available on the interaction of temperature and water quality.

The results observed in field operations support those obtained through research. One of the first reports of water temperature affecting the toxicity of TFM in the field was in connection with an incomplete kill of larval lamprey in the Sucker River, Michigan. Shortly after the application of TFM, the temperature dropped from 55 to 39° F, which apparently retarded the activity of the free phenol and resulted in inadequate exposure (U. S. Bureau of Commercial Fisheries, 1958b). A later report found one of the causes for lamprey surviving a treatment in the lower Brunsweiler, a tributary of the Bad River, Wisconsin, was a drop of 11° F in temperature which reduced the effectiveness of TFM (Smith and King, 1970). Workers also observed that winter treatments required too much chemical and resulted in mechanical failure of equipment due to freezing (U. S. Bureau of Commercial Fisheries, 1961). In addition, winter treatments made traveling, sampling, and observations difficult because of the ice and snow (Tibbles et al., 1961).

**Water chemistry**

Water from 16 streams in the Lakes Huron, Michigan, and Superior watersheds was used in bioassays at 55° F in the laboratory to check the effects of pH, conductivity, alkalinity, and turbidity on TFM. The chemical is most effective in soft, acid waters where the minimum lethal concentration is as low as 0.5 ppm. The hardest and most alkaline waters require 8 ppm. Turbidity caused no change in toxicity in a few simulated stream trials (Applegate et al., 1961). The dissolved oxygen was not checked because most streams to be treated have high oxygen concentrations.

The biological activity of TFM is generally best at about pH 7.1, but is reduced below 7.0 and as alkalinity increases. Attempts to change pH of streams have not been effective (U. S. Bureau of Commercial Fisheries, 1960b and 1960c). Lamprey larvae were exposed to six concentrations of TFM (1, 2, 3, 9, 11, and 13 ppm) for 20 hours at four pH values (6.6, 7.2, 7.8, and 8.4). All larvae died when exposed to 2 and 3 ppm of TFM at pH 6.6 to 7.8. Above pH 7.8, complete kills were not attained even at concentrations of 13 ppm (LeMaire, 1961).

In testing for comparative toxicity of TFM, Applegate and King (1962) selected water from three different sources which encompassed nearly all conditions in streams of Lakes Huron and Michigan. At pH 7.8, methyl orange alkalinity of 95.4 ppm, CO₂ of 1.8 ppm, and conductivity of 176.3 micromhos (at 18° C), the MLC of TFM was 4 ppm in 9 of 11 tests; at pH 7.7, methyl orange alkalinity of 141.7 ppm, CO₂ of 3.2 ppm, and conductivity of 219.1
micromhos, the MLC of TFM was 6 ppm in 6 of 11 tests, and at pH 7.7, methyl orange alkalinity of 203.3 ppm, CO₂ of 5.1 ppm, and conductivity of 338.7 micromhos, the MLC of TFM was 9 ppm in 5 of 10 tests. Thus, TFM is more toxic in waters having low alkalinity and conductivity.

Kanayama (1963) worked on a method to define the minimum lethal concentration of TFM. He measured alkalinity in tributaries of Lakes Superior and Michigan, and tested TFM at the various levels. The MLC of TFM ranged from 1 ppm at 10 to 19 ppm of CaCO₃ to 6.7 ppm at 160 to 169 ppm of CaCO₃. He tested conductivity values from 40 to 279 micromhos (at 20°C), and found the MLC of TFM ranges from 1 ppm at 40 to 59 micromhos to 5.7 ppm at 260 to 279 micromhos. His results confirmed the fact that TFM is more toxic to lampreys at low levels of alkalinity and conductivity.

An investigation was made on the water quality of streams tributary to Lakes Superior and Michigan to determine the natural levels and seasonal fluctuations in concentrations of aluminum, copper, iron, magnesium, calcium, chloride, nitrate, nitrite, silica, sulfate, tannin-like and lignin-like compounds, phenolphthalein alkalinity, total alkalinity, total hardness, pH, and conductivity. This was done to facilitate determination of the minimum lethal concentrations of TFM to larval lamprey (Zimmerman, 1965; Smith, 1966).

A need to correlate these constituents with the biological activity of TFM has been demonstrated many times in field situations. Thus, investigators in Canada used water from various streams in bioassays, and analyzed the water at the same time. In addition to the constituents evaluated by Zimmerman (1965), they measured oxygen consumed, chemical oxygen demand, carbon dioxide, color, turbidity, suspended matter, residue on evaporation, loss on ignition, manganese, zinc, sodium, potassium, ammonia, fluoride, and phosphate. No single constituent was linked consistently with the results of bioassays in the three streams tested; thus, no one factor was completely responsible for change in activity. More work needs to be done in this area (Johnson, 1970).

A few management experiences illustrate the problems related to differences in water chemistry. On one occasion when the concentration of dissolved oxygen in the Kalamazoo River, Michigan, was low (0.6 ppm to 2.4 ppm), 4 ppm of TFM and 2 percent Bayluscide® were required to get a complete kill of lamprey, but numbers of northern pike, carp, white sucker, and channel catfish were killed. In southern tributaries of Lake Michigan, 10 to 12 ppm of TFM were needed because of the water quality (Smith, 1967a). Manion (1969) found that effective concentrations of TFM range from 6 to 9 ppm and exposures range from 7 to 8 hours in waters of 4 to 10°C, 49 to 56 ppm of CaCO₃, and 109 to 113 micromhos.

Natural factors

Certain physical and meteorological conditions can reduce the effectiveness of TFM treatments. Lamprey control crews have observed the following: 1) dilution of chemical concentration caused by excessive rain, merging streams, melting snow, and other volumetric increases; 2) high and low water levels interfere with distribution of the toxicant; 3) unless the sample is filtered, turbidity makes measurement of concentration difficult; 4) any naturally occurring substance or pollutant absorbing light at 395 nm may interfere with the determination of TFM; 5) escape of lampreys from TFM by burrowing deeper into the mud or traveling into untreated areas; 6) variation in chemical characteristics of the stream water, especially pH, which changes the biological activity of TFM; and 7) natural formations such as beaver dams which obstruct dispersion of the chemical (U.S. Bureau of
Management results

Control of the sea lamprey has been the greatest fish control endeavor ever attempted (Bardach, 1964). The success of this program is evidenced in the number of self-sustaining populations of game and food fish which are not seriously threatened by lamprey predation (Baldwin, 1968). Great recoveries of valuable fish stocks have been noted in Lake Michigan and Lake Superior (Crowe, 1965; Lennon et al., 1970; Tody, 1966; Wiegert, 1966). Observations by experts attribute this success to the reduction in numbers of sea lamprey to 10 percent of their pre-control abundance (Lawrie, 1970; Anonymous, 1967).

Indications are that the sea lamprey will be reduced further by improved survey and treatment techniques and by complete treatment of lamprey-producing tributaries of all Great Lakes. The total benefits to be derived from the control program greatly exceed the cost of research and management that must continue in order to suppress and maintain the sea lamprey at low numbers (Brinser et al., 1968; Lawrie, 1970; Lennon et al., 1970).

TOXICITY--NON-TARGET SPECIES

Aquatic plants

At the concentrations used, TFM does not appear to affect adversely either algae or higher aquatic plants (Howell, 1966). However, TFM and its salts applied at concentrations from 15 to 100 ppm control rooted aquatic plants (Josephs, 1961). The lower doses are used in standing waters while the higher concentrations are needed in moving waters. Each concentration requires about 2 hours of exposure. TFM and its salts and esters in liquid or dust form have also been used to protect seeds and make them resistant to attack by organisms causing damping off, seed rot, and root rot (Baker, 1962).

Haas (1970) treated streams with 1 and 4 ppm of TFM to determine the effect on periphyton. He weighed the standing crops before and after treatment, and found no significant difference in the growth rates of the two groups.

Invertebrates

Scherer, Stähler, and Frensch (1957) and Schrader (1961) studied the toxicity of the phosphoric acid ester of TFM to the common house fly, Musca domestica. They found that this compound is nontoxic to warm-blooded animals.

Scherer, Frensch, and Stähler (1960 and 1964) observed during field studies that lower aquatic organisms such as leeches (Hemiclepsis spp. and Glossiphonia spp.) and tubificids are affected at 3 to 7.5 mg/l (milligrams per liter) of TFM. On the other hand, fish-food forms such as Daphnidae, Coleoptera, Odonata, Notonectidae, and Gammaridae are not affected by TFM until concentrations reach 20 to 24 mg/l.

The Great Lakes Biological Laboratory (1963) reported a German study on the effect of TFM on invertebrates. This study determined that animals with a strong exoskeleton are not affected by a concentration of 10 ppm for 5 days. Gammarids tolerated 8 ppm and some insect larvae 6 ppm. Thin-shelled invertebrates died readily at the same concentrations. Leeches, Tubifex, and Daphnia tolerated 1.5, 3.75, and 3.75 to 4.0 ppm, respectively.

Applegate et al (1961) in their preliminary field tests of TFM noticed premature
emergence of mayfly nymphs, but treatments do not appear to seriously affect other groups of invertebrates.

To gain further knowledge on effects of TFM to common aquatic invertebrates, assays were completed with 14 groups representing five phyla and using 2 to 20 ppm of the toxicant for each species. Mortality was insignificant in exposures to 20 ppm among isopods, gammarids, crayfish, dragonflies, water boatmen, and case-building caddisflies. Concentrations below 10 ppm were harmless to leeches in the family Glossiphanidae, stoneflies, bloodworms, and snails, but mortalities for this group were 10 to 55 percent at concentrations between 10 to 20 ppm. Mortality was significant with Hydra at 2 ppm, leeches (Herpobdellidae) at 8 ppm, burrowing mayflies at 6 ppm, net-building caddisflies at 13 ppm, blackflies at 3 ppm, and clams at 8 ppm (Erkkila, 1962). These results were much the same as those obtained in Germany, excluding the fact that the leeches tolerated 1.5 ppm there and 20 ppm here (Erkkila, 1964).

Smith (1967) tested invertebrates in the laboratory, and found that 100 percent of the hydras, turbellarians, and blackflies were affected when exposed to 10 ppm of TFM for an extended period. Other invertebrates such as burrowing mayflies would be reduced by 99 percent, Herpobdellidae by 89 percent and clams by 50 percent.

In the field, freshwater scud (Gammarus spp), burrowing mayflies, aquatic earthworms, and clams have been found dead in significant numbers after certain TFM treatments (U.S. Bureau of Commercial Fisheries, 1958b, 1959b, 1960b, and 1961).

In field tests in five tributaries of Lake Superior and four tributaries of Lake Michigan, Torblaa (1968) noted that one week after treatment 77 percent of the invertebrate groups present in sand and detritus areas had decreased, 17 percent increased, and 6 percent showed no change. In riffle areas 64 percent had decreased, 19 percent increased, and 17 percent showed no change. In two untreated riffle areas 33 percent had decreased, 50 percent increased, and 17 percent showed no change. Elmidae and Helidae declined in sand areas, and Trichoptera, Coleoptera, Ephemeroptera, and Diptera declined in riffle areas. Six weeks after treatment, the numbers of organisms increased in three streams, were partially restored in another, and were reduced in one. In one year, complete recoveries were made (Smith, 1966).

Haas (1970) evaluated the effect of TFM on bottom fauna. He selected 12 taxa from riffle fauna and 8 taxa from pool fauna, and treated the stream with 1 ppm and 4 ppm of the lampricide. No change in riffle or pool fauna was observed from a TFM treatment at 1 ppm. All taxa, except two, decreased in numbers in the experimental riffle area, and all taxa decreased in the pool at 4 ppm of TFM. However, the bottom fauna varied greatly even without TFM, so it was not possible to determine the exact effect of TFM on bottom fauna.

TFM does not have molluscidal properties at levels used against sea lamprey, but at 15 mg/l for 6 hours the sodium salt of TFM (Eelicide--TFM) had a LC 99.5 rating (lethal concentration - concentration producing a 99.5 percent mortality within a specified period of time) for the snail (Australorbis glabratus) that is an intermediate host of schistosomiasis. At that level it was not toxic to the guppy and other small fish tested (Jobin and Unrau, 1967).

**Fishes**

European species were not affected by TFM until levels of 15 to 18 mg/l were reached (Scherer, Frensch, and Stahler, 1964). In preliminary tests in the United States TFM as a free phenol was toxic to
brown trout at 7 ppm and to rainbow trout at 9 ppm. Rainbow trout were affected at a 7 ppm concentration of the sodium salt of TFM (Applegate, Howell, and Smith, 1958; McKee and Wolf, 1963). Raceway studies included 15 species of fish, TFM at 1.5 to 13 ppm, and temperatures from 45 to 55°F. Brown trout, brook trout, and panfish tolerated TFM as well as did rainbow trout. Brown trout and rock bass were affected at a concentration of 9 ppm, adult white sucker and yellow perch above 7 ppm, logperch at 5 ppm, and bullheads above 3 ppm (Applegate et al., 1961).

Applegate et al. (1961) observed in field trials that only a few species were affected adversely by TFM. Of 25 species of fish and four species of native lamprey in Silver River, Michigan, only logperch were killed in large numbers. Among 18 species of bony fishes only sculpins suffered great mortalities in the Pancake River system, Ontario.

Because lamprey control was extended to streams containing large numbers of warm-water fishes, toxic levels of TFM had to be established for bluntnose minnow, fathead minnow, white sucker, yellow bullhead, pumpkinseed, bluegill, smallmouth bass, largemouth bass, yellow perch, and walleye (U.S. Bureau of Commercial Fisheries, 1960a and 1960b). Lethal concentrations were established in three dilution waters for all of the above species except the bluntnose minnow and pumpkinseed. Tolerances also were established for golden shiner and blacknose shiner. TFM is as toxic to cyprinids as it is to rainbow trout. Centrarchids are more tolerant than the cyprinids. White sucker, yellow bullhead, yellow perch, and walleye are relatively susceptible, with the walleye the least tolerant. The MAC (maximum allowable concentration - concentration killing 25 percent of the specimens within 24 hours) ranges from 5 to 44 ppm depending upon the species of fishes present and the water quality conditions at the time of application (Applegate and King, 1962).

Recent toxicity studies were performed at the Fish Control Laboratory, La Crosse, Wisconsin, on fingerling-size fish of 12 species. Using standard reconstituted water Marking (1971) found that the toxicity ranged from 1.39 to 16.2 ppm in 96-hour static exposures. Green sunfish and bluegill were the most resistant, and channel catfish were the most sensitive. The toxicity easily defined at 1, 3, and 6 hours of exposure. In tests to determine the effect of temperature on the biological activity of TFM, yellow perch were exposed to 12, 17, and 22°C, but very little difference was observed. On the other hand, in tests with rainbow trout TFM was found to be more toxic at 17°C than at 12 or 7°C (Lennon, 1971). Changes in toxicity did occur in different water qualities with TFM being more toxic in soft water. The LC50 for yellow perch ranges from 2.28 ppm in soft water (10 ppm total hardness) to 28.4 ppm in hard water (300 ppm total hardness) at 96-hour exposures. Also, TFM is more toxic to fish in water with low pH than high pH (Lennon, 1971).

In stream treatments several workers have observed fish mortalities when the water temperatures increased or changed drastically. A rapid rise in temperature of 8° F in the Muskegon River, Michigan, and variable temperatures in the Au Gres River, Michigan, possibly contributed to fish mortalities (Smith and King, 1969 and 1970). During the treatment of the Nottawasaga River, Ontario in June 1968, extreme water temperatures stressed the fish enough that normally safe TFM dosages caused fish mortalities (Lamsa, Dustin, and Davis, 1969; Davis and Shera, 1969).

The physiological effects of TFM on bony fishes differ in some respects from those in lamprey. Both bony fishes and lamprey accumulate a large amount of fluid in the tissue between the respiratory epithelium
and the vascular endothelium. Both exhibit mucous accumulation and vasodilation. However, their activity response differs in that lamprey become narcotized and hemorrhage, but in contrast, rainbow trout surface, not hemorrhaging, but suffocating (Christie and Battle, 1963; Keller, 1966). Plasma concentrations of potassium, calcium, magnesium, lactic acid, and glucose increased, but sodium declined when adult white suckers were exposed to 5 ppm of TFM (Hunn, 1971; Lennon, 1971). Preliminary studies seem to indicate that the mode of action of TFM involves the release of potassium and the blocking of glucose utilization, resulting in increased plasma concentrations of lactic acid and glucose (Lennon, 1971).

Toxicity of TFM mixed with 2 percent of Bayluscide® to fishes changes somewhat, as compared to TFM alone. In the hard-water streams of Lake Michigan the mixture of toxicants increases the mortality of fish (Smith, 1967a; U. S. Bureau of Commercial Fisheries, 1965). If the amount of Bayluscide® is increased, the selectivity to lampreys over fish decreases (Smith, 1967b; Lamsa, 1968). In waters with high alkalinity, the toxicity of the mixture to fish increases (Smith, 1968).

Tests were performed on chinook salmon and coho salmon to determine the comparative effects of TFM and TFM with 1 percent of Bayluscide® (TFM-1B). The mixture was less toxic than TFM to both salmon. Coho salmon were affected less than chinook salmon by either compound. Care should be taken, however, not to treat streams when jack chinook salmon are running (Smith and King, 1969).

The toxicity of TFM to different fishes as reported from actual treatments varies according to conditions, but generally the species cited most as being affected by TFM are central mudminnow, white sucker, bullheads, stonecat, trout-perch, logperch, walleye, and sculpins. Occasionally brown trout are susceptible, mainly because treatments are made in September and October when they are spawning (U. S. Bureau of Commercial Fisheries, 1959b and 1960b; Erkkila, 1964; Smith, 1967a; Johnson, 1959). Howell (1966) found that native lamprey of the genera Lampetra and Ichthyomyzon are affected almost as much as the sea lamprey in stream treatments.

Davis and Wilson (1965) compared the susceptibility of Ichthyomyzon spp. and American brook lamprey in field bioassays of TFM and TFM plus Bayluscide® at three exposure times on three rivers. The lethal concentrations using only TFM ranged from 0.9 to 4.8 ppm at 9 hours, 2.7 to 3.7 ppm at 12 hours, and 1.8 to 2.5 at 18 hours. Canadian investigators found that TFM is more toxic to sea lamprey than native lampreys; therefore, bioassays against native lampreys tend to indicate too high a concentration for safe use in streams (Great Lakes Fishery Commission, 1970; Davis, 1970). Furthermore, Davis (1970) contends that no simple correction factor is available which would provide accurate concentration determinations from tests with native lamprey genera.

Amphibians

There are no records of laboratory tests of TFM on amphibians. Observations in the field have shown that amphibians generally are not affected by TFM treatments in streams. In the post-treatment operations on the Pancake River in 1958, Johnson (1959) found dead only one each of tadpoles and Necturus. Howell (1966) states that Necturus maculosus seems to be as susceptible as lamprey to TFM. According to tests run in a 0.1-acre pond by the Fish Farming Experimental Station, Stuttgart, Arkansas, a complete kill of tadpoles is possible with an application of 12 ppm or more of TFM (Anonymous, 1964).
Reptiles

Small numbers of turtles were exposed to 3, 5, and 10 ppm at temperatures of 7.7, 7.2, and 6.4° C, respectively, causing no mortalities (Scherer, Frensch, and Stahler, 1960). Chrysemys picta and Chelydra serpentina were exposed to the same dosages of TFM at temperatures from 43 to 45° F with none dying (Applegate et al., 1961). No observations of dead reptiles have been recorded from the field.

Birds

No laboratory or field data exist for the effects of TFM on birds. Currently, the Denver Wildlife Research Center is investigating the oral toxicity of TFM to waterfowl and upland gamebirds (Lennon, 1971).

Mammals

Scherer, Frensch, and Stähler (1964) state that TFM, like other halogenated mononitrophenols, is toxic to warm-blooded animals at certain concentrations, and requires care in transporting and applying. Pure TFM has an oral LD50 (lethal dose that produces a 50 percent mortality within a specified period of time) of 30 mg/kg (milligram per kilogram) for the rat when injected intraperitoneally, but formulations consisting either of 50 percent of the sodium salt of TFM or 51 percent of TFM have LD50's of 300 mg/kg and 200 mg/kg to rats, respectively. According to Scherer, Frensch, and Stähler (1964), TFM in a free phenol formulation becomes very toxic orally and dermally.

Tests made by the Wisconsin Alumni Research Foundation on a 20 percent by weight formulation of TFM showed an acute oral LD50 for rabbit of 0.16 g/kg (grams per kilogram) and dermal LC50 of 1.6 g/kg. TFM is harmless to the eyes at concentrations of 1 to 9 ppm but should be taken in handling concentrated forms (Applegate et al., 1961; U.S. Bureau of Commercial Fisheries, 1957b).

Lech (1971) injected rats with TFM in 0.9 percent saline and found no signs of toxicity at 18 mg/kg, but toxic effects appeared at 24 mg/kg and mortality at 40 mg/kg.

The oral LD50 ranges recorded by Frear (1969) were from 0.5 to 1.0 g/kg of body weight for rats.

To determine the effects that TFM might have on mammals, the Michigan Conservation Department administered TFM in the drinking water given to four white-tail deer. According to the author, two deer had their water contaminated with the maximum of the chemical that would be used in the stream work. After 6 weeks no effects were observed although all four had drunk freely of treated and non-treated water (Johnson, 1957). Six 1,000-pound cows and four calves were exposed to water containing 13 ppm of TFM. Again no harmful effects were observed, and no phenol was detected in the milk of the animals (Applegate et al., 1961).

When higher concentrations of TFM up to 11 ppm were used in Lake Michigan tributaries, the Wisconsin Alumni Research Foundation found that they were not toxic to mammals (Erkkila, 1964).

In 1971, the WARF Institute, Inc. was awarded a contract to conduct acute and 90-day studies on the oral toxicity of TFM to laboratory animals (Lennon, 1971).

MODE OF ACTION
ON SEA LAMPREY

The biological activity of TFM is affected by various factors which cause minimum lethal concentrations to range from 0.5 ppm to 12 ppm. The lower concentrations are
effective in soft, acid waters, and the higher doses are needed for hard, alkaline waters (Applegate et al., 1961; Scherer, Frensch, and Stähler, 1964; Applegate and King, 1962).

The physiological effects of TFM on the sea lamprey are not completely understood. The nervous tissue, cardiac muscle, notochord, alimentary canal, and mesonephros do not seem to be affected, but the gills, circulatory system, liver, and skeletal muscle are. In particular, the gills hemorrhage and become covered with mucous (Christie and Battle, 1963). Keller (1966) proposed that death was due to circulatory failure and suffocation. Applegate, Smith, and Willeford (1961) think lamprey die of a combination of circulatory and respiratory failure. One of the symptoms is a state of hypotension. The theory that death was due to anoxia was tested by Agris (1966 and 1967). He found that the electrophysiological events in the heart differ from those observed following anoxia. In another test he observed that lamprey killed with TFM did not have the methemoglobin which is present with anoxia. Smith and King (1969) found that oxygen consumption increased in lamprey exposed to TFM and Bayluscide®. Recently Dr. John Lech at the Medical College of Wisconsin, Milwaukee, Wisconsin, reported that the toxic action may be related to catecholamine metabolism. This theory is being tested by the use of the drug, Dibenzylene® (Fish Control Laboratories, 1971a).

RESIDUES

Federal regulations on the use of pesticides require that residue levels of TFM be determined in natural waters, bottom sediments, fish and other organisms exposed to the lampricide. Index streams were selected for observation of any long-term effects and toxic residues which might build up in the stream fauna (Erkkila, 1964). Analytical procedures for separating, concentrating, and detecting these residues had to be developed. The first method studied involved the adsorption on activated carbon of TFM residues from natural waters. The water quality, temperature, and site of sample were believed to have some effect on the quantitative measurement. Thus, the whole procedure needed more study and was finally considered inadequate to detect lampricide residues (Daniels et al., 1963 and 1965).

The next method made use of ion-exchange resin and solvent extraction of residues from natural waters, fish tissue, and bottom sediments (Daniels et al., 1965). Colorimetric methods were available to detect TFM in natural waters, but only concentrations of 0.1 ppm or greater could be measured. Therefore, ion-exchange resins were used to separate TFM residues. These compounds then could be recovered as concentrates by elution with selective solvent mixtures. TFM was removed from the whole fish by three extraction methods. At that time only the colored isomeric compounds, which absorb light at 395 nm, could be detected and measured (Daniels et al., 1965). These methods were not effective for detecting TFM in fish, bottom sediments, and water exposed to normal concentrations of the toxicant (Smith, 1966; Billy et al., 1965). By using an infrared recording spectrophotometer, various amounts of TFM residues were recovered from green sunfish exposed to extremely high concentrations of TFM. The value of this method is limited because only high concentrations of TFM can be detected (Smith, 1966).

Magadanz and Kempe (1968) observed that TFM disappeared in 2 weeks from natural waters that were in contact with bottom sediments. The rapid rate of removal is decreased if phenol is added to the bottom sediment. The residues in the bottom sediment apparently degrade, liberating the fluoride ion. With TFM in water alone, no color loss was observed.
In further studies on the removal of TFM by river muds, Sutton (1970) found that high temperature and organic content increase the rate of removal. Phenol stops the removal process by destroying the bacteria which degrade TFM. In a test to determine the toxicity of the degradation products of TFM, a concentration of 30 ppm of TFM was allowed to degrade 3 months. It was tested then against goldfish and lampreys, but none of them died.

In a related study Kempe (in review) reported on his attempts to determine whether TFM remains in the aquatic environment or is degraded to simpler compounds. Apparently, TFM degrades in bottom muds due to the action of bacteria, probably Pseudomonas spp. The products of this degradation, when tested against sea lamprey and goldfish, are not toxic. Only one-fourth of the fluorine added was recovered, according to other tests.

Lech (1971) has attempted to define metabolites of TFM in rats so that analytical methods may be developed for residues in organisms and the environment. The major metabolite appears to be 3-trifluormethyl-4-aminophenol (RTFM). Both TFM and RTFM are excreted in the urine as polar derivatives, some of which appear to be glucuronides. Dr. Lech is being assisted by the Fish-Pesticide Research Laboratory, Columbia, Missouri, in the identification of TFM metabolites through mass spectrometry (Lennon, 1971).

In an effort to develop methods for detection of TFM in the ppb (parts per billion) range, the General Electric Company (1971) is investigating the analysis of TFM by luminescence spectrophotometry. If successful, the method will enable simple and rapid detection of small amounts of TFM in water, bottom sediments and field organisms. The Fish Control Laboratories are investigating the use of gas chromatographic methods to detect and measure residues of TFM in fish tissue (Hunn, 1971). The method utilizing solvent extraction, acid-base partitioning, and gas chromatography, is sensitive to 0.005 ppm of TFM or less, and preliminary studies indicate excellent recovery (Fish Control Laboratories, 1971b).

APPLICATION METHODS

Successful application of TFM requires good equipment, proper formulations, and trained men using proven techniques. Many procedures were developed during the first three treatments of experimental streams in 1958. These included: 1) preliminary survey of lamprey distribution, of kinds and abundance of lampreys, fishes, and other fauna, and of potential treatment points; 2) pre-treatment analyses to determine the amount and exposure to TFM needed as influenced by discharge and velocity of water, and the chemical and physical properties of the water; 3) actual application techniques such as operating the controlled pumping system and measuring the concentration of TFM in the streams; and, 4) post-treatment surveys of dead fauna (Applegate et al., 1961; Johnson, 1959 and 1961; Kanayama, 1963; Baldwin, 1964; Wadden, 1968; Schneider, 1969). Smith, Applegate, and Johnson (1960 and 1961) used a colorimetric method to detect the distribution and concentration of TFM as it traveled downstream. The intense yellow color of TFM in an alkaline solution was measured and analyzed.

Several years were required to develop adequate equipment for survey and treatment procedures. A light, portable shocker was developed to survey the abundance and distribution of ammocoetes in inaccessible areas (Braem and Ebel, 1961). An anchor dredge was modified by Thomas (1960) to sample the larvae populations at the mouths of rivers. Marking larval lamprey with cadmium sulfide and mercuric sulfide yielded population statistics (Smith and
McLain, 1962; Hansen and Stauffer, 1964). Electrical barriers have been installed at various streams to determine the reduction of lamprey populations by TFM treatments (Tibbles, 1965). Portable metering devices (gravity, fuel, and electric) were developed to add precise volumes of liquid TFM into streams (Anderson, 1962). A pour-portioner drum meter, for example, was adapted to improve application of small volumes of TFM into streams (Tibbles, Lamsa, and Johnson, 1970; Dustin, 1970). Mobile wet laboratories were developed to facilitate bioassays in the field (Howell and Marquette, 1962). A photoelectric amplifier was modified for use as a dye detector to determine water movement (Ebel, 1962). It provided a continuous record of the duration and intensity of the tracer dye in a stream (U. S. Bureau of Commerical Fisheries, 1961).

Various compounds that might augment the activity of TFM were tested with the intent of reducing the amount of TFM needed. The most successful of these was Bayluscide® (5, 2'-dichloro-4'-nitrosalicylanilide). Addition of 2 percent by weight of this compound to the toxicant mixture reduced the amount of TFM needed by 50 percent (Howell et al., 1964; Johnson and Lamsa, 1964; Howell and King, 1966a). Unfortunately the mixture had several disadvantages that TFM alone did not have. It was barely soluble in water, clogged the feeder apparatus, and caused more fish kills when applied in lower Michigan streams by standard methods and in other areas from aircraft (Johnson and Lamsa, 1964; Smith, 1966 and 1967b; Lamsa, 1968; Smith and King, 1970).

Granular Bayluscide® and other nitro-salicylanilides have been tried alone as sea lamprey larvicides in deep water as bottom poisons, lamprey irritants, and survey tools, but many of these substances do not have a wide enough safety margin for fish and invertebrates, are influenced strongly by water quality, or information on their residues is lacking (Jacob, 1966; Marking et al., 1970; French and Swartz, 1968; Howell and King, 1966b; Starkey and Howell, 1966; Taborsky, 1970; Morman, 1969; King and Howell, 1970; Lennon et al., 1970).

Another compound, toxaphene, was reconsidered for treatment of lakes and estuaries after being tested by the Canadians. Although a large number of amo­coetes were killed at 100 ppb and most fish populations recovered within 1 year, the use of toxaphene was discontinued by the U. S. Bureau of Commerical Fisheries and the Great Lakes Fishery Commission (Gaylord and Smith, 1966).

A registered fish toxicant, antimycin, may offer a possible solution to treating selectively such difficult areas as oxbows, estuaries, and bays off the mouths of rivers. Ayerst Laboratories, Inc., is experimenting with various formulations that would allow the toxicant to perform as desired (Lennon, 1971).

Because TFM is less toxic in hard waters than soft, a group of compounds was tested to find a chelating agent that would suppress the ionization of interfering divalent metal ion (Johnson, 1970). Although the results proved that divalent metal ions cause a decrease in activity of TFM, the amount of chelating agent needed to offset the decrease would be too expensive.

The experiences of the men in the field brought about recommendations and changes in field procedures. Johnson (1963 and 1964) reported details of bioassays performed from 1958 to 1962, and changed the design and interpretation of bioassays to suit management needs. Observations by control crews indicated a need for consideration of the following factors: 1) synchronization of serial applications of TFM in a stream through accurate measurement of stream
velocity and of changes in velocity; 2) im­
proved efficiency of control in areas of
difficult access by spot treatments, longer
treatments, and multiple applications of
TFM; and, 3) acclimatization of healthy
bioassay animals in proper habitats
(Johnson, 1959; Johnson and Tibbles, 1962).

The need for a multifaceted, flexible,
evolving system for suppressing sea
lamprey may bring about integrated con­
trols that include both chemical and bi­
ological components (Hanson, 1970).

REGISTRATION

The U. S. Bureau of Commerical
Fisheries obtained registration of TFM on
August 21, 1964, for limited use as a sea
lamprey larvicide. Use was restricted to
trained operators and authorized personnel
only. On May 13, 1970, the U. S. Depart­
ment of the Interior was notified that the
registration was to be cancelled by the
Environmental Protection Agency on
December 31, 1970, because no tolerances
for TFM in fish and water has been estab­
lished (Fish Control Laboratory, 1971).
An application for extension until Decem­
ber 31, 1971, however, was granted to the
Bureau of Sport Fisheries and Wildlife in
order that additional data on methodology
and toxicology may be obtained (Anony­
mous, 1970). An outline of the research
needed on the chemical and physical proper­
ties, toxicity, efficacy, and residues was
prepared, and assignments of contracts
for the research were executed early in 1971
(Fish Control Laboratory, 1971). Hope­
fully, the research will be sufficient to re­
register TFM as a badly needed lampricide.

SUMMARY

TFM is a halogenated mononitrophenol
that was developed and registered as a
selective toxicant for the sea lamprey. Its
biological activity against the sea lamprey
is affected only slightly by temperature,
but it is affected by high alkalinity and
conductivity and by pH's below 7.0 and
above 7.8. Generally, aquatic organisms
are not affected adversely by stream treat­
ments, except when concentrations have
to be increased because conditions interfere
with the chemical activity. TFM does not
harm mammals at concentrations used in
stream treatments. Various methods have
been employed to detect TFM residues in
water, organisms, and bottom sediments,
but no method at present detects TFM in
the ppb range. Methods of application and
equipment have been improved through ob­
servations in the field and research. There
are still many unanswered questions re­
garding TFM, but research in progress
may answer them sufficiently for TFM to
remain registered as a lampricide.

ACKNOWLEDGMENTS

Special thanks are due to Mrs. Ruth
Rehfus, Librarian, Great Lakes Research
Laboratory, Ann Arbor, Michigan; Mr. Lee
Hanson, Fishery Biologist, Hammond Bay
Biological Station, Millersburg, Michigan;
the late Mr. Norman Baldwin, former
Executive Secretary, Great Lakes Fishery
Commission, Ann Arbor, Michigan; and
Miss Sandy Hamilton, Librarian, Regional
Office, Bureau of Sport Fisheries and
Wildlife, Minneapolis, Minnesota, for
technical assistance. Appreciation is also
due Dr. J. James Tibbles, Director, Sea
Lamprey Control Experiment, Sault Ste.
Marie, Ontario; Mr. John A. Howell,
Chief, Hammond Bay Biological Station,
Millersburg, Michigan; Mr. Robert W.
Saalfeld, Executive Secretary, Great Lakes
Fishery Commission, Ann Arbor, Michigan;
and Mr. Ralph M. Burress, Chief,
Southeastern Fish Control Laboratory,
Warm Springs, Georgia, for review of the
manuscript.

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APPENDIX A - TECHNICAL DATA ON TFM

Alternative names:
- 3-trifluoromethyl-4-nitrophenol (Beilstein, 1966)
- 3-trifluoromethyl-4-nitrophenol (Smith, 1967)
- ααα-trifluoro-4-nitro-m-cresol (Frear, 1969)
- 1,3,6-nitrotrifluorocresol (DeBrouwer, 1930)
- ααα-trifluoro-4-nitro-metacresol (Baker, 1962)
- 2-nitro-5-hydroxybenzotrifluoride (Whalley, 1949)
- 6-nitro-3-hydroxy-1-trifluoromethyl-benzol (Beilstein, 1966)
- ααα-trifluoro-6-nitro-3-hydroxy-toluol (Beilstein, 1966)
- Lamprecid 2770 (Moffett, 1958a)
- Dowlap F40 (U.S. Bureau of Commercial Fisheries, 1958b)
- Dowlap® F (Frear, 1969)
- Eelicide - TFM (Jobin and Unrau, 1967)

Chemical names:
- CF₃C₆H₃(NO₂)OH (Rose and Rose, 1966)
- C₇H₄F₃NO₃ (Beilstein, 1966)

Formulations:
- Crystalline solid, liquid (Applegate et al., 1961; Rose and Rose, 1966)

Primary use:
- Selective toxicant for larvae of sea lamprey; Re-registration of lampricide in progress (Fish Control Laboratory, 1971).

Secondary uses:
- Dye intermediate (Anonymous, 1959)
- Snail control (Jobin and Unrau, 1967)
- Housefly control with phosphoric ester of TFM (Scherer, Stähler, and Frensch, 1957)
- Seed protectants (Baker, 1962)
- Aquatic weed control (Josephs, 1961)

Toxicity to fish:
- \( \text{MAC}_{25} \) to 44 ppm (Applegate and King, 1962)

Toxicity to birds:
- Not tested

Toxicity to mammals:
- No acute effects in deer and dairy cattle;
- acute oral LD₅₀ for rabbit is 0.16 g/kg,
- acute dermal LD₅₀ at 1.6 g/kg (Applegate et al., 1961)
- Oral LD₅₀ for rat is 0.5 to 1.0 g/kg of body weight (Frear, 1969)
- Pure TFM LD₅₀ for rat is 30 mg/kg (Scherer, Frensch, and Stähler, 1964)
- 50 percent of sodium salt of TFM oral LD₅₀ for rat is 300 mg/kg (Scherer, Frensch, and Stähler, 1964)
- 51 percent of TFM LD₅₀ for rat is 200 mg/kg (Scherer, Frensch, and Stähler, 1964)

Safety hazards:
- Extreme care needed in handling concentrated forms of toxicant; protective clothing, rubber gloves, and face masks recommended (Applegate et al., 1961)

Persistence in environment:
- Non-persistent (Billy et al., 1965; Magadan and Kempe, 1968; Sutton, 1970)
APPENDIX B - COMMON AND TECHNICAL NAMES OF FISHES

The following fish classification was obtained by utilizing Bailey (1970).

<table>
<thead>
<tr>
<th>Common name</th>
<th>Technical name</th>
<th>Common name</th>
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<tbody>
<tr>
<td>LAMPREYS</td>
<td>PETROMYZONTIDAE</td>
<td>FRESHWATER CATFISHES</td>
<td>ICTALURIDAE</td>
</tr>
<tr>
<td></td>
<td>Ichthyomyzon spp</td>
<td>Bullheads</td>
<td>Ictalurus spp</td>
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<td>TROUTPERCHES</td>
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<td>Oncorhynchus kisutch</td>
<td>Trout-perch</td>
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As the Nation's principal conservation agency, the Department of the Interior has basic responsibilities for water, fish, wildlife, mineral, land, park, and recreational resources. Indian and Territorial affairs are other major concerns of this department of natural resources.

The Department works to assure the wisest choice in managing all our resources so that each shall make its full contribution to a better United States now and in the future.