WATER QUALITY ADVISORY

CHLORPYRIFOS

CRITERIA AND STANDARDS DIVISION

OFFICE OF WATER REGULATIONS AND STANDARDS

UNITED STATES

ENVIRONMENTAL PROTECTION AGENCY

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WATER QUALITY ADVISORY
Number 11

CHLOROPYRIFOS

Criteria and Standards Division
Office of Water Regulations and Standards
United States Environmental Protection Agency

Advisory - Aquatic Life.

No aquatic life advisory is given because publication of a final ambient water quality criterion document for chloropyrifos is scheduled for September, 1986.

Advisory - Human Health.

The advisory concentration for chloropyrifos in ambient water for the protection of human health is estimated to be 62 ug/L when exposure is assumed to include consumption of 6.5 grams of contaminated fish only. These concentrations do not take relative source contributions from other media into account. Care should be taken in the application of this advisory, with consideration of its derivation, as stated in the attached support document.

HUMAN HEALTH EFFECTS
LITERATURE SEARCH AND
DATA EVAULATION FOR
CHLOROPYRIFOS

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF WATER REGULATIONS AND STANDARDS
CRITERIA AND STANDARDS DIVISION
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INTRODUCTION

Advisories have been developed to give the best available scientific information on the aquatic and human health effects of chemicals in surface waters. They are issued in cases where information is needed quickly, but where there is not sufficient data to calculate national ambient water quality criteria.

An advisory concentration for the protection of human health can be derived from a number of sources: The Office of Drinking Water Health Effects Advisories; Acceptable Daily Intake (ADI) values from EPA; Office of Pesticides and Toxic Substances risk assessments; Carcinogen Assessment Group (CAG) cancer risk estimates; risk estimates derived from the open literature; or othe rsources which will be cited in the support document. The advisory concentrations derived from these sources will vary in confidence and usefulness, based on the amount and quality of data used as well as the assumptions behind the original estimates. The user is advised to read the background information carefully before using the advisory concentrations to determine the strengths or deficiencies of the values given in the advisory.

Human Health Section
Water Quality Advisory (Chlorpyrifos)

Identifying the most appropriate set of Advisory numbers (fish only, water only, fish plus water) requires an appreciation of several parameters:

(1) Relative source contribution analysis or all sources of exposure expressed in percent

(2) Toxicokinetics or the uptake, distribution, retention, and metabolism of the pollutant

(3) Health effects including both non-carcinogenic and carcinogenic bioeffects

(4) Quantification of the toxicological effects

A. Relative Source Contribution

The average ambient water concentration(s) of 0, 0-diethyl 0- (3, 5, 6-trichloro-2-pyridyl) phosphorothioate is not known. It is known, however, that Chlorpyrifos is an active ingredient of Dursban and Lorsban (No 84). Dursban is used to control fire ants, turf and ornamental plant insects, mosquitoes, cockroaches, termites, lice and horseflies on cattle (FCH85). Lorsban is used on corn as a soil insecticide for the control of rootworms, cutworms, billbugs, wireworms, seed corn maggots, etc. (FCH85). Agricultural application is via ground, aerial spray and dust. It would be reasonable to assume that some percentage of Chlorpyrifos does run off into streams where aquatic exposure would occur. Furthermore, should the ambient water be used for human consumption, the potable water tainted with Chlorpyrifos would contribute to one's total exposure to the insecticide.

The OPP, EPA has established tolerances for Chlorpyrifos and its metabolite for several food crops and maximum residue limits are available via Codex Alimentarius (OPP 84).

An arbitrary assumption that Chlorpyrifos exposure via water contributes some 20% of one's exposure will be made in this Water Quality Advisory to conform to the same prudent procedure used by the NAS(77) and ODW, EPA(85). Both the NAS and the ODW arbitrarily assumed that drinking water is responsible for 20% of one's total exposure to organic chemicals when other sources are known to exist qualitatively but not quantitatively.

B. Toxicokinetics

Based on human kinetics data, Chlorpyrifos is known to have a gastrointestinal absorption rate of approximately 70% (No 84). Dermal absorption is much less (1-3%) than absorption orally. Microsomal enzymes catalyze the oxidative desulfuration of Chlorpyrifos to form an oxon, and both Chlorpyrifos and the oxon are rapidly hydrolyzed to 3, 5, 6-trichloro-2-pyridinol (3, 5, 6-TCP). The average gastrointestinal absorption half-life in humans is 0.5 hr. and the elimination half-life is approximately 27 hrs. (No 84). Toxicokinetic data by The Dow Chemical Company suggest that Chlorpyrifos and its metabolite, 3, 5, 6-TCP have a low potential to bioaccumulate in man via repeated low level exposure. If high concentrations of Chlorpyrifos are ingested continuously, bioaccumulation may be a possibility.

Bioconcentration factors (BCF) for fish of 450 and 320 via flowing vs. static water tests were conducted by Kenaga and Goring (80). For this Advisory a bioconcentration factor of 385 will be assumed.

C. Health Effects

Chlorpyrifos can impact the nervous system. High level exposures can cause a headache, dizziness, weakness, atoxia, tiny pupils, twitching, tremors, nausea, slow heartbeat, pulmonary edema, and sweating (EPA 86). Continual absorption at intermediate dosages may cause influenza-like illness which includes such symptoms as weakness, anorexia, and malaise. At low exposure levels interference of nerve conduction may be impaired.

A summary of the toxicity by Battelle (85) shows that 50-500 ppm may cause death to humans. The LD50 values for rats, mice, and guinea pigs range from and 100-500 ppm, respectively.

Chlorpyrifos acts by inhibiting the production of acetyl-cholinesterase, a necessary chemical in nerve impulse transmission (EPA 86). Plasma cholinesterase depression appears to be the best indicator of Chlorpyrifos exposure. Plasma cholinesterase depression is more sensitive than erythrocyte cholinesterase depression as demonstrated by a recent study by Dow Chemical (No 84).

This organophosphorothioate insecticide and its principal metabolite (3, 5, 6-trichloro-2-pyridinol) were investigated by Nolan et al. (84) in which six healthy male volunteers were administered first a single oral dose of 0.5 mg/kg, followed by either a dermal dose of 0.5 or 5.0 mg/kg approximately one month later. Plasma cholinesterase was depressed to 15% of predose levels by

the 0.5 mg/kg oral exposure some 12 hours post-exposure. Normalcy of plasma cholinesterase was reached approximately one month later. The dermal exposures apparently did not alter the plasma cholinesterase levels. No significant changes in erythrocyte cholinesterase activity were reported for either the oral or dermal exposures even though on Day 3 post-exposure the data showed that the erythrocyte cholinesterase activity was some 70% of predose levels. Blood Chlorpyrifos concentrations were extremely low (<30 ng/ml). Mean blood concentrations of 3, 5, 6-TCP peaked at 0.93 ug/ml 6 hrs. after ingestion. The metabolite peaked at 0.063 ug/ml 24 hrs. after the 5.0 mg/kg dermal dose. No signs of toxicity were observed in volunteers administered either a single 0.5 mg/kg oral dose or the 0.5 or 5 mg/kg dermal dose.

Chlorpyrifos appears not to be carcinogenic since two studies proved to be negative (OPP 85). This insecticide is not teratogenic at levels up to 25 mg/kg/day (OPP 85). Furthermore, two reproductive studies (two generation) have been shown not to produce bioeffects at least up to 1.2 mg/kg/day. The impact on the nervous system then should be the focus of any advisory.

D. Quantification of Toxicological Effects

In 1982, OPP, EPA reviewed the toxicological data of two 2-year dog and rat feeding studies (EPA 82). The NOELS based on rbc cholinesterase activity were 0.1 mg/kg/day. Using a safety factor of only 10, the human ADI was calculated to be 0.01 mg/kg/day. For a 70 kg adult, the ADI could have been calculated to be 0.7 mg/day.

Using a paper by Nolan et al. (84), an ADI of 0.005 mg/kg via a precursor bioeffect of 0.5 mg/kg could be calculated using a safety factor of 100. In this human volunteer study, 0.5 mg/kg via one oral exposure caused a significant depression in plasma, but not erythrocyte cholinesterase. The ADI for a 70 kg adult then could be calculated to be 0.35 mg/day.

$$\frac{(0.5 \text{ mg/kg})(70 \text{ kg})}{100 \text{ S.F.}} = 0.35 \text{ mg/day}$$

In 1972 Coulston et al. reported that 0.1 mg/kg/day for 20 days resulted in a plasma but not erythrocyte cholinesterase depression in human volunteers. Furthermore a level of 0.03 mg/kg/day administered over the two-week study was found not to influence even the plasma cholinesterase level. Applying a safety factor of 10, an ADI of 0.003 mg/kg/day or 0.210 mg/day for the 70 kg adult could be calculated. The OPP, EPA calculated an ADI of 0.18 mg/day via using an adult weight of 60 rather than 70 kg.

$$\frac{(0.03 \text{ mg/kg/day})(70 \text{ kg})}{10.\ S.F.} = 0.210 \text{ mg/day}$$

Utilizing human data rather than animal data and averaging the two ADIs calculated from Nolan et. al. (84) and that specified by OPP, EPA of 0.35 and 0.21 mg/day, respectively, a consensus ADI of 0.28 mg/day could be obtained.

Without consideration of other sources of exposure, it is possible to calculate:

a. Lifetime acceptable level in drinking water via ADI/2

b. Lifetime acceptable level in ambient water if only fish were consumed but the water was not consumed via ADI/RF

c. Lifetime acceptable level in which the water was consumed and the fish living within the water were consumed at the rate of 0.0065 kg/day via ADI/2
plus 385 (0.0065).

The three values for drinking water only, fish only, water plus fish are 0.14 mg/L, 0.112 mg/L, and 0.062 mg/L, respectively:

- Drinking water only:

$$\frac{ADI}{2} = \frac{0.28 \text{ mg/day}}{2 \text{ 1/day}} = 0.14 \text{ mg/L}$$

- Fish only:

$$\frac{ADI}{RF} = \frac{0.28 \text{ mg/day}}{(385 \text{ BCF})\ (0.0065 \text{ kg/day})} = 0.112 \text{ mg/L}$$

- Ambient water or fish plus drinking water:

$$\frac{ADI}{2 + RF} = \frac{0.28 \text{ mg/day}}{2 \text{ 1/day} + (385)\ (0.0065 \text{ kg/day})} = 0\ 062 \text{ mg/L}$$

Since water is arbitrarily assumed to contribute some 20% of man's Chlorpyrifos intake, all initial Advisory levels should be modified by a factor of five (Table 1). Should other sources of exposure be determined on a case-by-case basis, values other than 10, 20, and 30 ug/L for fish plus potable, fish only and potable only, respectively, would be more appropriate.

Table I

WATER QUALITY ADVISORY FOR CHLORPYRIFOS (ug/L)

Water Use	Relative Source Contribution	
	No	Yes
Fish plus potable	62	10
Fish only	112	20
Potable only	140	30

It should be remembered that Chlorpyrifos is not the only chemical known to depress cholinesterase levels and possibly inhibit nerve transmission. Should other pollutants affecting this organ system be present, a dose-addition analysis of all pollutants affecting the nervous system via this mechanism should be considered (EPA 85, La 86). The Water Quality Advisory for Chlorpyrifos should be modified accordingly in those circumstances.

References

Ba 85. Battelle. Human Health & Aquatic Life Literature Search & Data Base Evaluation for Chlorpyrifos. Final Report to OWRS, EPA.

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EPA 85. U.S. EPA. Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures 50(6):1170-1175.

EPA 86. U.S. EPA. Pesticide Tolerances for Chlorpyrifos. 40 CFR Part 180, Vol. 51(53):9449-9450.

EPA 86. U.S. EPA. Chemical Fact Sheet: Chlorpyrifos. OPP/WDC.

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La 86. Lappenbusch. Contaminated Drinking Water & Your Health. 6480 Overlook Drive, Alexandria, Virginia 22312.

No 84. Nolan et al. Chlorpyrifos: Pharmacokinetics in Human Volunteers. Toxicol. & Appl. Pharm. 73:8-15.

OPP 86. U.S. EPA. Chemical Fact Sheet for Chlorpyrifos. OPP, EPA.