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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: July 6, 1998

SUBJECT: **TEMEPHOS**: HED Chapter for the Reregistration Eligibility Decision (RED) Document. Chemical No. 059001 Case No. 0006 Barcode D243662.

FROM: Nicole C. Paquette, Ph.D. Nicole C Paquette
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THROUGH: Alan P. Nielsen, Branch Senior Scientist Al Nielsen 7/7/98
Reregistration Branch 2
Health Effects Division (7509C)

TO: Larry Schnaubelt
Reregistration Branch I
Special Review and Reregistration Division (7508W).

The ~~Human~~ Health Assessment for the Reregistration Eligibility Decision (RED) Document for temephos is attached. This chapter includes the Hazard Identification Assessment Review Committee (HIARC) Report from David Liem (HED), the Occupational/Residential Exposure Assessment from Jonathan Becker (HED), the Product and Residue Chemistry Assessment from Ken Dockter (HED).

Attachments:
Attachment 1: HED RED Chapter. Nicole C. Paquette (7/6/98)
Attachment 2: HED HIARC Report. David Liem/Jess Rowland (5/12/98)
Attachment 3: Occupational and Residential Exposure Assessment. Jonathan Becker (5/21/98)
Attachment 4: Product and Residue Chemistry Assessment. Ken Dockter (6/30/98)

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Temephos HED RED CHAPTER

I. EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human health assessment for the active ingredient temephos (O,O,O',O'-tetramethyl O,O'-(thiodi-4,1-phenylene) phosphorothioate for purposes of making a reregistration eligibility decision. In making its determination of safety finding for health risks, HED considered potential exposure of occupational workers only, since temephos has no registered food uses or residential uses and therefore, there are no concerns for potential exposures to infants and children.

A. Hazard Characterization

The toxicology database for temephos is inadequate with several data gaps. Most of the available studies were conducted in the 60s and 70s and do not meet the requirements of Subdivision F Guidelines. However, the available data are adequate to support the non-food use and non-residential use.

Temephos has relatively low to moderate acute toxicity compared to other organophosphate insecticides. In acute toxicity studies, temephos is more toxic than malathion and considerably less toxic than ethyl parathion and diazinon. Temephos is moderately toxic by the oral and dermal route, and has low toxicity through inhalation. Signs of toxicity observed in animals treated with high doses of temephos are typical of acute toxicity signs induced by cholinesterase inhibition (ChEI) which include; hypoactivity, labored breathing, rough coat, chromodacryorrhea, salivation, muscle spasms and tremors. Temephos is a slightly irritating to eyes but is not a skin irritant or a dermal sensitizer.

In subchronic toxicity studies in rats and dogs, the most sensitive toxicological endpoint is cholinesterase inhibition. Dose-related inhibition of plasma, red blood cell (RBC) and brain cholinesterase (ChE) activity occurs following repeated exposures of various durations. The severity of cholinergic symptoms correlates with the level of inhibition of plasma and RBC ChE activity. Rats are the more sensitive species to ChEI and male rats are the more sensitive sex. In rats, dietary temephos reduced plasma and RBC ChE activity at doses as low as 0.46 mg/kg. In dogs given 12.5 mg/kg of dietary temephos also had reduced plasma and RBC ChE activity and showed cholinergic symptoms after 1 week of dosing which persisted throughout the 90-day study period. In addition to ChEI, the only other systemic effect in subchronic studies was decreased body weight gain in rats. This effect in rats, however, occurred at doses higher (17.5 mg/kg) than the dose which produced ChEI.

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A complete assessment of the neurotoxic potential of temephos cannot be made since acute or subchronic neurotoxicity studies in rats are not available. Nevertheless, temephos belongs to the class of organophosphorus insecticides which exert their toxic action by inhibiting cholinesterases in the peripheral and central nervous systems and therefore, neurotoxicity is implied in this class of chemicals.

Temephos is not considered to be a reproductive or developmental toxicant. However, this determination is based in part on a lack of adequate study database and should be viewed as an interim conclusion until more definitive data are available. Since there are no registered food or residential uses, there are no concerns for potential exposure to infants and children.

Temephos is not classified as a carcinogen mainly because of the inadequate database, therefore, the cancer potential was not presented in this risk assessment. The only study available was a 2- year chronic study in rats, in which the highest dose (15 mg/kg) did not induce tumor formation. In addition, several *in vitro* mutagenicity studies were considered not adequate to evaluate the genotoxic potential of temephos. Because this chemical is for non food use only, a chronic/ carcinogenicity study in another species is not required.

B. Exposure Characterization

Temephos is used as a mosquito larvicide for application to aquatic non-crop sites. The use sites include outdoor non-food and non-domestic aquatic areas such as standing waters (tidal areas, woodland pools, shallow ponds, tire and refuse piles), ponds, lakes, tidal waters, catch basin, marshlands, margins of streams, and intertidal zones of sandy beaches. These use sites are polluted or saline waters and are therefore, unusable as a source of drinking water.

Temephos is formulated as a granular and as an emulsifiable concentrate. It can be applied by fixed-wing aircraft, helicopter, hand-held sprayers, power backpack blowers, and by spoon. Application rates are based on the organic content of the standing water being treated and range up to 0.5 lb ai per acre. Areas can be treated multiple times per year, as needed.

Potential **occupational exposure routes** for handlers, mixers, loaders and applicators are dermal and inhalation and may be of short-term (1 to 7 days), intermediate-term (1 week to several months), and chronic durations (more than several months).

HED has identified 14 major scenarios for which there are potential for occupational exposure. **The use of maximum PPE and engineering controls results in acceptable risk estimates (i.e.,MOEs >100) for 4 of the 14 scenarios;** mixing/loading liquids for right-of-way sprayer, loading granulars for aerial application

and flagging during aerial application of granulars and liquid sprays. **Two exposure scenarios lack data and occupational risks could not be assessed. The remaining 8 of the 14 occupational exposure scenarios have MOEs are less than 100 and exceed HED's level of concern despite maximum mitigation measures.**

HED believes that **it is unlikely that significant postapplication exposures would occur** based on the low application rate (0.5 lb ai per acre), the short duration spent by the worker in a treated area, and the low exposure activities performed by the worker.

There are **no residential uses of temephos**. Because of the areas in which temephos is aerially applied (e.g., tidal marshes) and the presumed large droplet size of the spray, HED believes it is unlikely that significant exposure via spray drift would occur. However, because of the diversity of sites that temephos may be used, **HED is concerned that bystander spray drift exposure may occur in some situations.** Although temephos may be used in areas (e.g., temporary pools along the side of the road, standing water in discarded tires, and refuse piles) that may occasionally be visited by the general population, HED believes that postapplication exposure would be minimal. This belief is based on the low application rate, the likelihood of a brief duration spent in such environments, and the probability of low exposure activities of the residents.

A **drinking water risk assessment is not required** because; 1) temephos is applied to water that cannot be used as a source of surface water/drinking water and 2) temephos is not expected to reach ground water that would be used for drinking water because of its lack of an hydraulic gradient and its short half-life.

Risk Characterization

Risks of Concern: Occupational combined dermal and inhalation MOEs of less than 100 for short-term exposure, intermediate term and chronic term exposure durations are considered ~~to be~~ of risk concern.

- Occupational handler combined dermal and inhalation baseline MOEs range from **0.02 to 12** for **short-term, intermediate-term and chronic exposures.** These MOEs are not mitigated by the addition of PPE or engineering controls except for four scenarios: mixing / loading liquids for rights-of-way sprayer (MOE=121), loading granulars for aerial application (MOE= 290-590), and flagging during aerial application of granulars (MOE=1000-2000) and liquid sprays (MOE=260-530).

Aggregate Exposure and Risk (water and residential sources): There is no risk concern for drinking water exposure because temephos is applied to shallow, brackish polluted waters which are unsuitable for human consumption. The Environmental Fate

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and Effects Division (EFED) does not expect temephos to reach ground water (used for drinking water) because of the lack of hydraulic gradient and the short half-life. Since residential exposure to temephos is not a risk concern, a quantitative aggregate exposure assessment has not been conducted.

Uncertainties Impacting Exposure and Risk Estimates: Dermal and inhalation exposure estimates for occupational handlers are based on surrogate exposure data from PHED V1.1. Assumptions regarding amount of temephos handled are believed to be reasonable and representative of central tendency exposures.

Because there are no acceptable dermal toxicity or dermal absorption study data, acute toxicity via the oral and dermal routes have been compared. Dermal and oral toxicity via these routes are similar; therefore, a dermal absorption rate of 100% is assumed. Overall, the assumption of 100% dermal absorption likely results in an overestimation of risk.

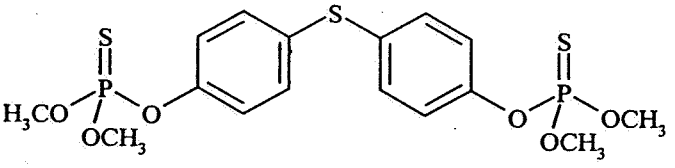
Determination of Safety: The MOEs estimated for all-occupational exposure scenarios indicates that there is a risk concern for currently registered uses of temephos. These MOE calculations were based on inhibition of plasma ChE activity in subchronic oral toxicity study in the rat.

II. SCIENCE ASSESSMENT

A. Physical and Chemical Properties Assessment

1. Identification of Active Ingredient

Pure temephos is a white crystalline solid with a melting point of 30 C; technical temephos is a brown viscous liquid which decomposes at 120-125 C, and has a specific gravity of 1.3, an octanol/water partition coefficient of 80,900 and vapor pressure of 7.17×10^{-8} mm Hg at 25 C. Technical temephos is essentially insoluble in water (0.03 ppm), and is insoluble in hexane and methyl cyclohexane. Temephos is soluble at 100g/100 mL in acetone, acetonitrile, dichloromethane, and toluene at 20 C. It is also soluble in carbon tetrachloride, chloroform, diethyl ether, ethytlene dichloride, and lower molecular weight alkyl ketones.



Empirical Formula:	$C_{16}H_{20}O_6P_2S_3$
Molecular Weight:	466.4
CAS Registry No.:	3383-96-8
PC Code:	059001

2. Manufacturing-Use Products

A search of the Reference Files System (REFS) conducted 6/24/98 identified a single temephos manufacturing-use product (MP) registered under PC Code 059001: the Clarke Mosquito Control Products Inc. 90% technical (T; EPA Reg. No. 8329-56). The Clarke Mosquito Control Products 90% T was transferred from American Cyanamid Company (EPA Reg. No. 241-220) on 9/9/97. Only the Clarke Mosquito Control Products 90% T is subject to a reregistration eligibility decision.

3. Product Chemistry Data

Most product chemistry data requirements remain outstanding for the Clarke Mosquito 90% T (see Table; Attachment 4). Provided that the registrant submits the data required in the attached data summary table for the 90% T, and either certifies that

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the suppliers of beginning materials and the manufacturing process for the temephos technical product/MP have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, HED has no objections to the reregistration of temephos with respect to product chemistry data requirements.

B. Hazard Profile

1. Hazard Assessment

The toxicological data base for temephos is inadequate to support reregistration. However, the available data are adequate to support the non-food use/non-residential use pattern.

a. Table 1. Acute Toxicity

Guideline#	Study Type	MRID	Results	Tox Category
81-1	Acute Oral (Rats)	00001902	LD_{50}= 444 mg/kg	II
81-2	Acute Dermal (Rabbits)	140124 1906/1907	LD_{50} = 1850 mg/kg (Males) LD_{50} = 970 mg/kg (Females)	II II
81-3	Acute Inhalation	00101656	LC_{50} > 1.3 mg/L	III
81-4	Primary Eye Irritation	001907	Corneal opacity 72 hrs	III
81-5	Primary Skin Irritation	140124	PIS = 1.4	IV
81-6	Dermal Sensitization	00157836	Not a sensitizer	

b. Dermal Absorption

No acceptable dermal absorption studies are available. Dermal studies conducted in rabbits are not considered adequate. Dermal rabbit studies can be expected to underestimate the toxicity of sulfur-containing organophosphates because rabbit blood has high concentrations of arylesterases, a class of enzymes which

detoxify the compounds before they can be converted to the activated form in the liver. For this reason, the rat is the preferred species for dermal studies. Therefore, a default assumption of 100% dermal absorption was used in this assessment.

b. The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

Table 2. Summary of Toxicology Endpoint Selection

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY	MOE
Acute Dietary	None	No registered food or residential uses; risk assessment is not required.		NA
Chronic Dietary	None	No registered food or residential uses; risk assessment is not required.		NA
Short-Term (Dermal) [a]	Oral NOEL= 0.3	RBC ChE Inhibition	90-day Feeding Study in Rats	100
Intermediate-Term (Dermal) [a]	Oral NOEL= 0.3	RBC ChE Inhibition	90-day Feeding Study in Rats	100
Long-Term (Dermal)	Oral NOEL= 0.3	RBC ChE Inhibition	90-day Feeding Study in Rats	100
Inhalation (Any Time Period)[a]	Oral NOEL= 0.3	RBC ChE Inhibition	90-day Feeding Study in Rats	100

a = Since an ~~oral~~ NOEL was selected a dermal absorption (100%) and inhalation absorption (100%) factors should be used for these risk assessments (i.e., corrected for dermal and inhalation exposures).

Determination of the FQPA Safety Factor:

A FQPA safety factor for the protection of infants and children from exposure to temephos as required by FQPA will not be necessary since there are no registered food or residential uses and thus there are no concerns for potential exposures of infants and children to temephos.

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C. Occupational Exposure and Risk Assessment

Temephos is a restricted use pesticide formulated as a granular (1 to 5 percent active ingredient) and as an emulsifiable concentrate (40 to 45 percent active ingredient). It is used to control mosquito larvae in standing water (tidal areas, woodland pools, shallow ponds, tire and refuse piles). It can be applied by fixed-wing aircraft, helicopter, hand-held sprayers, power backpack blowers, and by spoon. Application rates are based on the organic content of the standing water being treated and range up to 0.5 lb ai per acre. Areas can be treated multiple times per year, as needed.

Potential occupational exposure routes are dermal and inhalation and may be of short-term (1 to 7 days), intermediate-term (1 week to several months), and chronic durations (more than several months). The largest United States end user of temephos (Lee County Mosquito Control District, Florida) reports that in a "typical" year they apply temephos 5 to 6 days per week from May through October and possibly 2 days per week for the rest of the year (about 160 applications per year). Variation in amount of rainfall in a specific geographical region can greatly prolong or shorten the seasonal duration of required mosquito larvicide treatments. There are no homeowner uses of temephos.

1. Occupational Exposure

Application Rates: Temephos may be applied up to 0.5 lbs a.i. per acre.

Submitted Studies: HED is not aware of any handler exposure study submitted to the Agency for review.

Handler Exposure Scenarios: HED has identified the potential for occupational exposure for 14 major scenarios, as follows: (1) mixing / loading liquids for aerial application; (2) mixing / loading liquids for rights-of-way sprayer; (3) loading granulars for aerial application; (4) applying liquids using fixed-wing aircraft; (5) applying liquids using helicopter; (6) applying liquids using rights-of-way sprayer; (7) applying granulars using fixed-wing aircraft; (8) applying granulars using helicopter; (9) flagging during aerial application of liquid sprays; (10) flagging during application of granulars; (11) mixing / loading / applying sprays with a backpack sprayer; (12) loading / applying granulars with a power backpack blower; (13) loading / applying granulars with belly grinder; and (14) applying granulars by spoon.

Occupational handler dermal and inhalation exposures for all durations (developed using PHED Version 1.1 surrogate data) are presented in the attached spreadsheet. The assumptions and the formulas that were used in the exposure / risk calculations are as follows:

- Daily exposure (mg/day) = Unit exposure (mg/lb ai) * Application rate (lb ai/acre) * Acres treated.
- Daily dose (mg/kg/day) = Daily exposure (mg/kg) / Body weight (70 kg).
- MOE = NOEL (mg/kg/day) / Daily dose (mg/kg/day).

- Body weight for an adult handler is assumed to be 70 kg.
- PHED clothing and risk mitigation scenarios are as follows: Baseline - long sleeved shirt, long pants, no respirator; Maximum PPE - coveralls over long pants, long sleeved shirt, chemical-resistant gloves, organic vapor respirator; Engineering Controls - long pants, long sleeved shirt, no gloves in an enclosed cab or cockpit, closed mixing/loading.

Handler Exposure Scenario Results: Results for the occupational handler scenarios are presented in the attached spreadsheet and are summarized below in Table 2.

Table 3. Highest estimated MOE for each temephos exposure scenario for all exposure durations.

Exposure Scenario	Range of MOEs		
	Baseline	Maximum PPE	Engineering Controls
Mixer/Loader			
Mixing / loading liquids for aerial application	0.02 - 0.04	3.5 - 7.0	7 - 14
Mixing / loading liquids for rights-of-way sprayer	0.36	61	121
Loading granulars for aerial application	5.9 - 12	17 - 34	290 - 590
Applicator			
Applying liquids using fixed-wing aircraft	No data	Scenario not feasible	12 - 24
Applying liquids using helicopter	No data	Scenario not feasible	32 - 63
Applying liquids using rights-of-way sprayer	0.81	3.6	Scenario not feasible
Applying granulars using fixed-wing aircraft	No data	Scenario not feasible	21- 41
Applying granulars using helicopter	No data	Scenario not feasible	No data
Flagger			
Flagging during aerial application of liquid sprays	5.3 - 11	6 - 12	260 - 530
Flagging during application of granulars	20 - 41	37 - 74	1000 - 2000
Mixer/Loader/Applicator			
Mixing / loading / applying sprays with a backpack sprayer	3.3	5.2	Scenario not feasible
Loading / applying granulars with a power backpack blower	No data	No data	Scenario not feasible
Loading / applying granulars with belly grinder	0.83	1.0	Scenario not feasible
Applying granulars by spoon (by hand used as a surrogate)	26	46	Scenario not feasible

Postapplication Exposure Scenarios: HED believes that postapplication exposures would be minimal. This belief is based on the low application rate (0.5 lb ai/acre) of temephos, the short duration spent by the worker in a treated area (typically a few minutes), and the low exposure activity of the worker

(typically dipping water from a temporary pool with a long handled dipper and examining the collected water for mosquito larvae).

2. Residential Exposure Assessment

Residential Handler Exposure: There are no residential uses of temephos. Because of the areas in which temephos is aerially applied (e.g., tidal marshes) and the presumed large droplet size of the spray, it is unlikely that significant exposure via spray drift would occur. However, because of the diversity of sites that temephos may be used, HED remains concerned that bystander spray drift exposure may occur in some situations. HED reserves the decision concerning the magnitude of bystander spray drift exposure and the required buffer zone until data can be supplied.

Residential Postapplication Exposure: Although temephos may be used in areas (e.g., temporary pools along the side of the road, standing water in discarded tires, and refuse piles) that may occasionally be visited by the general population, HED believes that it is unlikely that significant postapplication exposure would occur. This belief is based on the low application rate, the likelihood of a brief duration spent in such environments, and the probability of low exposure activities of the residents.

Incident Reports: There are no temephos incidents in the Incident Data System, in California's database (1982-1995), and it was not a data call in for Poison center data. (Jerry Blondell 6/3/98)

Summary of Risk Concerns for Occupational Exposures

Based on the above occupational exposure and risk assessment, HED concludes:

- The use of risk mitigation measures for occupational handlers (i.e., maximum PPE and engineering controls) results in **MOEs greater than 100** for the following scenarios: mixing / loading liquids for rights-of-way sprayer, loading granulars for aerial application, and flagging during aerial application of granulars and liquid sprays.

- The use of risk mitigation measures form occupational handlers (i.e., maximum PPE and engineering controls) results in **MOEs less than 100** for the following scenarios: mixing / loading liquids for aerial application, applying liquids using fixed-wing aircraft, applying liquids using helicopter, applying liquids using rights-of-way sprayer, applying granulars using fixed-wing aircraft, mixing / loading / applying sprays with a backpack sprayer, loading / applying granulars with belly grinder, and applying granulars by spoon.

- Two scenarios lack exposure data that are needed to assess risk to temephos handlers. These scenarios are applying granulars using a helicopter and loading / applying granulars with a power backpack blower. A power backpack blower is frequently the method of choice for applying granulars to tire piles.

- HED remains concerned that bystander spray drift exposure may occur in some situations and requests supporting data concerning bystander spray drift exposure from the registrant.

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Conclusion

Temephos, formulated as a granular and as an emulsifiable concentrate, is a restricted use pesticide used as an insecticide for the control of mosquito larvae. Based on HED's occupational and risk assessment, MOEs are less than 100 for many of the commonly used exposure scenarios. Exposure scenarios with MOEs greater than 100 include mixing / loading liquids for rights-of-way sprayer, loading granulars for aerial application, and flagging during aerial application of granulars and liquid sprays. Two exposure scenarios could not be assessed because of the lack of exposure data. HED also requests supporting data concerning bystander spray drift exposure from the registrant.

Because the default assumption of 100 percent dermal absorption was used in this assessment, many of the calculated MOEs are less than 100. If the registrant has dermal absorption data, and if the Agency reviews and accepts these data, this assessment could be further refined and it is likely that the MOEs would be substantially greater.

Data requirements

a. Toxicology

▸ Acute Delayed Toxicity - Hen	§81-7
▸ Acute Neurotoxicity -Rat	§81-8
▸ Subchronic Neurotoxicity-Rat	§82-5
▸ Developmental Toxicity -Rat or Rabbit	§83-3 a, b

b. Occupational and Residential Exposure

The Agency would like to meet with the registrant to discuss the need for the following data:

- Supporting data concerning bystander spray drift exposure.
- Occupational exposure data for application of granulars by helicopter
- Occupational exposure data for application of granulars by power back pack blower

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