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Agency

Health Effects Support Document for S-Ethyl dipropylthiocarbamate (EPTC)

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for
S-Ethyl dipropylthiocarbamate (EPTC)

U.S. Environmental Protection Agency
Office of Water (4304T)
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FOREWORD

The Safe Drinking Water Act (SDWA), as amended in 1996, requires the Administrator of the Environmental Protection Agency (EPA) to establish a list of contaminants to aid the Agency in regulatory priority setting for the drinking water program. In addition, the SDWA requires EPA to make regulatory determinations for no fewer than five contaminants by August 2001 and every five years thereafter. The criteria used to determine whether or not to regulate a chemical on the Contaminant Candidate List (CCL) are the following:

- The contaminant may have an adverse effect on the health of persons.
- The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern.
- In the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

The Agency's findings for all three criteria are used in making a determination to regulate a contaminant. The Agency may determine that there is no need for regulation when a contaminant fails to meet one of the criteria. The decision not to regulate is considered a final Agency action and is subject to judicial review.

This document provides the health effects basis for the regulatory determination for s-ethyl dipropylthiocarbamate (EPTC). In arriving at the regulatory determination, The Office of Water used the Re-registration Eligibility Document (RED) for EPTC published by the Office of Pesticides Programs (OPP), as well as any OPP health assessment documents that supported the RED. The following publications from OPP were used in development of this document.

U.S. EPA (United States Environmental Protection Agency). 1999. Reregistration eligibility decision. EPTC. EPA 738-R-99-006. Washington, DC: U.S. EPA Office of Prevention, Pesticides and Toxic Substances.

U.S. EPA (United States Environmental Protection Agency). 1987. S-Ethyl dipropylthiocarbamate (EPTC) Integrated Risk Information System. Office of Research and Development. Washington DC.

Information from the OPP risk assessment was supplemented with information from the primary references for key studies where they have been published and recent studies of EPTC identified in a literature search conducted 2004.

A Reference Dose (RfD) is provided as the assessment of long-term toxic effects other than carcinogenicity. RfD determination assumes that thresholds exist for certain toxic effects, such as cellular necrosis, significant body or organ weight changes, blood disorders, etc. It is expressed in terms of milligrams per kilogram per day (mg/kg-day). In general, the RfD is an

estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The carcinogenicity assessment for EPTC includes a formal hazard identification and an estimate of tumorigenic potency when available. Hazard identification is a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen via the oral route and of the conditions under which the carcinogenic effects may be expressed.

Development of these hazard identification and dose-response assessments for EPTC has followed the general guidelines for risk assessment as set forth by the National Research Council (1983). EPA guidelines that were used in the development of this assessment may include the following: *Guidelines for the Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 1986a), *Guidelines for Mutagenicity Risk Assessment* (U.S. EPA, 1986b), *Guidelines for Developmental Toxicity Risk Assessment* (U.S. EPA, 1991), *Guidelines for Reproductive Toxicity Risk Assessment* (U.S. EPA, 1996a), *Guidelines for Neurotoxicity Risk Assessment* (U.S. EPA, 1998a), *Guidelines for Carcinogen Assessment* (U.S. EPA, 2005), *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988), (proposed) *Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity* (U.S. EPA, 1994a), *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994b), *Use of the Benchmark Dose Approach in Health Risk Assessment* (U.S. EPA, 1995), *Science Policy Council Handbook: Peer Review* (U.S. EPA, 1998b, 2000a), *Science Policy Council Handbook: Risk Characterization* (U.S. EPA, 2000b), *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2000c), *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 2000d), and *A Review of the Reference Dose and Reference Concentration Processes* (U.S. EPA, 2002a).

The chapter on occurrence and exposure to EPTC through potable water was developed by the Office of Ground Water and Drinking Water. It is based primarily on Unregulated Contaminant Monitoring Regulation 1 (UCMR1) data collected under the SDWA. The UCMR1 data are supplemented with ambient water data, as well as data from the States, and published papers on occurrence in drinking water.

ACKNOWLEDGMENT

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TABLE OF CONTENTS

FOREWORD iii

ACKNOWLEDGMENT v

LIST OF TABLES viii

LIST OF FIGURES ix

1.0 EXECUTIVE SUMMARY 1-1

2.0 IDENTITY: CHEMICAL AND PHYSICAL PROPERTIES 2-1

3.0 USES AND ENVIRONMENTAL FATE 3-1
- 3.1 Production and Use 3-1
- 3.2 Environmental Release 3-1
- 3.3 Environmental Fate 3-2
- 3.4 Summary 3-3

4.0 EXPOSURE FROM DRINKING WATER 4-1
- 4.1 Introduction 4-1
- 4.2 Ambient Occurrence 4-1
  - 4.2.1 Data Sources and Methods 4-1
  - 4.2.2 Results 4-3
- 4.3 Drinking Water Occurrence 4-4
  - 4.3.1 Data Sources, Data Quality, and Analytical Methods 4-4
  - 4.3.2 CCL Health Reference Level 4-5
  - 4.3.3 Results 4-5
- 4.4 Summary 4-8

5.0 EXPOSURE FROM MEDIA OTHER THAN WATER 5-1
- 5.1 Exposure from Food 5-1
  - 5.1.1 Concentration in Non-Fish Food Items 5-1
  - 5.1.2 Concentrations in Fish and Shellfish 5-1
  - 5.1.3 Intake of EPTC from Food 5-1
- 5.2 Exposure from Air 5-1
  - 5.2.1 Concentration of EPTC in Air 5-1
  - 5.2.2 Intake of EPTC from Air 5-1
- 5.3 Exposure from Soil 5-2
  - 5.3.1 Concentration of EPTC in Soil 5-2
  - 5.3.2 Intake of EPTC from Soil 5-2
- 5.4 Other Residential Exposures 5-2
- 5.5 Occupational Exposures 5-2
  - 5.5.1 Description of Industries and Workplaces 5-2
  - 5.5.2 Types of Exposure 5-3

5.6 Summary 5-3

6.0 HAZARD AND DOSE-RESPONSE ASSESSMENT 6-1
6.1 Characterization of Hazard 6-1
6.1.1 Synthesis and Evaluation of Major Noncancer Effects 6-1
6.1.2 Synthesis and Evaluation of Carcinogenic Effects 6-2
6.1.3 Mode of Action and Implications in Cancer Assessment 6-3
6.1.4 Weight of Evidence Evaluation for Carcinogenicity 6-3
6.1.5 Potentially Sensitive Populations 6-3
6.2 Reference Dose 6-4
6.2.1 Choice of Principle Study and Critical Effect 6-4
6.2.2 Dose-response Characterization (dose conversion if needed) 6-4
6.2.3 Method of Analysis 6-4
6.2.4 Application of Uncertainty Factor(s) and Modifying Factor(s) 6-4
6.3 Carcinogen Assessment 6-5
6.4 Sensitive Population Considerations 6-5
6.5 Post Re-registration Health Effects Publications 6-5
6.6 CCL Health Reference Level 6-5

7.0 REGULATORY DETERMINATION AND CHARACTERIZATION OF RISK FROM DRINKING WATER 7-1
7.1 Regulatory Determination for Chemicals on the CCL 7-1
7.1.1 Criteria for Regulatory Determination 7-1
7.1.2 National Drinking Water Advisory Council Recommendations 7-2
7.2 Health Effects 7-2
7.2.1 Health Criterion Conclusion 7-2
7.2.2 Hazard Characterization and Mode of Action Implications 7-3
7.2.3 Dose-Response Characterization and Implications in Risk Assessment 7-3
7.3 Occurrence in Public Water Systems 7-4
7.3.1 Occurrence Criterion Conclusion 7-5
7.3.2 Monitoring Data 7-5
7.3.3 Use and Fate Data 7-6
7.4 Risk Reduction 7-6
7.4.1 Risk Criterion Conclusion 7-7
7.4.2 Exposed Population Estimates 7-7
7.4.3 Relative Source Contribution 7-7
7.4.4 Sensitive Populations 7-7
7.5 Regulatory Determination Decision 7-8

8.0 REFERENCES 8-1

APPENDIX A: Abbreviations and Acronyms . . . . . Appendix A-1

LIST OF TABLES

Table 2-1 Chemical and Physical Properties of S-Ethyl dipropylthiocarbamate 2-2

Table 3-1 Environmental releases (in pounds) of EPTC in the United States, 1995-2002 3-2

Table 4-1 USGS National Synthesis Summary of NAWQA Monitoring of EPTC in Ambient Surface Water, 1992-2001 4-3

Table 4-2 USGS National Synthesis Summary of NAWQA Monitoring of EPTC in Ambient Ground Water, 1992-2001 4-4

Table 4-3 Summary UCMR1 Occurrence Statistics for EPTC in Small Systems (Based on Statistically Representative National Sample of Small Systems) 4-6

Table 4-4 Summary UCMR1 Occurrence Statistics for EPTC in Large Systems (Based on the Census of Large Systems) 4-7

LIST OF FIGURES

Figure 2-1 Chemical Structure of S-Ethyl dipropylthiocarbamate 2-1

1.0 EXECUTIVE SUMMARY

The U.S. Environmental Protection Agency (EPA) has prepared this Health Effects Support Document for S-Ethyl dipropylthiocarbamate (EPTC) to support a determination regarding whether to regulate EPTC with a National Primary Drinking Water Regulation (NPDWR). The available data on occurrence, exposure, and other risk considerations suggest that, because EPTC does not occur in public water systems at frequencies and levels of public health concern, regulating EPTC will not present a meaningful opportunity to reduce health risk. EPA will present a determination and further analysis in the Federal Register Notice covering the CCL proposals.

EPTC (Chemical Abstracts Services Registry Number 759-94-4) is a thiocarbamate used to control the growth of germinating annual weeds such as broadleaves, grasses, and sedges. It is a light yellowish, non-corrosive liquid with an aromatic odor. EPTC is released primarily into the environment through spraying and, at times, through irrigation methods. EPTC is listed as a Toxic Release Inventory (TRI) chemical, with air emissions constituting the majority of on-site releases.

The primary route of exposure to EPTC is through the ingestion of residues of the herbicide in food and drinking water. Dermal and inhalation exposure may occur in occupational or residential settings during handling activities such as mixing, loading, or applying.

EPTC is a reversible cholinesterase (ChE) inhibitor. In acute toxicity studies, EPTC is moderately toxic via oral and dermal routes but displays higher toxicity when inhaled. Similar to other thiocarbamates, EPTC does not produce a consistent ChE inhibition profile. There were no consistent patterns observed in any of the toxicity studies with regard to species, duration of treatment, or type of ChE enzyme measured. An increase in the incidence and severity of cardiomyopathy was observed in subchronic and chronic studies performed in both rats and dogs. The central and peripheral nervous systems also are affected by EPTC exposure with rats and dogs exhibiting an increase in the incidence and severity of degenerative effects (neuronal and/or necrotic degeneration).

In addition to its neurotoxic effects, EPTC has the ability to induce maternal and reproductive toxicity and secondary developmental toxicity in exposed rats and rabbits. In a rat developmental toxicity study, as well as a rabbit developmental toxicity study, toxicity indications (decreased fetal body weight and litter size for rats; decreased fetal body weight for rabbits) were observed, but were considered secondary to observed marked maternal toxicity (increased mortality and decreased body weight for rats; decreased body weight and increased mortality for rabbits). In a two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels that resulted in parental toxicity.

The available data for EPTC production and environmental releases all show a downward trend. Drinking water monitoring of EPTC is conducted under the Unregulated Contaminant Monitoring (UCM) program. As a List 1 contaminant, EPTC is scheduled to be monitored by all large community water systems (CWSs) and non-transient non-community water systems

(NTNCWSs) and a statistically representative sample of small CWSs and NTNCWSs. According to current data, there were no detections of EPTC found in any of the large (i.e., serving more than 10,000 people) CWSs and large NTNCWSs. There were no detections of EPTC found in the statistically representative national sample of 800 small (i.e., serving 10,000 people or fewer) CWSs and NTNCWSs.

The Agency used long-term studies in mice and rats and short-term studies of mutagenicity to evaluate the potential for carcinogenicity. Based on these data and using EPA's 2005 Guidelines for Carcinogen Risk Assessment, EPTC is not likely to be carcinogenic to humans. Based on a 2-generation feeding study in rats, the oral Reference Dose (RfD) was determined to be 0.025 mg/kg/day. The CCL health reference level (HRL) is 0.175 mg/L and was derived from the RfD.

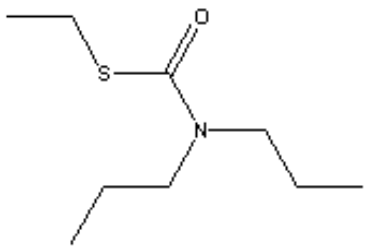
It appears that the general population is not exposed to EPTC through water consumption or use. Therefore, the impact of regulating EPTC concentrations in drinking water on health risk reduction is likely to be small. Regulation of EPTC in public water systems does not appear to present a meaningful opportunity for health risk reduction.

2.0 IDENTITY: CHEMICAL AND PHYSICAL PROPERTIES

S-Ethyl dipropylthiocarbamate (EPTC) is a light yellowish, non-corrosive liquid with an aromatic odor. It is highly volatile (vapor pressure 1.60 x 10^{-2} mm Hg at 20°C). The compound is soluble in water (370 mg/L at 20°C) and miscible with some common organic solvents such as acetone, ethanol, isopropanol, benzene, xylene, and kerosene. EPTC is also miscible with hydrogen sulfide. The compound is hydrolyzed when heated in the presence of strong acids (HSDB, 2004).

The technical grade purity of EPTC is 98.5%. Formulated products of the chemical include granular formulations containing up to 25% active ingredient, and emulsifiable concentrate liquids containing up to 87.8% active ingredient (U.S. EPA, 1999). Sometimes, EPTC is supplied in a mixture with N,N-diallyl-2,2-dichloroacetamide, which is supposed to be less toxic to maize, one of the crops to which this compound is applied (HSDB, 2004).

Figure 2-1 Chemical Structure of S-Ethyl dipropylthiocarbamate



Source: Chemfinder.com (2004)

The chemical structure of EPTC is shown above (Figure 2-1). Its physical and chemical properties, and other reference information are listed in Table 2-1.

Table 2-1 Chemical and Physical Properties of S-Ethyl dipropylthiocarbamate

Property	Information
Chemical Abstracts Registry (CAS) No.	759-94-4
EPA Pesticide Chemical Code	041401
Synonyms	EPTC Ethyl N,N-dipropylthiocarbamate Dipropylcarbamothioic acid S-ethyl ester
Registered Trade Name(s)	EPTAM; Eradicane
Chemical Formula	$C_9H_{19}NOS$
Molecular Weight	189.32
Physical State	Light yellow liquid
Boiling Point	127°C
Melting Point	No data
Density (at 20°C)	0.9633 g/mL (at 25°C)
Vapor Pressure:	
At 20°C	1.60×10^{-2} mm Hg
At 25°C	2.4×10^{-2} mm Hg
Partition Coefficients:	
Log K_{ow}	$2.2 \times 10^3 \pm 0.1 \times 10^3$ at 25°C
Log K_{oc}	2.23 - 2.58
Solubility in:	
Water	370 mg/L at 20°C 344 ± 5 mg/L at 25°C
Other Solvents	Acetone, Ethanol, Isopropanol, Benzene, Xylene, Kerosene, Hydrogen sulfide
Conversion Factors (at 25°C, 1 atm)	1 ppm= 7.743 mg/m^3 1 mg/m^3 = 0.1291 ppm

Source(s): U.S. EPA (1999); HSDB (2004)

3.0 USES AND ENVIRONMENTAL FATE

3.1 Production and Use

EPTC is a pre-emergence or early post-emergence herbicide used to control the growth of germinating annual weeds such as broadleaves, grasses, and sedges. It is used in every region of the United States in the production of a variety of food crops. The major usage, in terms of total pounds of active ingredient, is for crops like corn, potatoes, dry beans and peas, alfalfa, and snap beans (U.S. EPA, 1999). The herbicide is also used on non-food plants such as trees, shrubs, and ornamentals. In addition, EPTC is used at residential and public sites such as parks, gardens, and golf course sand traps (HSDB, 2004).

Based on available pesticide survey usage information for the years of 1987 through 1996, an annual estimate of EPTC total domestic usage averaged approximately 20 million pounds for almost 6 million acres treated throughout the United States (U.S. EPA, 1999).

EPTC can be synthesized by reacting ethyl mercaptan with phosgene to produce ethyl chlorothioformate, which subsequently is reacted with di-n-propylamine. Another method for production of EPTC is by reacting ethanethiol and dipropylcarbamoyl chloride (HSDB, 2004).

3.2 Environmental Release

EPTC is released primarily into the environment through pesticide spraying operations. EPTC is expected to volatilize from the soil and exist primarily in the vapor phase in the air, where it can redeposit onto earth through wet deposition (e.g., rain). Studies of rainwater have indicated the presence of EPTC. Moderate soil affinity allows EPTC to travel moderately, allowing some leaching to occur (HSDB, 2004).

The primary route of exposure to EPTC is through the ingestion of residues of the herbicide in food and drinking water. Dermal and inhalation exposure may occur in occupational or residential settings during handling activities such as mixing, loading, or applying. Post-application exposure to EPTC during harvesting is unlikely as EPTC is normally sprayed well before harvest time and is quickly volatilized from the soil.

Toxic Release Inventory (TRI) data for EPTC (see Table 3-1) are reported for the years 1995 to 2002 (U.S. EPA, 2004a). Total reported EPTC releases fluctuated widely in the range of thousands of pounds per year during this period. On-site releases were dominated by air emissions and sometimes underground injections. On-site surface water releases did not exceed 300 pounds per year; no land releases were reported. Off-site releases were significant, but declined steadily after 1998.

Table 3-1 Environmental releases (in pounds) of EPTC in the United States, 1995-2002

Year	On-Site Releases				Off-Site Releases	Total On- & Off-site Releases
	Air Emissions	Surface Water Discharges	Underground Injection	Releases to Land		
2002	1,917	98	0	0	708	2,723
2001	2,034	99	1,146	0	1,655	4,934
2000	2,034	95	6,083	0	2,798	11,010
1999	2,574	156	903	0	3,570	7,203
1998	2,008	115	2,088	0	4,565	8,776
1997	2,208	113	9,501	0	2,778	14,600
1996	7,325	2	29	0	590	7,946
1995	2,363	291	373	0	9,366	12,393

Source: U.S. EPA (2004a)

3.3 Environmental Fate

Direct releases of EPTC to the environment are expected due to its application as an herbicide. The most important dissipation pathways for EPTC in the environment stem from microbial degradation in the soil and volatilization, which can occur concurrently, making it difficult to distinguish the primary environmental fate of the chemical. However, based on a vapor pressure of 1.60 x 10^{-2} mm Hg at 20ºC, a Henry's Law constant of ~1 x 10^{-5} atm-m^3/g-mol at 25ºC, and a water solubility of 375 mg/L, EPTC is likely to quickly volatilize from moist soil after application and predominantly remain in the vapor phase while in the atmosphere. Limited data suggest that degradation of EPTC vapor in the atmosphere occurs rapidly through reaction with photochemically produced hydroxyl radicals (estimated half-life of 14 hours). EPTC vapor may be removed from the atmosphere through wet deposition as indicated by the presence of EPTC in rainwater samples (U.S. EPA, 1999).

EPTC is not expected to be rapidly incorporated into the soil with a fairly moderate log octanol/water coefficient of 3.21 (Hansch et al., 1995). Laboratory test results inadequately determine the relative rates of metabolism and volatilization from soils (U.S. EPA, 1999). Data indicate that abiotic hydrolysis and direct photolysis and photo degradation are not significant degradation pathways for EPTC in soil or water although microbial breakdown is a significant soil removal process (HSDB, 2004). While some studies indicate that EPTC is degraded microbially in water, there is not enough evidence to confirm this.

Based on data from terrestrial field studies, which indicate a range of dissipation half-lives between 2 and 18.8 days, EPTC is not considered an environmentally persistent chemical. Laboratory tests to measure dissipation rates indicate half-lives in the range of 36-75 days (U.S. EPA, 1999). The contribution of volatilization to these dissipation rates has yet to be determined. However, data indicate that volatilization significantly contributes to dissipation within the first few days following application (U.S. EPA, 1999). Volatilization significantly increases if EPTC is applied to moist surfaces, having an observed half-life of 3.4 hours under these conditions (Nash, 1983). Studies using loam soil (25°C) inoculated with microbes proven to degrade EPTC demonstrated an almost complete removal of EPTC from the soil within 15 days. A comparison to a sterile sample indicates that 45% of the loss was due to biodegradation

and 55% was attributed to volatilization (Nagy et al., 1987). The biodegradation half-life of EPTC (at a concentration of 5 ppm) in Regina heavy clay soil (pH 7.5) and Weyburn loam (pH 7.0) at 25°C was 4-5 wks and 4 wks, respectively (Smith and Fitzpatrick, 1971). Soil biodegradation studies suggest that EPTC is, somewhat, more persistent under anaerobic conditions with half-lives of 31 to 127 days (U.S. EPA, 1999).

The primary (soil/water) degradates of EPTC are EPTC-sulfoxide and dipropylamine. EPTC-sulfone, N, N-dipropylformamide, dipropylamine, and ethanesulfonic acid also were identified as degradates in one improperly conducted study which used black light; black light does not represent sunlight (U.S. EPA, 1999). The limited data available suggest that EPTC degradates are less persistent than their parent compound. In one study of aerobic soil metabolism of EPTC, EPTC-sulfoxide was found to be ≤6% of applied EPTC (U.S. EPA, 1999).

Since EPTC has a moderate affinity for soil with a high potential for mobility in soil and a moderate solubility in water, it may leach into groundwater (HSDB, 2004). However, due to its low persistence, based on its short half-life and high volatility in soil, the potential for leaching is significantly reduced. In unaged leaching columns, 9 percent of applied EPTC was found in leachate of loam and clay loam soils, and 55 and 78 percent were found in leachate for loamy sand and sandy loam soils, respectively. In aged soil columns, an average of 22% of the parent was detected in the leachate. Less than 0.01 percent of applied radiolabeled (^{14}C) found in the leachate was attributed to degradates (U.S. EPA, 1999). Ground-water monitoring studies indicate few occurrences of EPTC at concentrations greater than detection limits and in general, concentrations are lower than those detected in surface waters. These data support the conclusion that significant concentrations of EPTC will not reach groundwater (U.S. EPA, 1999).

In aqueous systems, EPTC may adsorb to suspended solids and sediment; however, it does not have the highest affinity for carbon rich species as evident with its moderate Koc. Accordingly, it is unlikely that EPTC will accumulate to a high level in subaqueous sediments of ambient surface waters. Abiotic degradation, such as hydrolysis, is not expected in aqueous systems. Biodegradation and volatilization of EPTC are expected to occur in water through similar processes as it does in soil. Based on estimations from its Henry's Law constant and vapor pressure, the calculated half-lives for a model river and model lake are 3 and 28 days, respectively (HSDB, 2004).

The bioaccumulation and elimination of ^{14}C-EPTC by bluegill sunfish were investigated in a dynamic flow-through system, where the fish were exposed for 28 days at 22°C, followed by depuration in EPTC free water for 14 days. Estimated bioconcentration factors for EPTC were 37, 60, and 110, respectively, in the edible, whole fish, and non-edible fish tissues. According to a classification scheme, the whole-fish bioaccumulation factor (BCF) value suggests the potential for bioconcentration in aquatic organisms is moderate (U.S. EPA, 1999).

3.4 Summary

Despite widespread use, the limited available data indicate that EPTC does not persist in the environment due to rapid dissipation rates. EPTC is highly volatile. Terrestrial field studies

indicate a range of dissipation half-lives between 2 and 18.8 days while laboratory tests to measure dissipation rates indicated half-lives in the range of 36-75 days (U.S. EPA, 1999). The risk of exposure to EPTC through food or groundwater is minimal due to its rapid rate of dissipation and normally early (pre-emergent) plant application. However, estimated bioconcentration rates in aquatic organisms are moderate, assuming the chemical persists long enough to be taken up by an organism (U.S. EPA, 1999).

4.0 EXPOSURE FROM DRINKING WATER

4.1 Introduction

EPA used data from several sources to evaluate the potential for occurrence of EPTC in Public Water Systems (PWSs). The primary source of drinking water occurrence data for EPTC was the Unregulated Contaminant Monitoring Regulation 1 (UCMR1) program. The Agency also evaluated ambient water quality data from the United States Geological Survey (USGS).

4.2 Ambient Occurrence

4.2.1 Data Sources and Methods

USGS instituted the National Water Quality Assessment (NAWQA) program in 1991 to examine ambient water quality status and trends in the United States. NAWQA is designed to apply nationally consistent analytical methods to provide a consistent basis for comparisons among study basins across the country and over time. These occurrence assessments serve to facilitate interpretation of natural and anthropogenic factors affecting national water quality. For more detailed information on the NAWQA program design and implementation, please refer to Leahy and Thompson (1994) and Hamilton and colleagues (2004).

Study Unit Monitoring

The NAWQA program conducts monitoring and water quality assessments in significant watersheds and aquifers referred to as "study units." NAWQA's sampling approach is not "statistically" designed (i.e., it does not involve random sampling), but it provides a representative view of the nation's waters in its coverage and scope. Together, the 51 study units monitored between 1991 and 2001 include the aquifers and watersheds that supply more than 60% of the nation's drinking water and water used for agriculture and industry (NRC, 2002). NAWQA monitors the occurrence of chemicals such as pesticides, nutrients, volatile organic compounds (VOCs), trace elements, and radionuclides, and the condition of aquatic habitats and fish, insects, and algal communities (Hamilton et al., 2004).

Monitoring of study units occurs in stages. Between 1991 and 2001, approximately one-third of the study units at a time were studied intensively for a period of three to five years, alternating with a period of less intensive research and monitoring that lasted between five and seven years. Thus, all participating study units rotated through intensive assessment in a ten-year cycle (Leahy and Thompson, 1994). The first ten-year cycle was called "Cycle 1." Summary reports are available for the 51 study units that underwent intensive monitoring in Cycle 1 (USGS, 2001). Cycle 2 monitoring is scheduled to proceed in 42 study units from 2002 to 2012 (Hamilton et al., 2004).

Pesticide National Synthesis

Through a series of National Synthesis efforts, the USGS NAWQA program is preparing comprehensive analyses of data on topics of particular concern. These data are aggregated from the individual study units and other sources to provide a national overview.

The Pesticide National Synthesis began in 1991. Results from the most recent USGS Pesticide National Synthesis analysis, based on complete Cycle 1 (1991-2001) data from NAWQA study units, are posted on the NAWQA Pesticide National Synthesis website (Martin et al., 2003; Kolpin and Martin, 2003; Nowell, 2003; Nowell and Capel, 2003). USGS considers these results to be provisional. Data for surface water, ground water, bed sediment, and biota are presented separately, and results in each category are subdivided by land use category. Land use categories include agricultural, urban, mixed (deeper aquifers of regional extent in the case of ground water), and undeveloped. The National Synthesis analysis for pesticides is a first step toward the USGS goal of describing the occurrence of pesticides in relation to different land use and land management patterns, and developing a deeper understanding of the relationship between spatial occurrence of contaminants and their fate, transport, persistence, and mobility characteristics.

The surface water summary data presented by USGS in the Pesticide National Synthesis (Martin et al., 2003) only include stream data. Sampling data from a single one-year period, generally the year with the most complete data, were used to represent each stream site. Sites with few data or significant gaps were excluded from the analysis. NAWQA stream sites were sampled repeatedly throughout the year to capture and characterize seasonal and hydrologic variability. In the National Synthesis analysis, the data were time-weighted to provide an estimate of the annual frequency of detection and occurrence at a given concentration.

The USGS Pesticide National Synthesis only analyzed ground water data from wells; data from springs, and agricultural tile drains were not included. The sampling regimen used for wells was different than that for surface water. In the National Synthesis analysis (Kolpin and Martin, 2003), USGS uses a single sample to represent each well, generally the earliest sample with complete data for the full suite of analytes.

NAWQA monitored bed sediment and fish tissue at sites considered likely to be contaminated and sites that represent various land uses within each study unit. Most sites were sampled once in each medium. In the case of sites sampled more than once, a single sample was chosen to represent the site in the Pesticide National Synthesis analysis (Nowell, 2003). In the case of multiple bed sediment samples, the earliest one with complete data for key analytes was used to represent the site. In the case of multiple tissue samples, the earliest sample from the first year of sampling that came from the most commonly sampled type of fish in the study unit was selected.

As part of the National Pesticide Synthesis, USGS also analyzed the occurrence of select semivolatile organic compounds (SVOCs) in bed sediment at sites considered likely to be contaminated and sites that represent various land uses within each study unit (Nowell and Capel, 2003). Most sites were sampled only once. When multiple samples were taken, the earliest one was used to represent the site in the analysis.

Over the course of Cycle 1 (1991-2001), NAWQA analytical methods may have been improved or changed. Hence, reporting levels (RLs) varied over time for some compounds. In the summary tables, the highest RL for each analyte is presented for general perspective. In the ground water, bed sediment, and tissue data analyses, the method of calculating concentration percentiles sometimes varied depending on how much of the data was censored at particular levels by the laboratory (i.e., because of the relatively large number of non-detections in these media).

4.2.2 Results

Under the NAWQA program, USGS monitored EPTC between 1992 and 2001 in representative watersheds and aquifers across the country. Reporting limits varied but did not exceed 0.002 µg/L. Results for surface water and ground water are presented in Tables 4-1 and 4-2. EPTC was not monitored in bed sediment or biota.

Table 4-1 USGS National Synthesis Summary of NAWQA Monitoring of EPTC in Ambient Surface Water, 1992-2001

Land Use Type	No. of Samples (and No. of Sites)	Detection Frequency	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration
Agricultural	1,884 (78)	14.11%	<RL	0.018 µg/L	7.30 µg/L
Mixed	1,000 (47)	11.88%	<RL	0.009 µg/L	29.6 µg/L (E)
Undeveloped	60 (4)	1.64%	<RL	<RL	0.004 µg/L
Urban	892 (33)	4.81%	<RL	<RL	0.038 µg/L

Source: Martin et al. (2003)
RL = Reporting limit. Reporting limits for EPTC varied, but did not exceed 0.002 µg/L.
E = Estimated (outside normal calibration limits)
The USGS Pesticide National Synthesis used one year of data, generally the year with the most sampling results, to represent each site in this analysis. The sampling results were time-weighted, to eliminate bias from more frequent sampling at certain times of year. Detection Frequencies and Percentile Concentrations can be interpreted as representing annual occurrence. For instance, the detection frequency can be thought of as the percent of the year in which detections are found at a typical site in this land use category, and the 95th percentile concentration can be thought of as a concentration that is not exceeded for 95% of the year at a typical site in this land use category.

In surface water, EPTC was detected at frequencies ranging from 1.64% of samples in undeveloped settings to 4.81% in urban land use settings, 11.88% in mixed land use settings, and 14.11% in agricultural settings. The 95th percentile concentrations were less than the reporting limit in undeveloped and urban settings, 0.009 µg/L in mixed land use settings, and 0.018 µg/L in agricultural settings. The highest concentration, estimated at 29.6 µg/L, was found in a mixed land use setting (Martin et al., 2003).

Table 4-2 USGS National Synthesis Summary of NAWQA Monitoring of EPTC in Ambient Ground Water, 1992-2001

Land Use Type	No. of Wells	Detection Frequency	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration
Agricultural	1,443	0.49%	<RL	<RL	0.45 µg/L
Mixed (Major Aquifer)	2,717	0.33%	<RL	<RL	0.182 µg/L
Undeveloped	67	0.0%	<RL	<RL	<RL
Urban	834	0.72%	<RL	<RL	0.02 µg/L

Source: Kolpin and Martin (2003)
RL = Reporting limit. Reporting limits for EPTC varied, but did not exceed 0.002 µg/L.
The USGS Pesticide National Synthesis considered each well a distinct site in this analysis. Each well was represented by one sample: normally the first one taken, but possibly a later sample if the first sample was not analyzed for the full range of analytes.
Percentile Concentrations were drawn from the range of detects and non-detects. The method for calculating Percentile Concentrations varied depending on how much of the data was censored at particular levels by the laboratory.

In ground water, EPTC detection frequencies ranged from 0.0% in undeveloped settings to 0.33% in mixed land use (major aquifer) settings, 0.49% in agricultural settings, and 0.72% in urban settings. The 95th percentile concentrations were less than the reporting limit in all settings. The highest concentration, 0.45 µg/L, was found in an agricultural setting (Kolpin and Martin, 2003).

4.3 Drinking Water Occurrence

4.3.1 Data Sources, Data Quality, and Analytical Methods

In 1999, EPA developed the UCMR1 program in coordination with the CCL and the National Drinking Water Contaminant Occurrence Database (NCOD) to provide national occurrence information on unregulated contaminants. EPA designed the UCMR1 data collection with three parts (or tiers), primarily based on the availability of analytical methods. EPTC belonged to the first tier, List 1.

List 1 Assessment Monitoring was performed for a specified number of chemical contaminants for which analytical methods have been developed. With the exception of transient non-community systems and systems that purchase 100% of their water, EPA required all large PWSs (systems serving more than 10,000 people), plus a statistically representative national sample of 800 small PWSs (systems serving 10,000 people or fewer) to conduct Assessment Monitoring. Approximately one-third of the participating small systems were scheduled to monitor for these contaminants during each calendar year from 2001 through 2003. Large systems could conduct one year of monitoring anytime during the 2001-2003 UCMR1 period. EPA specified a quarterly monitoring schedule for surface water systems and a twice-a-year, six-month interval monitoring schedule for ground water systems. Although UCMR1

monitoring was conducted primarily between 2001 and 2003, some results were not collected and reported until as late as 2005.

The objective of the UCMR1 sampling approach for small systems was to collect contaminant occurrence data from a statistically selected, nationally representative sample of small systems. The small system sample was stratified and population-weighted, and included some other sampling adjustments such as ensuring the selection of at least two systems from each State. With contaminant monitoring data from all large PWSs and a statistical, nationally representative sample of small PWSs, UCMR1 List 1 Assessment Monitoring provides a contaminant occurrence data set suitable for national drinking water estimates.

4.3.2 CCL Health Reference Level

To evaluate the systems and populations exposed to EPTC through PWSs, the monitoring data were analyzed against the Minimum Reporting Level (MRL) and a benchmark value for health that is termed the Health Reference Level (HRL). Two different approaches were used to derive the HRL, one for chemicals that cause cancer and exhibit a linear response to dose and the other applies to noncarcinogens and carcinogens evaluated using a non-linear approach.

The RfD for EPTC is 0.025 mg/kg/day based on decreased weight and cardiomyopathy in treated rats given the chemical in feed (Mackenzie, 1986). Additional detail concerning the RfD can be found in section 6.2. The Agency established the HRL for EPTC using the RfD and a 20 percent relative source contribution as follows:

HRL = [(0.025 mg/kg/day x 70 kg)/2 L/day] x 20% = 0.175 mg/L (or 175 µg/L)

4.3.3 Results

As a List 1 contaminant, EPTC was scheduled to be monitored by all large CWSs and NTNCWSs and a statistically representative sample of small CWSs and NTNCWSs. The data presented in this report reflect UCMR1 analytical samples submitted and quality-checked under the regulation as of July 2005. EPTC data were collected and submitted by 797 (99.6 percent) of the 800 small systems selected for the small system sample and 3,069 (99.0 percent) of the 3,100 large systems defined as eligible for the UCMR1 large system census. EPTC data have been analyzed at the level of simple detections (at or above the minimum reporting level, ≥MRL, or ≥1 µg/L), exceedances of the health reference level (>HRL, or >175 µg/L), and exceedances of one-half the value of the HRL (>½HRL, or >87.5 µg/L).

Results of the analysis are presented in Table 4-3 and 4-4. No detections of EPTC were found in any samples, and thus there were also no exceedances of the HRL or one-half the HRL.

Table 4-3 Summary UCMR1 Occurrence Statistics for EPTC in Small Systems (Based on Statistically Representative National Sample of Small Systems)

Frequency Factors	UCMR Data - Small Systems		National System & Population Numbers[1]
Total Number of Samples	3,251		--
Percent of Samples with Detections	0.00%		--
99th Percentile Concentration (all samples)	< MRL		--
Health Reference Level (HRL)	175 µg/L		--
Minimum Reporting Level (MRL)	1 µg/L		--
Maximum Concentration of Detections	< MRL		--
99th Percentile Concentration of Detections	< MRL		--
Median Concentration of Detections	< MRL		--
Total Number of PWSs	797		60,414
Number of GW PWSs	590		56,072
Number of SW PWSs	207		4,342
Total Population	2,760,570		45,414,590
Population of GW PWSs	1,939,815		36,224,336
Population of SW PWSs	820,755		9,190,254
Occurrence by System	**Number**	**Percentage**	**National Extrapolation[2]**
PWSs (GW & SW) with Detections (≥ MRL)	0	0.00%	0
PWSs (GW & SW) > 1/2 HRL	0	0.00%	0
PWSs (GW & SW) > HRL	0	0.00%	0
Occurrence by Population Served			
Population Served by PWSs with Detections	0	0.00%	0
Population Served by PWSs > 1/2 HRL	0	0.00%	0
Population Served by PWSs > HRL	0	0.00%	0

1. Total PWS and population numbers are from EPA September 2004 Drinking Water Baseline Handbook, 4th edition.
2. National extrapolations are generated by multiplying the system/population percentages and the national Baseline Handbook system/population numbers.

Abbreviations:
PWS = Public Water Systems; GW = Ground Water; SW = Surface Water; N/A = Not Applicable; Total Number of Samples = the total number of samples on record for the contaminant; 99th Percentile Concentration = the concentration in the 99th percentile sample (out of either all samples or just samples with detections); Median Concentration of Detections = the concentration in the median sample (out of samples with detections); Total Number of PWSs = the total number of PWSs for which sampling results are available; Total Population Served = the total population served by PWSs for which sampling results are available; PWSs with detections, PWSs > ½HRL, or PWSs > HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively; Population Served by PWSs with detections, by PWSs >½HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively.

Notes:
-Small systems are those that serve 10,000 persons or fewer.
-Only results at or above the MRL were reported as detections. Concentrations below the MRL are considered non-detects.
-Due to differences between the ratio of GW and SW systems with monitoring results and the national ratio, extrapolated GW and SW figures might not add up to extrapolated totals.
-The HRL used in this analysis is a draft value for working review only.

Table 4-4 Summary UCMR1 Occurrence Statistics for EPTC in Large Systems (Based on the Census of Large Systems)

Frequency Factors	UCMR Data - Large Systems	
Total Number of Samples	30,384	
Percent of Samples with Detections	0.00%	
99th Percentile Concentration (all samples)	< MRL	
Health Reference Level (HRL)	175 µg/L	
Minimum Reporting Level (MRL)	1 µg/L	
Maximum Concentration of Detections	< MRL	
99th Percentile Concentration of Detections	< MRL	
Median Concentration of Detections	< MRL	
Total Number of PWSs Number of GW PWSs Number of SW PWSs	3,069 1,375 1,694	
Total Population Population of GW PWSs Population of SW PWSs	223,361,341 53,303,000 170,058,341	
Occurrence by System	**Number**	**Percentage**
PWSs (GW & SW) with Detections (≥ MRL)	0	0.00%
PWSs (GW & SW) > 1/2 HRL	0	0.00%
PWSs (GW & SW) > HRL	0	0.00%
Occurrence by Population Served		
Population Served by PWSs with Detections	0	0.00%
Population Served by PWSs > 1/2 HRL	0	0.00%
Population Served by PWSs > HRL	0	0.00%

Abbreviations:
PWS = Public Water Systems; GW = Ground Water; SW = Surface Water; N/A = Not Applicable; Total Number of Samples = the total number of samples on record for the contaminant; 99th Percentile Concentration = the concentration in the 99th percentile sample (out of either all samples or just samples with detections); Median Concentration of Detections = the concentration in the median sample (out of samples with detections); Total Number of PWSs = the total number of PWSs for which sampling results are available; Total Population Served = the total population served by PWSs for which sampling results are available; PWSs with detections, PWSs > ½HRL, or PWSs > HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively; Population Served by PWSs with detections, by PWSs >½HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively.

Notes:
-Large systems are those that serve more than 10,000 persons.
-Only results at or above the MRL were reported as detections. Concentrations below the MRL are considered non-detects.
-The HRL used in this analysis is a draft value for working review only.

4.4 Summary

Under the NAWQA program, USGS monitored EPTC between 1992 and 2001 in representative watersheds and aquifers across the country. The 95th percentile concentrations in surface water were less than the reporting limit in undeveloped and urban settings, 0.009 µg/L in mixed land use settings, and 0.018 µg/L in agricultural settings. The highest concentration, estimated at 29.6 µg/L, was found in a mixed land use setting. The 95th percentile concentrations in ground water were less than the reporting limit in all settings. EPTC was detected more frequently in ambient surface water than ambient ground water in all land use settings (1.64% vs. 0% for undeveloped land samples; 4.81% vs. 0.72% for urban samples; 11.88% vs. 0.33% for mixed land use area samples; and 14.11% vs. 0.49% for agriculture samples).

For UCMR1, EPTC was scheduled to be monitored by all large CWSs and NTNCWSs and a statistically representative sample of small CWSs and NTNCWSs. The data available in July of 2005 were analyzed at the level of simple detections (at or above the minimum reporting level, ≥MRL, or ≥1 µg/L), exceedances of the health reference level (>HRL, or >175 µg/L), and exceedances of one-half the value of the HRL (>½HRL, or >87.5 µg/L). No detections of EPTC were found in any samples and, thus, there were also no exceedances of the HRL or one-half the HRL.

5.0 EXPOSURE FROM MEDIA OTHER THAN WATER

5.1 Exposure from Food

5.1.1 Concentration in Non-Fish Food Items

Based on the EPA's Reregistration Eligibility Decision (U.S. EPA, 1999), a single reported EPTC residue of toxicological concern was found in goats (EPTC-cysteine conjugate) and hens (unmetabolized EPTC) fed "highly exaggerated doses" of EPTC (doses were not provided). In both cases, the residue was found in low concentrations only (the values were not presented). EPA concluded that residues of EPTC in animal commodities represent a Category 3 situation under 40 CFR §180.6(a), in which it is impossible to clearly establish whether finite residues will be incurred under reasonable worst-case exposure scenarios, and there is no reasonable expectation that finite residues will be present in animal commodities. Therefore, tolerances for residues of EPTC in animal commodities need not be established (U.S. EPA, 1999). No other studies of EPTC residues in animals were located.

Residues of EPTC and its three hydroxylated metabolites were nondetectable (<0.05 ppm) in the majority of samples of raw and processed agricultural commodities obtained from submitted field trials (U.S. EPA, 1999).

5.1.2 Concentrations in Fish and Shellfish

Information concerning the concentrations of EPTC found in fish and shellfish was not found in the literature reviewed.

5.1.3 Intake of EPTC from Food

Based on the information presented, EPTC was not readily detected in food items. Consequently, the typical average daily intake of EPTC from food for the general population is anticipated to be close to zero.

5.2 Exposure from Air

5.2.1 Concentration of EPTC in Air

The maximum concentration of EPTC detected over the Mississippi River, encompassing an area from New Orleans, LA to St. Paul, MN during June 1994, was 1.5 ng/m^3 (Majewski et al., 1998). No other data are currently available.

5.2.2 Intake of EPTC from Air

Estimates of nonoccupational exposures to EPTC for adults can be derived from the ambient air concentration encompassing an area from New Orleans, LA to St. Paul, MN during June 1994 (Majewski et al., 1998) using the assumption that adult humans breath 15.2 m^3 air per day (U.S. EPA, 1996b).

$$1.5\ ng/m^3 \times 15.2\ m^3/day = 22.8\ ng/day \text{ rounded to } 23\ ng/day$$

For children the average rate for air exchange is 8.7 m^3 /day leading to an exposure of

$$1.5\ ng/m^3 \times 8.7\ m^3/day = 13.05\ ng/day \text{ rounded to } 13\ ng/day$$

5.3 Exposure from Soil

5.3.1 Concentration of EPTC in Soil

The mean concentration of EPTC at agrochemical facilities in Illinois was determined to be 110 µg/kg (Krapac, 1995). No other data were available.

5.3.2 Intake of EPTC from Soil

Human exposure to contaminants in soils is usually from dust that infiltrate homes, automobiles etc. in the adult, and from dusts and incidental soil ingestion in children. Estimates of intake for soil often assume an ingestion rate of 100 mg/day for children and 50 mg/day for adults (U.S. EPA, 1996b). Using the data from Krapac et al. (1995) of 0.110 mg EPTC/kg soil and the assumption that infants ingest 0.000001 kg/soil per day (100 mg), exposure of infants to EPTC from soils would be about 0.11 ng/day and that for adults would be 0.55 ng/day.

$$0.110\ mg/kg\ soil \times 0.000001\ kg\ soil = 0.00000011\ mg/day\ (0.11\ ng/day)$$

$$0.110\ mg/kg\ soil \times 0.0000005\ kg\ soil = 0.00000055\ mg/day\ (0.55\ ng/day)$$

5.4 Other Residential Exposures

Residential handler exposure to EPTC via dermal and inhalation routes can occur during application activities. The exposure duration of these activities was classified as short-term (1-7 days), because EPTC is usually applied only once per year or during well-spaced intervals. This prevents excessive concentration buildup.

5.5 Occupational Exposures

5.5.1 Description of Industries and Workplaces

The potential for exposure is greatest at agrochemical production facilities and during direct (manual) application to crops and non-food flora. Protective measures are necessary to reduce exposure risks (e.g., personal protective equipment and engineering controls).

5.5.2 Types of Exposure

Occupational and residential exposure to EPTC residues via dermal and inhalation routes can occur during handling activities such as mixing, loading, and applying. The exposure duration of application activities was classified as short-term (1-7 days), because EPTC is usually applied only once per year or applications are well-spaced in time, preventing excessive concentration buildup.

The potential for post-application occupational exposure is minimal. There is little chance for post-application dermal exposure because EPTC is directly applied to soil, or injected into soil well before plants are mature and dissipates rapidly.

5.6 Summary

Based on the data, the general population should not be exposed to EPTC from food items. Nonoccupational inhalation exposure to EPTC for adults is approximately 23 ng/day. For children, exposure from ambient air is approximately 13 ng/day. Estimates of EPTC intake from soils are 0.11 ng/day for infants and 0.55 ng/day for adults. Other residential exposures to EPTC can occur via dermal and inhalation routes during application activities. The exposure duration of these activities was classified as short-term (1-7 days) because EPTC is usually applied only once per year or during well-spaced intervals.

6.0 HAZARD AND DOSE-RESPONSE ASSESSMENT

6.1 Characterization of Hazard

6.1.1 Synthesis and Evaluation of Major Noncancer Effects

In a recent human study (Hoppin et al., 2002), EPTC exposure was shown to be associated with a slight but significant increase in the in the odds ratio for wheezing in farmers (odds ratio = 1.32; 95% confidence interval = 1.05-1.65; p=0.01). In acute animal toxicity studies, EPTC is most toxic when exposure is via inhalation; acute responses following oral and dermal exposures are less severe. In a primary eye irritation study in rabbits, technical EPTC was shown to be slightly irritating (U.S. EPA, 1999).

An increase in the incidence and severity of cardiomyopathy was observed in subchronic and chronic studies performed in both rats and dogs. In two chronic/oncogenicity feeding studies and in 90-day feeding and inhalation studies, all rats exhibited myocardial degeneration during the histopathology examination (Mackenzie, 1986; U.S. EPA, 1999). In dogs, two chronic oral dosing studies revealed degenerative changes in the cardiac muscle when EPTC was administered in a capsule, but not when it was administered at comparable doses in the diet. Electrocardiograms were performed in both dog studies; however, only one high-dose male in the capsule study exhibited changes which were described as "potentially" treatment-related (U.S. EPA, 1999).

EPTC is a reversible cholinesterase (ChE) inhibitor. Similar to other thiocarbamates, EPTC does not produce a consistent ChE inhibition profile. There were no consistent patterns observed in any of the toxicity studies with regard to species, duration of treatment, or type of ChE enzyme measured. Typically studies showed inhibition of plasma ChE with dose-related increases in red blood cells and brain ChE inhibition. Some studies have shown that brain ChE activity was inhibited without any effect on either plasma or erythrocyte ChE activities. Other studies illustrated erythrocyte ChE inhibition with no inhibition of either plasma or brain ChE. This inconsistent ChE inhibition profile is illustrated when comparing the results of a chronic dog oral dosing study, in which only plasma ChE was inhibited, and a developmental rabbit study, in which plasma and erythrocyte ChE were inhibited (U.S. EPA, 1999). In another study with rats at or near the acute median lethal dose, EPTC inhibited only erythrocyte and brain ChE, but not plasma ChE (U.S. EPA, 1999).

Exposure to EPTC, as well as other thiocarbamates (molinate, cycloate, pebulate, vernolate, and butylate), also is associated with toxic effects on the central and peripheral nervous systems. Both rats and dogs have exhibited increases in incidence and severity of neuronal necrosis/degeneration in both the central and peripheral nervous systems. In a rat neurotoxicity study, dose-related increases in the incidence of neuronal necrosis were observed in the brain after acute and subchronic exposure to EPTC. However, in an acute delayed neurotoxicity study of EPTC in hens, delayed neurotoxicity was not observed (U.S. EPA, 1999). Treatment-related neuromuscular lesions were observed in both chronic toxicity/oncogenicity studies in rats and in a chronic oral (capsule) study in dogs. In all of these studies, hindquarter weakness was observed and, at necropsy evaluation, atrophy and degeneration of the skeletal

muscle was observed. In the dog study, the lesions were described as Wallerian-type degeneration in the spinal cords and various peripheral nerves (U.S. EPA, 1999).

Smulders et al. (2003) recently investigated effects of several carbamate pesticides on neuronal nicotinic acetylcholine receptors (nAChRs) heterologously expressed in Xenopus laevis oocytes. The potencies of carbamate effects on the nAChRs were then compared to the potencies of rat brain AChE inhibition and the differential sensitivities of specific subtypes of ganglionic and brain neuronal nAChRs. The results of this study indicate that in oocytes expressing the rat α4β4 nAChR, EPTC caused nearly complete inhibition when applied at a concentration of 100 μM. In contrast, concentrations up to 1 mM of EPTC did not cause a marked reduction in rat brain AChE activity. The nicotinic acetylcholine receptors subtypes (α42, α3β4, and α3β2) also were inhibited by EPTC, with similar potencies to those of α4β4 receptors. Based on these observations, it was concluded that carbamate pesticides affect different subtypes of neuronal nicotinic receptors independent of acetylcholinesterase inhibition potential, and that these effects may contribute to long-term changes in the nervous system.

Maternal and parental developmental and reproductive toxicity were observed in rats and rabbits exposed to EPTC. In a rat prenatal developmental toxicity study, developmental toxicity indications (decreased fetal body weight and litter size) were observed, but were considered secondary to marked maternal toxicity (i.e., increased mortality and decreased body weight) (U.S. EPA, 1999). Similar results were observed in a rabbit developmental toxicity study in which a developmental toxicity index (decreased fetal body weight) was observed in the presence of marked maternal toxicity indices (decreased body weight and increased mortality) (U.S. EPA, 1999).

A two-generation study conducted in rats fed diets containing 0, 50, 200 or 800 ppm EPTC. Effects in the offspring were observed only at or above treatment levels that resulted in parental toxicity. There was a slight decrease in pup body weight in the 800 ppm dose group. Toxicity was observed in the F1 generation dams as reflected in a dose-related increase in cardiomyopathy and reduced body weights. Degenerative cardiomyopathy is an abnormality in the function of the heart muscle, which reduces physical abilities of the affected animal its including the ability to compete for food and reproductive dominance (U.S. EPA, 1999; Cal EPA, 1995).

Although the data do not provide evidence of reproductive or developmental toxicity except at maternally toxic doses, the OPP did register a concern for developmental neurotoxicity because of the neurodegenerative effects observed in studies in adult animals and for that reason suggested that a food Quality Protection Act factor of 10 be applied when assessing the pesticidal uses of this product (U.S. EPA, 1999).

6.1.2 Synthesis and Evaluation of Carcinogenic Effects

In a study conducted by Alavanja et al. (2003), there was no exposure-response association between EPTC exposure and prostate cancer. In another study, Zheng et al. (2001) examined the risk of non-Hodgkin lymphoma (NHL) from carbamate insecticide exposure using a pooled analysis of three-population based case-control studies. There was an increased risk of

NHL (30 to 50%) among farmers who had used carbamate pesticides as a group when compared to non-farmers. For those who used EPTC plus protectant (protectant not specified) for less than 7 years the association was not as strong (odds ratio = 2.2; 95% confidence interval = 1.1-4.4); the odds ratio among the farmers that used EPTC for $7 years was not significant but this may be due to the small number of cases.

There are a number of chronic animal studies of EPTC which included evaluation of the cancer endpoint. A 78-week study in mice (Tisdel et al., 1986) and a 2-year study in rats (Dickie, 1987), both demonstrated that there was no significant increase in tumors when the exposed animals were compared to the controls. The Tisdale et al., (1986) study used dietary concentrations ranging from 0 to 1,800 ppm; the Dickie study used doses of 0 to 72 mg/kg/day technical grade EPTC in the diet.

Based on the information provided, it does not appear that exposure to EPTC is carcinogenic. Limited studies in humans do not implicate carbamate in the etiology for prostate cancer and show only a weak association with NHL. Bioassays in rats and mice indicate that exposure to EPTC does not result in an increased incidence of neoplastic lesions.

6.1.3 Mode of Action and Implications in Cancer Assessment

This section is not applicable because EPTC shows no evidence of carcinogenicity (as described in Section 6.1.2, Synthesis and Evaluation of Carcinogenic Effects).

6.1.4 Weight of Evidence Evaluation for Carcinogenicity

Applying the criteria described in EPA's draft final guidelines for assessment of carcinogenic risk (U.S. EPA, 2005), EPTC may be classified as not likely to be carcinogenic to humans. This group is for agents with animal evidence that demonstrate lack of carcinogenic effects in well-designed and well-conducted studies in at least two appropriate animal species (in the absence of other animal or human data suggesting a potential for cancer effects); extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans; convincing evidence that carcinogenic effects are not likely to occur by a particular exposure route; or convincing evidence that carcinogenic effects are not likely to occur below a defined dose range.

6.1.5 Potentially Sensitive Populations

Results from both developmental and reproductive studies indicate that minimal adverse effects on body weight occur in pups in animal studies at maternally toxic doses after EPTC exposure. However, additional studies focusing on the potential for neurotoxic effects (neuronal necrosis and degeneration) after pre- and post-natal exposures are needed. Accordingly, there is some hypothetical concern that children may be a sensitive population for EPTC exposure.

6.2 Reference Dose

The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is derived from the no observed adverse effect level (NOAEL) in the critical or most sensitive study, which is then divided by a variable uncertainty factor. The RfD for EPTC is 0.025 mg/kg/day. The subsections below describe how this value was determined.

6.2.1 Choice of Principle Study and Critical Effect

The principal study for determining the RfD is a 2-generation rat reproductive study, in which Crl:CD(SD)Br rats (30/sex/group) were fed diets providing 0, 50, 200, and 800 ppm EPTC (equivalent to 0, 2.5, 10, and 40 mg/kg/day, respectively) (Mackenzie, 1986). At doses of 200 ppm and above, parental toxicity consisted of reduced body weights and weight gains, and a dose-related increased incidence of degenerative cardiomyopathy. Reproductive/developmental toxicity consisted of reduced pup weights at 800 ppm in both generations. The 50 ppm concentration was identified as the NOAEL in this study.

6.2.2 Dose-response Characterization (dose conversion if needed)

Doses in the Mackenzie (1986) study were converted from ppm to mg/kg/day using the assumption that 1 ppm was equivalent to 0.05 mg/kg/day (U.S. EPA, 1987). Accordingly, the NOAEL of 50 ppm is equivalent to a dose of 2.5 mg/kg/day (U.S.EPA, 1987).

6.2.3 Method of Analysis

U.S. EPA (1987) derived the RFD for EPTC using the NOAEL/LOAEL approach. The RfD was calculated as follows:

$$\text{RfD} = \frac{2.5\ \text{mg/kg/day}}{100} = 0.025\ \text{mg/kg/day}$$

Where:

2.5 mg/kg/day =	The NOAEL for cardiomyopathy in the dams from a two-generation study.
100 =	An uncertainty factor that includes a 10 to adjust for interspecies variability and a 10 for interspecies variability.

6.2.4 Application of Uncertainty Factor(s) and Modifying Factor(s)

An uncertainty factor of 100 was used for the RfD derivation (10 for interspecies extrapolation and 10 for intraspecies variability). The Agency did not apply uncertainty factors for the database or for a duration adjustment. However, the need for a study of developmental neurotoxicity was noted and the Office of Pesticide Programs recommended use of a Food

Quality Protection Act factor of 10 when setting tolerances for EPTC until this data need is filled.

6.3 Carcinogen Assessment

This section is not applicable because EPTC shows no evidence of carcinogenicity (as described in Section 6.1.2, Synthesis and Evaluation of Carcinogenic Effects).

6.4 Sensitive Population Considerations

The OPP identified children as a potentially sensitive population because of the neuronal degeneration noted in the central and peripheral nervous system in mature rats and dogs and because these same effects have been observed in studies of other thiocarbamates. Although the RfD is protective of these effects in mature animals, a study of developmental neurotoxicity was identified as a data need by the Office of Pesticide Programs.

6.5 Post Re-registration Health Effects Publications

Not applicable

6.6 CCL Health Reference Level

The CCL health reference level is 0.175 mg/L. EPA derived the HRL using an RfD approach as follows: HRL = (RfD ×70 kg)/2 L/day × RSC, where:

RfD = An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure (mg/kg/day) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from an NOAEL, LOAEL, or BMD, with uncertainty factors generally applied to reflect limitations of the data used;

70 kg = The assumed body weight of an adult;

2 L = The assumed daily water consumption of an adult;

RSC = The relative source contribution, or the level of exposure believed to result from drinking water when compared to other sources (e.g., air), and is assumed to be 20% unless noted otherwise.

$$\text{Therefore, the HRL} = \frac{0.025\ \text{mg/kg/day} \times 70\text{kg} \times 0.20}{2\text{L/day}} = 0.0.175\ \text{mg/L}$$

A discussion of the HRL as a benchmark for evaluating occurrence using monitoring data from public water systems is found in Section 4.3.2.

7.0 REGULATORY DETERMINATION AND CHARACTERIZATION OF RISK FROM DRINKING WATER

7.1 Regulatory Determination for Chemicals on the CCL

The Safe Drinking Water Act (SDWA), as amended in 1996, required the Environmental Protection Agency (EPA) to establish a list of contaminants to aid the Agency in regulatory priority setting for the drinking water program. EPA published a draft of the first Contaminant Candidate List (CCL) on October 6, 1997 (62 Federal Register [FR] 52193, U.S. EPA, 1997). After review of and response to comments, the final CCL was published on March 2, 1998 (63 FR 10273, U.S. EPA, 1998c).

On July 18, 2003 EPA announced final Regulatory Determinations for one microbe and 8 chemicals (68 FR 42897, U.S. EPA, 2003) after proposing those determinations on June 3, 2002 (67 FR 38222, U.S. EPA, 2002b). The remaining 40 chemicals and ten microbial agents from the first CCL became CCL 2 and were published in the Federal Register on April 2, 2004 (69 FR 17406, U.S. EPA 2004b).

The SDWA requires EPA to make regulatory determinations for no fewer than five contaminants from CCL 2 by August, 2006. In cases where the Agency determines that a regulation is necessary, the regulation should be proposed by August 2008 and promulgated by February 2010. The Agency is given the freedom to determine that there is no need for a regulation if a chemical on the CCL fails to meet one of three criteria established by the SDWA and described in section 7.1.1.

7.1.1 Criteria for Regulatory Determination

These are the three criteria used to determine whether or not to regulate a chemical on the CCL:

- The contaminant may have an adverse effect on the health of persons.
- The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern.
- In the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

The findings for all criteria are used in making a determination to regulate a contaminant. As required by the SDWA, a decision to regulate commits the EPA to publication of a Maximum Contaminant Level Goal (MCLG) and promulgation of a National Primary Drinking Water Regulation (NPDWR) for that contaminant. The Agency may determine that there is no need for a regulation when a contaminant fails to meet one of the criteria. A decision not to regulate is considered a final Agency action and is subject to judicial review. The Agency can choose to

publish a Health Advisory (a nonregulatory action) or other guidance for any contaminant on the CCL independent of the regulatory determination.

7.1.2 National Drinking Water Advisory Council Recommendations

In March 2000, the EPA convened a Working Group under the National Drinking Water Advisory Council (NDWAC) to help develop an approach for making regulatory determinations. The Working Group developed a protocol for analyzing and presenting the available scientific data and recommended methods to identify and document the rationale supporting a regulatory determination decision. The NDWAC Working Group report was presented to and accepted by the entire NDWAC in July 2000.

Because of the intrinsic difference between microbial and chemical contaminants, the Working Group developed separate but similar protocols for microorganisms and chemicals. The approach for chemicals was based on an assessment of the impact of acute, chronic, and lifetime exposures, as well as a risk assessment that includes evaluation of occurrence, fate, and dose-response. The NDWAC protocol for chemicals is a semi-quantitative tool for addressing each of the three CCL criteria. The NDWAC requested that the Agency use good judgment in balancing the many factors that need to be considered in making a regulatory determination.

The EPA modified the semi-quantitative NDWAC suggestions for evaluating chemicals against the regulatory determination criteria and applied them in decision-making. The quantitative and qualitative factors for s-ethyl dipropylthiocarbamate (EPTC) that were considered for each of the three criteria are presented in the sections that follow.

7.2 Health Effects

The first criterion asks if the contaminant may have an adverse effect on the health of persons. Because chemicals have adverse effects at some level of exposure, the challenge is to define the dose at which adverse health effects are likely to occur, and estimate a dose at which adverse health effects are either not likely to occur (threshold toxicant), or have a low probability for occurrence (non-threshold toxicant). The key elements that must be considered in evaluating the first criterion are the mode of action, the critical effect(s), the dose-response for critical effect(s), the reference dose (RfD) for threshold effects, and the slope factor for nonthreshold effects.

A full description of the health effects information and dose-response assessment associated with exposure to ETPC is presented in Chapter 6 of this document and summarized below in Sections 7.2.1, 7.2.2 and 7.2.3.

7.2.1 Health Criterion Conclusion

Results of studies have shown that EPTC is a reversible cholinesterase (ChE) inhibitor. Similar to other thiocarbamates, EPTC does not produce a consistent ChE inhibition profile; consequently, there is no consistent pattern observed in any of the toxicity studies with regard to species, duration of treatment, or the type of ChE enzyme measured (U.S. EPA, 1999). EPTC

exposure also is associated with toxic effects on the central and peripheral nervous system. In acute animal toxicity studies, EPTC was shown to be moderately toxic via oral and dermal routes, and highly toxic via inhalation. In subchronic and chronic studies performed in both rats and dogs, there was an increase in the incidence and severity of cardiomyopathy (Mackenzie, 1986; U.S. EPA, 1999).

The oral RfD for EPTC is 0.025 mg/kg/day, and the health reference level (HRL) for EPTC is calculated to be 0.175 mg/L. EPTC is classifiable as *not likely to be carcinogenic to humans* based on lack of evidence of carcinogenic effects in long term studies in rats and mice (U.S. EPA, 1987; U.S. EPA, 2005). Based on these considerations, the evaluation of the first criterion for EPTC is positive; EPTC may have an adverse effect on human health.

7.2.2 Hazard Characterization and Mode of Action Implications

In an epidemiological study of farmers, EPTC was associated with a slight increase in the relative risk for wheezing. In animals, acute toxicity studies have shown that EPTC is moderately toxic via oral and dermal routes, and is highly toxic when exposure is via inhalation. EPTC also is a reversible cholinesterase (ChE) inhibitor. Similar to other thiocarbamates, EPTC does not produce a consistent ChE inhibition profile. There were no consistent patterns observed in any of the toxicity studies with regard to species, duration of treatment, or type of ChE enzyme measured. Typically studies showed inhibition of erythrocyte and brain ChE; however, some studies have shown that brain ChE activity was inhibited without any effect on either plasma or erythrocyte ChE activities while others have identified erythrocyte ChE inhibition with no inhibition of either plasma or brain ChE (U.S. EPA, 1999). In a primary eye irritation study in rabbits, technical-grade EPTC was shown to be slightly irritating (U.S. EPA, 1999).

An increase in the incidence and severity of cardiomyopathy was observed in subchronic and chronic studies performed in both rats and dogs (Mackenzie, 1986; U.S. EPA, 1999). Additionally, the central and peripheral nervous systems also are affected by EPTC exposure with rats and dogs exhibiting an increase in the incidence and severity of degenerative effects (neuronal and/or necrotic degeneration) (U.S. EPA, 1999).

In addition to its neurotoxic effects, EPTC has the ability to induce maternal and reproductive toxicity and secondary developmental toxicity in exposed rats and rabbits. In a rat developmental toxicity study, as well as a rabbit developmental toxicity study, toxicity indications (decreased fetal body weight and litter size for rats; decreased fetal body weight for rabbits) were observed, but were considered secondary to observed marked maternal toxicity (increased mortality and decreased body weight for rats; decreased body weight and increased mortality for rabbits) (U.S. EPA, 1999). In a two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels that resulted in parental toxicity (Mackenzie, 1986; U.S. EPA, 1999).

7.2.3 Dose-Response Characterization and Implications in Risk Assessment

The RfD for EPTC is 0.025 mg/kg/day (U.S. EPA, 1987; U.S. EPA, 1999). This value was calculated using an NOAEL of 2.5 mg/kg/day from a study by Mackenzie (1986) and

applying an uncertainty factor of 100 for inter- and intraspecies differences. The critical effect associated with the RfD is cardiomyopathy (disease of the heart muscle). EPA determined that the HRL is 0.175 mg/L or 175 µg/L for EPTC, using the RfD of 0.025 mg/kg/day and a 20 percent relative source contribution.

The Agency used long-term studies in mice and rats and short-term studies of mutagenicity to evaluate the potential for carcinogenicity. Based on these data and using EPA's 2005 Guidelines for Carcinogen Risk Assessment, EPTC is not likely to be carcinogenic to humans (U.S. EPA, 2005).

EPA also evaluated whether health information is available regarding the potential effects on children and other sensitive populations. Data do not suggest increased pre- or post-natal sensitivity of children and infants to EPTC exposure because developmental adverse effects observed were considered secondary to maternal effects (U.S. EPA, 1999). Although results from both developmental and reproductive studies indicate that minimal adverse effects occur in fetuses or offspring in animal studies after EPTC exposure, additional studies focusing on the neurotoxic effects (neuronal necrosis and degeneration) are needed. The behavior patterns of children that lead to heightened opportunities for exposure in the indoor environment and the need for a developmental neurotoxicity study lead OPP to recommend the application of a ten-fold FQPA factor for EPTC.

7.3 Occurrence in Public Water Systems

The second criterion asks if the contaminant is known to occur or if there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern. In order to address this question the following information was considered:

- Monitoring data from public water systems
- Ambient water concentrations and releases to the environment
- Environmental fate

Data on the occurrence of EPTC in public drinking water systems were the most important determinants in evaluating the second criterion. EPA looked at the total number of systems that reported detections of EPTC, as well those that reported concentrations of EPTC above an estimated drinking-water HRL. For noncarcinogens, the estimated HRL level was calculated from the RfD assuming that 20% of the total exposure would come from drinking. For carcinogens, the HRL was the 10^{-6} risk level (i.e, the probability of 1 excess tumor in a population of a million people). The HRLs are benchmark values that were used in evaluating the occurrence data while the risk assessments for the contaminants were being developed.

The available monitoring data, including indications of whether or not the contaminant is a national or a regional problem, are included in Chapter 4 of this document and summarized below. Additional information on production, use, and fate are found in Chapters 2 and 3.

7.3.1 Occurrence Criterion Conclusion

There were no detections of EPTC found in any of the large (i.e., serving more than 10,000 people) community water systems (CWSs) and large non-transient non-community water systems (NTNCWSs) (USGS, 2001). There were no detections of EPTC found in the statistically representative national sample of 800 small (i.e., serving 10,000 people or fewer) CWSs and NTNCWSs. Additionally, the available data for EPTC production and environmental releases all show a downward trend (NCFAP, 2004).

The physiochemical properties of EPTC suggest that EPTC does not persist in the environment due to rapid dissipation rates and high volatility. However, estimated bioconcentration rates in aquatic organisms is moderate, assuming the chemical persists long enough to be taken up by an organism (U.S. EPA, 2005).

Based on the occurrence data, it is unlikely that EPTC will occur in public water systems at frequencies or concentration levels that are of public health concern. Thus, the evaluation for the second criterion is negative.

7.3.2 Monitoring Data

Under the National Water-Quality Assessment (NAWQA) program, the US Geological Survey (USGS) monitored EPTC between 1992 and 2001 in representative watersheds and aquifers across the country. Reporting limits varied but did not exceed 0.002 µg/L. In surface water, EPTC was detected at frequencies ranging from 1.64% of samples in undeveloped land settings to 4.81% in urban land-use settings, 11.88% in mixed land use settings, and 14.11% in agricultural land use settings. The 95th percentile concentrations in all land-use settings were below the reporting limit in undeveloped and urban settings, 0.009 µg/L in mixed land-use settings, and 0.018 µg/L in agricultural settings. The highest maximum concentration, estimated at 29.6 µg/L, occurred in an agricultural land-use setting (Martin et al., 2003).

In ground water, EPTC detection frequencies ranged from 0.0% of samples in undeveloped settings to 0.33% in mixed land-use (major aquifer) settings, 0.49% in agricultural settings, and 0.72% in urban settings. The 95th percentile concentrations were less than the reporting limit in all settings. The highest concentration, 0.45 µg/L, occurred in an agricultural setting (Kolpin and Martin, 2003).

Additionally, the Unregulated Contaminant Monitoring Regulation 1 (UCMR1) collects information on the national occurrence of select emerging contaminants in drinking water. The program operates on a five-year cycle, and the first cycle (which provided occurrence data used in this report) extended from 2001 to 2005. There are two components to the monitoring methods. The first monitoring component, Assessment Monitoring, is for the UCMR1 contaminants with well-developed analytical methods ("List 1" contaminants). The second component of the UCMR1, the Screening Survey, is for those contaminants with analytical methods that may need to be further refined for use in a large national survey ("List 2" contaminants) (USGS, 2001). EPTC is a "List 1" contaminant; consequently, all large (i.e., serving more than 10,000 people) CWSs and large NTNCWSs, plus a statistically representative

national sample of 800 small (i.e., serving 10,000 people or fewer) CWSs and NTNCWSs are required to participate. The small system sample is population-weighted and was expressly designed to provide UCMR1 contaminant monitoring results that are statistically representative of national contaminant occurrence.

Monitoring operates on a five-year cycle, and the first cycle extended from 2001 to 2005. The monitoring data available July 2005 were analyzed and indicate that there were no detections of EPTC in any of the samples. Consequently, there also were no exceedances of the HRL or one-half of the HRL. These results should be interpreted with some caution because they represent only approximately 90% of large systems in the census.

7.3.3 Use and Fate Data

EPTC is a pre-emergence or early post-emergence herbicide used to control the growth of germinating annual weeds such as broadleaves, grasses, and sedges. The major usage, in terms of total pounds of active ingredient, is in fields used to grow crops like corn, potatoes, dry beans and peas, alfalfa, and snap beans (U.S. EPA, 1999). EPTC also is used at residential and public sites such as parks, gardens, and golf courses (HSDB, 2004).

The physiochemical properties of EPTC suggest that it does not persist in the environment due to rapid dissipation rates. EPTC is highly volatile. Terrestrial field studies indicated a range of dissipation half-lives between 2 and 18.8 days while laboratory tests to measure dissipation rates indicated half-lives in the range of 36-75 days (U.S. EPA, 1999). The risk of exposure to EPTC through food or groundwater is minimal due to its rapid rate of dissipation and normally early (pre-emergent) plant application. However, estimated bioconcentration rates in aquatic organisms are moderate, assuming the chemical persists long enough to be taken up by an organism (U.S. EPA, 1999).

The available data for EPTC production and environmental releases all show a downward trend (NCFAP, 2004). EPTC mover from being the eighth most common pesticide ingredient in 1987 to the nineteenth in 1999. Toxic Release Inventory (TRI) data for EPTC are reported for the years 1995 to 2002 (U.S. EPA, 2004a). Total reported EPTC releases fluctuated widely in the range of thousands of pounds per year during this period but generally displayed a declining trend for most years; releases to surface waters are low.

Monitoring data from finished water are supportive of a decline of its presence in the environment. Monitoring data to date indicate that there were no detections of EPTC in any of the finished water samples. Consequently, there also were no exceedances of the HRL or one-half of the HRL. Results should be interpreted with some caution because they represent only approximately 90% of large systems in the census.

7.4 Risk Reduction

The third criterion asks if, in the sole judgment of the Administrator, regulation presents a meaningful opportunity for health risk reduction for persons served by public water systems. In evaluating this criterion, EPA looked at the total exposed population, as well as the population

exposed to levels above the estimated HRL. Estimates of the populations exposed and the levels to which they are exposed were derived from the monitoring results. These estimates are included in Chapter 4 of this document and summarized in section 7.4.2 below.

In order to evaluate risk from exposure through drinking water, EPA considered the net environmental exposure in comparison to exposure through drinking water. For example, if exposure to a contaminant occurs primarily through ambient air, regulation of emissions to air provides a more meaningful opportunity for EPA to reduce risk than does regulation of the contaminant in drinking water. In making the regulatory determination, the available information on exposure through drinking water (Chapter 4) and information on exposure through other media (Chapter 5) were used to estimate the fraction that drinking water contributes to the total exposure. The EPA findings are discussed in Section 7.4.3 below.

In making its regulatory determination, EPA also evaluated effects on potentially sensitive populations, including the fetus, infants and children. Sensitive population considerations are included in section 7.4.4.

7.4.1 Risk Criterion Conclusion

The presence of EPTC in water is rare. To date, there have been no detections of EPTC in any of the samples. Consequently, there also have been no exceedances of the HRL or one-half of the HRL. Thus, the evaluation of the third criterion is negative.

7.4.2 Exposed Population Estimates

EPTC is being monitored in all large (i.e., serving more than 10,000 people) community water systems (CWSs) and large non-transient non-community water systems (NTNCWSs), with the additon of a statistically representative national sample of 800 small (i.e., serving 10,000 people or fewer) CWSs and NTNCWSs. To date (July 2005), there have been no detections of EPTC in any of the samples. Therefore, it appears that the general population is not exposed to EPTC through water consumption or use.

7.4.3 Relative Source Contribution

Relative source contribution analysis compares the magnitude of exposure expected via drinking water to the magnitude of exposure from intake of EPTC in other media, such as food, air, and soil. In situations where EPTC occurs in drinking water, the water is likely to be the major source of exposure. Intake values found in food, soil, and air are very low (if detectable at all), and therefore, the RSC value should remain the default value of 20% were a lifetime HA to be developed for noncancer effects.

7.4.4 Sensitive Populations

Data do not suggest increased pre- or post-natal sensitivity of children and infants to EPTC exposure because developmental adverse effects observed were considered secondary to maternal effects. Although results from both developmental and reproductive studies indicate

that minimal adverse effects occur in fetuses or offspring in animal studies after EPTC exposure, additional studies focusing on the neurotoxic effects (neuronal necrosis and degeneration) have been recommended by the Office of Pesticide programs under the Food Quality Protection Act requirements.

7.5 Regulatory Determination Decision

As stated in Section 7.1.1, a positive finding for all three criteria is required in order to make a determination to regulate a contaminant. In the case of EPTC, only the finding for the criterion on health effects is positive. EPTC may have an adverse effect on the health of persons. To date, there have been no detections of EPTC found in any of the samples. Therefore, it appears that the general population is not exposed to EPTC through water consumption or use. On the basis of these observations, the impact of regulating EPTC concentrations in drinking water on health risk reduction is likely to be small. Regulation of EPTC in public water systems does not appear to present a meaningful opportunity for health risk reduction.

8.0 REFERENCES

Alavanja M.C.R., C. Samanic, M. Dosemeci, et al. 2003. Use of agricultural pesticides and prostate cancer risk in the agricultural health study cohort. Am. J. Epidemiol. 157:800-814.

Cal EPA (California. Environmental Protection Agency). 1995. EPTC (S-ethyl-dipropylthiocarbamamte) risk characterization document. Medical Toxicology and Worker Health and Safety Branches. Department of Pesticide Registration. California Environmental Protection Agency. Available from: <http://www.cdpr.ca.gov/docs/risk/rcd/eptc.pdf>.

Chemfinder.com. 2004. CambridgeSoft Corporation. Available from: <http://chemfinder.cambridgesoft.com/result.asp>.

Dickie, B.C. 1987. Two-year oral feeding study of the oncogenicity and chronic toxicity of EPTC in rats: Hazelton Laboratories America, Inc. PPG Industries, Inc. Study No. 6100-106. DPR Vol. 117-069 #55491 (as cited in Cal EPA, 1995).

Hamilton, P.A., T.L. Miller, and D.N. Myers. 2004. Water quality in the nation's streams and aquifers: overview of selected findings, 1991-2001. USGS Circular 1265. Available from: <http://water.usgs.gov/pubs/circ/2004/1265/pdf/circular1265.pdf>. Link to document from: <http://water.usgs.gov/pubs/circ/2004/1265/>.

Hansch, C., A. Leo, and D. Hoekman. 1995. Exploring QSAR - Hydrophobic, electronic, and steric constants. Washington, DC: American Chemical Society. p. 65 (as cited in HSDB, 2004).

Hoppin J.A., D.M. Umbach, S.J. London, et al. 2002. Chemical predictors of wheeze among farmer pesticide applicators in the Agricultural Health Study. Am. J. Respir. Crit. Care Med. 165:683–689.

HSDB (Hazardous Substance Data Bank). 2004. EPTAM. Division of Specialized Information Services, National Library of Medicine. Available from: <http://toxnet.nlm.nih.gov/>.

Kolpin, D.W. and J.D. Martin. 2003. Pesticides in Ground water: summary statistics; preliminary results from Cycle I of the National Water Quality Assessment Program (NAWQA), 1992-2001. Available from: <http://ca.water.usgs.gov/pnsp/pestgw/Pest-GW_2001_Text.html>. Link to document from: <http://ca.water.usgs.gov/pnsp/>.

Krapac, I.G., W.R. Roy, C.A. Smyth, et al. 1995. Occurrence and distribution of pesticides in soil at agrichemical facilities in Illinois. J. Soil Contam. 4:209-226 (as cited in HSDB, 2004).

Leahy, P.P. and T.H. Thompson. 1994. The National Water-Quality Assessment Program. U.S. Geological Survey Open-File Report 94-70. p. 4. Available from: <http://water.usgs.gov/nawqa/NAWQA.OFR94-70.html>.

Mackenzie, K. 1986. Two-generation reproduction study with EPTC in rats: Report: Study No. 6100-108 [unpublished study]. Hazleton Laboratories America, Inc.

Majewski, M.S., W.T. Foreman, D.A. Goolsby, et al. 1998. Airborne pesticide residues along the Mississippi River. Environ. Sci. Technol. 32:3689-98 (as cited in HSDB, 2004).

Martin, J.D., C.G. Crawford, and S.J. Larson. 2003. Pesticides in Streams: summary statistics; preliminary results from Cycle I of the National Water Quality Assessment Program (NAWQA), 1992-2001. Available from: <http://ca.water.usgs.gov/pnsp/pestsw/Pest-SW_2001_Text.html.> Link to document from: <http://ca.water.usgs.gov/pnsp/.>

Nagy I. et al. 1987. Proceedings British Crop Protection Conference - Weeds 2:525-30 (as cited in HSDB, 2004).

Nash, R.G. 1983. Determining environmental fate of pesticides with microagroecosystems. Residue Rev. 85:199-215 (as cited in HSDB, 2004).

NCFAP (National Center for Food and Agricultural Policy). 2004. National Pesticide Use Database. Available from: <http://www.ncfap.org/database/national/default.asp>.

Nowell, L. 2003. Organochlorine pesticides and PCBs in bed sediment and aquatic biota from United States rivers and streams: summary statistics; preliminary results of the National Water Quality Assessment Program (NAWQA), 1992-2001. Available from: <http://ca.water.usgs.gov/pnsp/rep/sedbiota/>.

Nowell, L. and P. Capel. 2003. Semivolatile organic compounds (SVOC) in bed sediment from United States rivers and streams: summary statistics; preliminary results of the National Water Quality Assessment Program (NAWQA), 1992-2001. Available from: <http://ca.water.usgs.gov/pnsp/svoc/SVOC-SED_2001_Text.html>.

NRC (National Research Council). 1983. Risk assessment in the federal government: managing the process. Washington, DC: National Academy Press.

NRC (National Research Council). 2002. Opportunities to improve the U.S. geological survey National Water Quality Assessment Program. National Academy Press. p. 238. Available from: <http://www.nap.edu/catalog/10267.html>.

Smith, A.E. and A. Fitzpatrick. 1971. A thin-layer chromatographic procedure for the detection in soils and waters of herbicide residues commonly used in Saskatchewan. J. Chromatogr. 57:303-8 (as cited in HSDB, 2004).

Smulders C.J.G.M., T.J.H. Bueters, R.G.D.M. Van Kleef, et al. 2003. Selective effects of carbamate pesticides on rat neuronal nicotinic acetylcholine receptors and rat brain acetylcholinesterase. Toxicol. Appl. Pharmacol. 193:139-146.

Tisdel, M., S. Kehoe, J.L. Carter, et al. 1986. Oncogenicity study in mice with EPTC: Hazelton Laboratories America, Inc. PPG Industries Inc. Study No 6100-I 04. DPR Vol. 117-049 #45704 (as cited in Cal EPA, 1995).

U.S. EPA (United States Environmental Protection Agency). 1986a. Guidelines for the health risk assessment of chemical mixtures. Fed. Reg. 51:34014-34025.

U.S. EPA (United States Environmental Protection Agency). 1986b. Guidelines for mutagenicity risk assessment. Fed. Reg. 51:34006-34012.

U.S. EPA (United States Environmental Protection Agency). 1987. S-Ethyl dipropylthiocarbamate (EPTC) Integrated Risk Information System. Available from: <http://www.epa.gov/iris/subst/0237.htm>.

U.S. EPA (United States Environmental Protection Agency). 1988. Recommendations for and documentation of biological values for use in risk assessment. EPA 600/6-87/008. Available from: National Technical Information Service, Springfield, VA; PB88-179874/AS.

U.S. EPA (United States Environmental Protection Agency). 1991. Guidelines for developmental toxicity risk assessment. Fed. Reg. 56:63798-63826.

U.S. EPA (United States Environmental Protection Agency). 1994a. Interim policy for particle size and limit concentration issues in inhalation toxicity studies. Fed. Reg. 59:53799.

U.S. EPA (United States Environmental Protection Agency). 1994b. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry. EPA/600/8-90/066F. Available from: National Technical Information Service, Springfield, VA; PB2000-500023, and <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 1995. Use of the benchmark dose approach in health risk assessment. U.S. Environmental Protection Agency. EPA/630/R-94/007. Available from: National Technical Information Service (NTIS) , Springfield, VA; PB95-213765, and <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency. 1996a. Guidelines for reproductive toxicity risk assessment. Fed. Reg. 61:56274-56322.

U.S. EPA (United States Environmental Protection Agency). 1996b. Exposure factors handbook. U.S. Environmental Protection Agency, Office of Research and Development, Washington, D.C. EPA/600/8-89/043.I

U.S. EPA (United States Environmental Protection Agency). 1997. Announcement of the draft Drinking Water Contaminant Candidate List. Fed. Reg.62:52193-52219.

U.S. EPA (United States Environmental Protection Agency). 1998a. Guidelines for neurotoxicity risk assessment. Fed. Reg. 63:26926-26954.

U.S. EPA (United States Environmental Protection Agency). 1998b. Science policy council handbook: peer review. Prepared by the Office of Science Policy, Office of Research and Development, Washington, DC. EPA 100-B-98-001. Available from: National Technical

Information Service, Springfield, VA; PB98-140726, and <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 1998c. Announcement of the draft Drinking Water Contaminant Candidate List. Fed. Reg. 63:10273-10287.

U.S. EPA (United States Environmental Protection Agency). 1999. Reregistration eligibility decision. EPTC. EPA 738-R-99-006. Washington, DC: U.S. EPA Office of Prevention, Pesticides and Toxic Substances.

U.S. EPA (United States Environmental Protection Agency). 2000a. Science policy council handbook: peer review. 2nd edition. Prepared by the Office of Science Policy, Office of Research and Development, Washington, DC. EPA 100-B-00-001. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 2000b. Science policy council handbook: risk characterization. Prepared by the Office of Science Policy, Office of Research and Development, Washington, DC. EPA 100-B-00-002. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 2000c. Benchmark dose technical guidance document [external review draft]. EPA/630/R-00/001. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 2000d. Supplemental guidance for conducting for health risk assessment of chemical mixtures. EPA/630/R-00/002. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 2002a. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P-02/0002F. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 2002b. Announcement of preliminary regulatory determinations for priority contaminants on the drinking water. Fed. Reg. 67:38222-38244.

U.S. EPA (United States Environmental Protection Agency). 2003. Announcement of regulatory determinations for priority contaminants on the Drinking Water Contaminant Candidate List. Fed. Reg. 68:42897-42906.

U.S. EPA (United States Environmental Protection Agency). 2004a. TRI Explorer: trends. Search for ethyl dipropylthiocarbamate. Available from: <http://www.epa.gov/triexplorer/trends.htm>.

U.S. EPA (United States Environmental Protection Agency). 2004b. Drinking Water Contaminant Candidate List 2; Notice. Fed. Reg. 69:17406-17415.

U.S. EPA (United States Environmental Protection Agency). 2005. Guidelines for carcinogen risk assessment. Risk Assessment Forum, Washington, DC; EPA/630/P-03/001B. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

USGS (United States Geological Survey). 2001. Summary publications from 51 NAWQA study units sampled in 1991-2001. Available from: <http://water.usgs.gov/pubs/nawqasum>.

Zheng T., S.H. Zahm, K.P. Cantor, et al. 2001. Agricultural exposure to carbamate pesticides and risk of non-Hodgkin lymphoma. J. Occup. Environ. Med. 43:641–649.

APPENDIX A: Abbreviations and Acronyms

atm	atmosphere
BCF	bioaccumulation factor
BMD	benchmark dose
CAS	Chemical Abstracts Registry
CCL	Contaminant Candidate List
ChE	cholinesterase
cm	centimeter
CWS	community water system
EPA	Environmental Protection Agency
EPTC	S-Ethyl dipropylthiocarbamate
FR	Federal Register
Hg	mercury
HRL	health reference level
HSDB	Hazardous Substances Database
kg	kilogram
K_{oc}	organic carbon partitioning coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LOAEL	lowest observed adverse effect level
m	meter
MCLG	Maximum Contaminant Level Goal
mg	milligram
mL	milliliter
mm	millimeter
mM	millimolar
MRL	minimum reporting level
nAChR	nicotinic acetylcholine receptor
NAWQA	National Water Quality Assessment
NCFAP	National Center for Food and Agricultural Policy
NCOD	National Drinking Water Contaminant Occurrence Database
NDWAC	National Drinking Water Advisory Council
NOAEL	no observed adverse effect level
NPDWR	National Primary Drinking Water Regulation
NHL	non-Hodgkin lymphoma
NTNCWS	non-transient non-community water system
OPP	Office of Pesticides Programs
PBPK	physiologically-based pharmacokinetic
ppm	parts per million
PWS	Public Water Systems
QAPP	Quality Assurance Project Plan
RED	Re-registration Eligibility Document
RfD	reference dose
RL	reporting level
RSC	relative source contribution

SDWA	Safe Drinking Water Act
SVOCs	select semivolatile organic compounds
UCMR1	Unregulated Contaminant Monitoring Regulation 1
UF	uncertainty factor
µg	microgram
U.S. EPA	United States Environmental Protection Agency
USGS	United States Geological Service
TRI	Toxic Release Inventory
VOC	volatile organic compound