

Health Effects Support Document for Fonofos

**Health Effects Support Document
for
Fonofos**

U.S. Environmental Protection Agency
Office of Water (4304T)
Health and Ecological Criteria Division
Washington, DC 20460

www.epa.gov/safewater/ccl/pdf/fonofos.pdf

EPA Document Number: 822-R-08-009
January, 2008



Printed on Recycled Paper

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 fonofos. In arriving at the regulatory determination, The Office of Water used the Re-registration Eligibility Decision document (RED) for fonofos 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). 1999a. RED facts: O-Ethyl S-phenylethylphosphonodithiolate (Fonofos). EPA 738-F-99-019. U.S. Environmental Protection Agency, Prevention, Pesticides and Toxic Substances. Available from: <<http://www.epa.gov/REDs/factsheets/0105fact.pdf>>.

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 fonofos identified in a literature search conducted in 2004 and updated in 2007.

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 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 carcinogenicity assessment for fonofos 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 fonofos 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, 2005a), *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988a), (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 fonofos through potable water was developed by the Office of Ground Water and Drinking Water. It is based primarily on first Unregulated Contaminant Monitoring Regulation (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

This document was prepared under the U.S. EPA contract No. 68-C-02-009, Work Assignment No. 2-54 and 3-54 with ICF Consulting, Fairfax, VA. The Lead U.S. EPA Scientist is Amal Mourad Mahfouz, Ph.D., Health and Ecological Criteria Division, Office of Science and Technology, Office of Water.

TABLE OF CONTENTS

FOREWORD	v
ACKNOWLEDGMENT	vii
LIST OF TABLES	xii
LIST OF FIGURES	xiv
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	3-1
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	4-4
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 Fonofos from Food	5-1
5.2 Exposure from Air	5-1
5.2.1 Concentration of Fonofos in Air	5-1
5.2.2 Intake of Fonofos from Air	5-2
5.3 Exposure from Soil	5-2
5.3.1 Concentration of Fonofos in Soil	5-2
5.3.2 Intake of Fonofos from Soil	5-2
5.4 Summary	5-2
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 and Mode of Action	6-3
6.1.3	Weight of Evidence Evaluation for Carcinogenicity	6-3
6.1.4	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	Method of Analysis	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	7-6
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	7-7
8.0	REFERENCES	8-1
	APPENDIX A: Abbreviations and Acronyms	Appendix A-1

LIST OF TABLES

Table 2-1	Chemical and Physical Properties of Fonofos	2-2
Table 4-1	USGS National Synthesis Summary of NAWQA Monitoring of Fonofos in Ambient Surface Water, 1992-2001	4-3
Table 4-2	USGS National Synthesis Summary of NAWQA Monitoring of Fonofos in Ambient Ground Water, 1992-2001	4-4
Table 4-3	Summary UCMR1 Occurrence Statistics for Fonofos in Small Systems	4-6
Table 4-4	Summary UCMR1 Occurrence Statistics for Fonofos in Large Systems	4-7

LIST OF FIGURES

Figure 2-1	Chemical Structure of Fonofos	2-1
------------	-------------------------------------	-----

1.0 EXECUTIVE SUMMARY

The U.S. Environmental Protection Agency (EPA) has prepared this Health Effects Support Document for Fonofos to support a determination regarding whether to regulate fonofos with a National Primary Drinking Water Regulation (NPDWR). The available data on occurrence, exposure, and other risk considerations suggest that, because fonofos does not occur in public water systems at frequencies and levels of public health concern, regulating fonofos 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.

Fonofos is an organophosphate used as a soil insecticide against insect pests on a variety of agricultural crops, vegetables, and fruits. It is a clear, light yellow liquid with an aromatic odor. Production of fonofos was cancelled on May 6, 1998 (63 Federal Register [FR] 25033), with an effective date of November 2, 1998, plus a one-year grace period to permit the exhaustion of existing stocks before the end of 1999.

Fonofos, like many organophosphates, is toxic to humans and animals. Case human poisoning reports and acute oral toxicity studies in animals indicate that oral exposure to fonofos induces clinical signs of toxicity that are typical of cholinesterase inhibitors. Accidental ingestion of fonofos by humans results in signs and symptoms of acute intoxication, including muscarinic, nicotinic, and central nervous system (CNS) manifestations. Acute oral toxicity studies in animals reported clinical signs such as depression, tremors, salivation, diarrhea, and labored breathing.

Organophosphates irreversibly bind to cholinesterase, causing the phosphorylation and deactivation of acetylcholinesterase. The subsequent accumulation of acetylcholine at the neural synapse causes an initial overstimulation, followed by eventual exhaustion and disruption of postsynaptic neural transmission in the central nervous system and peripheral nervous systems. This effect is the critical endpoint of concern for fonofos as noted in the animal studies in hens, rats, and dogs. Consequently, these studies were used to establish the no observed adverse effect level (NOAEL) for this critical endpoint of toxicity and to calculate the reference dose (RfD) for fonofos.

Fonofos is classified as *not likely to be carcinogenic to humans* because there is no evidence of carcinogenic potential in the available long-term feeding studies in rats and mice. The RfD is 0.002 mg/kg/day and is based on a one-year dog feeding study where animals exhibited cholinesterase inhibition. This RfD was used to calculate the drinking water health reference level (HRL) for fonofos at 0.01 mg/L. This value also is protective of children, as the sensitive population of potential concern, because it used an RfD based on **an** NOAEL that is below the level where developmental effects occurred.

Drinking water monitoring of fonofos was conducted under the first Unregulated Contaminant Monitoring Regulation (UCMR1). As a List 2 contaminant, fonofos was scheduled to be monitored by 300 public water systems. Data were received from 295 systems. The data have been analyzed at three levels as follows: level of simple detections (\geq minimum reporting limit, \geq MRL, or ≥ 0.5 $\mu\text{g/L}$), at the level of exceedances of the HRL ($>$ HRL, or >10 $\mu\text{g/L}$), and

at the level of exceedances of one-half the value of the HRL ($>1/2$ HRL, or $>5 \mu\text{g/L}$). No detections of fonofos were found in any samples, and thus there were no exceedances of the HRL or one-half the HRL.

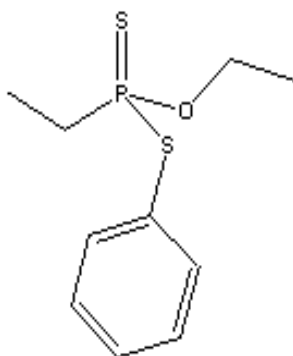
It appears that the general population is not exposed to fonofos through water consumption or use. Therefore, the impact of regulating fonofos concentrations in drinking water on health risk reduction is likely to be small. Regulation of fonofos in public water systems does not appear to present a meaningful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

2.0 IDENTITY: CHEMICAL AND PHYSICAL PROPERTIES

Fonofos is a clear, light yellow liquid with an aromatic odor. It also is flammable and corrosive to steel. The compound exists in two chiral forms which are interconverted in solutions of carbon tetrachloride, cyclohexane, and methanol. The (R)-isomer is more toxic to insects and mice and a stronger inhibitor of cholinesterase than the (S)-isomer (HSDB, 2004).

Commercially, fonofos once was available in granules or as an emulsifiable concentrate with a wide range of percent active ingredient. Commercial fonofos preparations were sold under the Dyfonate trade name (U.S. EPA, 1999a). The manufacturer voluntarily withdrew fonofos from the market, and it is not a commercially available pesticide in the United States (U.S. EPA, 1998c, 1999b).

Figure 2-1 Chemical Structure of Fonofos



Source: Chemfinder (2004)

The chemical structure of fonofos 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 Fonofos

Property	Information
Chemical Abstracts Registry (CAS) No.	944-22-9
EPA Pesticide Chemical Code	041701
Synonyms	difonate; difonatal; dyfonate®; ENT 25; fonophos; stauffer N2790
Registered Trade Name(s)	dyfonate; ENT-25, 796; stauffer -2790; -2790
Chemical Formula	C ₁₀ H ₁₅ OPS ₂
Molecular Weight	246.32
Physical State	light yellow liquid
Boiling Point	130°C
Melting Point	No data
Density (at 20°C)	1.16 at 25°C
Vapor Pressure:	
At 20 °C	No data
At 25°C	3.38x10 ⁻⁴ mm Hg
Partition Coefficients:	
Log K _{ow}	3.94
Log K _{oc}	1.18 - 3.03
Solubility in:	
Water	15.7 mg/L (20°C)
Other Solvents	Acetone, Ethanol, Kerosene, Methyl isobutyl ketone, Xylene
Conversion Factors (at 25 °C, 1 atm)	1 ppm= 10.074 mg/m ³ 1 mg/m ³ = 0.0993 ppm

Source(s): U.S. EPA (1989); HSDB (2004)

3.0 USES AND ENVIRONMENTAL FATE

3.1 Production and Use

Fonofos is produced by reacting thiophenol with O-ethyl ethyl or using phosphonochloridothioate (HSDB, 2004). It was used as a soil insecticide against insect pests (worms, maggots, flies, and crickets) on a variety of agricultural crops, vegetables and fruits (U.S. EPA, 1999a).

Fonofos was scheduled for a re-registration decision in 1999. However, before the review was completed, the registrant requested voluntary cancellation. The cancellation was announced in the Federal Register on May 6, 1998 (63 Federal Register [FR] 25033), with an effective date of November 2, 1998, plus a one-year grace period to permit the exhaustion of existing stocks before the end of 1999 (U.S. EPA, 1999a).

3.2 Environmental Release

Cancellation of the fonofos registration limited its potential to contaminate the environment through agricultural uses.

3.3 Environmental Fate

Fonofos was usually applied directly to the soil. Fonofos is moderately mobile to essentially immobile in soil with Freundlich K_{ads} (adsorption coefficient that most closely fits empirical data) values ranging from 3-13 mL/g (U.S. EPA, 1999a). It has a wide range of organic carbon partitioning coefficient (K_{oc}) values estimated to be 68 ($\log K_{oc} = 1.83$) (Swann et al., 1983) to 5,128 (Rao et al., 1985); these values provide little predictive information on the affinity of fonofos for organic carbon. K_{oc} values ranging from 50 to 150 (equivalent to $\log K_{oc}$ values of 1.7 and 2.18, respectively) are expected to be highly mobile in carbon rich environments, whereas, values greater than 3.7 indicate a compound could be relatively immobile. Laboratory and field leaching studies indicate that fonofos has low to very low mobility in highly carbon rich soils such as silt loam, sandy loam, and organic soil, but is relatively mobile in quartz sand (Lichtenstein et al., 1972; Chapman et al., 1984; Lichtenstein and Liang, 1987). Therefore, it can be assumed from experimental data that fonofos binds to highly carbon rich soils. The adsorption of fonofos increases with decreasing temperature and increasing organic content, particularly humic acid and an associated cation content of soil (Choudhry, 1983). A certain fraction of both fonofos and its oxon metabolite form bound residues in soil and the latter fraction increases with time (Khan and Belanger, 1987).

Fonofos may volatilize from moist soils and exist in the vapor phase as evident from its estimated Henry's Law constant of 7.0×10^{-6} atm-m³/mole, which was based on its vapor pressure and water solubility constants of 3.38×10^{-4} mm Hg (USDA, 2003) and 15.7 mg/L (Yalkowsky and He, 2003), respectively. In a laboratory volatility study, approximately 35% of the fonofos that was applied to soil volatilized after 24 hours; most of the remaining fonofos was extractable from soil (U.S. EPA, 1999a). In another study, volatilization losses of fonofos were almost twice the rate from no-till agricultural soils (6.1%) compared with conventional tilled

soils (4.0%) following application of 530 mg/m², measured over 26 days. Volatilization rates quickly decreased when compared to loss of total fonofos suggesting adsorption to soil (Whang et al., 1993).

Adsorption to highly carbon rich soils may attenuate the volatilization of fonofos. Estimated and experimental soil half-lives of 120 and 150 days (Johnson, 1991) and 121-133 days (U.S. EPA, 1999a) under aerobic and anaerobic conditions, respectively, indicate that biodegradation may be an important environmental fate process in soil. Fonofos' major route of degradation in the soil is biodegradation (Miles et al., 1979). The conditions of the environment and soil will affect the half-life of fonofos in a field as shown by three studies that determined the half-lives of the compound to range from 18-82 days (Racke, 1992; Huckins et al., 1986; Miles et al., 1979).

The major metabolite of biodegradation in fonofos-treated soil is carbon dioxide; dyphonate-oxon, methyl phenyl sulfone, and other unidentified polar products are minor metabolites (Racke and Coats, 1988). The degradates of fonofos, fonofos oxon, and methylphenyl sulfone were very mobile to moderately mobile in soil with Freundlich K_{ads} values of 0.66-3.3 mL/g and 0.05-66 ml/g, respectively (U.S. EPA, 1999a).

Fonofos is only slightly soluble in water (15.7 mg/L) and is therefore not expected to migrate into water rapidly following soil application. Fonofos may adsorb onto organic material in water systems such as suspended solids and sediment as observed in moist high carbon rich soils. Fonofos may volatilize from water surfaces, but the process will be slowed by adsorption to organic material. Fonofos was stable to hydrolysis with a range of half-lives of 128-435 days (U.S. EPA, 1999a). Estimated volatilization half-lives for a model river and model lake are 8 and 66 days, respectively, and from a model pond is 2.3 yrs if adsorption is considered (U.S. EPA, 1987). The hydrolysis half-lives of fonofos in water at 25°C and pH 5, 6, 7 and 8 were 50, 41, 22 and 6.9 weeks, respectively (Chapman and Cole, 1982); however, at pH 5 in the presence of cupric ion, a catalytic accelerator, the half-life was less than 1 day (Chapman and Harris, 1984). Fonofos may undergo photodegradation; in the presence of anthraquinone (electron transfer agent involved in photosynthesis), this process is complete in 1 hr (Ivie and Casida, 1971a). Other compounds that significantly photosensitized dyphonate were anthracene, rotenone and chloroplasts (Ivie and Casida, 1971a,b). Photosensitizers such as rotenone and chloroplasts that occur naturally in some plants may enhance photodegradation of fonofos (Ivie and Casida, 1971b).

Fonofos does not bioaccumulate significantly in fish. For example, the mosquito fish (*Gambusia affinis*) had a bioaccumulation factor (BCF) of less than 2 (Metcalf, 1977). A BCF of 300 for whole fish and 140 for the edible tissues was observed in another study however, 90% depuration was observed within 14 days (U.S. EPA, 1999a). There is evidence that aquatic organisms readily metabolize organophosphates (Freed et al., 1976), and they can be altered chemically (Boethling and Mackay, 2000) once released into the environment to make them less bioavailable.

According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere (Bidleman, 1988) and the vapor pressure of fonofos (3.38×10^{-4} mm Hg at 25°C)

(USDA, 2003), fonofos was determined to exist in both the vapor and particulate phases in the ambient atmosphere. Fonofos in the vapor-phase is degraded by photochemically-produced hydroxyl radical reactions; the half-life for this reaction in air is estimated to be 4.5 hrs, based on calculations from its rate constant of 8.9×10^{-11} cm³/molecule-sec at 25°C (Atkinson, 1988). Fonofos in the particulate phase may be removed from the air by wet or dry deposition. Some photodegradation was observed when fonofos was deposited on silica gel chromatoplates and exposed to sunlight (Ivie and Casida, 1971a). This corresponds to an atmospheric half-life of about 4.5 hours at an atmospheric concentration of $5 \times 10^{+5}$ hydroxyl radicals/cm³ (Meylan and Howard, 1993).

3.4 Summary

Fonofos has been released directly to the environment in the past, based on its historic use as a direct soil insecticide in the U.S. Upon release into the soil, fonofos is expected to have very high to no mobility based on the large range of K_{oc} values of 68 to 5,128 (equivalent to log K_{oc} values of 1.83 and 3.7, respectively); however, fonofos has demonstrated that it binds to highly carbon rich soils and is relatively mobile in soils with quartz content. Fonofos adsorbs onto soils more readily with decreasing temperature and increasing organic content, particularly humic acid and associated cation content. Fonofos is expected to volatilize from moist soil surfaces based upon the estimated Henry's Law constant of 7.0×10^{-6} atm-m³/mole, but adsorption may attenuate volatilization. Estimated soil half-lives of 120 and 150 days under aerobic and anaerobic conditions, respectively, indicate that biodegradation may be an important environmental fate process in soil as opposed to volatilization.

Fonofos in ambient air will exist in both the vapor and particulate phases as expected from the vapor pressure at 25°C of 3.38×10^{-4} mm Hg. The vapor-phase fonofos will undergo reactions with photochemically-produced hydroxyl radicals with an estimated half-life of 4.5 hrs. Wet and dry deposition is expected to remove particulate-phase fonofos from the atmosphere. Fonofos in the water systems may adsorb to carbon-rich particles, suspended solids, and sediment as predicted by the upper-end K_{oc} values.

Volatilization from water surfaces is expected to be an important fate process based upon the estimated Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 8 and 66 days, respectively. As with volatilisation for moist soils, volatilization from water surfaces may be attenuated by adsorption to suspended solids and sediment in the water column. The estimated volatilization half-life from a model pond was 2.3 years when adsorption was considered. The reported hydrolysis half-life range is 110-435 days indicating the relative stability of fonofos to this process.

The available data indicate that fonofos does not bioconcentrate extensively in fish. Although an estimated BCF of 300 was reported for whole fish in one study, the compound was found to be metabolized in tissues at a later time, indicating a lower potential for accumulation. Aquatic organisms readily metabolize organophosphates and upon release into the water they can be altered abiotically; thus, the BCF potential is mitigated by these factors.

4.0 EXPOSURE FROM DRINKING WATER

4.1 Introduction

EPA used data from several sources to evaluate the potential for occurrence of fonofos in Public Water Systems (PWSs). The primary source of drinking water occurrence data for fonofos was the **first** Unregulated Contaminant Monitoring Regulation (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 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 limits (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 fonofos between 1992 and 2001 in representative watersheds and aquifers across the country. Reporting limits varied but did not exceed 0.003 µg/L. Results for surface water and ground water are presented in Tables 4-1 and 4-2. Fonofos was not monitored in bed sediment or biota.

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

Land Use Type	No. of Samples (and No. of Sites)	Detection Frequency	50 th Percentile (Median) Concentration	95 th Percentile Concentration	Maximum Concentration
Agricultural	1,889 (78)	3.05%	<RL	<RL	1.20 µg/L
Mixed	1,020 (47)	1.20%	<RL	<RL	0.014 µg/L
Undeveloped	60 (4)	0.00%	<RL	<RL	<RL
Urban	900 (33)	0.92%	<RL	<RL	0.084 µg/L

Source: Martin et al. (2003)

RL = Reporting limit. Reporting limits for fonofos varied, but did not exceed 0.003 µg/L.

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, fonofos was detected at frequencies ranging from 0.0% of samples in undeveloped land settings to 0.92% in urban land use settings, 1.20% in mixed land use settings, and 3.05% in agricultural land use settings. The 95th percentile concentrations in all land use settings were below the reporting limit. The highest concentration, 1.20 µg/L, occurred in an agricultural land use setting (Martin et al., 2003).

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

Land Use Type	No. of Wells	Detection Frequency	50 th Percentile (Median) Concentration	95 th Percentile Concentration	Maximum Concentration
Agricultural	1,443	0.07%	<RL	<RL	0.009 µg/L
Mixed (Major Aquifer)	2,717	0.07%	<RL	<RL	0.003 µg/L
Undeveloped	67	0.0%	<RL	<RL	<RL
Urban	835	0.0%	<RL	<RL	<RL

Source: Kolpin and Martin (2003)

RL = Reporting limit. Reporting limits for fonofos varied, but did not exceed 0.003 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, fonofos detection frequencies ranged from 0.0% of samples in urban and undeveloped settings to 0.07% in agricultural and mixed land use (major aquifer) settings. The 95th percentile concentrations were less than the reporting limit in all settings. The highest concentration, 0.009 µg/L, occurred 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. Fonofos belonged to the second tier, List 2.

The List 2 Screening Survey was designed for monitoring of contaminants for which analytical methods had been developed but were not widely used. For the Screening Survey, EPA randomly selected 300 public water systems (120 large and 180 small systems) from the pool of systems required to conduct the more extensive UCMR1 List 1 Assessment Monitoring. The UCMR1 List 2 Screening Survey included systems from 48 States, two U.S. Territories, and Tribal lands in one EPA Region.

4.3.2 CCL Health Reference Level

To evaluate the systems and populations exposed to fonofos 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 fonofos is 0.002 mg/kg/day based on plasma and blood cholinesterase inhibition and signs of toxicity in a one-year dog feeding study (Hodge, 1995). Additional detail concerning the RfD can be found in section 6.2. The Agency established the HRL for fonofos using the RfD and a 20 percent relative source contribution as follows:

$$\text{HRL} = [(0.002 \text{ mg/kg/day} \times 70 \text{ kg}) / 2 \text{ L/day}] \times 20\% = 0.014 \text{ mg/L (rounded to 0.010 mg/L or } 10 \text{ } \mu\text{g/L)}$$

4.3.3 Results

As a List 2 contaminant, fonofos was scheduled to be monitored by 300 public water systems, including both large and small systems. These included the following systems in states where fonofos use is particularly intensive: two systems in South Dakota; twelve systems in North Carolina; and four systems in South Carolina. **Data were received from 295 systems.** The data have been analyzed at the level of simple detections (at or above the minimum reporting level, \geq MRL, or $\geq 0.5 \mu\text{g/L}$), exceedances of the health reference level ($>$ HRL, or $> 10 \mu\text{g/L}$), and exceedances of one-half the value of the HRL ($> \frac{1}{2}$ HRL, or $> 5 \mu\text{g/L}$).

Results of the analysis are presented in Tables 4-3 and 4-4. No detections of fonofos 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 Fonofos in Small Systems

Frequency Factors	UCMR Data - Small Systems		National System & Population Numbers ¹
Total Number of Samples	643		--
Percent of Samples with Detections	0.00%		--
99 th Percentile Concentration (all samples)	< MRL		--
Health Reference Level (HRL)	10 µg/L		--
Minimum Reporting Level (MRL)	0.5 µg/L		--
Maximum Concentration of Detections	< MRL		--
99 th Percentile Concentration of Detections	< MRL		--
Median Concentration of Detections	< MRL		--
Total Number of PWSs	178		60,414
Number of GW PWSs	114		56,072
Number of SW PWSs	64		4,342
Total Population	508,136		45,414,590
Population of GW PWSs	275,185		36,224,336
Population of SW PWSs	232,951		9,190,254
Occurrence by System	Number	Percentage	National Extrapolation²
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 > 1/2HRL, or PWSs > HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the 1/2HRL benchmark, or exceeding the HRL benchmark, respectively; Population Served by PWSs with detections, by PWSs >1/2HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the 1/2HRL 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 since the registration for fonofos had been withdrawn.

Table 4-4 Summary UCMR1 Occurrence Statistics for Fonofos in Large Systems

Frequency Factors	UCMR Data - Large Systems	
Total Number of Samples	1,663	
Percent of Samples with Detections	0.00%	
99 th Percentile Concentration (all samples)	< MRL	
Health Reference Level (HRL)	10 µg/L	
Minimum Reporting Level (MRL)	0.5 µg/L	
Maximum Concentration of Detections	< MRL	
99 th Percentile Concentration of Detections	< MRL	
Median Concentration of Detections	< MRL	
Total Number of PWSs	117	
Number of GW PWSs	50	
Number of SW PWSs	67	
Total Population	40,259,344	
Population of GW PWSs	8,000,122	
Population of SW PWSs	32,259,222	
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 > 1/2HRL, or PWSs > HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the 1/2HRL benchmark, or exceeding the HRL benchmark, respectively; Population Served by PWSs with detections, by PWSs >1/2HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the 1/2HRL 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 since the registration for fonofos has been withdrawn.

4.4 Summary

In ambient surface and ground water monitoring by USGS, the 95th percentile concentrations in all land use settings were below the reporting limit. There were no detections in undeveloped settings. In other settings, fonofos was detected more frequently in surface water than in ground water (0.92% vs. 0% of urban samples; 3.05% vs. 0.07% of agriculture samples; and 1.20% vs. 0.07% of samples from mixed land use settings).

For UCMR1, fonofos also was monitored by **295** public water systems. The data have been analyzed at the level of simple detections (at or above the minimum reporting limit, \geq MRL, or ≥ 0.5 $\mu\text{g/L}$), exceedances of the HRL ($>$ HRL, or >10 $\mu\text{g/L}$), and exceedances of one-half the value of the HRL ($>1/2$ HRL, or >5 $\mu\text{g/L}$). No detections of fonofos were found in any samples, and thus there were no exceedances of the HRL or one-half the HRL.

5.0 EXPOSURE FROM MEDIA OTHER THAN WATER

Fonofos registration was cancelled in 1999. Therefore, it is not considered as an environmental contaminant of concern at the present time.

5.1 Exposure from Food

5.1.1 Concentration in Non-Fish Food Items

During the period when fonofos was used (before 1999), it was detected at a low frequency in raw agricultural commodities and adult total diet samples (detection limit of 0.1 mg/kg) (Yess et al., 1991a,b; Schattenberg and Hsu, 1992; Minyard and Roberts, 1991). After its cancellation, a mean value of 0.650 ppm of fonofos was detected in dry, roasted peanuts (n = 1) (U.S. FDA, 2003). Fonofos was detected, but not quantified, in domestic and imported food samples analyzed in fiscal year 1994 (U.S. FDA, 1995). The compound was detected in 2 of 416 carrot samples at 2.0 and >2.0 ppm, respectively; 1 of 137 onion samples at 0.10 ppm; 1 of 769 potato samples at <0.05 ppm, analyzed as part of a Canadian fruit and vegetable commodity survey of 21,982 samples conducted over a 27-month period from 1/1/92 to 3/31/94 (Neidert and Saschenbrecker, 1996).

5.1.2 Concentrations in Fish and Shellfish

Analysis of fish tissue for fonofos did not detect the chemical.

5.1.3 Intake of Fonofos from Food

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

5.2 Exposure from Air

5.2.1 Concentration of Fonofos in Air

Weekly composite air samples were collected from early April through to mid-September 1995 at three paired urban and agricultural sites along the Mississippi River region of the Midwestern United States. The paired sampling sites were located in Mississippi, Iowa, and Minnesota. A background site, removed from dense urban and agricultural areas, was located on the shore of Lake Superior in Michigan. Two urban sites along the Mississippi River (Jackson, Mississippi and Minneapolis, Minnesota), a rural area (Eagle Harbor, Lake Superior, Michigan), and two agricultural areas (Rolling Fork, Mississippi and Princeton, Minnesota) were sampled from early April to mid-September 1995. Fonofos was not detected in weekly composite samples. A 3.75% detection frequency was reported for Iowa City, Iowa (Foreman et al., 2000).

5.2.2 Intake of Fonofos from Air

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

5.3 Exposure from Soil

5.3.1 Concentration of Fonofos in Soil

Fonofos was used as a soil insecticide, which resulted in its direct release to the environment. Fonofos was either not detected (detection limit 0.01 mg/kg) or concentrations were up to 1.10 mg/kg in 28 farms of 6 vegetable growing areas in Southwestern Ontario in 1976 (Miles and Harris, 1978). The sediment of tailwater pits from irrigated corn and sorghum fields in Kansas had a median range concentration of 4.0-48.4 µg/kg with a maximum of 771 µg/kg in one pit (Kadoum and Mock, 1978). The loading and rinse areas of a farm chemical supply in Iowa had a maximum concentration that exceeded 1000 µg/kg in (Hallberg, 1989). In Illinois, 822 soil samples from 49 agrichemical facilities were analyzed. Fonofos was handled in 32 facilities, and 5 soil samples tested positive. Concentrations at four of the positive sites were: 96 µg/kg, median; 238 µg/kg, mean; and 34-4,300 µg/kg, range. Detection limits were 20-60 µg/kg (Krapac et al., 1995). Canadian agricultural soils had fonofos concentrations ranging from not detected to 72 µg/kg dry wt (Webber and Wang, 1995).

5.3.2 Intake of Fonofos 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 0.238 mg fonofos/kg soil and the assumption that infants ingest 0.0001 kg/soil per day (100 mg), exposure of infants to fonofos from soils would be about 24 ng/day. The value for adults would be about 12 ng/day.

$$0.238 \text{ mg/kg soil} \times 0.0001 \text{ kg soil} = 0.0000238 \text{ mg/day (23.8 ng/day)}$$

$$0.238 \text{ mg/kg soil} \times 0.00005 \text{ kg soil} = 0.0000119 \text{ mg/day (11.9 ng/day)}$$

5.4 Summary

Fonofos registration was cancelled in 1999, and it is not considered to be an environmental contaminant of concern at the present time. Residues no longer are present in agricultural produce. Levels once found in ambient air and soils have dissipated over time.

6.0 HAZARD AND DOSE-RESPONSE ASSESSMENT

6.1 Characterization of Hazard

6.1.1 Synthesis and Evaluation of Major Noncancer Effects

Fonofos is toxic in humans and animals. In humans, signs and symptoms of acute intoxication by organophosphorus insecticides like fonofos include muscarinic, nicotinic, and central nervous system (CNS) manifestations (HSDB, 2004). Such symptoms have been documented in several case reports in which fonofos was accidentally ingested. In one reported case of accidental ingestion, a 19-year-old woman who ate pancakes prepared with ingredients containing fonofos (unknown dose level) developed nausea, vomiting, salivation, sweating, and was found to have muscle fasciculation, blood pressure of 64/0 mm Hg, a pulse rate of 46, pinpoint pupils, and profuse salivary and bronchial secretions. She also suffered a cardiorespiratory arrest and developed a pancreatic pseudocyst. A second individual who also ate the contaminated pancakes died (Hayes, 1982). Additionally, there was an outbreak of acute food poisoning, in which nine individuals ate game-birds that showed the presence of nitrogen or phosphorus atoms. This discovery was compatible with the pattern of fonofos toxicity and uses on the hunting estate where the birds were located. The clinical picture showed: high level of the creatine phosphokinase enzyme, general myalgias, vomiting or nausea and visual problems (Gonzalez et al., 1996).

Acute oral toxicity studies in animals indicate that oral exposure to fonofos induces clinical signs of toxicity that are typical of cholinesterase inhibitors. Such clinical signs include depression, tremors, salivation, diarrhea, and labored breathing. Reported values for the oral LD₅₀ for female rats ranged from 3.2 to 7.9 mg/kg, while oral LD₅₀ for male rats ranged from 6.8 to 18.5 mg/kg (Horton 1966a,b; Dean, 1977). Because fonofos is lipophilic, dermal exposure also can result in toxic effects. Reported dermal LD₅₀ values in rabbits ranged from 121 to 147 mg/kg (Horton 1966a,b). Reported dermal LD₅₀ values in rabbits are 25 mg/kg for females and 100 mg/kg for males (Dean, 1977).

Organophosphates irreversibly bind to cholinesterase, causing the phosphorylation and deactivation of acetylcholinesterase. The subsequent accumulation of acetylcholine at the neural synapse causes an initial overstimulation, followed by eventual exhaustion and disruption of postsynaptic neural transmission in the central nervous system and peripheral nervous system. The neurotoxicity of fonofos has been questioned because it is an organophosphate pesticide. Generally, fonofos has been shown to inhibit cholinesterase in hens, rats, and dogs; consequently, studies have established no observed adverse effect levels (NOAELs) and lowest observed adverse effect levels (LOAELs) based on this effect (Banerjee et al., 1968; Cockrell et al., 1966; Hodge, 1995; Horner, 1993a,b; Miller, 1987; Miller et al., 1979; Pavkov and Taylor, 1988; Woodard et al., 1969).

Similar results of cholinesterase inhibition have been shown in chronic exposure studies. Hodge (1995) conducted a study in which groups of 4 beagle dogs/sex/dose were administered fonofos (94.6% a.i.) by capsule at dose levels of 0, 0.2, 1, or 1.75 mg/kg/day in corn oil for a period of at least one year. The NOAEL was determined to be 0.2 mg/kg/day; however, this NOAEL was considered to be a borderline NOAEL/LOAEL because there was minimal plasma

cholinesterase inhibition at 0.2 mg/kg/day which was generally weak and was not consistent. The LOAEL, 1.0 mg/kg/day, was based on plasma and erythrocyte cholinesterase inhibition, increases in alkaline phosphatase levels, clinical signs of toxicity, decreases in selected blood chemistry values, increases in liver weights, and histologic changes in the ileum (Hodge, 1995). (Note: There is a discrepancy in secondary source reporting of the middle dose. U.S. EPA [2001] reports the dose as 0.4 mg/kg/day and California EPA [Cal EPA, 1998] reports it as 1 mg/kg/day. Both references identify the LOAEL as being 1 mg/kg/day, which, therefore, is believed to be the true mid-dose.)

Woodard et al. (1969) also conducted a dog study, in which technical fonofos (99.5% and 99.8-99.9%) was administered via diet to male and female beagle dogs at 0, 16/8.0, 60 and 240 ppm (equivalent to 0, 0.4/0.2, 1.5, 6 mg/kg/day, respectively [Lehman, 1959]) for 2 years. After 14 weeks, the low dose was reduced from 16 ppm to 8 ppm. Four dogs/sex/dose were tested. The cholinesterase NOAEL was 0.2 mg/kg/day, the cholinesterase LOAEL was 0.4 mg/kg/day, the systemic NOAEL was 0.4/0.2 mg/kg/day, and the systemic LOAEL was 1.5 mg/kg/day. However, there were major deficiencies with this study, which included an unusual feeding pattern. There was no information on the frequency of diet preparation, storage, stability of the test chemical in the diet, homogeneity of mixing, or concentration analyses. In the high-dose group, a replacement dog was started 6 weeks into the study and did not appear to be kept an extra 6 weeks at the other end of the study. Electrolytes were not measured for the clinical chemistry analyses, the microscopic examinations were incomplete, and statistical calculations were not conducted.

Technical fonofos (94%) was administered in the diet to groups of 50 Sprague Dawley CD rats/sex/dose for 24 months at levels of 0, 4, 15, or 60 ppm and groups of 20/sex at 120 ppm for 12 months. The mean compound intake (averaged across sexes) was approximately 0.17, 0.65, 2.6, and 6.6 mg/kg/day at 4, 15, 60, or 120 ppm, respectively. The systemic NOAEL was determined to be 2.6 mg/kg/day and the LOAEL was 6.6 mg/kg/day based on decreases in body weight and body weight gain (Pavkov and Taylor, 1988). In the same study, the NOAEL for cholinesterase inhibition was 0.65 mg/kg/day and the LOAEL was 2.6 mg/kg/day based on inhibition of cholinesterase activity (brain, serum and erythrocyte).

Other than cholinesterase inhibition, rats and dogs have shown decreases in body weights and body weight gains after fonofos exposure in chronic exposure (Hodge, 1995; Pavkov and Taylor, 1988; Woodard et al., 1969). Additionally, a common endpoint exhibited by dogs in both studies was increased liver weights (Hodge, 1995; Woodard et al., 1969).

Two developmental studies with rabbits or mice were identified (Minor et al., 1982; Pulsford, 1991; Sauerhoff, 1987). There were no developmental effects observed in rabbits that were administered 0, 0.2, 0.5, or 1.5 mg/kg/day of technical fonofos (94% a.i.) via gavage (Sauerhoff, 1987). Groups of 30 pregnant mice received 10 daily doses of technical fonofos (95.6% a.i.) via gavage (Minor et al., 1982; Pulsford, 1991). The test article was administered in corn oil at concentration of 0, 2, 4, 6, or 8 mg/kg/day from gestation days 6 through 15. Developmental effects included an increase in the incidence of variant sternbrae ossifications at dose levels of 6 mg/kg/day or greater. There also was a slight dilation of the fourth brain ventricle observed in offspring in dose groups that received 4 mg/kg/day or greater. The

NOAEL for developmental effects in this study is 2 mg/kg/day, and the LOAEL is 4 mg/kg/day based on the brain ventricle effect.

Only one reproductive study was identified, in which three generations of rats were exposure to fonofos via diet at concentrations of 0, 10, or 31.6 ppm (equivalent to 0, 0.5, and 1.58 mg/kg/day, respectively, assuming that 1 ppm in the diet is equivalent to 0.05 mg/kg/day [Lehman, 1959]) (Woodard et al., 1968). There were no treatment-related, adverse effects observed at any dose level.

Fonofos did not exhibit mutagenic nor clastogenic characteristics in a bacterial reverse mutation assay (Callander, 1990), chromosomal aberration test (James and Mackay, 1991), or *in vivo* mouse micronucleus test (Jones and Mackay, 1990). Additionally, fonofos, with or without metabolic activation, was not mutagenic in each of five microbial assay systems (the Ames [*Salmonella typhimurium*] test; reverse mutation in *Escherichia coli* strain; mitotic recombination in yeast, *Saccharomyces cerevisiae* D3; and differential toxicity assays in strains of *Escherichia coli* and *Bacillus subtilis*) and in a test for unscheduled DNA synthesis in human fibroblast (WI-38) cells (Simmon, 1979).

6.1.2 Synthesis and Evaluation of Carcinogenic Effects and Mode of Action

Currently, there is no evidence of carcinogenic potential in long term studies in rats (Banerjee et al., 1968; Pavkov and Taylor, 1988) and mice (Sprague and Zwicker, 1987).

6.1.3 Weight of Evidence Evaluation for Carcinogenicity

Fonofos is classified as *not likely to be carcinogenic to humans* (U.S. EPA, 1998c, 2005a). This is because animal evidence failed to demonstrate a carcinogenic effect in at least two well-designed and well-conducted studies in two appropriate animal species.

6.1.4 Potentially Sensitive Populations

The effect of concern for fonofos is cholinesterase (ChE) inhibition and the potential aftermath on brain development in the young. There are no developmental neurotoxicity studies with fonofos available at the present time. Children appear, however, potentially to be a sensitive population based on developmental effects observed in studies with mice. Fonofos treated groups had an increased incidence of variant ossifications of the sternbrae at dose levels of 6 mg/kg/day or greater. Those exposed to 4 mg/kg/day or greater developed a slight dilation of the fourth ventricle of the brain (Minor et al., 1982; Pulsford, 1991). Because the current RfD for fonofos is based on an NOAEL of 0.2 mg/kg/day (Hodge, 1995), which is far below the levels that caused developmental effects, this leads us to believe that children should be adequately protected.

6.2 Reference Dose

6.2.1 Choice of Principle Study and Critical Effect

The principal study for determining the RfD is a chronic toxicity study, in which fonofos (94.6% a.i.) was administered to groups of 4 beagle dogs/sex/dose by capsule at dose levels of 0, 0.2, 0.4 or 1.75 mg/kg/day in corn oil for a period of at least one year. Results showed that at 0.2 mg/kg/day, minimal sporadic plasma cholinesterase inhibition was observed in both sexes (7-13%; 20% only once at 52 weeks in females). At 1.0 mg/kg/day, there were increases in alkaline phosphatase levels (130-194% of control values). There also was inhibition of erythrocyte (51% in males, 53% in females) and plasma cholinesterase (50% in both sexes) activities. At 1.75 mg/kg/day, there were clinical signs of toxicity in one animal, decreases in serum albumin and total protein levels, increases in alkaline phosphatase levels (up to 217%), inhibition of erythrocyte (62% in males, 63% in females), plasma (57% in males, 58% in females) and brain (20% in females) cholinesterase activities and increases in absolute liver weights in males (18.5%). Consequently, the NOAEL was 0.2 mg/kg/day and was considered to be a borderline NOAEL/LOAEL because there was minimal plasma cholinesterase inhibition at 0.2 mg/kg/day that was generally weak and inconsistent. The LOAEL, 1.0 mg/kg/day, was based on plasma and erythrocyte cholinesterase inhibition and increases in alkaline phosphatase levels at 1.0 mg/kg/day and above, and clinical signs of toxicity, decreases in selected blood chemistry values, increases in liver weights and histologic changes in the ileum at 1.75 mg/kg/day (Hodge, 1995).

6.2.2 Method of Analysis

The derivation of the reference dose (RfD) is described below. 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 NOAEL for the most sensitive endpoint in the critical study, which is then divided by a variable uncertainty factor.

$$\text{RfD} = \frac{0.2 \text{ mg/kg/day}}{100} = 0.002 \text{ mg/kg/day}$$

where:

0.2 mg/kg/day = NOAEL derived from a one-year dog feeding study (Hodge, 1995), based on plasma and erythrocyte cholinesterase inhibition, increases in alkaline phosphatase levels, clinical and hematological toxicity, increased liver weight, and histologic changes in the ileum.

100 = Uncertainty factor (UF), which includes a 10-fold UF for intraspecies variability, and another 10-fold UF to account for interspecies extrapolation, as noted by NAS and EPA.

As noted from the above equation, the RfD for fonofos is 0.002 mg/kg/day. The subsection above describes the study used in support of this RfD.

6.3 Carcinogen Assessment

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

6.4 Sensitive Population Considerations

Because fonofos is a ChE inhibitor there is a concern about its potential to cause neurodevelopmental effects. However, the Agency believes that the current RfD is adequately protective of children. Because the current fonofos RfD of 0.002 mg/kg/day is based on an NOAEL of 0.2 mg/kg/day and includes an additional uncertainty factor of 100, this RfD value is 1,000-fold below the NOAEL noted in the Woodward et al. (1986) developmental studies.

6.5 Post Re-registration Health Effects Publications

A literature search was conducted, and no studies were identified. All fonofos pesticide uses have been cancelled.

6.6 CCL Health Reference Level

The CCL health reference level is 0.014 mg/L (0.01 mg/L when rounded to one significant number). EPA derived the HRL using an RfD approach as follows: $HRL = (RfD \times 70 \text{ kg}) / 2 \text{ L/day} \times RSC$, 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.

Therefore, the $HRL = \frac{0.002 \text{ mg/kg/day} \times 70\text{kg}}{2\text{L/day}} \times 0.20 = 0.014 \text{ mg/L}$

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 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, 1998d).

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 2004) and finalized on February 24, 2005 (70FR:9071) (U.S. EPA, 2005b).

EPA proposed Regulatory Determinations for 11 chemicals from CCL2 on May 1, 2007 (72FR 24016) (U.S. EPA, 2007). Determinations for all 11 chemicals were negative based on a lack of national occurrence at levels of health concern. 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. After review of public comments and submitted data the negative determinations for the 11 contaminants have been retained. Each contaminant will be considered in the development of future CCLs if there are changes in health effects and/or occurrence.

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 fonofos 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 all 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 fonofos is presented in Chapter 6 of this document and summarized below in Section 7.2.2 and 7.2.3.

7.2.1 Health Criterion Conclusion

Fonofos (like many organophosphates) is toxic to humans and animals. Case reports and acute oral toxicity studies in animals indicate that oral exposure to fonofos induces clinical signs of toxicity that are typical of cholinesterase inhibitors. In humans, accidental exposure

included signs and symptoms of acute intoxication, nausea, vomiting, salivation, sweating, muscle twitches, decreased blood pressure and pulse rate, pinpoint pupils, profuse salivary and bronchial secretions, cardiorespiratory arrest and even death in one accidentally exposed individual (Hayes, 1982; Gonzalez et al., 1996).

In animals, clinical signs of exposure include tremors, salivation, diarrhea, and labored breathing (U.S. EPA, 2001). Subchronic and chronic exposure studies also indicate that oral administration of fonofos inhibits cholinesterase (Banerjee et al., 1968; Cockrell et al., 1966; Hodge, 1995; Horner, 1993b; Miller, 1987; Miller et al., 1979; Pavkov and Taylor, 1988; Woodard et al., 1969). Cholinesterase inhibition is one of the critical effects associated with the RfD, which was verified by EPA (1991) at 0.002 mg/kg/day. This RfD value was calculated using an NOAEL of 0.2 mg/kg/day (Hodge, 1995) and divided by a 100-fold uncertainty factor to account for inter- and intraspecies differences. The Agency derived an HRL for fonofos using the RfD of 0.002 mg/kg/day and a 20 percent relative source contribution. The Agency derived an HRL of 0.014 mg/L and rounded to 0.01 mg/L (or 10 µg/L).

In accordance with the U.S. EPA 2005 Guidelines for Carcinogen Risk Assessment, fonofos is classifiable as not likely to be carcinogenic to humans based on no evidence of carcinogenic potential in long term studies in rats and mice (Banerjee et al. 1968; Pavkov and Taylor, 1988; Sprague and Zwicker, 1987; U.S. EPA, 2005a). Fonofos is not mutagenic.

7.2.2 Hazard Characterization and Mode of Action Implications

Fonofos (like many organophosphates) is toxic to humans and animals. Case reports and acute oral toxicity studies in animals indicate that oral exposure to fonofos induces clinical signs of toxicity that are typical of cholinesterase inhibitors. Fonofos exposure through accidental ingestion in humans results in signs and symptoms of acute intoxication by organophosphorus insecticides including muscarinic, nicotinic, and central nervous system (CNS) manifestations (HSDB, 2004). In acute oral toxicity studies, animals exhibited such clinical signs include depression, tremors, salivation, diarrhea, and labored breathing.

Organophosphates irreversibly bind to cholinesterase, causing the phosphorylation and deactivation of acetylcholinesterase. The subsequent accumulation of acetylcholine at the neural synapse causes an initial overstimulation, followed by eventual exhaustion and disruption of postsynaptic neural transmission in the central nervous system and peripheral nervous systems. The neurotoxicity of fonofos has been questioned because it is an organophosphate pesticide. Generally, fonofos has been shown to inhibit cholinesterase in hens, rats, and dogs; consequently, studies have established NOAELs and LOAELs based on this effect (Banerjee et al., 1968; Cockrell et al., 1966; Hodge, 1995; Horner, 1993b; Miller, 1987; Miller et al., 1979; Pavkov and Taylor, 1988; Woodard et al., 1969).

7.2.3 Dose-Response Characterization and Implications in Risk Assessment

Cholinesterase inhibition is one of the critical effects associated with the RfD, which was determined to be 0.002 mg/kg/day by EPA. This RfD value was calculated using an NOAEL of 0.2 mg/kg/day (Hodge, 1995), which was divided by a 100-fold uncertainty factor to account for

inter- and intraspecies differences. The HRL for fonofos is 0.014 mg/L and rounded to 0.01 mg/L (or 10 µg/L) and was derived using the RfD (0.002 mg/kg/day) and a 20 percent relative source contribution.

Fonofos is classified as *not likely to be carcinogenic to humans* because there is no evidence of carcinogenic potential in the available long-term feeding studies in rats and mice (Banerjee et al. 1968; Pavkov and Taylor, 1988; Sprague and Zwicker, 1987), and fonofos does not appear to be mutagenic (Callander, 1990; James and Mackay, 1990; James and Mackay, 1991; Simmon, 1979).

EPA also evaluated whether health information is available regarding the potential effects on children and other sensitive populations. Children appear potentially to be a sensitive population based on developmental effects observed in studies with mice. Fonofos treated groups had an increased incidence of variant ossifications of the sternbrae at dose levels of 6 mg/kg/day or greater. Those exposed to 4 mg/kg/day or greater developed a slight dilation of the fourth ventricle of the brain (Minor et al., 1982; Pulsford, 1991). Because the current RfD for fonofos is based on an NOAEL of 0.2 mg/kg/day (Hodge, 1995), which is far below the levels that caused developmental effects, this leads us to believe that children should be adequately protected.

7.3 Occurrence in Public Water Systems

The second criterion for regulating a chemical on the CCL 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 fonofos 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 fonofos, as well those that reported concentrations of fonofos 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

The available data for fonofos production, use and environmental releases all show a downward trend. This is because cancellation of the pesticide was announced in the Federal Register on May 6, 1998 (63 FR 25033), with an effective date of November 2, 1998 plus a one-year grace period to permit the exhaustion of existing stocks (U.S. EPA, 1999a). Consequently, the National Center for Food and Agricultural Policy (NCFAP) estimated that 3.2 million pounds of active ingredient were applied annually to 24 types of crops on 2.6 million acres in 1992, as compared to approximately 0.4 million pounds of active ingredient being applied annually to 19 types of crops on 0.3 million acres in 1997 (NCFAP, 2004). Additionally, there were no detections of fonofos found in any of the 300 public water systems sampled.

Based on the occurrence data, it is unlikely that fonofos 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. Cancellation of the pesticide was announced in the Federal Register on May 6, 1998 (63 FR 25033), with an effective date of November 2, 1998 plus a one-year grace period to permit the exhaustion of existing stocks (U.S. EPA, 1999a).

7.3.2 Monitoring Data

Under the National Water-Quality Assessment (NAWQA) program, US Geological Survey (USGS) monitored fonofos between 1992 and 2001 in representative watersheds and aquifers across the country. Reporting limits varied but did not exceed 0.003 µg/L. In surface water, fonofos was detected at frequencies ranging from 0.0% of the samples from undeveloped land settings to 0.92% in urban land use settings, 1.20% in mixed land use settings, and 3.05% in agricultural land use settings. The 95th percentile concentrations in all land use settings were below the reporting limit. The highest maximum concentration, estimated at 1.20 µg/L, occurred in an agricultural land use setting (Martin et al., 2003).

In ground water, fonofos detection frequencies ranged from 0.0% of the samples from urban and undeveloped settings to 0.07% in agricultural and mixed land use (major aquifer) settings. The 95th percentile concentrations were less than the reporting limit in all settings. The highest concentration, 0.009 µg/L, occurred in an agricultural setting (Kolpin and Martin, 2003).

Additionally, the first Unregulated Contaminant Monitoring Regulation (UCMR1) collected information on the national occurrence of select emerging contaminants in drinking water. There were 2 components to the monitoring. The first monitoring component, Assessment Monitoring, was for the UCMR1 contaminants with well-developed analytical methods (“List 1” contaminants). The second component of the UCMR1, the Screening Survey was for those contaminants with analytical methods that may need to be further refined for use in a large national survey (“List 2” contaminants) (U.S. EPA, 2001). Fonofos was a “List 2” contaminant; consequently, the Screening Survey was designed to be conducted by a total of 300 public water systems (120 large and 180 small systems). List 2 monitoring was conducted between 2001 and 2003.

Data were reported from 295 systems. There were no detections of fonofos in any samples when the data were analyzed at the level of simple detections (\geq minimum reporting limit MRL, or $\geq 0.5 \mu\text{g/L}$), at the level of exceedances of the HRL ($>\text{HRL}$, or $>10 \mu\text{g/L}$), and at the level of exceedances of one-half the value of the HRL ($>1/2\text{HRL}$, or $>5 \mu\text{g/L}$).

7.3.3 Use and Fate Data

Fonofos was used as a soil insecticide (Spencer, 1982; Tomlin, 2002, U.S. EPA, 1999a), and in recent years, the chemical was predominantly used on agricultural crops. Cancellation of the pesticide was announced in the Federal Register on May 6, 1998 (63 FR 25033), with an effective date of November 2, 1998 plus a one-year grace period to permit the exhaustion of existing stocks.

Monitoring data from public water systems are supportive of a decline in the presence of fonofos in the water. In fact, there were no detections of fonofos found in any of the 295 public water systems reporting data. Fonofos is strongly sorptive in soil and insoluble in water; therefore it is more likely to remain in soil overtime.

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 (0.01 mg/L). 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 from all potential sources/media in comparison to the exposure from 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 fonofos in water is rare. There were no detections of fonofos in any samples when the data were analyzed at the level of simple detections ($\geq\text{MRL}$ or $\geq 0.5 \mu\text{g/L}$), at the level of exceedances of the HRL ($>\text{HRL}$ or $>10 \mu\text{g/L}$), and at the level of exceedances of

one-half the value of the HRL ($>1/2$ HRL, or >5 $\mu\text{g/L}$). On the basis of these observations, the impact of regulating fonofos concentrations in drinking water on health risk reduction is likely to be small. Thus, the outcome of the evaluation of the third criterion is negative.

7.4.2 Exposed Population Estimates

Fonofos was scheduled to be monitored by 300 public water systems. There were no detections of fonofos found in any of the samples. Therefore, it appears that the general population is not exposed to fonofos through drinking 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 fonofos in other media, such as food, air, and soil. In situations where fonofos occurs in drinking water, the water is likely to be the major source of exposure. Intake values found in food, air, and soil are very low but the available data are not complete, and therefore, the RSC value should remain the default value of 20% if a lifetime HA were to be developed for noncancer effects.

7.4.4 Sensitive Populations

Children appear potentially to be the most sensitive population based on developmental effects observed in studies with mice. Fonofos treated groups had an increased incidence of variant ossifications of the sternbrae at dose levels of 6 mg/kg/day or greater. Those exposed to 4 mg/kg/day or greater developed a slight dilation of the fourth ventricle of the brain (Minor et al., 1982; Pulsford, 1991). Because the current RfD is based on an NOAEL of 0.2 mg/kg/day (Hodge, 1995), children should be adequately protected. This is because the determined NOAEL from the Hodge study is far below the NOAELs available from the developmental and reproductive studies for fonofos.

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 fonofos, only the finding for the criterion on health effects is positive. Fonofos may have an adverse effect on the health of persons. To date, there have been no detections of fonofos found in any of the samples. Because use of this pesticide was cancelled, it is unlikely that it will be found in water supplies in the future. Therefore, it appears that the general population is not exposed to fonofos through water consumption or use. On the basis of these observations, the impact of regulating fonofos concentrations in drinking water on health risk reduction is likely to be small. Regulation of fonofos in public water systems does not appear to present a meaningful opportunity for health risk reduction.

8.0 REFERENCES

- Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem.* 7:435-462 (as cited in HSDB, 2004).
- Banerjee B.M., D. Howard, and M.W. Woodard. 1968. Dyfonate (-2790) safety evaluation by dietary administration to rats for 105 weeks. Woodard Research Corporation (as cited in U.S. EPA, 1988b).
- Bidleman, T.F. 1988. Atmospheric processes. *Environ. Sci. Technol.* 22:361-367 (as cited in HSDB, 2004).
- Boethling, R.S. and D. Mackay. 2000. *Handbook of Property Estimation Methods for Chemicals*. Boca Raton, FL: Lewis Pub. p. 317 (as cited in HSDB, 2004).
- Cal EPA (California. Environmental Protection Agency). 1998. Summary of toxicological data: fonofos. Revised 3/31/98.
- Callander, R. 1990. Fonofos: An evaluation of mutagenic potential using *S. typhimurium*: Lab Project Number: CTL/P/3153: YV2906. ICI Central Toxicology Laboratory. p. 34 (as cited in U.S. EPA, 2001).
- Chapman, R.A., C.R. Harris, H.J. Svec, et al. 1984. Persistence and mobility of granular insecticides in an organic soil following furrow application for onion maggot (*Delia antiqua*) control. *J. Environ. Sci. Health B*.19:259-270 (as cited in HSDB, 2004).
- Chapman, R.A. and C. Harris. 1984. The chemical-stability of formulations of some hydrolyzable insecticides in aqueous mixtures with hydrolysis catalysts. *J. Environ. Sci. Health B*.19:397-407 (as cited in HSDB, 2004).
- Chapman, R.A. and C.M. Cole. 1982. Observations on the influence of water and soil pH on the persistence of pesticides. *J. Environ. Sci. Health B*.17:487-504 (as cited in HSDB 2004).
- Chemfinder.com. 2004. CambridgeSoft Corporation. Available from: <<http://chemfinder.cambridgesoft.com/result.asp>>.
- Choudhry, G.G. 1983. Humic substances. Part III: Sorptive interactions with environmental chemicals. *Toxicol. Environ. Chem.* 6:127-171 (as cited in HSDB, 2004).
- Cockrell, K.O., M.W. Woodard, and G. Woodard. 1966. -2790 Safety evaluation by repeated oral administration to dogs for 14 weeks and to rats for 13 weeks. Woodard Research Corporation (as cited in U.S. EPA, 1988b).
- Dean, W.P. 1977. Acute oral and dermal toxicity (LD₅₀) in male and female albino rats. Study No. 153-047. International Research and Development Corporation (as cited in U.S. EPA, 1988b).

Foreman, W.T., M.S. Majewski, D.A. Goolsby, et al. 2000. Pesticides in the atmosphere of the Mississippi River Valley, Part II—Air. *Sci. Total Environ.* 248:213-226 (as cited in HSDB, 2004).

Freed, V.H., R. Haque, D. Schmedding, et al. 1976. Physicochemical properties of some organophosphates in relation to their chronic toxicity. *Environ. Health Perspect.* 13:77-81 (as cited in HSDB, 2004).

Gonzalez, P., J. Perez-Rendon Gonzalez, E. Dominguez Alberdi, et al. 1996. Epidemic outbreak of acute food poisoning caused by pesticides [article in Spanish]. *Aten Primaria* 17:467-70. Available from: <<http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~akWcXa:1>>.

Hallberg, G.R. 1989. Pesticide pollution of groundwater in the humid USA. *Agric. Ecosystems Environ.* 26:299-367 (as cited in HSDB, 2004).

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/>>.

Hayes, W.J. 1982. *Pesticides Studied in Man*. Baltimore, MD: Williams and Wilkins. p. 413 (as cited in U.S. EPA, 1988b).

Hodge, M. 1995. Fonofos: 1 year old toxicity study in dogs. Report Number CTL/P/4499, Study Number PD044. Zeneca Central Toxicology Lab (as cited in U.S. EPA, 2001).

Horner, H. 1993a. Fonofos: Acute neurotoxicity study in rats: Lab Project Number: CTL/P/3946: AR5434. Zeneca Central Toxicology Lab. p. 318 (as cited in U.S. EPA, 2001).

Horner, J. 1993b. Fonofos: Subchronic neurotoxicity study in rats: Lab Project Number: CTL/P/3879: PR0889. Zeneca Central Toxicology Lab. p. 381 (as cited in U.S. EPA, 2001).

Horton R.J. 1966a. -2790: Acute oral LD₅₀ - rats; acute dermal toxicity study - rabbits; acute eye irritation - rabbits. Technical Report T-986. Stauffer Chemical Company (as cited in U.S. EPA, 1988b).

Horton R.J. 1966b. -2790: Acute oral LD₅₀ - rats; acute dermal toxicity study - rabbits; acute eye irritation - rabbits. Technical Report T-985. Stauffer Chemical Company (as cited in U.S. EPA, 1988b).

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

Huckins, J.N., J.D. Petty, and D.C. England. 1986. Distribution and impact of trifluralin atrazine and fonofos residues in microcosms simulating a northern prairie wetland USA. *Chemosphere* 15:563-588 (as cited in HSDB, 2004).

Ivie, G.W. and J.E. Casida. 1971a. Sensitized photodecomposition and photosensitizer activity of pesticide chemicals exposed to sunlight on silica gel chromatoplates. *J. Agric. Food Chem.* 19:405-409 (as cited in HSDB, 2004).

Ivie, G.W. and J.E. Casida. 1971b. Photosensitizers for the accelerated degradation of chlorinated cyclodienes and other insecticide chemicals exposed to sunlight on bean leaves. *J. Agric. Food Chem.* 19:410-416 (as cited in HSDB, 2004).

James, N. and J. Mackay. 1991. Fonofos: An evaluation in the *in vitro* cytogenetic assay in human lymphocytes: Lab Project Number: CTL/P/3263: SV0481. ICI Central Toxicology Lab. p.32 (as cited in U.S. EPA, 2001).

Johnson, B. 1991. Setting revised specific numerical values. April 1991. CA Dept. Food Agric., Div. Pest. Manag., Environ. Haz. Prog. EH 91-6. p. 17 (as cited in HSDB, 2004).

Jones, J. and J. Mackay. 1990. Fonofos: An evaluation in the mouse micronucleus test: Lab Project Number: CTL/P/2827: SM0365. ICI Central Tox. Lab. p. 35 (as cited in U.S. EPA, 2001).

Kadoum, A.M. and D.E. Mock. 1978. Herbicide and insecticide residues in tailwater pits: water and pit bottom soil from irrigated corn and sorghum fields. *J. Agric. Food Chem.* 26(1):45-50 (as cited in HSDB, 2004).

Khan, S.U., and A. Belanger. 1987. Formation of bound carbon-14 fonofos residues in an organic soil and a vegetable crop under field conditions. *Chemosphere* 16:167-70 (as cited in HSDB, 2004).

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>>.

Lehman, A.J. 1959. Appraisal of the safety of chemical in foods, drugs, and cosmetics. United States Food and Drug Association (as cited in U.S. EPA, 1988b).

Lichtenstein, E.P., E. Coppola, and D.A. Aikens. 1972. Selective potentiometric titration of calcium with EGTA [ethylene glycol bis(2-aminoethylether)-N,N'-tetraacetic acid] using silver ion indicator. *J. Agric. Food Chem.* 20:831-838 (as cited in HSDB, 2004).

Lichtenstein, E.P. and T.T. Liang. 1987. Effects of simulated rain on the transport of fonofos and carbofuran from agricultural soils in a three-part environmental microcosm. *J. Agric. Food Chem.* 35:173-8 (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/>>.

Metcalf, R.L. 1977. Biological fate and transformation of pollutants in water. *Adv. Environ. Sci. Technol.* 8:195-221 (as cited in HSDB, 2004).

Meylan, W.M., and P.H. Howard. 1993. *Chemosphere* 26:2293-2299 (as cited in HSDB, 2004).

Miles, J.R.W. and C.R. Harris. 1978. Insecticide residues in water, sediment, and fish of the drainage system of the Holland Marsh, Ontario, Canada. *J. Econ. Entomol.* 71:125-31.

Miles, J.R.W., C.M. Tu, and C.R. Harris. 1979. Persistence of eight organophosphorus insecticides in sterile and non-sterile mineral and organic soils. *Bull. Environ. Contam. Toxicol.* 22:312-318 (as cited in HSDB, 2004).

Miller, J. 1987. Neurotoxicity of oral administration of technical Dyfonate to adult hens: T-6237: Final Report. Stauffer Chemical Co. p. 59 (as cited in U.S. EPA, 1988b and 2001).

Miller, J.L., L. Sandvik, G.L. Sprague, et al. 1979. Evaluation of delayed neurotoxic potential of chronically administered Dyfonate in adult hens. *Toxicol. Appl. Pharmacol.* 22:312-318.

Minor, J., J. Downs, G. Zwicker, et al. 1982. A teratology study in CD-1 mice with Dyfonate technical T-10192. Final report. Stauffer Chemical Company (as cited in U.S. EPA, 1988b).

Minyard, J.P. and W.E. Roberts. 1991. State findings on pesticide residues in foods: 1988 and 1989. *J. Assoc. Off. Anal. Chem.* 74:438-452 (as cited in HSDB, 2004).

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

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

Neidert, E. and P.W. Saschenbrecker. 1996. Occurrence of pesticide residues in selected agricultural food commodities available in Canada. *J. AOAC Int.* 79: 549-566 (as cited in HSDB, 2004).

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.

Pavkov, K. and D. Taylor. 1988. Rat chronic toxicity and oncogenicity study with dyfonate. Laboratory Project ID T-11997. ICI Americas Inc. 2053 p. 842a (as cited in U.S. EPA, 2001).

Pulsford, A. 1991. First amendment to a teratology study in cd 1 mice with dyfonate technical (MRID No. 118423): Lab Project No. T-10192, T-10192C. Stauffer Chemical Co. p. 8 (as cited in U.S. EPA, 2001).

Racke, K.D. 1992. Degradation of organophosphorous insecticides in environmental matrices. In: Organophosphates: Chemistry, Fate, and Effects. Chambers J.E. and P.E. Levi (eds). San Diego, CA: Academic Press, Inc. pp. 47-78 (as cited in HSDB, 2004).

Racke, K.D. and J.R. Coats. 1988. Enhanced degradation and the comparative fate of carbamate insecticides in soil. J. Agric. Food Chem. 36:193-9 (as cited in HSDB, 2004).

Rao P.S.C. A.G. Hornsby, and R.E. Jessup. 1985. Indices for ranking the potential for pesticide contamination of groundwater. Soil Crop Sci. Soc. Florida Proc. 44:1-8 (as cited in HSDB, 2004).

Sauerhoff, N. 1987. A teratology study in rabbits with dyfonate technical: T-12630: Volume 1: Final Report: Laboratory Project ID: WIL 27027. Wil Research Laboratories, Inc. p.199 (as cited in U.S. EPA, 2001).

Schattenberg, H.J. and J.-P. Hsu. 1992. Pesticide residue survey of produce from 1989 to 1991. J. Assoc. Off. Anal. Chem. Int. 75: 925-933 (as cited in HSDB, 2004).

Simmon, V.F. 1979. *In vitro* microbiological mutagenicity and unscheduled DNA synthesis studies of eighteen pesticides. National Technical Information Service, Springfield, VA. EPA-600/1-79-041, Research Triangle Park, NC. p.164 (as cited in U.S. EPA, 1988b).

Spencer, E.Y. 1982. Guide to the Chemicals Used in Crop Protection. 7th ed. Publication 1093. Research Institute, Agriculture Canada, Ottawa, Canada: Information Canada. p. 308 (as cited in HSDB, 2004).

Sprague, G. and G. Zwicker. 1987. 18 month dietary oncogenicity study with dyfonate technical in mice: Final Report: T-11995. Stauffer Chemical Co. p.1399 (as cited in U.S. EPA, 2001).

Swann, R.L., D.A. Laskowski, P.J. McCall, et al. 1983. A rapid method for the estimation of the environmental parameters octanol/water partition coefficient, soil sorption constant, water to air ratio and water solubility. *Res. Rev.* 85: 17-28 (as cited in HSDB, 2004).

Tomlin, C.D.S (ed.). 2002. Fonofos (944-22-9). In: *The e-Pesticide Manual, Version 2.2*. Surrey UK, British Crop Protection Council (as cited in HSDB, 2004).

USDA (United States Department of Agriculture). 2003. ARS Pesticide Prop Database. Fonofos. Available from: <http://www.arsusda.gov/acsl/ppdb.html> (as of July 22, 2003).

U.S. EPA (United States Environmental Protection Agency). 1986a. Guidelines for the health risk assessment of chemical mixtures. *Fed. Reg.* 51(185):34014-34025.

U.S. EPA (United States Environmental Protection Agency). 1986b. Guidelines for mutagenicity risk assessment. *Fed. Reg.* 51(185):34006-34012.

U.S. EPA (United States Environmental Protection Agency). 1987. EXAMS II Computer Simulation.

U.S. EPA (United States Environmental Protection Agency). 1988a. 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). 1988b. Fonofos. Health Advisory. Washington, DC: U.S. EPA Office of Drinking Water.

U.S. EPA (United States Environmental Protection Agency). 1989. Fonofos. In: *Drinking Water Health Advisory: Pesticides*. Chelsea, MI: Lewis Publishers, Inc. pp. 443-457.

U.S. EPA (United States Environmental Protection Agency). 1991. Guidelines for developmental toxicity risk assessment. *Fed. Reg.* 56(234):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(206):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(212):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.

U.S. EPA (United States Environmental Protection Agency). 1997. Announcement of the Draft Drinking Water Contaminant Candidate List. Fed. Reg. 62(193):52193-52219.

U.S. EPA (United States Environmental Protection Agency). 1998a. Guidelines for neurotoxicity risk assessment. Fed. Reg. 63(93):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. Notice of receipt of requests to voluntarily cancel certain pesticide registrations. Fed. Reg. 63(52):13249-13254.

U.S. EPA (United States Environmental Protection Agency). 1998d. Announcement of the Draft Drinking Water Contaminant Candidate List. Fed. Reg. 63(40):10273-10287.

U.S. EPA (United States Environmental Protection Agency). 1999a. RED facts: O-Ethyl S-phenylethylphosphonodithiolate (Fonofos). EPA 738-F-99-019. U.S. Environmental Protection Agency, Prevention, Pesticides and Toxic Substances. Available from: <<http://www.epa.gov/REDS/factsheets/0105fact.pdf>>.

U.S. EPA (United States Environmental Protection Agency). 1999b. Dalapon, fluchloralin, et al; various tolerance revocations. Fed. Reg. 64(139):39072-39078.

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). 2001. 030443. Phosphonodithioic acid, ethyl-, O-ethyl. Washington, DC: HED Records Center Series 361 Science Reviews.

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(138):42897-42906.

U.S. EPA (United States Environmental Protection Agency). 2004. Drinking Water Contaminant Candidate List 2; Notice. Fed. Reg. 69(64):17406-17415.

U.S. EPA (United States Environmental Protection Agency). 2005a. 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>>.

U.S. EPA (United States Environmental Protection Agency). 2005b. Drinking Water Contaminant Candidate List 2; Final Notice. Fed. Reg. 70(36):9071-9077.

U.S. EPA(United States Environmental Protection Agency). 2007. Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List - Preliminary Determinations: Proposed Rule Fed. Reg. 72(83):24016-24058.

U.S. FDA (United States Food and Drug Administration). 1995. Pesticide Program. Residue Monitoring - 1995. J. AOAC Int. Vol. 78 (as cited in HSDB, 2004).

U.S. FDA (United States Food and Drug Administration). 2003. FDA Total Diet Study. Available from: <<http://www.cfsan.fda.gov/~acrobat/tds1byps.pdf>>.

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>>.

Webber, M.D. and C. Wang. 1995. Industrial organic compounds in selected Canadian soils. Can. J. Soil. Sci. 75:513-524 (as cited in HSDB, 2004).

Whang, J.M., C.J. Schomburg, D.E. Glotfelty, et al. 1993. Volatilization of fonofos, chlorpyrifos, and atrazine from conventional and no-till surface soils in the field. *J. Environ. Qual.* 22:173-180 (as cited in HSDB, 2004).

Woodard, M.W., C.I. Donoso, and J.P. Gray. 1969. Dyfonate (N 2790) safety evaluation by dietary administration to dogs for 106 weeks. Prepared by Woodard Research Corp., submitted by Stauffer Chemical Co., Richmond, Calif.; CDL: 091638 C (as cited in U.S. EPA, 1988b and 2001).

Woodard, M.W., C.L. Leigh, and G. Woodard. 1968. Dyfonate (-2790) three-generation reproduction study in rats. Woodard Research Corporation (as cited in U.S. EPA, 2001).

Yalkowsky, S.H. and Y. He (eds.). 2003. *Handbook of Aqueous Solubility Data*. Boca Raton, FL: CRC Press p. 692 (as cited in HSDB, 2004).

Yess, N.J., M.G. Houston, and E.L. Gunderson. 1991a. Food and Drug Administration pesticide residue monitoring of foods: 1983-1986. *J. Assoc. Off. Anal. Chem.* 74: 273-80 (as cited in HSDB, 2004).

Yess, N.J., M.G. Houston, and E.L. Gunderson. 1991b. Food and Drug Administration pesticide residue monitoring of foods: 1978-1982. *J. Assoc. Off. Anal. Chem.* 74:265-272 (as cited in HSDB, 2004).

APPENDIX A: Abbreviations and Acronyms

a.i.	active ingredient
atm	atmosphere
BCF	bioaccumulation factor
Cal EPA	California EPA
CAS	Chemical Abstracts Registry
CCL	Contaminant Candidate List
ChE	cholinesterase
cm	centimeter
CNS	central nervous system
CWS	community water system
EPA	Environmental Protection Agency
FR	Federal Register
Hg	mercury
HRL	health reference level
HSDB	Hazardous Substances Database
K_{ads}	adsorption coefficient
kg	kilogram
K_{oc}	organic carbon partitioning coefficient
L	liter
LOAEL	lowest observed adverse effect level
m	meter
MCLG	Maximum Contaminant Level Goal
mg	milligram
mL	milliliter
mm	millimeter
MRL	minimum reporting level
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
NTNCWS	non-transient non-community water system
OPP	Office of Pesticides Programs
ppm	parts per million
PWS	Public Water Systems
QAPP	Quality Assurance Project Plan
RED	Re-registration Eligibility Document
RfD	reference dose
RL	reporting limit
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
USDA	United States Department of Agriculture
U.S. EPA	United States Environmental Protection Agency
U.S. FDA	United States Food and Drug Administration
USGS	United States Geological Service
VOC	volatile organic compound