United States
Environmental Protection
Agency

Health Effects Support Document for Dacthal Degradates: Tetrachloroterephthalic Acid (TPA) and Monomethyl Tetrachloroterephthalic Acid (MTP)

Health Effects Support Document
for
Dacthal Degradates: Tetrachloroterephthalic Acid (TPA) and Monomethyl Tetrachloroterephthalic Acid (MTP)

U.S. Environmental Protection Agency
Office of Water (4304T)
Health and Ecological Criteria Division
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FOREWORD

The Safe Drinking Water Act (SDWA), as amended in 1996, requires the Administrator of the Environmental Protection Agency (EPA) to establish a list of contaminants to aid the Agency in regulatory priority setting for the drinking water program. In addition, the SDWA requires EPA to make regulatory determinations for no fewer than five contaminants by August 2001 and every 5 years thereafter. The following criteria are used to determine whether to regulate a chemical on the Contaminant Candidate List:

- 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 the dacthal degradates tetrachloroterephthalic acid (TPA) and monomethyl tetrachloroterephthalic acid (MTP). To arrive at the regulatory determination, data on toxicokinetics, human exposure, acute and chronic toxicity to animals and humans, epidemiology, and mechanisms of toxicity were evaluated. To avoid wasteful duplication of effort, information from the following risk assessments by the EPA and other government agencies was used in development of this document:

- U.S. EPA (United States Environmental Protection Agency). 1988b. DCPA (Dacthal) Health Advisory. Office of Drinking Water, U.S. Environmental Protection Agency. August, 1988.
- U.S. EPA (United States Environmental Protection Agency). 1994c. Integrated Risk Information System (IRIS): Dacthal. Cincinnati, OH.
- U.S. EPA (United States Environmental Protection Agency). 1998c. Reregistration eligibility decision DCPA. Washington, DC: Office of Prevention, Pesticides, and Toxic Substances (7508C), EPA738-R-98-005. November 1998.

Information from the published risk assessments was supplemented with information from the primary references for key studies and recent studies of the dacthal degradates TPA and MTP. This information was identified by a literature search conducted in 2004.

A reference dose (RfD) is provided as the assessment of long-term toxic effects other than carcinogenicity. RfD determination assumes that thresholds exist for certain toxic effects, such as cellular necrosis, significant body or organ weight changes, blood disorders, etc. It is expressed in terms of milligrams per kilogram per day (mg/kg-day). In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily 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 the dacthal degradates TPA and MTP includes a formal hazard identification and, when available, an estimate of tumorigenic potency. 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 the dacthal degradates TPA and MTP 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, 1996b), *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 Studies* (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, 1995a), *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 dacthal degradates TPA and MTP through potable water was developed by the Office of Ground Water and Drinking Water. It is based primarily on the first round of Unregulated Contaminant Monitoring Regulation (UCMR 1) data collected under the SDWA. The UCMR 1 data are supplemented with ambient water data, as well as data from the States, and published papers on occurrence in drinking water.

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1.0 EXECUTIVE SUMMARY

The U.S. Environmental Protection Agency (EPA) has prepared this Health Effects Support Document for Dacthal (DCPA) Degradates: tetrachloroterephthalic acid (TPA, or the di-acid degradate) and monomethyl tetrachloroterephthalic acid (MTP, or the mono-acid degradate) to assist in determining whether to regulate TPA and MTP with a National Primary Drinking Water Regulation (NPDWR). The available data on occurrence, exposure, and other risk considerations suggest that, because TPA and MTP do not occur in public water systems at frequencies and levels of public health concern, regulating TPA and MTP 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 Contaminant Candidate List (CCL) regulatory determinations.

DCPA (Chemical Abstracts Service Registry Number 1861-32-1) is a chlorinated terephthalic acid ester that is used as a pre-emergence herbicide to control annual grasses and some annual broad-leaved weeds. TPA (Chemical Abstracts Service Registry Number 2136-79-0) is the terminal DCPA degradate. It is extremely mobile and persistent in the environment and will leach to ground water wherever DCPA is used, regardless of soil properties. MTP (Chemical Abstracts Service Registry Number 887-54-7) is a minor DCPA metabolite. No data were found on the physical and chemical properties of TPA or MTP. The properties of both compounds have many similarities common with the parent dacthal. Their aqueous solubility is predicted to be higher than dacthal (0.5 mg/L at 25°C) because one or two of the ester functional groups are replaced by a free acid functional group. For the same reason, the vapor pressures of the acid derivatives are predicted to be lower than those for the parent (2.5×10^{-6} mm Hg at 0.25°C).

Although there are data evaluating the parent compound's (DCPA) exposure and intake, limited information is available to evaluate the amount of TPA or MTP present in the environment and what the intake may be for food, air, or workplace environments. On the basis of estimates derived from the available exposure data, it appears that food is the major source of exposure. Further monitoring data are needed to evaluate TPA or MTP exposure and intake.

TPA and MTP are degradates of DCPA and are present only in areas where DCPA has been used. DCPA and its derivatives have been detected in surface and ground water as well as in public water systems. TPA and MTP combined have been detected at the health reference level (HRL) in no large public water systems and 0.13% of small systems, affecting 0.02% of the population served, approximately equivalent to 113,000 individuals nationwide. DCPA, MTP, and TPA have also been detected in ambient waters in U.S. Geological Survey (USGS) studies. However, in all cases, concentrations have been below the HRL and one-half the HRL (½HRL). Accordingly, TPA and MTP are likely to occur in public water systems but not generally at concentrations of concern.

Both DCPA and TPA do cause adverse health effects in laboratory animals. Currently, no toxicological studies are available to assess the toxicological effects of MTP (the mono-acid degradate). Three studies in rats (30- and 90-day feeding studies and a developmental study) are available for TPA. The effects of exposure were mild (weight loss and diarrhea) and occurred at

doses greater than or equal to 2000 mg/kg/day. No reproductive effects were observed. The critical effects for DCPA, the parent compound, include effects on the lung, liver, kidney, and thyroid in male and female rats in a 2-year chronic bioassay (ISK Biotech, 1993). The available data indicate that the adverse effects associated with TPA are much milder than those for the parent and tend to occur at doses that are lower by approximately an order of magnitude.

No carcinogenicity studies have been performed with either TPA or MTP. Based on a comparison of TPA toxicity with that of its parent, as well as on TPA's lack of mutagenicity, the EPA (U.S. EPA, 2004b) concluded that TPA is unlikely to pose a cancer risk. Klopman et al. (1996) evaluated the carcinogenic potential of TPA on the basis of its chemical and biological properties, as well as by a variety of quantitative structure-activity relationships (QSAR) tools, and determined that it did not present any substantial carcinogenic risk.

There is suggestive evidence that DCPA could be carcinogenic, on the basis of an increased incidence of liver and thyroid tumors in rats and liver tumors in mice. The presence of hexachlorobenzene and dioxin as impurities could have contributed to the cancer risk. However, it is also possible that DCPA itself could have some tumorigenic activity. No liver or thyroid precursor events occurred with TPA at doses of 2000 mg/kg/day for 30 days or 500 mg/kg/day for 90 days, suggesting that it is toxicologically different from DCPA.

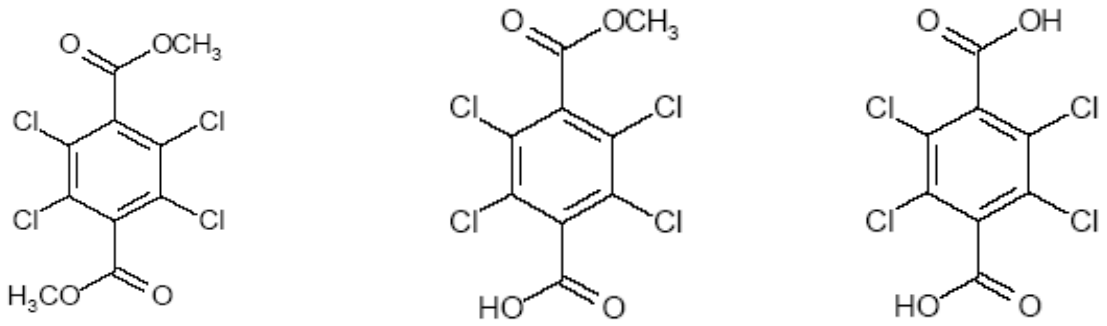
A reference dose (RfD) has not been set for either MTP or TPA because of the incomplete database on these compounds. The EPA (1998c), however, suggests that the RfD for the parent compound DCPA (i.e., 0.01 mg/kg/day) is sufficient to protect against any toxicity from its metabolites.

2.0 IDENTITY: CHEMICAL AND PHYSICAL PROPERTIES

Dacthal (dimethyl tetrachloroterephthalate, DCPA) is a chlorinated terephthalic acid ester that is used as a pre-emergence herbicide to control annual grasses and some annual broad-leaved weeds. Tetrachloroterephthalic acid (TPA, or di-acid) is the terminal DCPA degradate. It is extremely mobile and persistent in the environment and will leach to ground water wherever DCPA is used, regardless of soil properties. Monomethyl tetrachloroterephthalic acid (2,3,5,6-tetrachloro-, monomethyl ester 1,4-benzenedicarboxylic acid; MTP; mono-acid) is a minor DCPA metabolite (U.S. EPA, 1998c).

Currently, all registered DCPA products are in the form of single active-ingredient formulations: emulsifiable concentrate (20.7%), flowable concentrate (54.9%), granules (1.15%-10%), soluble concentrate/liquid (6%), wettable powder (25% and 75%), and formulation intermediates (20.7%, 75%, and 90%). Common impurities in technical DCPA are hexachlorobenzene (HCB) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) (U.S. EPA, 1998c). Recent changes in production have lowered the levels of impurities in commercial Dacthal (U.S. EPA, 2004b).

Figure 2-1 Chemical structure of (a) dacthal (DCPA), (b) tetrachloroterephthalic acid (TPA), and (c) monomethyl tetrachloroterephthalic acid (MTP) (U.S. EPA, 1998c)



(a) DCPA (b) MTP (c) TPA

The chemical structure of DCPA and of its two major metabolites, TPA and MTP, are shown above (Figure 2-1). The physical and chemical properties and other reference information are listed in Table 2-1. No data were found on the physical and chemical properties of TPA or MTP. The properties of both compounds are expected to have many similarities in common with the parent dacthal. Their aqueous solubility is predicted to be higher than dacthal, because one or two of the ester functional groups are replaced by the free acid functional group. For the same reason, the vapor pressures of the acid derivatives are predicted to be lower than those of the parent.

Table 2-1 Chemical and Physical Properties of Dacthal (DCPA), Tetrachloroterephthalic Acid (TPA), and Monomethyl Tetrachloroterephthalic Acid (MTP)

Property	DCPA	TPA	MTP
Chemical Abstracts Service (CAS) Registry no.	1861-32-1	2136-79-0	887-54-7
EPA Pesticide Chemical Code	078701	078702	Not identified
Synonyms	Chlorthal-dimethyl, dimethyl tetrachloroterephthalate, 2,3,5,6-tetrachloroterephthalic acid dimethyl ester	Tetrachloroterephthalic acid; chlorothal; perchloroterephthalic acid	Tetrachloroterephthalic acid, monomethyl-chlorthal monomethyl, monomethyl 2,3,5,6-tetrachloroterephthalate
Registered trade name(s)	Dacthal, DAC 893, Dacthalor	Not identified	Not identified
Chemical formula	$C_{10}H_6C_{14}O_4$	$C_8H_2C_{14}O_4$	$C_9H_4C_{14}O_4$
Molecular weight	331.97	303.9134	317.93916
Physical state	Colorless crystals	Not identified	Not identified
Boiling point	365°C	Not identified	Not identified
Melting point	155°C	Not identified	Not identified
Specific gravity	1.70	Not identified	Not identified
Vapor pressure:			
At 20°C	Not identified	Not identified	Not identified
At 25°C	2.5×10^{-6} mm Hg	Not identified	Not identified
Partition coefficients:			
Log K_{ow}	4.40	Not identified	Not identified
Log K_{oc}	4.28	Not identified	Not identified
Solubility in:			
Water	0.5 mg/L (25°C)	Not identified	Not identified
Dioxan Benzene Toluene Xylene Acetone Carbon tetrachloride	120 mg/L (25°C) 250 mg/L (25°C) 170 mg/L (25°C) 140 mg/L (25°C) 100 mg/L (25°C) 70 mg/L (25°C)	Not identified	Not identified
Conversion factors* (at 25°C, 1 atm)	1 ppm = 13.6 mg/m^3 1 mg/m^3 = 0.07 ppm	1 ppm = 12.4 mg/m^3 1 mg/m^3 = 0.08 ppm	1 ppm = 12.9 mg/m^3 1 mg/m^3 = 0.07 ppm

Source(s): ChemFinder (2004); U.S. EPA/OPP Chemical Database, Hazardous Substances Data Bank (HSDB, 2004)
*Calculated as follows: ppm = mg/m^3 × (24.45/molecular weight); mg/m^3 = ppm × (molecular weight/24.45).

3.0 USES AND ENVIRONMENTAL FATE

3.1 Production and Use

DCPA can be produced by esterification of TPA with methyl alcohol (Spencer, 1982), by chlorination of terephthaloyl chloride and subsequent reaction with methanol (Worthing, 1979), or by chlorination of *p*-xylene followed by conversion of the reaction products to 2,3,5,6-tetrachloroterephthaloyl chloride and finally reaction with methanol to yield the dimethyl ester (Frear, 1976).

DCPA is used as a selective, pre-emergence herbicide to control annual grasses and some annual broad-leaved weeds in turf, ornamentals, strawberries, certain vegetables, beans, and cotton (U.S. EPA, 1998c). Some uses, particularly on vegetable crops, were voluntarily terminated by the registrant in response to EPA concerns regarding the contamination of ground water with DCPA and its di-acid degradate, TPA (U.S. EPA, 2005b). Two products, Dacthal 1.92F and 90% Dimethyl-T, produced by ISK Biotech Corporation, are the starting material from which all other products are formulated. Today there are 66 registered products with dacthal as an active ingredient.

There are three DCPA manufactured products registered to ISK Biosciences Corporation (formerly Fermenta ASC Corporation): a 20.7% formulation intermediate (FI; EPA Reg. No. 50534-187), a 75% FI (EPA Reg. No. 50534-20), and a 90% FI (EPA Reg No. 50534-113). There is also a 98% minimum technical formulation (EPA File Symbol No. 50534-ROA).

3.2 Environmental Release

TPA and MTP are not released directly into the environment. They are byproducts of DCPA, which is a pre-emergence herbicide used for the control of annual grasses and some annual broad-leaved weeds.

3.3 Environmental Fate

DCPA should be immobile in the soil, based on the estimated log K_{oc} range of 3.77-3.81 (Lyman et al., 1990) and the experimental log K_{ow} of 4.40 (Hansch et al., 1995). DCPA has been found to adsorb onto clay and organic matter, and thus it moves minimally in the soil (Choi et al., 1988). Volatilization from moist soil surfaces has been illustrated in published data (Glotfelty and Schomburg, 1989; Glotfelty et al., 1984; Majewski et al., 1991); however, the estimated Henry's law constant of 2.18×10^{-6} atm/m^3/mol is low and the partitioning coefficient is high. Nash and Gish (1989) suggested that DCPA volatilization may be adsorption and diffusion controlled, which would explain the poor predictability of volatilization from vapor pressure. At a temperature of 35°C, volatility accounts for the loss of most of the DCPA applied to treated land.

In a field experiment, the loss of DCPA followed an apparent first-order dissipation rate over 85 days after application, having a calculated soil half-life of 33.8 days. The total estimated loss by volatilization from the soil surface after 21 days was approximately 36%-52%; 26% of

the total loss was attributed to compound degradation (Majewski et al., 1991). A majority of the loss by volatilization occurred after irrigation; when the soil surface was dry, loss was minimal (Majewski et al., 1991). DCPA was sprayed as a 75% wettable powder onto a moist Hatboro silt loam (23% sand, 57% silt, 20% clay, 1.2% organic matter); 2% was lost by volatilization after 34 hours and 50% was lost after 8 days (Glotfelty and Schomburg, 1989; Glotfelty et al., 1984).

DCPA's vapor pressure of 2.5×10^{-6} mm Hg and estimated Henry's law constant of 2.18×10^{-6} atm/m^3/mol at 25°C indicate that it may exist in the vapor phase or particulate phase in the atmosphere. Particulate-phase DCPA will redeposit onto the soil or water systems by wet deposition, whereas vapor-phase DCPA may undergo photodegradation. However, DCPA is reported to be stable to both heat and ultraviolet light (Tomlin, 1994; U.S. EPA, 1998c). In experiments using a thin layer of DCPA on a glass plate that was exposed to sunlight for 2 to 96 hours, a 50% decrease in DCPA was observed after exposure for 5 hours, and >95% decomposition was noted after 48 hours (HSDB, 2004). Degradation products from this study were MTP and TPA after a 2-hour exposure; 1,2,4,5-tetrachlorobenzene was detected after 4 hours of exposure. After 64 hours, more unidentified products were noted (HSDB, 2004). The rate constant for the vapor-phase reaction with photochemically produced hydroxyl radicals of DCPA has been estimated as 4.41×10^{-13} cm^3/molecule-sec at 25°C, and the half-life was estimated to be 36 days when the hydroxyl radical concentration is $5 \times 10^{+5}$ (Meylan and Howard, 1993).

In an early study, DCPA was stable under a sunlamp with a wavelength of 297 nm. After the equivalent of 38.5 days of radiation on a glass bead surface, 95.7% of the applied DCPA was present as parent DCPA. With the same sunlamp and DCPA on silica gel in the presence of a photosensitizer (unnamed), 90.8% remained as DCPA after the equivalent of 168 days of exposure. The primary photoproduct was MTP at 5.2% (U.S. EPA, 1998c). No photodegradation occurred under black light and fluorescent light, which have been shown to be similar to natural sunlight in the range of wavelengths where DCPA absorbs light (U.S. EPA, 1998c). Photodegradation may occur but is not considered a major degradation pathway for DCPA.

Biodegradation is expected to be a major route of DCPA decay; two successive dealkylations of the methyl groups at the ester linkages lead to the formation of MTP and TPA (Choi et al., 1988). Both TPA and MTP were determined to be highly mobile in all soils (U.S. EPA, 1998c); however, the organic carbon coefficient or octanol water coefficients were not reported. Several leaching studies performed for pesticide registration or reregistration of DCPA for U.S. EPA (1998c) illustrated that TPA is very mobile and more mobile in higher pH soils.

The optimal temperature and moisture conditions for the biodegradation of DCPA were investigated in two studies (Choi et al., 1988; Wettasinghe and Tinsley, 1993). At 20-30°C and 0.2 kg of H_2O/kg of soil, a half-life of 11 days was obtained (Choi et al., 1988). Soil with 0.1 kg of H_2O/kg was tested at 10-15°C; the half-life was 105 days (Choi et al., 1988). The half-life values of DCPA for coarse, medium, and fine soil textures were 44, 15, and 32 days, respectively, at optimal temperature and moisture conditions for microbial degradation (Choi et al., 1988). The half-life for DCPA was 16.6 days in soil with a 12.6% water content at 25°C and 289 days with a 9.6% water content at 5°C (Wettasinghe and Tinsley, 1993). The MTP

degradate was quickly hydrolyzed to TPA, which was determined to be persistent because there was no loss of the TPA metabolite over a 300-day period (Wettasinghe and Tinsley, 1993).

Measurable residues of DCPA and its two major degradates could be detected on land that had 5 years of application (cumulative total of 94 lb/acre) and was then untreated for 3 years (Gershon and McClure, 1966). Radiolableled ^{14}C-DCPA was added to soil or ground thatch, which was then tested for parent and degradation products at 0, 1, 2, 4, 8, 12, and 16 weeks. Thatch displayed faster degradation than did soil; in thatch, 55% and 25% dacthal remained at 4 and 16 weeks, respectively, whereas in soil, 96% and 78% dacthal remained at 4 and 16 weeks, respectively (Hurto et al., 1979).

Sandy loam field plots were sprayed with DCPA at 4.0 kg of a.i./ha, with three replicates in May and three replicates in October (Roberts et al., 1978). Soil residues of this herbicide were measured at 0, 38, 63, 101, and 128 days post-application for the May spraying, at which times 100%, 95%, 67%, 62%, and 45% of the DCPA remained, respectively (Roberts et al., 1978). The fall applications were measured after 0, 171, and 263 days, at which times 100%, 55%, and 11% remained, respectively (Roberts et al., 1978). Horowitz et al. (1974) described field plots that were sprayed for 4 years with DCPA (7.5 and 15.0 kg/ha per application) twice a year, in the spring and fall. Soil samples displayed negligible phytotoxic activity following a 5-month period after application, indicating that this herbicide is readily degraded. There was no decrease in nitrification processes in these plots over time.

New York soil treated for 5 years with DCPA at a rate of 19 lb/acre annually had nearly 3-times more actinomycetes in soil as compared to untreated soil (Tweedy et al., 1968). Cultures of actinomycetes from 1 of 20 soil samples were incubated for 96 hours with dacthal (10, 100, 1000, and 10,000 mg/L), which was the sole carbon source. The isolated actinomycetes were able to utilize dacthal as a carbon source. Using ^{36}Cl-labeled DCPA, it was determined that little if any chlorine was liberated from the ring structure during microbial degradation (Tweedy et al., 1968). Anaerobic soil conditions slowed DCPA degradation only slightly, with estimated half-lives of 37-59 days. TPA was also the final degradate under anaerobic conditions (U.S. EPA, 1998c).

DCPA has a water solubility of 0.5 mg/L. Since its estimated log K_{oc} ranges from 3.77 to 3.81 and its experimental log K_{ow} is 4.40 (Hansch et al., 1995), it is expected to bind strongly to particulate matter and sediment in the water column (Swann et al., 1983). DCPA was stable in water for 36 days at pH 5, 7, and 9 (U.S. EPA, 1998c). DCPA was stable to photolysis in unbuffered water. After the equivalent of 191 exposure days (12 hours/day), less than 10% of the parent DCPA had photolyzed (U.S. EPA, 1998c).

DCPA is expected to bioconcentrate in aquatic organisms; an estimated bioconcentration factor (BCF) value of 1300 was obtained using an experimental log K_{ow} of 4.40 (Hansch et al., 1995) and a recommended regression-derived equation (Leiker et al., 1991). DCPA bioaccumulates significantly in bluegill sunfish, having BCFs of 1894 in whole fish, 777 in edible tissue, and 2574 in viscera. Depuration (i.e., removal of impurities from the body) appears to be complete after 14 days. Little metabolism or degradation of DCPA occurs in fish tissues, although there is a detectable amount of demethylation (U.S. EPA, 1998c). DCPA has

been detected in fish at several locations in the United States, providing evidence that dacthal does bioaccumulate (DeVault, 1985; DeVault et al., 1988; Jaffé et al., 1985; Leiker et al., 1991; Miller and Gomes, 1974; Pereira et al., 1994; Saiki and Schmitt, 1986; Schmitt et al., 1985, 1990).

3.4 Summary

DCPA is released directly into the environment during its use as a herbicide. Upon release into the air, DCPA may exist in both the vapor and particulate phases. In the vapor phase, it should react slowly with hydroxyl radicals with an estimated half-life of 36 days. Particulate-phase dacthal may be removed physically from air by wet and dry deposition. DCPA is expected to be almost completely immobile in soil, based on an estimated high K_{oc} of 3900; therefore, it may bind strongly to organic matter. DCPA biodegrades into MTP or TPA by dealkylation of the methyl groups at the ester linkages. Volatilization of dacthal from moist soil surfaces is expected on the basis of its Henry's law constant of 2.18×10^{-6} atm/m^3/mol. During a 21-day period, 36%-52% of the total measured DCPA loss from soil was accounted for by volatilization and 26% by breakdown in soil. Photodegradation on soil surfaces may occur with a half-life of 5 hours; reaction products include MTP, TPA, and 1,2,4,5-tetrachlorobenzene. In water, DCPA binds strongly to particulate matter and sediment in the water column, based on its K_{oc} value. DCPA bioconcentrates in aquatic organisms, having an estimated BCF value of 1300, and has been detected in fish at several locations.

DCPA's two major metabolites, MTP and TPA, are expected to be more water soluble than the parent, because acids are more hydrophilic than methyl esters. Thus, it is expected that these metabolites will be more mobile than the parent compound in soil. Little physical or chemical data, however, have been presented on these compounds. TPA is unusually mobile and persistent in the field. Data suggest that TPA will leach to ground water wherever DCPA is used, regardless of soil properties (U.S. EPA, 1998c). TPA appears to be substantially more persistent than parent DCPA and exhibits low soil/water partitioning. Therefore, substantial quantities of TPA should be available for runoff for a longer period than the parent DCPA. TPA is extremely mobile and can leach to ground water under many different conditions. Although contrary to the data on environmental chemistry and environmental fate, which indicate that parent DCPA would not be very mobile, it appears that under certain conditions both the DCPA parent and the MTP metabolite can also find their way into the ground water. The persistence of TPA in ground water is not known.

4.0 EXPOSURE FROM DRINKING WATER

4.1 Introduction

EPA used data from several sources to evaluate the potential for occurrence of DCPA, MTP, and TPA in public water systems (PWSs). The primary source of drinking water occurrence data was the first Unregulated Contaminant Monitoring Regulation (UCMR 1) program. The Agency also evaluated ambient water quality data from the USGS.

4.2 Ambient Occurrence

4.2.1 Data Sources and Methods

The USGS instituted the National Water Quality Assessment (NAWQA) program in 1991 to examine ambient water quality status and trends in the United States. The NAWQA program 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 the interpretation of natural and anthropogenic factors affecting national water quality. (More detailed information on the design and implementation of the NAWQA program can be found in Leahy and Thompson [1994] and Hamilton et al. [2004].)

Study Unit Monitoring

The NAWQA program conducts monitoring and water quality assessments in significant watersheds and aquifers referred to as "study units." The program'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). The NAWQA program monitors the occurrence of chemicals such as pesticides, nutrients, volatile organic compounds (VOCs), trace elements, and radionuclides, as well as 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 3-5 years, alternating with a period of less intensive research and monitoring that lasted between 5 and 7 years. Thus, all participating study units rotated through intensive assessment in a 10-year cycle (Leahy and Thompson, 1994). The first 10-year cycle was designated 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 (Kolpin and Martin, 2003; Martin et al., 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 goals 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) include only stream data. Sampling data from a single 1-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 analyzed ground water data only from wells; data from springs and agricultural tile drains were not included. The sampling regimen used for wells was different from 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.

The NAWQA program monitored bed sediment and fish tissue at sites considered likely to be contaminated and at 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 Pesticide National Synthesis, USGS also analyzed the occurrence of select semivolatile organic compounds (SVOCs) in bed sediment at sites considered likely to be contaminated and at 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 according to 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

Surface Water and Ground Water

Under the NAWQA program, USGS monitored DCPA (listed as "dacthal") and DCPA mono-acid degradate (listed as "dacthal monoacid") between 1992 and 2001 in representative watersheds and aquifers across the country. Reporting limits varied but did not exceed 0.003 µg/L for DCPA and 0.070 µg/L for the degradate. Results for surface water and ground water are presented in Tables 4-1, 4-2, 4-3, and 4-4.

Table 4-1 USGS National Synthesis Summary of NAWQA Monitoring of DCPA (Dacthal) in Ambient Surface Water, 1992-2001

Land Use Type	No. of Samples (No. of Sites)	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration (µg/L)	Maximum Concentration (µg/L)
Agricultural	1890 (78)	11.46	<RL	0.003	40 (E)
Mixed	1020 (47)	15.4	<RL	0.004	0.179
Undeveloped	60 (4)	6.34	<RL	<RL	0.003
Urban	902 (33)	21.78	<RL	0.007	0.045

Source: Martin et al. (2003)
RL = reporting limit. Reporting limits for dacthal varied but did not exceed 0.003 µg/L.
E = estimated (outside normal calibration limits).
The USGS Pesticide National Synthesis used 1 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 considered the percentage of the year in which detections are found at a typical site in this land use category, and the 95th percentile concentration can be considered a concentration that is not exceeded for 95% of the year at a typical site in this land use category.

In surface water NAWQA samples, DCPA was found at frequencies ranging from 6.34% of samples in undeveloped areas to 11.46% of samples in agricultural settings, 15.4% of samples in mixed land use settings, and 21.78% of samples in urban areas. The higher frequency of occurrence in samples from urban areas may reflect that the majority of DCPA use is on turf (e.g., golf courses and lawns) rather than on agricultural crops. The 95th percentile concentrations were non-detectable in undeveloped settings, 0.003 µg/L in agricultural settings, 0.004 µg/L in mixed land use settings, and 0.007 µg/L in urban land use settings. The highest concentration, estimated at 40 µg/L, was found at an agricultural site (Martin et al., 2003).

Table 4-2 USGS National Synthesis Summary of NAWQA Monitoring of DCPA's Mono-acid Degradate in Ambient Surface Water, 1992-2001

Land Use Type	No. of Samples (and No. of Sites)	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration (µg/L)
Agricultural	1233 (48)	0.18	<RL	<RL	0.430
Mixed	561 (25)	0.00	<RL	<RL	<RL
Undeveloped	19 (1)	0.00	<RL	<RL	<RL
Urban	503 (18)	0.00	<RL	<RL	<RL

Source: Martin et al. (2003)
RL = Reporting limit. Reporting limits for dacthal mono-acid varied but did not exceed 0.070 µg/L.
The USGS Pesticide National Synthesis used 1 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 percentage of the year in which detections are found at a typical site in this land use category, and the 95th percentile concentration can be considered a concentration that is not exceeded for 95% of the year at a typical site in this land use category.

The DCPA mono-acid degradate was not detected in surface water samples in undeveloped areas, mixed land use settings, or urban areas. It was detected in 0.18% of surface water samples in agricultural settings. The 95th percentile concentrations were non-detectable in all land use settings. The maximum surface water concentration in agricultural settings was 0.430 µg/L (Martin et al., 2003).

Table 4-3 USGS National Synthesis Summary of NAWQA Monitoring of DCPA (Dacthal) in Ambient Ground Water, 1992-2001

Land Use Type	No. of Wells	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration (µg/L)
Agricultural	1443	1.18	<RL	<RL	10 (E)
Mixed (major aquifer)	2717	0.44	<RL	<RL	0.004
Undeveloped	67	0.00	<RL	<RL	<RL
Urban	834	0.96	<RL	<RL	0.011

Source: Kolpin and Martin (2003)
RL = reporting limit. Reporting limits for dacthal varied but did not exceed 0.003 µg/L.
E = estimated (outside normal calibration limits).
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 detectable and non-detectable measurements. The method for calculating percentile concentrations varied according to how much of the data was censored at particular levels by the laboratory.

In ground water, DCPA detection frequencies ranged from 0% (no detectable measurement) in undeveloped settings to 0.44% in mixed land use (major aquifer) settings, 0.96% in urban settings, and 1.18% in agricultural settings. The 95th percentile concentrations were non-detectable in all land use settings. The highest ground water concentration, estimated at 10 µg/L, was found at an agricultural site (Kolpin and Martin, 2003).

Table 4-4 USGS National Synthesis Summary of NAWQA Monitoring of DCPA's Mono-acid Degradate in Ambient Ground Water, 1992-2001

Land Use Type	No. of Wells	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration (µg/L)
Agricultural	1217	0.08	<RL	<RL	1.1
Mixed (major aquifer)	1474	0.00	<RL	<RL	<RL
Undeveloped	46	0.00	<RL	<RL	<RL
Urban	619	0.00	<RL	<RL	<RL

Source: Kolpin and Martin (2003)
RL = reporting limit. Reporting limits for dacthal mono-acid varied but did not exceed 0.07 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 detectable and non-detectable measurements. The method for calculating percentile concentrations varied according to how much of the data was censored at particular levels by the laboratory.

The DCPA mono-acid degradate was not detected in ground water samples in undeveloped areas, mixed land use (major aquifer) settings, or urban areas. It was detected in 0.08% of ground water samples in agricultural settings. The 95th percentile concentrations were non-detectable in all land use settings. The maximum ground water concentration in agricultural settings was 1.1 µg/L (Kolpin and Martin, 2003).

Bed Sediments and Biotic Tissue

The NAWQA program also investigated the occurrence of select organochlorine compounds, including DCPA, in bed sediments and biotic tissue. Sampling was conducted at 1310 sites from 1992 to 2001. Method detection limits were 5 µg/kg dry weight in sediment and 5 µg/kg wet weight in tissue. Details on sampling techniques and analytical methods are described by Nowell (2003). Organochlorines can be present in biotic tissue and bed sediments of aquatic systems, even when they are undetectable in the water column, using conventional methods. The occurrence of a toxic compound in stream sediments is pertinent to drinking water concerns because some desorption of the compound from sediments into water, albeit at low rates, may be expected to occur through equilibrium reactions.

Results of monitoring for DCPA in bed sediment and fish tissue are presented in Tables 4-5 and 4-6.

Table 4-5 USGS National Synthesis Summary of NAWQA Monitoring of DCPA in Bed Sediment, 1992-2001

Land Use Type	No. of Sites	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration (µg/kg)
Agricultural	282	1.8	<RL	<RL	25
Mixed	338	0.6	<RL	<RL	33.7
Undeveloped	224	0.5	<RL	<RL	5
Urban	166	0.0	<RL	<RL	<RL

Source: Nowell (2003)
RL = reporting limit. Reporting limits for DCPA varied but did not exceed 5 µg/kg.
For bed sediment, all weights are dry weights.
Most sites were sampled only once. In the case of sites sampled multiple times, USGS used a single sample (the earliest sample with complete data for key analytes) to represent each site in this analysis.
Percentile concentrations were drawn from the range of detectable and non-detectable measurements. The method for calculating percentile concentrations varied according to how much of the data was censored at particular levels by the laboratory.

NAWQA data indicate that DCPA occurred in bed sediment at detection frequencies ranging from 0.0% in urban settings to 0.5% in undeveloped settings, 0.6% in mixed land use settings, and 1.8% in agricultural land use settings. The 95th percentile concentrations in all land use settings were non-detectable. The highest concentration, 33.7 µg/kg dry weight, was found in a mixed land use setting (Nowell, 2003).

Table 4-6 USGS National Synthesis Summary of NAWQA Monitoring of DCPA in Whole Fish, 1992-2001

Land Use Type	No. of Sites	Detection Frequency (%)	50th Percentile (Median) Concentration	95th Percentile Concentration	Maximum Concentration (µg/kg)
Agricultural	204	5.0	<RL	<RL	78
Mixed	207	4.5	<RL	<RL	63
Undeveloped	162	1.9	<RL	<RL	32
Urban	100	2.0	<RL	<RL	8.5

Source: Nowell (2003)
RL = reporting limit. Reporting limits for DCPA varied but did not exceed 5 µg/kg.
For whole fish, all weights are wet weights.
Most sites were sampled only once. In the case of sites sampled multiple times, USGS used a single sample (from the first year of sampling, the earliest sample of the variety of fish most often sampled in that study unit) to represent each site in this analysis.
Percentile concentrations were drawn from the range of detectable and non-detectable measurements. The method for calculating percentile concentrations varied according to how much of the data was censored at particular levels by the laboratory.

In whole fish, DCPA detection frequencies ranged from 1.9% in undeveloped settings to 2.0% in urban settings, 4.5% in mixed settings, and 5.0% in agricultural settings. The 95th percentile concentrations in all settings were non-detectable. The highest concentration, 78 µg/kg wet weight, was found in an agricultural setting (Nowell, 2003).

4.3 Drinking Water Occurrence

4.3.1 Data Sources and Methods

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

List 1 assessment monitoring was performed for a specified number of chemical contaminants for which analytical methods have been developed. With the exception of transient non-community systems and systems that purchase 100% of their water, EPA required all large PWSs (systems serving more than 10,000 people), plus a statistically representative national sample of 800 small PWSs (systems serving 10,000 people or fewer) to conduct assessment monitoring. Approximately one-third of the participating small systems were scheduled to monitor for these contaminants during each calendar year from 2001 through 2003. Large systems could conduct 1 year of monitoring at any time during the 2001-2003 UCMR 1 period. EPA specified a quarterly monitoring schedule for surface water systems and a twice-a-year, 6-month interval monitoring schedule for ground water systems. Although UCMR 1 monitoring was conducted primarily between 2001 and 2003, some results were not collected and reported until as late as 2005.

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

4.3.2 Derivation of the Health Reference Level

To evaluate the systems and populations exposed to TPA and MTP 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 is used for chemicals that cause cancer and exhibit a linear response to dose, and the other applies to noncarcinogens and carcinogens evaluated with a non-linear approach. In the case of the dacthal degradates, the HRL was derived on the basis of noncancer effects, using the RfD for the parent compound, dacthal, as follows. The basis for the

calculation is detailed in Section 8.1.1. The EPA has not established an RfD for either TPA or MTP.

$$HRL = \frac{0.01\ mg/kg \times 70\ kg \times 20\%}{2L}$$

$$HRL = 0.07\ mg/L \text{ or } 70\ \mu g/L$$

where

0.01 mg/kg/day	=	the RfD for dacthal
70 kg	=	adult body weight
2L/day	=	daily adult drinking water intake
20%	=	the percentage of total daily dacthal intake allocated to drinking water

For comparison to the HRL, the total for the dacthal degradates was assumed to represent TPA, the more stable degradate, and the concentration was back-calculated to dacthal equivalents based on the ratio of the molecular weights for both compounds.

4.3.3 Results

As List 1 contaminants, DCPA mono- and di-acid degradates were scheduled to be monitored by all large community water systems (CWSs) and nontransient noncommunity water systems (NTNCWSs) and a statistically representative sample of small CWSs and NTNCWSs. The data presented in this report reflect UCMR 1 analytical samples submitted and quality-checked under the regulation as of July 2005. DCPA degradate data were collected and submitted by 797 (99.6 percent) of the 800 small systems selected for the small system sample and 3071 (99.1 percent) of the 3100 large systems defined as eligible for the UCMR 1 large system census. Because the analytical method approved for UCMR 1 use does not distinguish between the two degradates, they are measured and reported in aggregate. The DCPA degradate data have been analyzed at the level of simple detections (at or above the minimum reporting level, ≥MRL, or ≥1 µg/L), exceedances of the HRL (>HRL or >70 µg/L), and exceedances of one-half the value of the HRL (>½HRL or >35 µg/L). Results of these analyses are presented in Tables 4-7 and 4-8.

Among small systems, DCPA degradate detections (≥MRL or ≥1 µg/L) were reported by 2.13% of PWSs, representing 3.19% of the population served, equivalent to approximately 1.1 million people nationally. All but one of these systems was served by ground water. Only a single small system had a concentration >½HRL (>35 µg/L), and >HRL (>70 µg/L); this ground water system represented 0.13% of small PWSs and 0.02% of the population served by them, equivalent to 113,000 persons nationally.

Among large systems, 158 systems (5.14%) had detections ≥MRL (≥1 µg/L), affecting approximately 11.2 million people (5.05% of the population served). Most of these were ground water systems. A single large system had a concentration >½HRL (>35 µg/L); this surface

water system represented 0.03% of large PWSs and 0.33% of the population served by them (approximately 738,000 people). No large systems had detections at concentrations >HRL (>70 µg/L).

Table 4-7 Summary UCMR 1 Occurrence Statistics for DCPA Mono- and Di-acid Degradates in Small Systems (Based on Statistically Representative National Sample of Small Systems)

Frequency Factors	UCMR Data - Small Systems		National System & Population Numbers[1]
Total Number of Samples	3,272		--
Percent of Samples with Detections	1.16%		--
99th Percentile Concentration (all samples)	1.3 µg/L		--
Health Reference Level (HRL)	70 µg/L		--
Minimum Reporting Level (MRL)	1 µg/L		--
Maximum Concentration of Detections	190 µg/L		--
99th Percentile Concentration of Detections	190 µg/L		--
Median Concentration of Detections	1.8 µg/L		--
Total Number of PWSs	797		60,414
Number of GW PWSs	590		56,072
Number of SW PWSs	207		4,342
Total Population	2,760,570		45,414,590
Population of GW PWSs	1,939,815		36,224,336
Population of SW PWSs	820,755		9,190,254
Occurrence by System	**Number**	**Percentage**	**National Extrapolation[2]**
PWSs with Detections (≥ MRL)	17	2.13%	689
GW PWSs with Detections	16	2.71%	652
SW PWSs with Detections	1	0.48%	37
PWSs > 1/2 HRL	1	0.13%	373
GW PWSs > 1/2 HRL	1	0.17%	373
SW PWSs > 1/2 HRL	0	0.00%	0
PWSs > HRL	1	0.13%	373
GW PWSs > HRL	1	0.17%	373
SW PWSs > HRL	0	0.00%	0
Occurrence by Population Served			
Population Served by PWSs with Detections	87,933	3.19%	1,118,000
Pop. Served by GW PWSs with Detections	86,433	4.46%	1,074,000
Pop. Served by SW PWSs with Detections	1,500	0.18%	44,000
Population Served by PWSs > 1/2 HRL	500	0.02%	113,000
Pop. Served by GW PWSs > 1/2 HRL	500	0.03%	113,000
Pop. Served by SW PWSs > 1/2 HRL	0	0.00%	0
Population Served by PWSs > HRL	500	0.02%	113,000
Pop. Served by GW PWSs > HRL	500	0.03%	113,000
Pop. Served by SW 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 separately for each population-served size stratum and then added to yield the national estimate of GW PWSs with detections (and population served) and SW PWSs with detections (and population served). For intermediate calculations at the level of individual strata, see EPA's UCMR 1 Occurrence Report, entitled "The Analysis of Occurrence Data from the First Unregulated Contaminant Monitoring Regulation (UCMR 1) in Support of Regulatory Determinations for the Second Drinking Water Contaminant Candidate List."

Abbreviations and terms:
PWS = public water systems; GW = ground water; SW = surface water; N/A = not applicable; total number of samples = the total number of samples on record for the contaminant; 99th percentile concentration = the concentration in the 99th percentile sample (out of either all samples or just samples with detections); median concentration of detections = the concentration in the median sample (out of samples with detections); total number of PWSs = the total number of PWSs for which sampling results are available; total population served = the total population served by PWSs for which sampling results are available; PWSs with detections, PWSs >½HRL, or PWSs >HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively; population served by PWSs with detections, by PWSs >½HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively.

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

Table 4-8 Summary UCMR 1 Occurrence Statistics for DCPA Mono- and Di-acid Degradates in Large Systems (Based on the Census of Large Systems)

Frequency Factors	UCMR Data - Large Systems	
Total Number of Samples	30,480	
Percent of Samples with Detections	2.41%	
99th Percentile Concentration (all samples)	2.3 µg/L	
Health Reference Level (HRL)	70 µg/L	
Minimum Reporting Level (MRL)	1 µg/L	
Maximum Concentration of Detections	39 µg/L	
99th Percentile Concentration of Detections	16 µg/L	
Median Concentration of Detections	2.0 µg/L	
Total Number of PWSs	3,071	
Number of GW PWSs	1,384	
Number of SW PWSs	1,687	
Total Population	222,054,801	
Population of GW PWSs	53,434,814	
Population of SW PWSs	168,619,987	
Occurrence by System	**Number**	**Percentage**
PWSs with Detections (≥ MRL)	158	5.14%
GW PWSs with Detections	107	7.73%
SW PWSs with Detections	51	3.02%
PWSs > 1/2 HRL	1	0.03%
GW PWSs > 1/2 HRL	0	0.00%
SW PWSs > 1/2 HRL	1	0.06%
PWSs > HRL	0	0.00%
GW PWSs > HRL	0	0.00%
SW PWSs > HRL	0	0.00%
Occurrence by Population Served		
Population Served by PWSs with Detections	11,220,836	5.05%
Pop. Served by GW PWSs with Detections	6,034,379	11.29%
Pop. Served by SW PWSs with Detections	5,186,457	3.08%
Population Served by PWSs > 1/2 HRL	738,337	0.33%
Pop. Served by GW PWSs > 1/2 HRL	0	0.00%
Pop. Served by SW PWSs > 1/2 HRL	738,337	0.44%
Population Served by PWSs > HRL	0	0.00%
Pop. Served by GW PWSs > HRL	0	0.00%
Pop. Served by SW PWSs > HRL	0	0.00%

Abbreviations and terms:
PWS = public water systems; GW = ground water; SW = surface water; N/A = not applicable; total number of samples = the total number of samples on record for the contaminant; 99th percentile concentration = the concentration in the 99th percentile sample (out of either all samples or just samples with detections); median concentration of detections = the concentration in the median sample (out of samples with detections); total number of PWSs = the total number of PWSs for which sampling results are available; total population served = the total population served by PWSs for which sampling results are available; PWSs with detections, PWSs > ½HRL, or PWSs > HRL = PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively; population served by PWSs with detections, by PWSs >½HRL, or by PWSs >HRL = population served by PWSs with at least one sampling result greater than or equal to the MRL, exceeding the ½HRL benchmark, or exceeding the HRL benchmark, respectively.
Notes:
Large systems are those that serve more than 10,000 persons.
Only results at or above the MRL were reported as detections. Concentrations below the MRL are considered non-detects.
The HRL used in this analysis is a draft value for working review only.

Regional Patterns

The geographic distribution for systems with at least one sample that exceeded the MRL (Figures 4-1 and 4-2) was examined to evaluate whether there was a regional pattern to the occurrence of the dacthal degradates in public drinking water supplies.

Figure 4-1 Geographic Distribution of DCPA Degradates in UCMR 1 Monitoring -- States With At Least One Detection At or Above the MRL (1 µg/L)

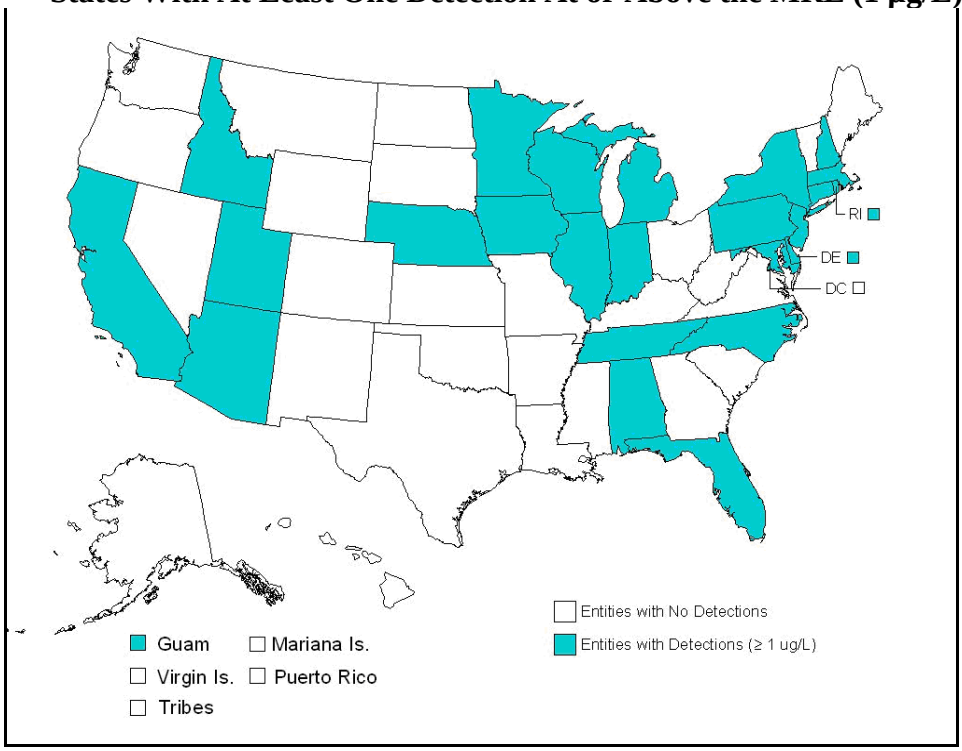
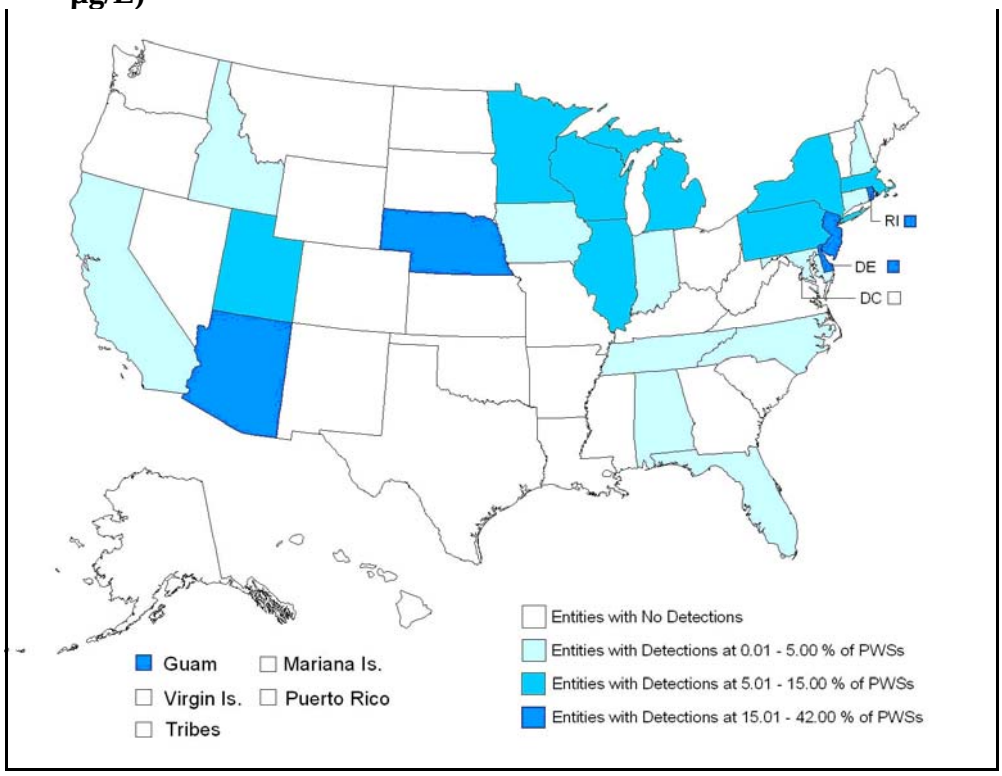


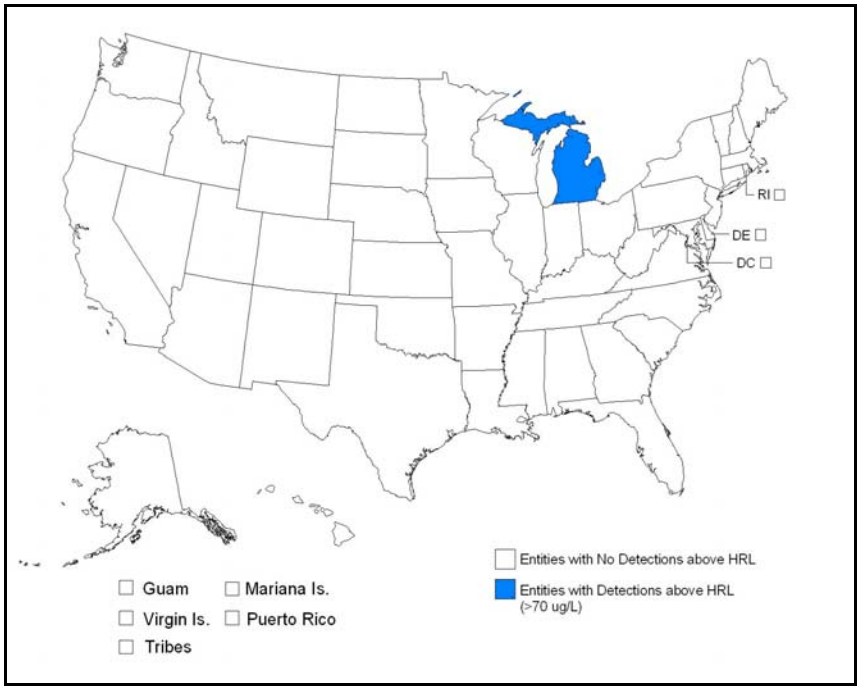
Figure 4-2 Geographic Distribution of DCPA Degradates in UCMR 1 Monitoring -- Percentage of PWSs With At Least One Detection At or Above the MRL (1 µg/L)



Note: This map depicts UCMR 1 results from both small systems and large systems. The statistical selection of UCMR 1 small systems was designed to be representative at the national level, but not at the state level. Therefore, this map should only be considered a rough approximation of state-level patterns of contaminant occurrence.

The dacthal degradates were detected in various states across the country. The highest concentrations of detections (15.1%-42% of PWSs) were seen in Arizona, Delaware, Nebraska, New Jersey, Rhode Island, and Guam. There appeared to be a cluster of states with detections that ranged from 5.01% to 15% of samples in the Northeast and the states surrounding the Great Lakes. The only state with a detection that exceeded the HRL was Michigan (Figure 4-2).

Figure 4-3 Geographic Distribution of DCPA Degradates in UCMR 1 Monitoring - States with at Least One Detection Above the HRL (>70 µg/L)



4.4 Summary

TPA and MTP are degradates of DCPA and are present only in areas where DCPA has been used. DCPA and/or its derivatives have been detected in ambient surface and ground water (DCPA and MTP), as well as in public water systems (MTP and TPA combined). TPA and MTP combined were not detected at the HRL in any large systems. They were found at levels exceeding the HRL in 0.13% of small systems, affecting 0.02% of the population served by small systems, approximately equivalent to 113,000 individuals nationwide. MTP was detected at a maximum concentration of 0.430 µg/L (median and 95th percentile concentrations were below the reporting level) in ambient surface waters near agricultural use but was not detected in ambient surface waters near mixed, undeveloped, or urban areas. MTP was detected at a maximum concentration of 1.1 µg/L (median and 95th percentile concentrations were below the reporting level) in ambient ground waters near agricultural use but was not detected in ambient surface waters near mixed, undeveloped, or urban areas. DCPA also has been measured in sediment, but there are no data available on TPA or MTP levels in sediment. TPA and MTP, however, have been determined to be more mobile in soil than the parent compound, DCPA.

5.0 EXPOSURE FROM MEDIA OTHER THAN WATER

5.1 Exposure From Food

5.1.1 Concentration in Non-Fish Food Items

Data were not available on the degradates MTP or TPA in foods. Most of the information is provided for DCPA or total DCPA, which combines degradate and parent compound data.

Plant residue analyses were submitted to the Office of Pesticides Programs (OPP) for reregistration of dacthal (DCPA) (U.S. EPA, 1998c). The analysis had limits of detection (LOD) of 0.01 parts per million (ppm) each for DCPA, MTP, and TPA. The plants analyzed were potatoes (including processed commodities), sweet potatoes, broccoli, celery, cucumbers, green and bulb onions, strawberries, sweet and bell peppers, cantaloupes, tomatoes (including processed commodities), summer squash, and processed commodities of beans and cottonseed (U.S. EPA, 1998c). A second, similar method was used to detect DCPA, MTP, and TPA in milk and beef fat (U.S. EPA, 1998c). Use of DCPA on beans, peppers, and squash has been terminated (U.S. EPA, 2005b), removing the residue concern for these crops in the future.

In 1963, a cattle feeding study was performed in which DCPA was fed to cattle at levels of 20 and 200 ppm. At the 20-ppm feeding level, combined residues of DCPA, MTP, and TPA were non-detectable in milk and fat. Muscle, liver, and kidney were not analyzed (U.S. EPA, 1998c). Further studies performed in a goat metabolism study indicated that a cattle feeding study is needed.

In 1973, poultry feeding studies were conducted. Chickens were fed 4- and 40-ppm DCPA for 30 days, and residue analyses for DCPA, MTP, and TPA were conducted. In hens fed 4 ppm, all residues were non-detectable in edible tissues, but at the 40-ppm level, detectable combined residues were observed only in fat at 0.14 ppm. Combined residues in egg yolk at the 4-ppm feeding level were 0.07 ppm on day 21 of the study. The animals given 40 ppm had 0.26 ppm in egg yolk residues after 21 days.

The values in food products in Table 5-1 are anticipated residues of DCPA, MTP, and TPA, not actual monitoring data. The data represented in Table 5-1 were derived from actual studies or calculated estimations of residues in food products from registrant field trials and processing studies, from monitoring data supplied by the U.S. Food and Drug Administration (FDA), and from survey data supplied by the U.S. Department of Agriculture (USDA) (U.S. EPA, 1998c). The limit of detection was 0.1 ppm for DCPA, MTP, and TPA for plant commodities analyzed by a gas chromatography/electron capture (GC/EC) method. Another GC/EC method, similar to those submitted for plants, is available for determining DCPA, MTP, and TPA in milk and beef fat; the LOD was 0.01 ppm (U.S. EPA, 1998c).

Table 5-1 Anticipated Residues of DCPA, Its Metabolites, and HCB From Use of DCPA on Food/Feed Crops as Modified From the Re-registration Eligibility Decision Document on DCPA[a]

Food Name	Residue Data Source DCPA	Anticipated Residues (ppm) DCPA, MTP, and TPA
Peppers, other	Field trials	0.17
Chili peppers	Field trials	0.17
Pimentos	Field trials	0.17
Tomatoes, whole	Field trials	0.11
Tomatoes, juice	Processing study	0.11
Tomatoes, puree	Processing study	0.15
Tomatoes, paste	Processing study	0.396
Tomatoes, catsup	Processing study	0.12
Broccoli	Field trial	0.1
Brussels sprouts	Field trials	0.04
Cauliflower	Brussels sprouts data	0.04
Cabbage, green/red	Field trials	0.35
Collards	Kale data	0.5
Kale	Field trials	0.5
Kohlrabi	Brussels sprouts data	0.04
Lettuce, leafy varieties[a,b]	FDA monitoring	0.65
Lettuce, unspecified[a,b]	FDA monitoring	0.65
Mustard greens[a]	Field trials	1
Turnip' tops	Field trials	0.775
Cress, upland	Field trials	0.36
Lettuce–head varieties[a,b]	FDA monitoring	0.65
Garlic	Onion data	0.02
Leeks	Field trials	0.57
Onions–dry bulb (cipollini)	Field trials	0.02
Potatoes, whole	Field trials	0.25
Potatoes, peeled	Field trials	0.25
Radishes, roots	Field trials	0.07
Radishes, tops	Field trials	9.12
Rutabagas, roots[b]	Tolerance	2
Shallots	Field trials	0.57
Sweet potatoes (including yams)	Field trials	0.64
Turnip, roots	Field trials	0.275
Corn, pop[b]	Tolerance	0.05
Beans–succulent, lima	Field trials	0.26
Beans, dry	Field trials	0.09
Black-eyed peas, dry	Field trials	0.36
Onions, green	Field trials	0.57
Cottonseed, oil Cottonseed, meal	Field trial	0.02
Soybeans–mature, seeds dry[b]	Tolerance	2
Milk, nonfat solids	Goat metabolism study	0.0000006
Milk, fat solids		
Milk sugar (lactose)		

Food Name	Residue Data Source DCPA	Anticipated Residues (ppm) DCPA, MTP, and TPA
Beef, goat, sheep, pork–meat byproducts	Goat metabolism study	0.0000011[c]
Beef, goat, sheep, pork (organ meats)–other		0.0000017
Beef, dried		0.0000006
Beef, goat, sheep, pork (boneless)–fat		0.0000011
Beef, goat, sheep, pork (organ meats)–kidney		0.0000057
Beef, goat, sheep, pork (organ meats)–liver		0.0000017
Beef, goat, sheep, pork (boneless)–lean (without removable fat)		0
Turkey, other poultry, chicken–by-products	Poultry feeding study	0.0000230[c]
Turkey, other poultry, chicken–giblets (liver)		0
Turkey, chicken–flesh (without skin, without bones)		0
Turkey, other poultry, chicken–flesh (with skin, without bones)		0.0000230[c]
Turkey, unspecified		0.0000230[c]
Eggs, whole (36.55 yolk)		0.0000011
Eggs, white only		0.0000009
Eggs, yolk only		0.0000138

Source: U.S. EPA (1998c)
a The residue values for these crops are based on FDA monitoring or USDA survey data and were not adjusted for the percentage of crop treated in the Dietary Risk Evaluation System analysis, the system EPA's OPP uses to calculate carcinogenic and chronic, noncarcinogenic risk of DCPA for all raw agricultural commodities in which DCPA tolerances have been established.
b There are no established uses on this crop; however, the registrant has expressed an interest in retaining a tolerance to cover potential residues from rotation of this crop into fields that have been previously treated with DCPA. The tolerance on this crop and anticipated residues will be reassessed in conjunction with review of rotational crop studies and registrant proposals for inadvertent residue tolerance and rotational crop restrictions on DCPA labels. Other crops of concern are sweet corn; corn grain, endosperm; corn grain, bran; corn sugar; corn grain, oil; soybeans, oil; soybeans, unspecified; and soybean, flour.
c The anticipated residue on this food is assumed to be the same as for fat.

Produce samples from 1989-1990 were tested for the presence of DCPA (n = 6970; approximately 80% domestic, 20% foreign); the detection limit was 0.125 ppm, and 50 samples were positive for DCPA. DCPA was detected in broccoli samples (n = 203; 2.5% incidence), greens (n = 153; 1.3%), lettuce (1.3%), onions (1.2%), and turnips (n = 44; 9.0%) (Schattenberg and Hsu, 1992). In the 1982-1984 Market Basket Study, DCPA residues were found in 2% of the total samples (n > 3000) (Gunderson, 1988). In the 1980-1982 Market Basket Study (27 locations) for adult diets, DCPA was detected in 9 samples of leafy vegetables (trace = 0.057 ppm), 12 samples of root vegetables (trace = 0.004 ppm), and 2 samples of garden fruits (trace = 0.002 ppm) (Gartrell et al., 1986a). Market Basket studies for 1974-1980 for adult diets detected DCPA in 11 samples of leafy vegetables (trace = 0.017 ppm), 7 samples of root vegetables (trace = 0.002 ppm), 9 samples of garden fruits (trace = 0.008 ppm), and 2 samples of oils/fats (0.002-0.004 ppm) (Gartrell et al., 1985a, 1985b; Johnson et al., 1977, 1981, 1984). Detection limits

were not specified in secondary literature for most of the studies cited in this paragraph. In the 1991-2001 Total Dietary Study, dacthal residues were detected in a variety of produce. The most frequent detections were found in leafy vegetables (spinach and collard greens) and root vegetables (radish and turnip). Green beans had a low incidence of detection but relatively high mean concentrations, whereas black olives had a high frequency of detection but a low average residue level (U.S. FDA, 2003).

5.1.2 Concentrations in Fish and Shellfish

Data were not available on the degradates MTP or TPA; all data were for DCPA or DCPA and degradates combined as total DCPA residues.

Tissue samples of catfish were collected along the Mississippi River and several major tributaries during July and August 1987 and analyzed for DCPA; catfish from Winfield, Missouri, to Chester, Illinois, had DCPA residues at concentrations ranging from 0 to 9 ng/g wet weight (Leiker et al., 1991). In another study, mature striped bass were taken from the Sacramento and the San Joaquin Rivers and analyzed for DCPA in May 1992 (n = 7); the levels were <0.1-8.7 ng/g wet weight (Pereira et al., 1994). Bluegill and carp were collected from the San Joaquin River, Merced River, and Salt Slough in California. Bluegills from four sites had DCPA concentrations of 0-0.01 mg/kg wet weight, and carp were 0-0.054 mg/kg wet weight (detection limit = 0.004 mg/kg) (Saiki and Schmitt, 1986). DCPA was analyzed in samples of spotted sea trout, perch, speckled trout, mullet, red drum, and menhaden collected from the Rio Grande River in Texas from 1971 to 1972, which had residue levels of 0-555 parts per billion (ppb) (Miller and Gomes, 1974). Great Lakes harbors and tributaries were tested for DCPA in a composite sampling of indigenous fish; 73% had detectable DCPA levels that ranged from 0.002 to 0.12 mg/kg (DeVault, 1985).

DCPA was detected in fish that were sampled via the National Contaminant Biomonitoring Program, in which composite fish samples are analyzed from 112 stations in major rivers and the Great Lakes in the United States. The percentages of samples with detections were as follows: 1978-1979, 34.3%; 1980-1981, 28%; and 1984, 45.5% (Schmitt et al., 1990). Between 1978 and 1979, DCPA measures were a maximum wet weight of 1.22 µg/g and 18.8 µg/g lipid weight; in 1980-1981, maximum wet weight was 0.40 µg/g wet weight and 6.1 µg/g lipid weight (Schmitt et al., 1985). Carp from major tributaries and embayments of Lake Superior and Lake Huron were analyzed for the presence of DCPA; the total composite concentration range was 2.2-17 ng/g fish fat (Jaffé et al., 1985). Carp from the mouths of tributaries to Lake Ontario and the Niagara River were analyzed for the presence of DCPA; the total composite concentration range was 93-2300 ng/g fish fat (Jaffé and Hites, 1986). Fall-run coho salmon from each of the Great Lakes were analyzed for DCPA, and the concentrations ranged from not detected at five sites to <0.05 µg/g at nine sites (DeVault et al., 1988).

5.1.3 Intake of DCPA and DCPA Degradates (TPA and MTP) From Food

Data were not available on the intake of MTP or TPA from the diet; data were provided as DCPA or total DCPA, which combined degradate and parent compound.

Data are available from several market basket surveys in which DCPA or DCPA and degradates in the diet were examined. In market basket surveys, foods are purchased from local suppliers and prepared as served. They are then analyzed for a variety of nutrients, pesticides, and/or xenobiotic compounds. Data are presented as either intakes for age/sex populations groupings and/or concentration in selected food groupings. The data for population groupings are summarized in Table 5-2.

Table 5-2 Estimates of Dietary Exposure to DCPA From Market Basket Survey Data

Survey Date	Population Group				
	Infant (ng/kg)	Child (ng/kg)	Adolescent (ng/kg)	Adult (ng/kg)	Reference/Notes
1976-1977				1.1	Johnson et al., 1984
1978	20	1			Gartrell et al., 1986a; 13 locations
1979	2	1	2	2.1[a]	Gartrell et al., 1985a, 1985b
1980-1982	ND[b]	ND–1		2.4[a]	Gartrell et al., 1986a, 1986b
1982-1984	1.9	2.4	1.2–1.9	1.1–1.8	Gunderson, 1988; 24 states

a Authors reported 145 ng/day in 1979 and 165 ng/day in 1980-1982. Assuming an average body weight of 70 kg gives the ng/kg presented in the table.
b ND = none detected.

A market basket survey performed in 27 locations during October 1980 to March 1982 reported the data for DCPA in adult foods as 0.137 µg/day from leafy vegetables, 0.0213 µg/day in root vegetables and 0.007 µg/day from garden fruits (Gartrell et al., 1986a, 1986b). The average daily intake of DCPA from October 1979 to July 1980 in adult foods was 0.0920 µg/day from leafy vegetables, 0.005 µg/day from root vegetables, and 0.0476 µg/day from garden fruits (Gartrell et al., 1985a, 1985b). Detection limits were not specified in secondary literature for most of the studies cited in this section. In both sets of data, the leafy vegetables seemed to provide the major exposures to DCPA.

5.2 Exposure From Air

Data were not available on the degradates MTP or TPA; most data were provided as DCPA or total DCPA, which combined degradate and parent compound data.

Nonoccupational exposure results from the inhalation of both indoor and outdoor air, particularly near agricultural areas (Tessari and Spencer, 1971; Whitmore et al., 1994; Lee, 1977; Kutz et al., 1976), and carpet dust (Starr et al., 1974; Lewis et al., 1994). Spray drift droplet spectrum analysis was not required by EPA because the pesticide producer was a participant in the Spray Drift Task Force. Spray drift is assumed to be 5% of the application rate (U.S. EPA, 1998c).

5.2.1 Concentration of DCPA and DCPA Degradates (TPA and MTP) in Air

Data were not available on the degradates MTP or TPA; most data were provided as DCPA or total DCPA, which combined degradate and parent compound data.

Indoor and outdoor air samples collected monthly for 1 year at homes of occupationally exposed men in Colorado showed the presence of DCPA at similar concentrations for all conditions: farmers indoor, incidence = 31/38, range = 0.08-12.04 µg/m^3; farmers outdoor, incidence = 31/37, range = 0.02-9.12 µg/m^3; formulators indoor, incidence = 48/52, range = 0.05-8.72 µg/m^3; formulators outdoor, incidence = 39/54, range = 0.08-38.26 µg/m^3 (Tessari and Spencer, 1971).

Indoor, outdoor, and personal air samples were collected in winter, spring, and summer in Jacksonville, Florida, and Springfield/Chicopee, Massachusetts, to assess nonoccupational exposure to DCPA. Residents from Jacksonville had low exposures, and the Springfield/Chicopee residents were exposed to higher levels of DCPA (see Table 5-3) (Whitmore et al., 1994). The arithmetic mean airborne pesticide concentration of DCPA in the United States in 1970-1971 equaled trace levels of this compound; 0.49% of the samples were positive, and the maximum DCPA value was 2.1 ng/m^3 (Lee, 1977; Kutz et al., 1976).

Table 5-3 DCPA concentrations in air samples from Jacksonville, Florida, and Springfield/Chicopee, Massachusetts

Season	Concentration (ng/cm^3)					
	Jacksonville, FL			Springfield/Chicopee, MA		
	Indoor Air	Outdoor Air	Personal Air	Indoor Air	Outdoor Air	Personal Air
Winter	0.3	ND	0.2	0.3	ND	0.3
Spring	ND	ND	ND	1.6	0.9	2.6
Summer	0.2	ND	0.6	—	—	—

ND = not detected.
— = not measured.

5.2.2 Intake of DCPA and DCPA Degradates (TPA and MTP) From Air

Estimates of nonoccupational exposures to DCPA for adults can be derived from the arithmetic mean ambient air concentration in 1970-1971 (Lee, 1977; Kutz et al., 1976), using the assumption that adult humans breathe 15.2 m^3 of air per day (U.S. EPA, 1996a).

$$2.1 \text{ ng/m}^3 \times 15.2 \text{ m}^3\text{/day} = 31.92 \text{ ng/day, rounded to 32 ng/day}$$

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

$$2.1 \text{ ng/m}^3 \times 8.7 \text{ m}^3\text{/day} = 18.27 \text{ ng/day, rounded to 18 ng/day}$$

The concentration in air reported by Whitmore et al. (1994) for Jacksonville, Florida, and Springfield/Chicopee, Massachusetts, indicates that ambient air exposures are often less than the estimate derived from the 1970-1971 data. Individual intakes vary depending on factors including activity, geographic location, and inhalation rate.

5.3 Exposure From Soil

5.3.1 Concentration of DCPA and DCPA Degradates (TPA and MTP) in Soil and Sediment

Data were not available on the degradates MTP or TPA; most data were provided as DCPA or total DCPA, which combined degradate and parent compound data.

In sediment samples taken in 1986 from the Moss Landing drainage area in California, 12% contained DCPA. The concentration ranged from not detected to 25-µg/kg dry weight, where the detection limit was 8.8 µg/kg (Fleck et al., 1988).

DCPA was detected in 39% of the soil samples from the Moss Landing drainage area. Concentrations ranged from not detected to 690-µg/kg dry weight. Of the samples taken from the Salinas and Carmel River Valley agricultural areas, 47% had a range of not detected to 700-µg/kg dry weight (detection limit, 4.4 µg/kg) (Fleck et al., 1988). In 1972, 1533 sites in 37 states had soil samples tested for DCPA; only 0.1% of the total samples had DCPA detected at a concentration of 0.18 ppm (Carey et al., 1979).

5.3.2 Intake of DCPA and DCPA Degradates (TPA and MTP) From Soil

Human exposure to contaminants in soils is usually from dust that infiltrates homes, automobiles, etc., in adults and from dust 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, 1996a). Using the data from Carey et al. (1979) of 0.18 mg/kg soil and the assumption that infants ingest 0.000001 kg (100 mg) of soil per day, the exposure to DCPA from soil would be about 0.2 ng/day for infants and 0.08 ng/day for adults.

$$0.18 \text{ mg/kg of soil} \times 0.000001 \text{ kg of soil} = 0.00000018 \text{ mg } (0.18 \text{ ng})/\text{day}$$

$$0.18 \text{ mg/kg of soil} \times 0.0000005 \text{ kg of soil} = 0.00000009 \text{ mg } (0.09 \text{ ng})/\text{day}$$

5.4 Other Residential Exposures

Data were not available on the degradates MTP or TPA; most data were provided as DCPA or total DCPA, which combined degradate and parent compound data.

Household dust samples from Colorado showed the presence of DCPA as follows: control group, incidence = 14/182, mean concentration = 7.11 ppb; farmers, incidence = 22/45, mean = 18.50 ppb; formulators, incidence = 19/95, mean = 7.28 ppb (Starr et al., 1974). DCPA was detected in carpet dust in two of nine houses in the Raleigh-Durham-Chapel Hill area, North Carolina (Lewis et al., 1994).

5.5 Occupational (Workplace) Exposures

Data were not available on the degradates MTP or TPA; most data were provided as DCPA or total DCPA, which combined degradate and parent compound data. DCPA was detected in the hand rinses from 2 of 11 people who were occupationally exposed to the herbicide. DCPA was detected up to 112 days after exposure (Kazen et al., 1974).

5.5.1 Description of Industries and Workplaces

DCPA is applied with tractor-mounted boom sprayers, tractor-drawn granular spreaders, shaker cans, and residential push-type and "whirly-bird" spreaders, and by aerial application (U.S. EPA, 1998c). Based on use patterns, the following 10 major exposure scenarios were identified for DCPA (U.S. EPA, 1998c):

1. Mixing/loading:
   a. of liquid flowable formulation
   b. of wettable powder formulations
2. Mixing and loading granular product for ground applications
3. Aerial application
   a. of liquid formulation
   b. of granular product
4. Applying the liquid and wettable powders with groundboom equipment
5. Applying with a granular spreader cultivator mounted
6. Flagger exposure:
   a. to liquids
   b. to granulars
7. Applying with a shaker can
8. Applying with a backpack
9. Mixing/loading and applying with a residential push-type spreader
10. Mixing/loading and applying with a whirly-bird spreader

All exposure patterns assume that workers wore long pants, long-sleeved shirts, and protective gloves.

5.5.2 Types of Exposure

Dermal and inhalation exposures are expected among agricultural and horticultural professionals who work with DCPA. The extent of the exposure will depend on how DCPA is used and applied.

5.6 Summary

There are data evaluating the parent compound's (DCPA's) exposure and intake, but limited information is available to evaluate the amount of TPA or MTP present in the environment and what the intake may be for food, air, or workplace environments. On the basis of estimates derived from the available exposure data, it appears that food is the major source of exposure. Further monitoring data are needed to evaluate TPA or MTP exposure and intake.

6.0 TOXICOKINETICS

TPA and MTP are metabolites and environmental degradates of dacthal (DCPA). However, there is little information on the toxicokinetics of either compound.

6.1 Absorption

Although there have been no oral absorption studies on TPA or MTP, studies indicate that the parent compound DCPA is poorly absorbed. In humans, at least 6% of a 25-mg dose and 12% of a 50-mg dose were determined to be absorbed, as indicated by the presence of metabolites in the urine (Tusing, 1963).

Dogs were determined to excrete 97% of a single dose of DCPA (capsules containing 100 or 1000 mg/kg) as the parent compound in the feces by 96 hours, indicating lack of absorption (Skinner and Stallard, 1963). Approximately 3% of dacthal was converted to MTP. Two percent was eliminated in the urine and 1% in the feces. Less than 1% (0.07%) of DCPA was converted to TPA, which was also excreted in the urine.

Radiolabeled DCPA was given to a lactating goat to determine absorption and distribution in a ruminant species. After dietary exposure to a concentration of 10 ppm for 4 days, radiolabel was detected in the tissues, indicating that absorption had occurred. Tissue residues accounted for 38.5% of the dose, suggesting that a minimum of this amount was absorbed (U.S. EPA, 1998c).

No studies are available on inhalation or dermal absorption of either TPA or MTP.

6.2 Distribution

No studies on the distribution of TPA or MTP after oral exposure are available. DCPA containing 1.1% MTP and 1.7% TPA was not found in the liver, kidneys, or adipose tissues of dogs treated with 10,000 ppm (250 mg/kg-day) in the diet for 2 years (Skinner and Stallard, 1963). After a single dose of 100 or 1000 mg of DCPA per kg was given to dogs, TPA was detected in kidney and MPA was found in kidney, liver, and adipose tissue. Some DCPA was also found in adipose tissue.

Processing of dietary components in ruminants can differ from that in other species. After a lactating goat was exposed to a concentration of 10-ppm radiolabeled DCPA for 4 days, tissue levels accounted for 38.5% of the dose, and 80%-98% was present as MTP (U.S. EPA, 1998c). Residue concentrations were highest in kidney (0.1007 ppm), followed by liver (0.0333 ppm), fat (0.0168-0.179 ppm), and muscle (0.0057-0.107 ppm). Deposits in fat were the only ones that contained the DCPA parent compound; in fat, DCPA was 10%-15% of the total residue.

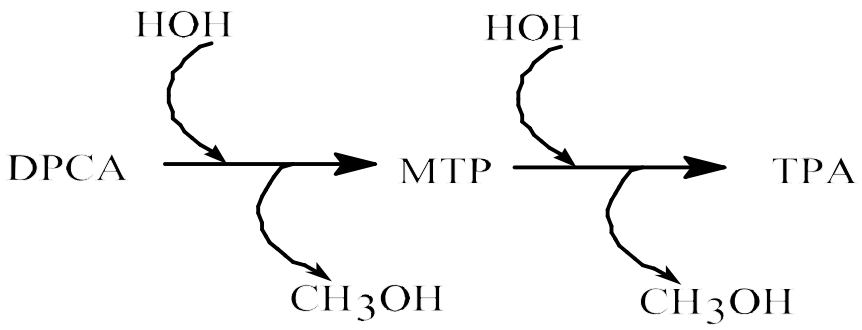
Some of the radiolabel (0.01 ppm) given to the lactating goat was found in the milk, indicating that DCPA or its metabolites are transferred to mammary secretions. The specific radiolabeled compound or compounds present in the milk were not identified (U.S. EPA, 1998c).

No studies are available on the distribution of TPA, MTP, or DCPA after inhalation or dermal exposure.

6.3 Metabolism

No studies are available on the metabolism of either TPA or MTP. Some animals excrete TPA and/or MTP as metabolites of DCPA, suggesting that dacthal is converted to the mono- and di-acid derivatives (U.S. EPA, 1998c; Skinner and Stallard, 1963; Tusing, 1963). Some of this probably occurs in the gastrointestinal tract by way of nonspecific esterases; additional hydrolysis may also occur in the liver and other tissues. Hydrolysis would be a two-step process, as indicated in Figure 6-1. Based on the metabolism of other phthalates, MPA is more likely formed in the gastrointestinal tract and TPA in the tissues. The identification of TPA as the terminal metabolite of DCPA is supported by the results of using the META metabolism and biodegradation expert system to predict the aerobic metabolism of DCPA. The META system predicted that, once formed, TPA is stable to further degradation (Klopman et al., 1996).

Figure 6-1 Metabolism of DCPA



Tusing (1963) reported that humans who took single oral doses of pure DCPA (25 or 50 mg) converted 3-4% of the dose to MTP within 24 hours. After 3 days, approximately 6% of the 25-mg dose and 11% of the 50-mg dose were converted to MTP. At both doses, less than 1% was converted to TPA in the 1- or 3-day period. The low levels of metabolites in relation to dose are, at least in part, a reflection of the limited absorption of DCPA. Skinner and Stallard (1963) and Hazleton and Dieterich (1963) reported that, in dogs administered single oral doses of DCPA, small amounts were converted to MTP (3%) and TPA (0.07%). The Skinner and Stallard (1963) study was a single-dose study, and the Hazleton and Dieterich (1963) study was a long-term study.

6.4 Excretion

Few studies are available on the excretion of TPA or MTP. In human studies (Tusing, 1963), 6% of a single 25-mg oral dose was excreted in urine as MTP and 0.5% as TPA over a 3-day period. Approximately 11% of the 50-mg dose was converted to MTP and 0.6% was converted to TPA. The parent compound was not found in the urine at either dose. A U.S. EPA study (2004a) predicts rapid urinary excretion of TPA on the basis of its structure. As noted earlier, however, only a minimal amount is predicted to be absorbed, at least in nonruminant species.

Skinner and Stallard (1963) reported that, after the administration of a single oral dose (100 or 1000 mg/kg) to dogs, 90% and 97% was eliminated unchanged in the feces at 24 hours and 96 hours, respectively. Approximately 3% was converted to MTP; of this, 3%, 2% was eliminated in the urine and 1% in the feces. MTP and TPA have also been identified in rat urine (U.S. EPA, 2004a).

7.0 HAZARD IDENTIFICATION

7.1 Human Effects

7.1.1 Short-Term Studies and Case Reports

There are no studies of intentional or accidental ingestion of TPA or MTP in humans. A single dose of 25 or 50 mg of DCPA, however, did not cause any observable effects in humans (Tusing, 1963).

7.1.2 Long-Term and Epidemiological Studies

There are no long-term exposure or epidemiology studies of TPA or MTP exposure.

7.2 Animal Studies

7.2.1 Acute Toxicity

There are no acute toxicity studies on TPA or MTP after oral exposure in animals. The 50% lethal dose (LD_{50}) for the parent compound DCPA is greater than 12,500 mg/kg in Spartan rats (Wazeter et al., 1974a) and greater than 10,000 mg/kg in beagle dogs (Wazeter et al., 1974b). These LD_{50} values are indicative of low acute toxicity for DCPA.

The dermal LD_{50} for DCPA in albino rabbits is greater than 10,000 mg/kg (Elsea, 1958). A single application of 3.0 mg of dacthal to the eyes of albino rabbits produced a mild degree of irritation that subsided completely within 24 hours after treatment (Elsea, 1958).

There are no acute toxicity studies on TPA or MTP via dermal or inhalation exposure.

7.2.2 Short-Term Studies

A 30-day intubation study using doses of 0, 100, 500, or 2000 mg of TPA per kg/day in 0.5% methylcellulose solution was conducted in groups of 10 male and 10 female Sprague Dawley rats (Major, 1985). There were no treatment-related mortality or changes in organ weights or histopathology. There were increases in hemoglobin and hematocrit in the males given high doses. A lowest observed adverse effect level (LOAEL) of 2000 mg/kg/day was based on soft stools in high-dose males and females as well as occult blood in the urine (U.S. EPA, 1994c). The no-effect level was 500 mg/kg/day. However, because the observed effects at the highest dose were not considered to be adverse, the 2000-mg/kg/day dose was identified by OPP as a no observed adverse effect level (NOAEL) (U.S. EPA, 1998c).

The results from the short-term TPA study differed from those for DCPA in a 28-day dietary study in groups of five male and female Sprague-Dawley rats given doses of 0, 250, 1000, or 2000 mg/kg/day (ISK Biotech Corp., 1990b). In the DCPA study, there was a dose-related increase in liver weight and centrilobular hypertrophy of hepatocytes. The lowest dose

tested (250 mg/kg/day) was the LOAEL for these effects (U.S. EPA, 1994c). The difference in the effect levels suggests that the parent DCPA is more acutely toxic than the TPA degradate.

No short-term studies of MTP were identified.

7.2.3 Subchronic Studies

A 90-day feeding study (Goldenthal et al., 1977) of TPA was performed in Charles River CD rats, using doses of 0, 50, 500, 1000, or 10,000 ppm in the diet. These doses were estimated to be equivalent to 0, 2.5, 25, 50, and 500 mg/kg/day, respectively. There were no adverse effects observed based on clinical observations, histopathology, and other standard measures of toxicity, such as hematology and organ weights. Therefore, the NOAEL was set at greater than or equal to the highest dose, 500 mg/kg/day, and an LOAEL could not be determined.

Like those of short-term studies, the results of subchronic exposures of Sprague-Dawley rats to DCPA differed from those for TPA. Groups of 15 male and 15 female animals were given doses of 0, 10, 50, 100, 150, or 1000 mg/kg/day in their diets for 13 weeks (ISK Biotech Corp., 1991). No clinical signs were observed and no effects on body weights were seen in the males, although there was a dose-related trend toward lower weight gain in the females. Liver weights and the incidence of centrilobular hepatocyte hypertrophy were increased in a dose-related manner. Kidney weights were increased, and there was evidence of tubular regenerative hyperplasia and follicular hypertrophy. The LOAEL was determined to be the 50-mg/kg/day dose and the NOAEL the 10-mg/kg/day dose (U.S. EPA, 1994c).

The liver was also the target organ in a subchronic study of DCPA in CD-1 mice (Fermenta Plant Protection Co., 1988). The lowest effect levels were 1235 mg/kg/day for males and 1049 mg/kg/day for females, based on minimal centrilobular hepatocyte enlargement. The NOAELs in males and females were 406 and 517 mg/kg/day, respectively (U.S. EPA, 1994c).

No subchronic studies of MTP were identified.

7.2.4 Neurotoxicity

No studies are available on the neurotoxicity of either TPA or MTP. Some dose-related signs of nervous system effects (ataxia, decreased motor activity, poor righting reflex) were seen in New Zealand White rabbits during a developmental study of DCPA after exposure to doses of 0, 500, 1000, or 1500 mg/kg/day during gd 6-19 (Fermenta Plant Production Co., 1989; U.S. EPA, 1994c).

7.2.5 Developmental/Reproductive Toxicity

Pregnant rats (25 per dose group) were administered 0, 625, 1250, or 2500 mg of TPA per kg/day via gavage on gd 6-15 (Mizen, 1985). Because no developmental effects were noted, the NOAEL for developmental effects was identified as 2500 mg/kg/day. The LOAEL for developmental effects could not be determined. Maternal toxicity, however, was noted at 2500 mg/kg/day, based on soft stools, red mucus in the feces, salivation, decreased body weight gain,

and decreased food consumption. An LOAEL of 2500 mg/kg/day and an NOAEL of 1250 mg/kg/day were set for the dams. There were no studies of the developmental or reproductive toxicity of MTP.

Reproductive and developmental testing of DCPA has been evaluated in rats (Sprague-Dawley) and rabbits (New Zealand White). The parent compound was minimally toxic. In the two-generation study, the NOAEL for reproductive toxicity was 63 mg/kg/day and the LOAEL was 319 mg/kg/day, based on decreased pup body weight (ISK Biotech Corp., 1990a). In the F1 generation, there was an apparent increase in stillbirths at the highest dose level (1273 mg/kg/day for the dams), which was more pronounced in the second generation than in the first. Decreased body weight gain in the parents established the LOAELs for the parents at 319 mg/kg/day for the dams and 952 mg/kg/day for the males. The NOAELs for the dams and males were 63 and 233 mg/kg/day, respectively (U.S. EPA, 1994c).

Developmental testing of CD rats exposed on gd 6-15 failed to identify an LOAEL; the NOAEL was 2000 mg/kg/day (SDS Biotech Corp., 1986). Similar results were seen in New Zealand White rabbits exposed to DCPA by gavage during gd 7-19. The NOAEL and highest dose tested was 500 mg/kg/day (Fermenta Plant Protection Co., 1989). In a second study in New Zealand White rabbits by the same company, there were some (four) maternal deaths at the lowest dose of 500 mg/kg/day. Thirteen maternal deaths occurred at a dose of 1000 mg/kg/day and 12 maternal deaths occurred at 1500 mg/kg/day. The animals that died had signs of neurotoxicity, and the mid- and high-dose groups had a higher incidence of gastric ulcerations than controls. No embryo or fetal toxicity or teratogenicity was observed (U.S. EPA, 1994c).

7.2.6 Chronic Toxicity

Long-term studies of DCPA have been conducted in dogs, rats, and mice. These studies evaluated both cancer and noncancer endpoints. Hazleton and Dieterich (1963) fed beagle dogs (four per sex per dose) DCPA in the diet at 0, 100, 1000, or 10,000 ppm for 2 years. Based on body weight and food consumption data provided in the report, these dietary levels are approximately 0, 2.6, 17.7, or 199 mg/kg/day for males and 0, 3, 20.7, or 238 mg/kg/day for females, respectively. Physical appearance, behavior, food consumption, hematology, biochemistry, urinalysis, organ weight, organ-to-body weight ratio, gross pathology, and histopathology were comparable in treated and control groups at all dose levels. An NOAEL of 10,000 ppm (199 mg/kg/day for males and 238 mg/kg/day for females), the highest dose tested, was identified for this study.

Paynter and Kundzin (1963) fed albino rats (35 per sex per dose; 70 per sex for controls) DCPA in the diet for 2 years at 0, 100, 1000, or 10,000 ppm. Based on food consumption and body weight data provided in the report, these dietary levels correspond approximately to 0, 5, 50, or 500 mg/kg/day. Interim sacrifices were conducted at 13 and 52 weeks. Physical appearance, behavior, hematology, biochemistry, organ weights, body weights, gross pathology, and histopathology of treated and control animals were monitored. After 3 months at 10,000 ppm, slight hyperplasia of the thyroid was reported in both sexes. After 1 year, increased hemosiderosis of the spleen occurred in females at 10,000 ppm, and there were slight alterations in the centrilobular cells of the liver of both sexes. Kidney weights were increased significantly

in males fed 10,000 ppm, and adrenal weights were increased in females at the end of the 2-year study. Based on these data, an NOAEL of 1000 ppm (50 mg/kg/day) was identified.

A second 2-year feeding study of DCPA in rats was conducted by ISK Biotech Corporation (1993). In this study, Sprague-Dawley rats (70 per sex per dose) were administered technical-grade DCPA in their diets at doses of 0, 1, 10, 50, 500, or 1000 mg/kg/day. The material used contained 0.13% hexachlorobenzene as an impurity. The animals were examined for body weights and clinical signs. After sacrifice, the organs were examined for gross pathology and tissue histopathology.

There was a dose-related increase in the incidence and severity of focal accumulation of foamy-appearing macrophages within the alveolar spaces in males and females. Increases in both the incidence and severity of centrilobular swelling (hepatocytic hypertrophy) were observed at both interim and terminal sacrifices. Chronic nephropathy was increased in severity in males and in incidence in females. Thyroid-stimulating hormone (TSH) was elevated at 52 weeks in a dose-related manner. It also was increased at 104 weeks, but the increase was not dose related. Thyroxin (T_4) was decreased throughout the study, and triiodothyronine (T_3) was decreased at 52 weeks. The LOAEL for systemic toxicity was determined to be 10 mg/kg/day on the basis of effects observed in the lungs, kidneys, thyroid, and thyroid hormone levels in both sexes. The NOAEL was determined to be 1 mg/kg/day (ISK Biotech Corp., 1993). Tumors of the thyroid and liver were also observed. The cancer findings from this study are discussed in Section 7.2.7.

Groups of CD-1 mice (90 per sex per dose) were administered dacthal in the diet for 2 years, using technical-grade DCPA (Fermenta Plant Protection Co., 1988). The dosage levels were 0, 100, 1000, 3500, or 7500 ppm, equivalent in males to 0, 12, 123, 435, and 930 mg/kg/day and in females to 0, 15, 150, 510, and 1141 mg/kg/day. The effects observed after exposure to the test material included corneal opacities and increased relative liver weight (in both sexes in the 7500-ppm group). Liver enzyme activities were increased, but not in a dose-related manner, in both sexes at dietary concentrations of greater than 1000 ppm. There was also a dose-related increase in cholesterol levels in females from the highest two dose groups and hepatocyte enlargement/vacuolation in both sexes at 7500 ppm. Therefore, based on liver effects, the LOAEL for systemic toxicity was identified as 7500 ppm (male, 930 mg/kg/day; female, 1141 mg/kg/day). The NOAEL for systemic toxicity is 3500 ppm (male, 435 mg/kg/day; female, 1141 mg/kg/day). A supplementary 2-year study in Sprague-Dawley rats (Fermenta ASC Corp., 1990) to investigate the finding on corneal opacity in CD-1 mice failed to replicate this effect.

7.2.7 Carcinogenicity

There are no carcinogenicity studies for either TPA or MTP. The parent compound (DCPA) was shown to induce thyroid tumors in male and female rats, liver tumors in female rats (ISK Biotech Corp., 1993), and liver tumors in female mice (Fermenta Plant Protection Co., 1988) in the chronic toxicity studies discussed in Section 7.2.6. There was no significant increase in tumor incidence in the Paynter and Kundzin (1963) study in albino rats with dietary doses of 1-10,000 ppm. However, the ISK Biotech Corporation (1993) and Fermenta Plant

Protection Company (1988) studies used technical-grade DCPA containing impurities (0.13% hexachlorobenzene), whereas the Paynter and Kundzin (1963) study used a purer grade of the chemical (Klopman et al., 1996).

In the ISK Biotech Corporation (1993) study, the incidence of liver combined adenoma, carcinomas and hepatocholangiocarcinomas in female Sprague Dawley rats was 0%, 0%, 3%, 1%, 11%, and 16 % for doses of 0, 1, 10, 50, 500, and 1000 mg/kg/day, respectively. The first adenoma appeared at week 53 and the first carcinoma at week 96; the numbers of adenomas was greater than the number of adenomas. The thyroid tumors were observed in both males and females. In males, neither the adenomas or adenomas and carcinomas combined demonstrated a dose-response trend with incidences of 2%, 4%, 4%, 17%, 19%, 13%, respectively, for the adenomas and 3%, 5%, 5%, 13%, 16%, 10%, respectively, for combined carcinomas and adenomas (U.S. EPA, 1995b). In females the situation was similar with adenoma incidences of 2%, 2%, 4%, 7%, 2%, and 7%, respectively, and combined carcinoma and adenoma incidences of 2%, 2%, 5%, 7%, 3%, 12%, respectively (U.S. EPA, 1995b).

Hepatocyte hypertrophy and thyroid follicular cell hyperplasia or hypertrophy occurred in subchronic (28-day and 90-day) rat studies of DCPA, as well as in the long-term ISK Biotech Corporation (1993) and Paynter and Kundzen (1963) studies. The short-term studies that have been conducted for TPA have not provided any evidence for either thyroid or liver effects at the doses tested, reducing concern that TPA might have tumorigenic properties (U.S. EPA, 2004a). No short- or long-term toxicity data are available for MTP.

Male and female CD-1 mice both developed carcinomas and ademomas in the liver (Fermenta Plant Protection Company, 1988). Tumors were found in the controls as well as the exposed animals. The tumors in male mice fell withing the range for historical controls from 9 studies in CD-1 mice (27-56% for adenomas and carcinomas combined; 4-27% for adenomas alone; U.S. EPA, 1995a). The incidence of adenomas the female mice at the high dose (11%) was slightly greater than that for the historic controls (2-8%). The same was true for combined adenomas and carcinomas (12%) when compared to the historic controls (4-10%). There was also a dose-response trend for the numbers of adenomas with incidences of 3%, 0%, 3%, 5%, and 11% for the 1, 100, 1000, 3500, and 7500 mg/kg/day doses, respectively (U. S. EPA, 1995b).

7.3 Other Key Data

7.3.1 Mutagenicity and Genotoxicity

TPA did not induce a mutagenic response in either the Ames or hypoxanthine guanine phosphoribosyl transferase assays with or without metabolic activation (U.S. EPA, 1998c). TPA also did not induce a significant increase in the frequency of sister chromatid exchange in Chinese hamster ovary cells with or without metabolic activation (U.S. EPA, 1998c).

TPA has not been found to induce an increase in unscheduled DNA synthesis. An in vivo mouse micronucleus assay was negative in females and equivocal in males (U.S. EPA, 1998c).

DCPA had no mutagenic activity, with or without activation, in *Salmonella* assays (Auletta et al., 1977), in *in vivo* cytogenetic tests (Kouri et al., 1977a), in DNA repair tests (Auletta and Kuzava, 1977), or in dominant lethal tests (Kouri et al., 1977b).

7.3.2 Immunotoxicity

No studies are available on the immunotoxicity of DCPA, TPA, or MTP.

7.3.3 Hormonal Disruption

No studies are available on the ability of TPA or MTP to influence hormone production or activity. However, DCPA caused histopathological changes in the thyroid, along with decreased levels of T_4 and T_3, in Sprague-Dawley rats at doses greater than or equal to 10 mg/kg/day. TSH levels were elevated at 50 and 104 weeks. The subchronic study of TPA did not reveal any histopathological changes in the thyroid at a dose of 500 mg/kg/day. There was no evaluation of thyroid hormones in this study.

7.3.4 Structure-Activity Relationship

Klopman et al. (1996) evaluated the carcinogenic potential of DCPA and TPA on the basis of their chemical and biological properties and the multiple computer automated structure evaluation (MULTICASE) artificial intelligence program (a QSAR model). The MULTICASE system training set for mutagenicity and cytotoxicity included all the Ames assay results from the National Toxicology Program (NTP). The cancer projections were trained with the NTP bioassay results as well as a carcinogen potency database by Gold et al. (1984, 1986, 1987, 1990, 1993). The QSAR program produced consistently negative findings for DCPA and TPA, leading to the conclusion that neither molecule was predicted to be carcinogenic or mutagenic.

The prediction for lack of carcinogenicity for DCPA was somewhat unexpected, because it had been found to have a weak tumorigenic response in rats (ISK Biotech Corp., 1993) and mice (Fermenta Plant Protection Co., 1988). In trying to develop a rationale for the positive response of dacthal in the study by ISK Biotech Corporation, Klopman et al. (1996) noted that the negative Paynter and Kundzin (1963) bioassay of DCPA in rats was conducted with pure dimethyl-tetrachloroterephthalate, whereas the later, weakly positive studies used technical-grade material. For that reason, Klopman et al. (1996) obtained a list of the impurities in technical-grade DCPA and evaluated those materials with the MULTICASE program. Although the authors did not present a list of the impurities they tested, they did report that most of them resulted in a positive carcinogenicity finding by the MULTICASE program. Hexachlorobenzene, the best-documented and most frequently mentioned impurity, was found to be carcinogenic in a bioassay conducted by NTP.

Klopman et al. (1996) also examined the alkylating properties of TPA in relation to those of DCPA, as reflected in the ability of these compounds to react with γ-4-nitrobenzylpyridine (γ4-NBP). Dacthal demonstrated some ability to react with γ4-NBP, whereas TPA did not react. The γ4-NBP reactivity opens the possibility that DCPA's alkylating potential, alone or in combination with the carcinogenicity of the product impurities, might explain the weak

tumorigenic response in the ISK Biotech Corporation (1993) study. This study supports the conclusion that TPA is unlikely to be tumorigenic.

7.4 Hazard Characterization

7.4.1 Synthesis and Evaluation of Major Noncancer Effects

The only noncancer health effects noted with TPA were soft stools and occult blood in urine at doses of greater than 2000 mg/kg/day (Major, 1985). Doses of 2500 mg/kg/day administered during gd 6-15 also caused soft stools, increased salivation, decreased body weight gain, and decreased food consumption (Mizen, 1985). No studies are available on the health effects of MTP.

The data available from chronic and subchronic studies of DCPA demonstrate that it can affect multiple organ systems (lungs, liver, thyroid) in rats and liver in mice. The LOAEL for the noncancer critical effects in rats is 10 mg/kg/day, whereas that in mice is approximately 100-fold higher (1000 mg/kg/day). No adverse health effects were observed in dogs at doses of about 200 mg/kg/day (Diamond Alkali Co. 1963; U.S. EPA, 1994c).

The data from chronic and subchronic studies of dacthal in rats and mice identify the rat as the most sensitive laboratory species. A comparison of the subchronic effect level from rats for DCPA (10 mg/kg/day) with the NOAEL for TPA (>500 mg/kg/day) supports the conclusion that TPA is at least an order of magnitude less toxic than its parent chemical.

7.4.2 Synthesis and Evaluation of Carcinogenic Effects

There are no carcinogenicity studies of either TPA or MTP. There is some evidence for the carcinogenic potential of the parent compound DCPA, based on the induction of thyroid and liver tumors in rats and of liver tumors in mice. The U.S. EPA (1998c) concluded that the evidence for the carcinogenicity of DCPA may reflect, at least in part, the carcinogenicity of several of the impurities in the test material.

In DCPA subchronic rat studies, thyroid and liver tumors were preceded by tissue lesions and hepatocyte hypertrophy, which occurred at a dose of greater than 215 mg/kg/day (the lowest dose tested) in a 28-day feeding study and a dose of 100 mg/kg/day in a 90-day feeding study. Thyroid follicular cell hyperplasia or hypertrophy occurred at a dose of 1720 mg/kg/day in a 28-day feeding study and at a dose of 1000 mg/kg/day in a 90-day feeding study (U.S. EPA, 2004a).

No liver or thyroid precursor events occurred in rats after a subchronic feeding study with up to 500-mg/kg/day doses of TPA. In addition, TPA has not been demonstrated to be mutagenic. The U.S. EPA (2004a, 2004b) concluded that TPA is unlikely to pose a cancer risk. As described in Section 7.3.4, Klopman et al. (1996) reached the same conclusion regarding the carcinogenic potential of TPA, using QSAR analysis combined with an evaluation of its chemical properties.

7.4.3 Mode of Action and Implications in Cancer Assessment

There are no cancer data for either MTP or TPA. The mode of action proposed for the tumors observed in the chronic studies of DCPA relates primarily to the presence of potentially carcinogenic impurities (polyhalogenated dibenzo-p-dioxins, dibenzofurans, and hexachlorobenzene) in the material tested. Early commercial preparations of DCPA could contain up to 0.3% hexachlorobenzene as an impurity. Dioxin/furanes also were present at times. Hexachlorobenzene is a probable human carcinogen and, like DCPA, is associated with liver, kidney, and thyroid tumors in laboratory animals (U.S. EPA, 1988c).

Although it is hypothesized that impurities contributed to the carcinogenic activity of DCPA, at the concentrations present, they cannot account for all of the DCPA cancer risk (U.S. EPA, 1998). It is possible that weak alkylation activity associated with the methyl ester conformation of DCPA and/or nongenotoxic mechanisms may also be involved in the tumor response (Klopman et al., 1996).

7.4.4 Weight-of-Evidence Evaluation for Carcinogenicity

Although there is little weight-of-evidence information available, the lack of precursor effects compatible with the DCPA data and QSAR projections supports the conclusion that TPA is probably not carcinogenic. Not enough data are available to perform a weight-of-evidence assessment on MTP.

There is suggestive evidence of the carcinogenic potential of the parent compound DCPA, based on the induction of thyroid and liver tumors in rats and liver tumors in mice (U.S. EPA, 1998c).

7.4.5 Potentially Sensitive Populations

No sensitive populations have been identified. Results of a single developmental study indicate that exposure of pregnant dams to doses of ≤2500 mg/kg/day via gavage on gd 6-15 did not cause a toxic effect to the fetuses.

8.0 DOSE-RESPONSE ASSESSMENT

8.1 Dose-Response for Noncancer Effects

An RfD has not been set for either MTP or TPA because of the incompleteness of the database on these compounds. The U.S. EPA (1998c), however, suggests that the RfD for the parent compound, DCPA, is sufficient to protect against any toxicity from its metabolites. 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 data needed to derive a reference concentration (RfC) for MTP, TPA, or DCPA are not available. The RfC is an estimate of the daily inhalation exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime.

8.1.1 RfD Determination

Choice of Principal Study and Critical Effect

A chronic 2-year feed study of DCPA (containing 0.13% of the impurity hexachlorobenzene) in Sprague-Dawley rats (70 per sex per dose) was used as the basis for determining the RfD (U.S. EPA, 1994c, 1998c). There was a dose-related increase in the incidence and severity of focal accumulation of foamy-appearing macrophages within the alveolar spaces in the lungs of both males and females. Increases in both the incidence and severity of centrilobular swelling (hepatocytic hypertrophy) were observed at both interim and terminal sacrifices. Chronic nephropathy was increased in severity in males and in incidence in females. TSH was elevated at 52 weeks in a dose-related manner. TSH also was increased at 104 weeks, but the increase was not dose related. T_4 was decreased throughout the study, and T_3 was decreased at 52 weeks. The LOAEL for systemic toxicity was 10 mg/kg/day, based on effects observed in the lungs, kidneys, thyroid, and thyroid hormones of both sexes. The NOAEL was determined to be 1 mg/kg/day (ISK Biotech Corp., 1993). This was chosen as a critical study for establishing the HRL for TPA and MTP in the absence of adequate studies on either DCPA degradate.

Dose-Response Characterization

As described above, the chronic 2-year feed study of DCPA (with the hexachlorobenzene impurity) in Sprague-Dawley rats is the critical study used in developing an RfD for DCPA, the parent compound for TPA and MTP, using the NOAEL/LOAEL approach as follows:

$$\text{RfD} = \frac{1\ \text{mg/kg/day}}{100} = 0.01\ \text{mg/kg/day}$$

where:

1 mg/kg/day = The NOAEL from a chronic study of DCPA in rats in which a variety of adverse effects were observed at an LOAEL of 10 mg/kg/day

100 = An uncertainty factor that includes a 10 to adjust for intraspecies variability and a 10 for interspecies variability

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

An uncertainty factor of 100 was used for the RfD derivation (10 for interspecies extrapolation and 10 for intraspecies variability). The Agency did not apply uncertainty factors for the database, use of NOAEL or LOAEL, or duration adjustment.

The RfD for DCPA is lower than the chronic level of concern of 0.05 mg/kg/day established by the EPA Office of Pesticide Programs (U.S. EPA, 2004b) for TPA. This determination is based on the NOAEL from the subchronic TPA study, using a total uncertainty factor of 1000 (10 for interspecies extrapolation, 10 for intraspecies variability, and 10 to adjust for the subchronic exposure duration). Accordingly, the use of the DCPA RfD to establish the HRL for regulatory determination for MTP and TAP is a health-risk-protective measure.

8.1.2 RfC Determination

There are insufficient data to determine an RfC for DCPA, MTP, or TPA.

8.2 Dose-Response for Cancer Effects

No data are available for cancer effects from TPA or MTP. DCPA has been demonstrated to cause liver and thyroid tumors in rats and liver tumors in mice. However, no liver or thyroid precursor events occurred in studies of TPA with dosing regimens of 2000 mg/kg/day for 30 days or 500 mg/kg/day for 90 days. This suggests that TPA is toxicologically different from DCPA. In addition, TPA has not been demonstrated to be mutagenic. Accordingly, the U.S. EPA (2004a) concluded that TPA is unlikely to pose a cancer risk. Klopman et al. (1996) demonstrated that TPA did not act as an alkylating agent in a chemical test system, and the results of QSAR analysis with the MULTICASE program supported the EPA's conclusion concerning the cancer risk of TPA. Lack of toxicity data for MTP, prevents a quantitative or qualitative assessment of its potential carcinogenicity.

A quantitative cancer assessment was conducted for dacthal by OPP (U.S. EPA., 1995b). Liver and thyroid tumors were observed in male and female Sprague Dawley rats (ISK Biotech Corp., 1993) using doses of 0-1000 mg/kg/day. No tumors were observed in Albino rats exposed to doses of 0 to 500 mg/kg/day (Paynter and Kundzin, 1963). The dose range achieve in the Paynter and Kundzin (1963) study was lower than that for the ISK Biotech Corporation (1993) study, and it also reportedly used a purer form of DCPA. Other than the tumors, the high-dose histological effects on the thyroid and liver were similar in both studies: thyroid hyperplasia and histological changes in the centrilobilar cells of the liver.

In CD-1 mice there was an increase primarily of adenoma's of the livers of the males and females compared to controls. In males, the incidence did not exhibit a dose-response trend and fell within the historic control range, while in females there was a weak dose-response with the incidence at the high dose slightly greater than that for the historic controls for adenomas (U.S. EPA, 1995b).

8.2.1 Choice of Study

The U.S, EPA (1995b) selected the liver tumors in the female rats from the ISK Biotech Corporation (1993) study as the basis for quantification of the carcinogenic potential of DCPA. Although it was concluded that the impurities in the tested material could, in part, account for the tumors observed, they could not unequivocally account for the total tumor response. DCPA was classified as a Group C (Possible) carcinogen.

8.2.2 Dose-Response Characterization

The dose-response data for the liver tumors in female Sprague Dawley rats are summarized in Table 8-1. Although, DCPA was evaluated against the U.S. EPA 1986 *Guidelines for Carcinogen Risk Assessment*, a body weight$^{3/4}$ conversion was used for the DCPA analysis rather than the then conventional body weight$^{2/3}$ (U.S. EPA, 1998). The body weight scaling factor is consistent with that used in the Agency 2005 cancer guidelines. Dose-response was modeled using the linear multistage model.

Table 8-1 Hepatocellular Tumors in Female Sprague-Dawley Rats

Tumor/Dose (mg/kg/day)	0	1	10	50	500	1000
Adenomas	0/69	0/69	1/67	1/68	5/70	7/68
Carcinomas	0/69	0/69	1/67	0/68	3/70	3/68
Hepatocholangeocarcinomas	0/69	0/69	0/67	0/78	0/70	2/68
Combined	0/69	0/69	2/67	1/68	8/70	11/68

Source: U.S. EPA (1995b)

8.2.3 Cancer Potency and Unit Risk

The calculated slope factor for DCPA is 1.49×10^{-3} (mg/kg/day)$^{-1}$ (U.S. EPA, 1998); the 10-6 risk concentration in water is 23 µg/L. There is uncertainty in these values because of the carcinogenicity of some of the impurities present in the material tested. The cancer assessment for the parent compound can be applied to its MTP and TPA degradates in the absence of tumorigencity data on either material.

9.0 REGULATORY DETERMINATION AND CHARACTERIZATION OF RISK FROM DRINKING WATER

9.1 Regulatory Determination for Chemicals on the Contaminant Candidate List

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

On July 18, 2003, EPA announced final Regulatory Determinations for one microbe and eight 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 41 chemicals and 10 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, 2004c).

The SDWA requires EPA to make regulatory determinations for no fewer than five contaminants from CCL 2 by August 2006. In cases where the Agency determines that a regulation is necessary, the regulation should be proposed by August 2008 and promulgated by February 2010. The Agency is given the freedom to determine that there is no need for a regulation if a chemical on the CCL fails to meet one of three criteria established by the SDWA and described in section 9.1.1.

9.1.1 Criteria for Regulatory Determination

Following are the three criteria used to determine whether 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 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.

9.1.2 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 NDWAC 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 NDWAC 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 semiquantitative tool for addressing each of the three CCL criteria. The NDWAC requested that the EPA use good judgment in balancing the many factors that need to be considered in making a regulatory determination.

The EPA modified the semiquantitative NDWAC suggestions for evaluating chemicals against the regulatory determination criteria and applied them in decision-making. The quantitative and qualitative factors for dacthal degradates (TPA and MTP) that were considered for each of the three criteria are presented in the sections that follow.

9.2 Health Effects

The first criterion asks whether 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 to estimate a dose at which adverse health effects are either not likely to occur (threshold toxicant) or to have a low probability for occurrence (nonthreshold 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 RfD for threshold effects, and the slope factor for nonthreshold effects.

A full description of the health effects associated with exposure to TPA and MTP is presented in Chapter 7 of this document and summarized below in Section 9.2.2. Chapter 8 and Section 9.2.3 present dose-response information.

9.2.1 Health Criterion Conclusion

The limited toxicological data on the health effects of the dacthal degradates MTP and TPA led to a two-level evaluation of these compounds for their heath effects. Following the recommendation of the EPA's Office of Pesticide Programs, both derivatives were first evaluated in terms of the health effects caused by the parent material (DCPA). Since the TPA

degradate has been studied for its toxicological properties, it was also evaluated independently. Because of a lack of data, the effects of the MTP degradate could be determined only in terms of the toxicity of the parent compound. However, intestinal conversion of much of DCPA to MTP for absorption provides justification for this approach.

Both DCPA and TPA cause adverse health effects in laboratory animals. However, the effects associated with TPA are much milder than those of the parent and tend to occur at doses that are lower by about an order of magnitude. TPA is weakly toxic, causing effects on weight gain and stool consistency at its lowest effect levels. DCPA can cause a variety of systemic effects on liver, kidney, thyroid, and, potentially, the eyes. It may also have some tumor-initiating or tumor-promoting properties.

9.2.2 Hazard Characterization and Mode of Action Implications

Currently, no subchronic or chronic studies are available to assess the toxicological effects of MTP (the mono-acid degradate). Three studies in rats (30- and 90-day feeding studies and a developmental study) are available for TPA (the di-acid degradate). The effects of exposure were mild (weight loss and diarrhea) and occurred at doses greater than or equal to 2000 mg/kg/day. No reproductive effects were observed. The critical effects for DCPA, the parent compound, include effects on the lung, liver, kidney, and thyroid in male and female rats in a 2-year chronic bioassay (ISK Biotech Corp., 1993).

No carcinogenicity studies have been performed with either TPA or MTP. Based on a comparison of TPA toxicity with that of its parent, and TPA's lack of mutagenicity, the EPA (U.S. EPA, 2004b) concluded that TPA is unlikely to pose a cancer risk. Klopman et al. (1996) evaluated the carcinogenic potential of TPA on the basis of its chemical and biological properties and, using a variety of QSAR tools, determined that it did not present any substantial carcinogenic risk.

There is suggestive evidence, based on an increased incidence of liver and thyroid tumors in rats and liver tumors in mice, that DCPA could be carcinogenic. The presence of hexachlorobenzene and dioxin as impurities could have contributed to the cancer risk. However, it is also possible that dacthal itself could have some tumorigenic activity.

The EPA evaluated whether health information is available regarding the potential effects of the dacthal degradates on children and other sensitive populations. There are no data that identify a particular sensitive population for the degradates or the parent compound exposure. Results of a single developmental study indicate that exposure to pregnant dams to doses of $\leq$2500 mg of TPA per kg/day via gavage did not have an adverse effect on the fetus. The EPA did not identify any data that suggest gender-related differences in toxicity or sensitivity in the elderly.

9.2.3 Dose-Response Characterization and Implications in Risk Assessment

The present toxicity database for MTP and TPA is not sufficient to derive RfDs for these two chemicals. However, because the available data indicate that neither MTP nor TPA is more

toxic than its parent compound, DCPA, the Agency suggests that the RfD for the DCPA parent would be protective against exposure from these two DCPA metabolites (U.S. EPA, 1998c). Both compounds are formed in the body from the DCPA parent, and therefore the toxicity of the degradates is reflected in the toxicity of the parent compound. The RfD for DCPA is 0.01 mg/kg/day, based on a chronic rat study (ISK Biotech Corp., 1993), with an NOAEL of 1.0 mg/kg/day and an uncertainty factor of 100 for interspecies and intraspecies variability.

The EPA derived the HRL for TPA and MTP using the DCPA RfD of 0.01 mg/kg/day (U.S. EPA, 1994c) and a 20% relative source contribution. The Agency calculated an HRL of 0.07 mg/L or 70 µg/L for DCPA and used this HRL for TPA and MTP.

9.3 Occurrence in Public Water Systems

The second criterion asks whether the contaminant is known to occur or whether there is a substantial likelihood that the contaminant will occur in PWSs with a frequency and at levels of public health concern. To address this question, EPA considered the following information:

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

Data on the occurrence of the dacthal degradates TPA and MTP 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 TPA and MTP, as well those that reported concentrations of TPA and MTP 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 water. For carcinogens, the HRL was the 10^{-6} risk level (i.e., the probability of one excess tumor in a population of 1 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 HRL for TPA and MTP is 70 µg/L. The combined concentrations of MTP and TPA were converted to their DCPA equivalents for the occurrence analysis.

The available monitoring data, including indications of whether the contaminant is a national or 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.

9.3.1 Occurrence Criterion Conclusion

TPA and MTP are degradates of DCPA and are present only in areas where DCPA has been used. DCPA and its derivatives have been detected in surface and ground water as well as in PWSs. States reporting detections of the dacthal degradates are located across the country, from east to west and north to south. TPA and MTP combined have not been detected at the health reference level (HRL) in any large systems. They were found at levels exceeding the

HRL in 0.13% of small systems, affecting 0.02% of the population served by small systems, approximately equivalent to 113,000 individuals nationwide. The one HRL exceedance occurred in one small system in Michigan. Dacthal, MTP, and TPA have also been detected in ambient waters in USGS surveys. However, in all cases, concentrations have been below the HRL and ½HRL. Accordingly, TPA and MTP are likely to occur in PWSs but not at concentrations of concern.

9.3.2 Monitoring Data

Drinking Water

Analytical methods for TPA and MTP cannot distinguish between the two compounds. Accordingly, the results from the UCMR 1 program report both compounds as one. The first cycle extended from 2001 to 2005. The MRL of the degradates was ≥1 µg/L. Results were provided for small systems and large systems separately. A total of 797 small PWSs (590 ground water and 207 surface water) were tested, and 3272 samples were obtained. Among the small systems, DCPA degradate detections (≥MRL or ≥1 µg/L) were reported in 2.13%. A single small system had a concentration greater than the HRL (>HRL or >70 µg/L). This ground water system represented 0.13% of small PWSs. A total of 3071 large PWSs (1384 ground water and 1687 surface water systems) were tested, and 30,480 samples were obtained. Among the large systems that reported results, 5.14% had detections (≥MRL or ≥1 µg/L). A single large surface water system had a concentration >½HRL. No large system had detections of concentrations >HRL (>70 µg/L).

Ambient Water

Occurrence data for dacthal and MTP were collected by the NAWQA program from 1992 to 2001 (Cycle 1) in representative watersheds and aquifers across the country. Reporting limits varied over the course of the cycle owing to improved methods of detection, but the level of detection did not exceed 0.070 µg/L for dacthal and MTP. The MTP degradate was not detected in ambient surface or ground water in mixed, undeveloped, or urban areas. In agricultural areas, 1233 samples from 48 ambient surface water sites were tested at a detection frequency of 0.18%. The maximum concentration was 0.430 µg/L; both the median and the 95th percentile concentrations were below the reporting limit. Ambient ground water samples in agricultural areas were obtained from 1217 wells. The detection frequency was 0.08%; the maximum concentration was 1.1 µg/L, and both the median and 95th percentile concentrations were below the reporting limit. The parent DCPA was detected in both ambient and ground water samples. The 95% concentrations for agricultural, mixed, and urban samples from ambient surface waters were below the HRL and ½ HRL. Levels were below the reporting limit for all ground water samples and from ambient surface waters sampled from undeveloped areas.

9.3.3 Use and Fate Data

DCPA is used as a selective, pre-emergence herbicide to control annual grasses and broad-leaved weeds in turf. It is also applied to ornamentals, strawberries, certain vegetables, nuts, and cotton (U.S. EPA, 1998c). Some use of DCPA on some vegetable and nut products was terminated in 2005 along with residential turf and ornamental plant use. Today, 66 registered products contain dacthal as an active ingredient as well as 2 manufactured products,

Dacthal 1.92F and 90% dimethyl-T, from which all other products are formulated. Agricultural use of DCPA is mainly on the east and west coasts and along the southern United States. TPA and MTP are likely to occur in these areas. Approximately 80% of DCPA is used for weed control on turf (e.g., golf courses) and home lawns, for which adequate estimations of use are not available. There is no commercial use for TPA or MTP. However, DCPA photodegrades on soil surfaces; after 5 hours of exposure to sunlight, 50% of this compound was degraded to MTP and TPA (Chen et al., 1976).

Both TPA and MTP were determined to be highly mobile in all soils (U.S. EPA, 1998c). MTP and TPA are expected to be more water soluble than the parent compound, based on hydrolysis of the ester bonds and resultant increased hydrophilicity of the products. Thus, it is expected that they will be more mobile in the soil. Limited physical or chemical data, however, are available for these compounds. Data suggest that TPA will leach to ground water wherever DCPA is used, regardless of soil properties (U.S. EPA, 1998c). TPA appears to be substantially more persistent than the parent compound (DCPA) and exhibits low soil/water partitioning. Therefore, substantial quantities of TPA should be available for runoff for a longer period than the parent DCPA.

9.4 Risk Reduction

The third criterion asks whether, in the sole judgment of the administrator, regulation presents a meaningful opportunity for health risk reduction for persons served by PWSs. In evaluating this criterion, EPA looked at the total exposed population, as well as the population exposed to levels above the estimated HRL. Estimates of the populations exposed and the levels to which they are exposed were derived from the monitoring results. These estimates are included in Chapter 4 of this document and summarized in section 9.4.2 below.

To evaluate risk from exposure through drinking water, EPA considered the net environmental exposure in comparison to the exposure through drinking water. For example, if exposure to a contaminant occurs primarily through ambient air, regulation of emissions to air provides a more meaningful opportunity for EPA to reduce risk than does regulation of the contaminant in drinking water. In making the regulatory determination, the available information on exposure through drinking water (Chapter 4) and information on exposure through other media (Chapter 5) were used to estimate the fraction that drinking water contributes to the total exposure. The EPA findings are discussed in Section 9.4.3 below.

In making its regulatory determination, EPA also evaluated effects on potentially sensitive populations, including fetuses, infants, and children. Sensitive population considerations are included in section 9.4.4.

9.4.1 Risk Criterion Conclusion

An estimated 113,000 individuals were served by systems with detections greater than the HRL (all served from small systems); an additional 738,337 individuals, all served by large systems, were exposed at levels >½HRL. Although additional monitoring data are needed, food and drinking water appear to be the major sources of exposure to DCPA. The impact of

regulating TPA and MTP concentrations in drinking water on health risk reduction is likely to be small, based on limited occurrence at levels of potential toxicological concern. Thus, the evaluation of the third criterion is negative.

9.4.2 Exposed Population Estimates

A total of 11,220,836 people were served by large PWSs in which TPA and MTP was greater than the MRL (≥1 µg/L). An estimated 1,118,000 people from small systems received water with mono- and di-acid concentrations greater than the MRL. These values are a function of the widespread use of DCPA, an herbicide, and the mobility of it and its degradates in the environment. The number of individuals exposed to concentrations greater than either the HRL or ½ the HRL was considerably smaller. An estimated 113,000 individuals served by small PWSs were exposed to levels greater than the HRL. In large systems, there were no exposures greater than the HRL, and 738,337 individuals were exposed to concentrations >½HRL from a single large system.

9.4.3 Relative Source Contribution

Relative source contribution (RSC) analysis compares the magnitude of exposure expected via drinking water to the magnitude of exposure from intake of TPA and MTP in other media, such as food, air, and soil. Lack of recent monitoring data for air, foods, and soils would preclude using a data-derived RSC value other than a default 20% at this time if a lifetime health advisory were to be developed for noncancer effects.

9.4.4 Sensitive Populations

No sensitive populations have been identified. The limited data available on TPA indicates that the rat fetus is not affected by oral exposure at levels below those that affect the dams. There are also no data to suggest gender-related differences in the toxicity of TPA or MTP.

9.5 Regulatory Determination Decision

As stated in Section 9.1.1, a positive finding for all three criteria is required in order to make a determination to regulate a contaminant. There are inadequate data to meet the regulatory determination criteria for TPA or MTP. Based on the monitoring of ambient water samples collected between 1992 and 2001 and of samples from PWSs collected between 2001 and 2005, TPA and MTP (combined) were detected in <3% of the systems tested, and approximately 113,000 individuals were exposed to a level greater than or equal to the HRL. Accordingly, it appears that TPA and MTP do not occur in PWSs with a frequency and at a level constituting a public health concern at the present time. Therefore, regulation of TPA and MTP does not present a meaningful opportunity for health risk reduction for persons served by PWSs.

10.0 REFERENCES

Auletta, A. and J. Kuzava. 1977. Activity of DTX-77-0005 in a test for differential inhibition of repair deficient and repair competent strains of *Salmonella typhimurium* [unpublished study]. Microbiological Associates Rpt. DS-0001. MRID 00100776 (as cited in U.S. EPA, 1988b).

Auletta, A., A. Parmar, and J. Kuzava. 1977. Activity of DTX-0003 in the *Salmonella*/microsomal assay for bacterial mutagenicity [unpublished study]. Microbiological Associates Rpt. DS-0002. MRID 00100774 (as cited in U.S. EPA, 1988b).

Carey, A.E., J.A. Gowen, H. Tai, et al. 1979. Pesticide residue levels in soils and crops from 37 states, 1972 - National Soils Monitoring Program (IV). Pestic. Monit. J. 12:209-229 (as cited in HSDB, 2004).

ChemFinder. 2004. Cambridge Soft Corporation, Cambridge, MA. Available from: <http://chemfinder.cambridgesoft.com>.

Chen, Y.L., et al. 1976. Chung-Kuo Nung Yeh Hua Hsueh Hui Chih 14:59-67 (as cited in HSDB, 2004).

Choi, J.S., T.W. Fermanian, D.J. Wehner, et al. 1988. Effect of temperature, moisture, and soil texture on DCPA degradation. Agron. J. 80:108-113 (as cited in HSDB, 2004).

DeVault, D.S. 1985. Contaminants in fish from Great Lakes harbors and tributary mouths. Arch. Environ. Contam. Toxicol. 14(5):587-594 (as cited in HSDB, 2004).

DeVault, D.S., J.M. Clark, and G. Lahvis. 1988. Contaminants and trends in fall run coho salmon. J. Great Lakes Res. 14:23-33 (as cited in HSDB, 2004) .

Diamond Alkali Company. 1963. MRID No. 00083584. HED doc. No. 003299, 005866. Available from EPA. Write to FOI, EPA, Washington DC 20460. (as cited in U.S. EPA, 1994c)

Elsea, J.R. 1958. Acute oral administration; acute dermal application; acute eye application [unpublished study]. MRID 00045823[1] (as cited in U.S. EPA, 1988b).

Fermenta Plant Protection Company. 1988. MRID 40958701. HED Doc. No. 007250, 008095. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

Fermenta ASC Corporation. 1989. MRID 41054820. HED Doc. No. 0088229, 008409 Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

Fermenta ASC Corporation. 1990. MRID 41349101, 41750102. HED Doc. No. 008373. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

[1]Confidential Business Information submitted to the EPA Office of Pesticide Programs.

Fleck, J.E., et al. 1988. Endosulfan and Chlorothal-dimethyl residues in soil and sediment of Monterey County. (Environ Hazards Assess Program, California Dep Food Agric, Sacramento, CA USA). Report 1988, EH-88-6; Order No. PB90-182635. pp. 47 (as cited in HSDB, 2004).

Frear, D.S. 1976. In: Kearney, P.C., and D.D. Kaufman (eds.). Herbicides: Chemistry Degradation and Mode Action, 2nd ed. 2:541-607 (as cited in HSDB, 2004).

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, et al. 1985a. Pesticides, selected elements, and other chemicals in adult total diet samples, October 1978–September 1979. J. Assoc. Off. Anal. Chem. 68:862-875 (as cited in HSDB, 2004).

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, et al. 1985b. Pesticides, selected elements, and other chemicals in adult total diet samples, October 1979–September 1980. J. Assoc. Off. Anal. Chem. 68:1184-1197 (as cited in HSDB, 2004).

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, et al. 1986a. Chemical contaminants monitoring. Pesticides, selected elements, and other chemicals in infant and toddler total diet samples, October 1980–March 1982. J. Assoc. Off. Anal. Chem. 69:123-145 (as cited in HSDB, 2004).

Gartrell, M.J., J.C. Craun, D.S. Podrebarac, et al. 1986b. Pesticides, selected elements, and other chemicals in adult total diet samples, October 1980–March 1982. J. Assoc. Off. Anal. Chem. 69: 146-161 (as cited in HSDB, 2004).

Gershon, H., and G.W. McClure, Jr. 1966. Approach to the study of the degradation of dimethyl tetrachloroterephthalate. Contributions from Boyce Thompson Institute 23:291-294 (as cited in HSDB, 2004).

Glotfelty, D.E., A.W. Taylor, B.C. Turner, et al. 1984. Volatilization of surface-applied pesticides from fallow soil. J. Agric. Food Chem. 32:638–643 (as cited in HSDB, 2004).

Glotfelty, D.E. and C.J. Schomburg. 1989. Volatilization of pesticides from soil. In: Reactions and Movement of Organic Chemicals in Soils. Soil Sci. Soc. Am. and Am. S. Agron. SSSA Special Publication 22:181-207 (as cited in HSDB, 2004).

Gold, L.S., C.B. Sawyer, R. Magaw, et al. 1984. A carcinogenic potency database of the standardized results of animal bioassays. Environ. Health Perspect. 58:9-319 (as cited in Klopman et al., 1996).

Gold, L.S., M. de Veciana, G.M. Backman, et al. 1986. Chronological supplement to the carcinogenic potency database: standardized results of animal bioassays published through December 1982. Environ. Health Perspect. 67:161-200 (as cited in Klopman et al., 1996).

Gold, L.S., T.H. Sloan, G.M. Backman, et al. 1987. Second chronological supplement to the carcinogenic potency database: standardized results of animal bioassays published through December 1984 and by the National Toxicology Program through May 1986. Environ. Health Perspect. 74:237-329 (as cited in Klopman et al., 1996).

Gold, L.S., T.H. Sloan, G.M. Backman, et al. 1990. Third chronological supplement to the carcinogenic potency database: standardized results of animal bioassays published through December 1986 and by the National Toxicology Program through June 1987. Environ. Health Perspect. 84:215-286 (as cited in Klopman et al., 1996).

Gold, L.S., N.B. Manley, T.H. Sloan, et al. 1993. The fifth plot of the carcinogenic potency database: results of animal bioassays published in the general literature through 1988 and by the National Toxicology Program through 1989. Environ. Health Perspect. 100:65-135 (as cited in Klopman et al., 1996).

Goldenthal, E., F. Wazeter, D. Jessup, et al. 1977. Ninety day toxicity study in rats. Compound: DTX 76-0010:239-044 [unpublished study]. Prepared by International Research and Development Corp. Submitted by Diamond Shamrock Agricultural Chemicals. MRID 00100773 (as cited in U.S. EPA, 1998c, 2004a).

Gunderson, E.L. 1988. FDA Total Diet Study, April 1982–April 1984. Dietary intakes of pesticides, selected elements, and other chemicals. J. Assoc. Off. Anal. Chem. 71:1200-1209 (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/>.

Hansch, C., et al. 1995. Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. In: Chihara, H., et al. (eds.). ACS Professional Reference Book. Washington, DC: American Chemical Society. p. 348 (as cited in HSDB, 2004).

Hazleton, L.N. and W.H. Dieterich.1963. Final report: two-year dietary feeding - dogs [unpublished study]. MRID 00083584 (as cited in U.S. EPA, 1988b).

Horowitz, M., T. Blumenfeld, G. Herzlinger, et al. 1974. Effects of repeated application of ten soil-active herbicides on weed population, residue accumulation and nitrification. Weed Res. 14:97-109 (as cited in HSDB, 2004).

HSDB (Hazardous Substances Data Bank). 2004. Dacthal. Searched December 1, 2004. Bethesda, MD: National Library of Medicine. Last updated January 31, 1996.

Hurto, K.A., A.J. Turgeon, and M.A. Cole. 1979. Degradation of benefin and DCPA in thatch and soil from a Kentucky bluegrass (*Poa pratensis*) turf. Weed Soil 27:154-157 (as cited in HSDB, 2004).

ISK Biotech Corporation. 1990a. MRID 41750103, 41905201. HED Doc. No. 008134, 008444. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

ISK Biotech Corporation. 1990b. MRID 41790901. HED Doc. No. 008408. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c)

ISK Biotech Corporation. 1991. MRID 41767901. HED Doc. No. 008366. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

ISK Biotech Corporation. 1993. MRID 42731001, 42998401 HED No. 010513. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c, 1998c, 2004a).

Jaffé, R., B. Eitzer, E. Stemmler, et al. 1985. Anthropogenic organic compounds in sedentary fish from Lakes Superior and Huron tributaries. J. Great Lakes Res. 11:156-162 (as cited in HSDB, 2004).

Jaffé, R. and R.A. Hites. 1986. Anthropogenic, polyhalogenated, organic compounds in non-migratory fish from the Niagara River area and tributaries to Lake Ontario. J. Great Lakes Res. 12(1):63-71 (as cited in HSDB, 2004).

Johnson, R.D. and D.D. Manske. 1977. Pesticides in food and feed. Pesticide and other chemical residues in total diet samples. XI. Pestic. Monit. J. 11:116-131 (as cited in HSDB, 2004).

Johnson, R.D., D.D. Manske, and D.S. Podrebarac. 1981. Pesticide, metal, and other chemical residues in adult total diet samples. XII. August 1975–July 1976. Pestic. Monit. J. 15:54-69 (as cited in HSDB, 2004).

Johnson, R.D., D.D. Manske, D.H. New, et al. 1984. Pesticide, metal, and other chemical residues in adult total diet samples. XIII. August 1976–September 1977. J. Assoc. Off. Anal. Chem. 67:154-166 (as cited in HSDB, 2004).

Kazen, C., A. Bloomer, R. Welch, et al. 1974. Persistence of pesticides on the hands of some occupationally exposed people. Arch. Environ. Health 29:315-318 (as cited in HSDB, 2004).

Klopman, G., D. Fercu, and H.S. Rosenkranz. 1996. The carcinogenic potential of dacthal and its metabolites. Environ. Toxicol. Chem. 15(2):80-84.

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/.

Kouri, R., A. Parmar, J. Kuzava, et al. 1977a. The activity of DTX 770006 in the in vivo cytogenetic assay in rodents for mutagenicity [unpublished study]. Microbiological Associates Proj. No. T1083. MRID 00107907 (as cited in U.S. EPA, 1988b).

Kouri, R., A. Parmar, J. Kuzava, et al. 1977b. Activity of DTX 770004 in the dominant lethal assay in rodents for mutagenicity [unpublished study]. Microbiological Associates Proj. No. T1077. Final Report. MRID 00100775 (as cited in U.S. EPA, 1988b).

Kutz, F.W., A.R. Yobs, and H.S.C. Yang. 1976. National pesticide monitoring networks. In: Lee, R.E. (ed.). Air Pollution From Pesticides and Agricultural Processes. Cleveland, OH: CRC Press. pp. 95-136 (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. Available from: <http://water.usgs.gov/nawqa/NAWQA.OFR94-70.html>.

Lee, R.E., Jr. 1977. Proceedings of the 4th International Clean Air Congress. Kasuga, S., et al. (eds). Research Triangle Park, NC: U.S. EPA Health Effects Lab. pp. 37-40 (as cited in HSDB, 2004).

Leiker, T.J., C.E. Rostad, C.R. Barnes, et al. 1991. A reconnaissance study of halogenated organic compounds in catfish from the lower Mississippi River and its major tributaries. Chemosphere 23:817-829 (as cited in HSDB, 2004).

Lewis, R.G., R.C. Fortmann, and D.E. Camann. 1994. Evaluation of methods for monitoring the potential exposure of small children to pesticides in the residential environment. Arch. Environ. Contam. Toxicol. 26(1):37-46 (as cited in HSDB, 2004).

Lyman, W.J., W.F. Reehl, and D.H. Rosenblatt. 1990. Handbook of Chemical Property Estimation Methods. Washington, DC: American Chemical Society. pp. 4-9 (as cited in HSDB, 2004).

Majewski, M.S., M.M. McChesney, and J.N. Seiber. 1991. A field comparison of two methods for measuring DCPA soil evaporation rates. Environ. Toxicol. Chem. 10:301-311 (as cited in HSDB, 2004).

Major, D. 1985. A 30-day oral intubation study in rats with tetrachloroterephthalic acid: SDS 954. Document No. 665-STX-84-0007001 [unpublished study]. MRID 00158011. Prepared by SDS Biotech Corp. p. 269.(as cited in U.S. EPA, 1998c, 2004a).

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/>.

Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere 26:213-218 (as cited in HSDB, 2004).

Miller, F.M. and E.D. Gomes. 1974. Detection of DCPA residues in environmental samples. Pestic. Monit. J. 8:53-58 (as cited in HSDB, 2004).

Mizen, M. 1985. A teratology dose range-finding study in rats with tetrachloroterephthalic acid (SDS-954) Document No. 687-5Tx-84-0034-002 [unpublished study]. Prepared by SDS Biotech

Corp. p. 120. (MRID 262303 as cited in U.S. EPA, 1998c; MRID 41064802 as cited in U.S. EPA, 1998c; MRID 00158010 as cited in U.S. EPA, 2004a).

Nash, R.G. and T.J. Gish. 1989. Halogenated pesticide volatilization and dissipation from soil under controlled conditions. Chemosphere 18(11/12):2353-2362 (as cited in U.S. EPA, 1998c).

NRC (National Research Council). 1983. Risk Assessment in the Federal Government: Managing the Process. Washington, DC: National Academy Press.

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

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 online at: <http://ca.water.usgs.gov/pnsp/svoc/SVOC-SED_2001_Text.html>.

Paynter, O.E. and M. Kundzin. 1963. Two-year dietary administration - rats. Final Report. MRID 00083577 (as cited in U.S. EPA, 1988b).

Pereira, W.E., F.D. Hostettler, J.R. Cashman, et al. 1994. Occurrence and distribution of organochlorine compounds in sediment and livers of striped bass (*Morone saxatilis*) from the San Francisco Bay–Delta Estuary. Marine Poll. Bull. 28:434-441 (as cited in HSDB, 2004).

Roberts, H.A., et al. 1978. Proc. Br. Crop Prot. Conf. - Weeds 14:87-92 (as cited in HSDB, 2004).

Saiki, M.K. and C.J. Schmitt. 1986. Organochlorine chemical residues in bluegills and common carp from the irrigated San Joaquin Valley floor, California. Arch. Environ. Contam. Toxicol. 15:357-366 (as cited in HSDB, 2004).

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

Schmitt, C.J., J.L. Zajicek, and M.A. Ribick. 1985. National pesticide monitoring program: residues of organochlorine chemicals in freshwater fish, 1980-81. Arch. Environ. Contam. Toxicol. 14:225-260 (as cited in HSDB, 2004).

Schmitt, C.J., J.L. Zajicek, and P.H. Peterman. 1990. National Contaminant Biomonitoring Program: residues of organochlorine chemicals in USA freshwater fish, 1976-1984. Arch. Environ. Contam. Toxicol. 19:748-781 (as cited in HSDB, 2004).

SDS Biotech Corporation. 1986. MRID 00160685. HED Doc. No. 005866, 009515. Available from EPA. Write to FOI, EPA, Washington, DC 20460 (as cited in U.S. EPA, 1994c).

Skinner, M.B. and D.E. Stallard. 1963. Dacthal animal metabolism studies. MRID 00083579[1] (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.126 (as cited in HSDB, 2004).

Starr, H.G. Jr, F.D. Aldrich, W.D. MacDougall III, et al. 1974. Contribution of household dust to the human exposure to pesticides. Pestic. Monit. J. 8:209-212 (as cited in HSDB, 2004).

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).

Tessari, J.D. and D.L. Spencer. 1971. Air sampling for pesticides in the human environment. J. AOAC Int. 54:1376-1382 (as cited in HSDB, 2004).

Tomlin, C. 1994. The Pesticide Manual - A World Compendium. 10th ed. Thornton Heath, UK: The British Crop Protection Council. p. 205 (as cited in HSDB, 2004).

Tusing, T.W. 1963. Oral administration - humans. MRID 0083583 (as cited in U.S. EPA, 1988b).

Tweedy, B.G., N. Turner, and M. Achituv. 1968. The interactions of soil-borne microorganisms and DCPA. Weed Sci. 16:470-473 (as cited in HSDB, 2004).

U.S. EPA (United States Environmental Protection Agency). 1986a. Guidelines for the health risk assessment of chemical mixtures. Fed. Reg. 51(185):34014-34025. Available from: <http://www.epa.gov/iris/backgr-d.htm>.

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). 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.

[1]Confidential Business Information submitted to the EPA Office of Pesticide Programs.

U.S. EPA (United States Environmental Protection Agency). 1988b. DCPA (Dacthal) Health Advisory. Office of Drinking Water, U.S. Environmental Protection Agency. August, 1988.

U.S. EPA (United States Environmental Protection Agency). 1988c. Hexachlorobenzene (CASRN 118-74-1). Integrated Risk Information System (IRIS). Office of Research and Development. Available from: http://www.epa.gov/iris/subst/0374.htm.

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). 1994c. Integrated Risk Information System (IRIS): Dacthal. Cincinnati, OH.

U.S. EPA (United States Environmental Protection Agency). 1995a. 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, Springfield, VA; PB95-213765, and <http://www.epa.gov/iris/backgr-d.htm>.

U.S. EPA (United States Environmental Protection Agency). 1995b. Carcinogenicity peer review of DCPA (dimethyl tetrachloroterephthalate or dacthal). U. S. Environmental Protection Agency. Office of Pesticide Programs TXR # 0050123. February 10, 1995.

U.S. EPA (United States Environmental Protection Agency). 1996a. Exposure Factors Handbook. U.S. Environmental Protection Agency, Office of Research and Development, Washington, DC. EPA/600/8-89/043.

U.S. EPA (United States Environmental Protection Agency). 1996b. Guidelines for reproductive toxicity risk assessment. Fed. Reg. 61(212):56274-56322.

U.S. EPA (United States Environmental Protection Agency). 1997. Announcement of the draft drinking water contaminant candidate list; notice. Fed. Reg. 62(193):522194-52219.

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. Reregistration eligibility decision DCPA. Washington, DC: Office of Prevention, Pesticides, and Toxic Substances (7508C), EPA738-R-98-005. November 1998.

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

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

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

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

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

U.S. EPA (United States Environmental Protection Agency). 2002b. Announcement of Preliminary Regulatory Determinations for Priority Contaminants on the Drinking Water. Fed. Reg 67(106):38222-38244.

U.S. EPA (United States Environmental Protection Agency). 2003. Announcement of Regulatory Determinations for Priority Contaminants on the Drinking Water Contaminant Candidate List. Fed. Reg. 68:42897-42906.

U.S. EPA (United States Environmental Protection Agency). 2004a. TPA (tetrachloroterephthalic acid)-metabolite of DCPA (Dacthal). Evaluation of potential for carcinogenicity. U.S. Environmental Protection Agency Office of Prevention, Pesticide, and Toxic Substances, Washington, DC 20460. May 25, 2004.

U.S. EPA (United States Environmental Protection Agency). 2004b. 2nd Revised drinking water and aggregate human health risk assessment for Chlorothal demethyl (DCPA) and the metabolite tetrachloroterephthalic acid (TPA) DP Barcode D 291641. Washington, DC 20460. June 8, 2004.

U.S. EPA (United States Environmental Protection Agency). 2004c. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005. Office of Water. Winter. Available from: <http://www.epa.gov/waterscience/drinking/standards/dwstandards.pdf>.

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. DCPA: Order to terminate uses. Fed. Reg. 70(143):43408-43410.

U.S. FDA (United States Food and Drug Administration). 2003. Food and Drug Administration total diet study: Sullary of residues found ordered by pesticide (Market Baskets 91-3 to 01-4). June.

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>.

Wazeter, F.X., E.I. Goldenthal, and W.P. Dean. 1974a. Acute oral toxicity (LD_{50}) male and female albino rats [unpublished study]. MRID 00031872[1] (as cited in U.S. EPA, 1988b).

Wazeter, F.X., E.I. Goldenthal, and W.P. Dean. 1974b. Acute oral toxicity (LD_{50}) in beagle dogs [unpublished study]. MRID 00031873[1] (as cited in U.S. EPA, 1988b).

Wettasinghe, A., and I.J. Tinsley 1993. Degradation of dacthal and its metabolites in soil. Bull. Environ. Contam. Toxicol. 50:226-231 (as cited in HSDB, 2004).

Whitmore, R.W., F.W. Immerman, D.E. Camann, et al. 1994. Non-occupational exposures to pesticides for residents of two U.S. cities. Arch. Environ. Contam. Toxicol. 26:47-59 (as cited in HSDB, 2004).

Worthing, C.R. (ed.). 1979. Pesticide Manual. 6th ed. Worcestershire, England: British Crop Protection Council. p. 121 (as cited in HSDB, 2004).

[1]Confidential Business Information submitted to the Office of Pesticide Programs.

APPENDIX A: Abbreviations

BCF	bioconcentration factor
CCL	Contaminant Candidate List
CWS	community water system
DCPA	dimethyl tetrachloroterephthalic acid
FR	Federal Register
GC/EC	gas chromatography/electron capture
gd	gestation days
HCB	hexachlorobenzene
HRL	health reference level
K_{oc}	organic carbon/water partitioning coefficient
K_{ow}	octanol-water partitioning coefficient
LOAEL	lowest observed adverse effect level
LOD	limits of detection
MRL	minimum reporting level
MTP	monomethyl tetrachloroterephthalic acid
MULTICASE	multiple computer automated structure evaluation
NAWQA	National Water Quality Assessment
γ4-NBP	γ-4-nitrobenzylpyridine
NDWAC	National Drinking Water Advisory Council
NOAEL	no observed adverse effect level
NPDWR	National Primary Drinking Water Regulation
NTNCWS	nontransient noncommunity water system
NTP	National Toxicology Program
OPP	Office of Pesticide Programs (U.S. EPA)
ppb	parts per billion
ppm	parts per million
PWS	public water system
QSAR	quantitative structure-activity relationship
RED	Re-registration Eligibility Decision
RfC	reference concentration
RfD	reference dose
RL	reporting level
RSC	relative source contribution
SDWA	Safe Drinking Water Act
T_3	triiodothyronine
T_4	thyroxine
TPA	tetrachloroterephthalic acid
TSH	thyroid-stimulating hormone
UCMR 1	first Unregulated Contaminant Monitoring Regulation
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 Survey