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

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

August 17, 2005

MEMORANDUM

SUBJECT: DIMETHOATE: The Post-SAP HED Chapter of the Reregistration Eligibility Decision Document (RED). PC Code: 035001, Case # 0088. DP Barcode D320518.

Regulatory Action: Phase 5 Reregistration Action
Risk Assessment Type: Single Chemical Aggregate

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The attached revised review of the Human Health Assessment for the dimethoate RED document (post-SAP) was generated as part of the post-phase 6 public participation process to reflect the comments received at the November 31 - December 1, 2004 Scientific Advisory Panel (SAP) meeting on dimethoate hazard issues, analysis of data received since the September 30, 2003 dimethoate risk assessment, policy changes, and the inclusion of benchmark dose (BMD) analysis for endpoint selection. The Health Effects Division's (HED) revised chapter reflects the Agency's guidelines concerning the retention of the Food Quality Protection Act (FQPA) factor and the risk assessment, and includes the results of a dietary risk evaluation using United States Department of Agriculture's (USDA) Continuing Surveys of Food Intake by Individuals (CSFII) in 1994-1996 and 1998, monitoring data from USDA's Pesticide Data Program (PDP) and from the Food and Drug Administration's (FDA) surveillance data program, and use of the Dietary Exposure Evaluation Model (DEEM-FCID™), version 2.02/2.03 software. This chapter includes a summary of the product and residue chemistry review from Bonnie Cropp-Kohlligian, acute and chronic dietary risk analysis and characterization from David Hrdy, toxicology review from Anna Lowit, Byong-Han Chin, Kathleen Raffaele, Elissa Reaves, Vicki Dellarco, Karl Baetcke, and Judy Facey, benchmark dose analysis from Philip Villanueva, occupational exposure and risk assessment from Alan Nielsen, environmental fate and drinking water exposures from R. David Jones [Environmental Fate and Effects Division (EFED)], as well as risk assessment and characterization from Diana Locke.

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TABLE OF CONTENTS

DIMETHOATE POST-SAP ASSESSMENT

PREFACE

Upon the completion of the Human Health Risk Assessment for the dimethoate post-mitigation RED document (*September 30, 2003. DP Barcode D291601*), the Agency concluded that there were potential risks of concern based on the registered post-mitigation uses of dimethoate through exposures from drinking water and occupational activities. Cheminova (primary registrant) had submitted a letter (*July 8, 2003, Diane Allemang to Dan Kenny*) requesting the voluntary cancellation of the following crops from their dimethoate technical registration: apples, grapes, cabbage, collards, spinach, and head lettuce (all other lettuces are retained). Other uses, not listed on the technical label, were also voluntarily cancelled, which included: broccoli raab, fennel, tomatillo, lespedeza, and trefoil [*Federal Register: September 10, 2003 (volume 68, number 175) Environmental Protection Agency (OPP-2003-0263; FRL-7321-2) pp 53371-53374*]. Based on the assumptions used in the food exposure assessment at that time, the removal of the above listed crops from dietary risk consideration reduced the potential exposures from food (alone) to all population subgroups to risks below the Agency's level of concern. However, since that time, data have become available to the Agency which suggests that exposures to additional metabolites of concern are expected to increase the acute and chronic dietary risks but could not, and cannot, be reliably quantified at this time. The Agency is asking for data to address these concerns; a comparative repeated dose cholinesterase inhibition (ChEI) study in rats to more accurately characterize the ChE inhibiting potential of the metabolites of concern and, magnitude of the residue data, in order to more accurately characterize the abundance of the residues of these metabolites of concern.

In the dimethoate post-mitigation RED document, the estimated drinking water exposures to all population subgroups and the occupational exposures remained potential risks of concern (see *D291601, 09/30/2003*). In addition, key scientific issues regarding the interpretation of the dimethoate developmental neurotoxicity (DNT) study, the hazard characterization and dose-response assessment remained unresolved. The EPA/HED, in collaboration with Canada's Pest Management Regulatory Agency (PMRA) developed a science issue paper entitled: *Dimethoate: Issues Related to the Hazard and Dose-response Assessment* (USEPA, 2004) which was reviewed by the FIFRA Scientific Advisory Panel (SAP) in December, 2004. The panel provided comments regarding the interpretation of ChEI in juvenile and adult rats along with pup mortality data from the DNT study and related special studies. The panel was also asked to comment on the information available for dimethoate which characterizes the underlying cause(s) of the pup mortality in the dimethoate DNT study and the degree to which this information can be used to determine the impact of maternal neglect/maternal toxicity on pup mortality. The panel agreed that "… the database is insufficient to characterize the underlying cause of pup mortality." Furthermore, the panel supported EPA's proposal that the use of the brain ChEI data for the critical effect in the risk assessment is protective of pup death (*FIFRA SAP, 2005*).

EPA has further refined the dose-response assessment for dimethoate compared to that from the dimethoate post-mitigation RED document (*September 30, 2003. DP Barcode D291601*) by using benchmark dose (BMD) analysis to develop points of departure (PoD) for oral, dermal, and inhalation exposures using route-specific studies in dimethoate and/or omethoate. This analysis was developed using an exponential dose-response model previously supported by the FIFRA SAP (2002).

1.0 EXECUTIVE SUMMARY

Dimethoate is a general use systemic, organophosphate (OP) insecticide/acaricide that is used to control a wide variety of insect pests. Some examples of the pests that dimethoate is intended to control include aphids, citrus thrips, grasshoppers, leafminers, spider mites, and whiteflies. For reregistration, Cheminova (primary data-submitter) is supporting the use of dimethoate on a variety of foods, feeds, and ornamentals. Manufacturing products contain between 95 and 96% active ingredient (ai). Formulated end-use products are available as emulsifiable concentrates (EC) and wettable powders (WP). However, the WP formulation is being supported during reregistration for use on pears, potatoes, and noncrop areas adjacent to vineyards only. Historically, several other types of formulated products have contained dimethoate, such as dusts, granulars, and a ready-to-use formulation. However, none of these other formulation types are being supported in the reregistration process and are not included in the risk assessment.

Tolerances are established for total residues of dimethoate and its oxon metabolite, omethoate (*40 CFR 180.204*). The Codex Alimentarius Commission has established separate maximum residue limits (MRLs) for dimethoate *per se* and omethoate *per se* in/on various commodities (see *Guide to Codex Maximum Limits for Pesticide Residues, Part 2, FAO CX/PR, 04/1993*). The Codex and U.S. tolerances are not harmonized with respect to MRL/tolerance expression since the U.S. tolerance expression is in terms of the combined residues of dimethoate and omethoate, as a metabolite.

Dimethoate is not a restricted use chemical, though no residential exposure and risk assessment is included in this document because the registrants are not supporting residential uses [*Federal Register: May 1, 2002 (Volume 67, Number 84, Page 21669 ENVIRONMENTAL PROTECTION AGENCY. OPP-2002-0023; FRL-6834-4. Dimethoate Product Cancellation Order and Label Amendment; Technical Correction*]. However, the Agency is currently in the process of expanding the scope of residential exposure assessments by developing guidance for characterizing exposures from sources other than residential uses, such as from spray drift; residential residue track-in; exposures to farm worker children; and exposures to children in schools. Modifications to this assessment will be incorporated as updated guidance becomes available.

As discussed in the Preface, HED has received and reviewed additional dimethoate and omethoate data, as well as conducted a BMD analysis. In two meetings (HazSPoC Part 1. TXR# 0052988 & HazSPoC Part 2. TXR# 0052992) with the HED's Hazard Science Policy Council (HazSPoC) it was agreed that the use of the BMDs/BMDLs for the critical effect, brain ChEI, is 1) protective of all other effects of concern, 2) agrees with the SAP's conclusions, and 3) is consistent with the approach that was used on the OP cumulative risk assessment.

The BMDs/BMDLs were calculated from route-specific studies for the following endpoints: acute dietary(all populations), chronic dietary, short- & intermediate-term dermal, and short- & intermediate-term inhalation. No long-term exposures are expected. Since HED has determined that brain ChEI is

the most protective critical effect and a 28-day dermal toxicity study in rats, with ChEI measurements, is available, a dermal absorption factor is not needed. Though no repeated-dose inhalation study on dimethoate is available, a 21-day inhalation study in rats using omethoate is available. The omethoate inhalation study is appropriate for endpoint selection and certainly protective, since omethoate is known to have higher toxicity relative to dimethoate.

Both dietary residue monitoring data and dislodgeable foliar residue (DFR) data show measurable levels of dimethoate and omethoate. Available data show that the oxon metabolite of dimethoate, omethoate, is a more potent ChE inhibitor than its parent. Based on new data and revised BMD modeling, the HED and the Agency's Office of Research and Development (ORD) determined that toxicity adjustment factors (TAF) of 12 for acute dietary and short-term occupational, and 3 for chronic dietary and intermediate-term occupational exposures, should be applied to omethoate exposures to be protective of more potent omethoate toxicities.

There are indications that additional metabolites of dimethoate are present and that some may also be ChE inhibitors. However, based on the available data, it is unlikely that exposure to these metabolites of dimethoate (other than omethoate) will make a significant contribution to potential risk. Therefore, they are not quantitatively included in the risk assessment. Confirmatory data are needed to both measure the ChE inhibiting potential of each metabolite and to measure the residues of each metabolite on a variety of representative crops.

An uncertainty factor (UF) of 100 was applied to the doses selected for risk assessment to account for both interspecies extrapolation and intraspecies variability. HED/OPP determined that for dimethoate, the special FQPA 10X factor, used to account for enhanced sensitivity of infants and children (as required by the FQPA), could be reduced to 1X (see Section 4.2).

HED performed a highly refined acute dietary analysis (Tier 3) incorporating updated dietary guidelines, a UF of 100, and exposure to ChEI residue levels of dimethoate and its metabolite, omethoate. The acute TAF of 12 was applied to all omethoate residues. The acute probabilistic dietary risk assessment is based primarily on USDA PDP monitoring data from years 2000 or more recent, when enough data existed, and FDA residue data; the USDA's 1994-1996 and 1998 CSFII food consumption survey; processing/cooking data; and percent crop treated (%CT) data. The DEEM-FCID™ software, version 2.02, was used in combining the residue data and consumption data to estimate the acute dietary exposures. The assessment showed that acute dietary exposures to dimethoate and omethoate in food alone are not expected to exceed the acute Population Adjusted Dose (aPAD) at the 99.9th percentile estimated exposure distribution (32% aPAD for children 1-2 years of age, highest exposed population subgroup) and are not of concern. The crops that appear to make the most significant contribution (dietary "drivers") to the risk for infants and children are broccoli, kale, cherries, turnip, celery and cauliflower. It should be noted that monitoring data, as well as processing/cooking factors, were available and used in the dietary assessment for the dietary drivers, or translations from monitoring data, and therefore, the risk estimates for these crops are considered highly refined and not an overestimate of potential risk.

The chronic dietary analysis was conducted incorporating similar refinements and a chronic TAF of 3 for omethoate residues, and used DEEM-FCID™ software, version 2.03. Based on a highly refined Tier 3 chronic dietary exposure analysis, risks from dietary exposures of dimethoate and omethoate from food alone to all population subgroups are not expected to exceed the chronic PAD (cPAD) and are not of concern (5% cPAD for children 1-2 years of age).

EFED derived estimated drinking water exposure concentrations (EDWECs) of dimethoate in surface and ground waters from water quality models that use conservative assumptions regarding the pesticide transport from the point of application to surface and ground water, and supplemented their estimates with limited monitoring data. Maximum applications (rate and frequency) of dimethoate to Florida and California citrus, were used in the models. Based on dimethoate-specific fate and drinking water treatment data, and based on treatment data on other OPs, EFED believes that dimethoate will be converted to omethoate during drinking water treatment (primarily by chlorination). Tier 2 estimated acute (peak) and chronic (average) surface water EDWECs are calculated to be 1654 µg/L and 73 µg/L, respectively, based on applications to Florida citrus (maximum). These acute and chronic estimates include the TAFs of 12 and 3, respectively, to account for the conversion to omethoate (100% assumed). The ground water acute and chronic EDWEC for dimethoate is 0.044 µg/L, based on Tier 1 modeling and limited monitoring data. The TAFs have only been applied to surface water, as ground water wells are likely to be privately owned and not chlorinated.

Surface water monitoring data from a number of sources are available but are limited and not nationally representative. One monitoring study, sampling over several years, and conducted by the California Department of Pesticide Regulation (CalDPR), found the highest concentration of dimethoate, 2.4 µg/L, in the San Joaquin River basin. Given the sampling pattern and frequency of the study, it is uncertain whether higher concentrations (peak) exist. Omethoate was not looked for in the study.

Dimethoate-specific treatment (chlorination) data are available but are limited. These data indicate that, under some conditions, conversion to omethoate may possibly be low as 20%. Since these data are limited, 100% conversion of dimethoate to omethoate during drinking water treatment of surface waters has been assumed as a protective measure for this assessment. More data are needed. Without actual drinking water monitoring data (at-the-tap), it is difficult to draw any conclusions about actual residues in drinking water of dimethoate, omethoate, or any of the other metabolites of concern. Dimethoate is not regulated under the Safe Drinking Water Act and the Agency's Office of Water (OW) has not established a Maximum Contaminant Level (MCL) for dimethoate or omethoate in water.

The aggregate acute risk estimate includes the contribution to risk from dietary (food + drinking water) sources only. The acute risk estimates from exposures to dimethoate and omethoate in food alone, do not exceed the Agency's level of concern (100% aPAD) and are not of concern. When combined with drinking water, aggregate acute risk estimates from exposures to food plus water, exceed HED's level of concern. The estimated aggregate acute dietary risk is 1773 % of the aPAD at the 99.9th percentile

for infants (< 1 year old, most highly exposed population subgroup) when EDWECs from applications to Florida citrus are included, and 1011% aPAD when EDWECs from applications to California citrus are included. For children 1-2 years of age, the estimated acute aggregate dietary risk is 771 % and 467% of the aPAD when EDWECs from applications to Florida and California citrus, respectively, are included (see *Hrdy, 2005b*).

Aggregate chronic (noncancer) risk estimates generally include the contribution of risk from dietary sources (food + water) and residential sources. However, no residential uses are being supported. Chronic risk estimates from exposures to dimethoate and omethoate in food alone, do not exceed HED's level of concern for all population subgroups and are not of concern. When combined with drinking water, chronic aggregate risk estimates from exposures to food plus water exceed HED's level of concern. The estimated chronic aggregate dietary risk is 231 % of the cPAD for infants (< 1 year old, most highly exposed population subgroup) when EDWECs from applications to Florida citrus are included, and 109% of the cPAD for children ages 1-2 years of age.

HED anticipates that most occupational exposures to dimethoate will occur over a short-term duration, since the HED defines short-term exposures as the use of a chemical up to 30 days. HED anticipates that there may also be intermediate-term exposures in some handler exposure scenarios, particularly those involving applications by commercial applicators to large-acreage crops (e.g., field corn, wheat, alfalfa, cotton). However, since the route-specific intermediate-term endpoint is the same as the short-term endpoint, the Margins of Exposure (MOEs) for intermediate-term exposures are the same as those calculated for short-term exposures. Surrogate data were used to develop the exposure risk assessment for handlers since no chemical-specific data are available. The calculations of short- and intermediate-term total risks to handlers indicate that most occupational handler risks are not of concern (i.e., MOEs are greater than 100) at some level of risk mitigation. However, MOEs are a concern (i.e., the MOEs are below 100), even with engineering controls, for: mixing/loading liquid formulations for aerial and chemigation applications to many crops (see section 9.1.2.4) at a variety of application rates; mixing/loading/applying with high pressure handwand sprayers to woody ornamentals, Christmas tree farms, and conifer seed orchards; mixing/loading/applying liquid formulations by aerial and chemigation applications to cottonwoods; and applying sprays with airblast equipment to seed orchards.

Postapplication occupational exposure is likely following applications of dimethoate to fruit, vegetable, grain, fiber, feed, conifer seed nursery, cottonwood grown for pulp, ornamental, and other crops and sites during typical postapplication activities such as harvesting, irrigating, scouting, pruning, thinning, and transplanting. Submitted dislodgeable foliar residue (DFR) data show measurable levels of dimethoate and omethoate on foliage. DFR data were submitted for grapes, apples, lettuce, and tomatoes and were translated to other crops, as appropriate. The results of the risk assessment for postapplication exposures indicate that the location and/or the environmental conditions near the time of application influence the length of time following application until risks are not of concern (i.e., MOEs are greater than or equal to 100) as does the type of plant to which the application is directed. For

most crops, the risk assessment indicates that following applications in arid areas (i.e., outdoor areas where average annual rainfall is less than 25 inches), residues persist longer than in non-arid areas, particularly in orchards and to ornamentals (see section 9.2.2.2). HED could potentially establish different entry restrictions for arid areas versus nonarid areas.

The Agency conducted a cumulative risk assessment for dimethoate and other OPs (*Revised Cumulative Risk Assessment. USEPA, 2002*), prior to the voluntary cancellation of some dimethoate uses.

In summary, the potential acute and chronic dietary risks to all population subgroups, based on dimethoate/omethoate exposures from food alone, are not of concern but, when drinking water (modeled or measured) is aggregated with food, there are potential risks of concern. There are potential occupational risks of concern to handlers, even with engineering controls, for aerial and chemigation applications to many crops at a variety of application rates; for applications with high pressure handwand sprayers to woody ornamentals and trees, and applications with airblast equipment to seed orchards. For postapplication exposures, the location and/or the environmental conditions near the time of application influence the length of time following application until risks are not of concern, as does the type of plant to which the application is directed. In general, arid climates require longer REIs. Exposures to additional metabolites of concern are expected to increase dietary and occupational risks but cannot be reliably quantified at this time.

2.0 PHYSICAL/CHEMICAL PROPERTIES

2.1 Description of Chemical

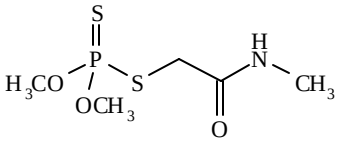
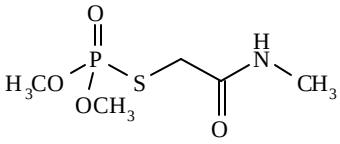
Dimethoate [O,O-dimethyl S-(N-methylcarbamoylmethyl) phosphorodithioate] is a systemic insecticide/acaricide registered for use on various food and feed crops.

Empirical Formula:	$C_5H_{12}NO_3PS_2$
Molecular Weight:	229.3
CAS Registry No.:	60-51-5
PC Code:	035001

2.2 Identification of Active Ingredient

Dimethoate is a white crystalline solid with a mercaptan odor and a melting point of 45-48^o C. Dimethoate is soluble in water at 25 g/L at 21^o C, is highly soluble in chloroform, methylene chloride, benzene, toluene, alcohols, esters, and ketones, and is only slightly soluble in xylenes, carbon tetrachloride, and aliphatic hydrocarbons. Dimethoate is stable in aqueous solutions at pH 2-7, but hydrolyzes in alkaline media.

Chemical structures of Dimethoate and Omethoate

Compound: Dimethoate	**Compound**: Omethoate
Dimethoate  *O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorodithioate	**Omethoate**  *O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorothioate

2.3 Manufacturing-Use Products

A search of the Reference Files System (REFS), conducted 12/1999, identified six dimethoate manufacturing-use products (MPs) registered under Shaughnessy No. 035001. A list of the MPs subject to a reregistration eligibility decision is presented below in Table 2.3.

TABLE 2.3

Formulation	EPA Reg. No.	Registrant
98% T	4787-7	Cheminova Agro A/S
96% T	10163-211	Gowan Company
94% T	19713-209	Drexel Chemical Company
82% FI	7969-32	BASF Corporation
96%	34704-788	Platte Chemical Co. Inc.
96%	51036-279	Micro-Flo Company

3.0 METABOLISM

3.1 Animal and Human Metabolism Data

3.1.1 Dimethoate

In the rat, dimethoate is metabolized via hydrolytic and oxidative pathways (based on urine analyses). The hydrolytic pathway (major) involves cleavage of the C-N bond to yield dimethoate carboxylic acid that was subsequently metabolized to dimethyldithiophosphate, dimethylthiophosphoric acid, and dimethylphosphoric acid. A minor metabolic pathway involves oxidation of dimethoate to its oxon analogue, omethoate, that was subsequently metabolized to dimethylthiophosphoric acid and dimethylphosphoric acid. Loss of the methoxy groups of the parent to yield carbon dioxide is a minor metabolic pathway.

Groups of male and female Wistar rats were dosed with ^{14}C-dimethoate (labeled in the O-methyl groups) at a single oral dose (10 or 100 mg/kg), an intravenous dose (10 mg/kg) or 14-day repeated oral doses of dimethoate at 10 mg/kg followed by a single oral dose of ^{14}C-dimethoate at 10 mg/kg. Dimethoate was rapidly absorbed, metabolized, and eliminated in rats for all dosing regimens. There were no remarkable sex-, dose- or treatment-related differences in the absorption, distribution, and elimination of dimethoate in rats. Total recovery of radioactivity ranged between 91% and 97% of the administered dose for all tested groups within 5 days after dosing. Most of the radioactivity (85-91% of the dose) was excreted in the urine. A small amount of radioactivity was found in feces (1-2% of the dose), in the tissues and remaining carcass (1-2%), and in the expired air as carbon dioxide (2-3%). ^{14}C-Concentrations in all tissues was less than 7 ppm after a single oral dose at 100 mg/kg and less than 0.3 ppm after a single or multiple oral doses at 10 mg/kg (14-daily dose) and an intravenous dose at 10 mg/kg.

Most (83-91%) of the administered dose in urine samples from orally or intravenously dosed rats were identified by HPLC analysis followed by confirmation by mass spectrometry. Four metabolites identified were as follows:

Ref II (Omethoate, 1-6% of dose),
Ref XVI (Dimethylthiophosphoric acid, 4-11% of dose),
Ref XV (Dimethyldithiophosphate, 20-30% of dose), and
Ref III (Dimethoate carboxylic acid, 29-46% of dose).

There were no qualitative or quantitative differences in the metabolite profiles for dose level and sex of rats after oral or intravenous administration of ^{14}C-dimethoate. Five radioactive components were not identified but no component in the urine samples represented more than 7% of the dose. Unchanged parent in the urine samples represented 0.4-2% of the dose. Biliary excretion of radioactivity by bile-cannulated rats accounted for 4-5% of the dose 2 days after a single oral administration of ^{14}C-dimethoate at 10 or 100 mg/kg.

A metabolism study (MRID# 46497601) with human volunteers was evaluated; however, due to the limitations of this study, including a limited number of subjects and only one dose, it was not useful for dose-response evaluation and was not relied upon in the risk assessment.

3.1.2 Omethoate

In a study (MRID# 46099808) conducted to examine the metabolism and disposition of omethoate, Wistar rats (5/sex/group) were given either single oral or intravenous doses of 0.5 mg/kg bw, a single 10 mg/kg bw oral dose, or a 14-day repeated oral dose (0.5 mg/kg bw/day) of unlabeled omethoate, followed by a single oral exposure to 0.5 mg/kg bw [^{14}C]-omethoate.

A single oral exposure to 10 mg/kg bw was used to monitor excretion of volatile radioactivity in expired air. At the high dose (10 mg/kg bw), male and female rats exhibited signs of toxicity at 0.5-4 hrs post-dosing including trembling, salivation, high breathing rate, and congestion of the eyes. Overall recovery of administered radioactivity was an acceptable 88.2-98.4%. Absorption rates were rapid and appeared similar in both males and females from all dose groups. Peak plasma concentrations were noted within one hour of dosing in single low, repeat low or single high oral dose groups. Omethoate was rapidly excreted within 48 hours following a single oral or intravenous dose of 0.5 mg/kg bw, a 14-day repeat oral dose of 0.5 mg/kg bw, or a single 10 mg/kg bw oral dose. Following single or multiple oral low doses (0.5 mg/kg bw) of [C^{14}]-omethoate, urinary excretion accounted for 92.6-97.3% or 87.3-96.7% of the administered radioactivity, respectively, suggesting that a multiple exposure regimen did not significantly affect the absorption/excretion processes. Urinary excretion was similar following a single 10 mg/kg dose with 84.7-97.4% of the administered radioactivity excreted in urine. Excretion via the feces accounted for the remainder of the administered radioactivity in all treatment groups (2.1-4.2%). Fecal excretion was similar following i.v. dosing (2.1-3.3%), suggesting that biliary excretion accounted for the majority of fecal metabolite content. Excretory patterns did not exhibit gender-related variability. At sacrifice, tissue residues of the administered radioactivity were low (<0.5% of the dose), with the highest concentrations found in the thyroid, testes, liver, spleen, and lung. Significantly elevated tissue burdens were found only in the thyroid of the high-dose group (1.5-2.0 μg eq/g). Based upon tissue burden data, omethoate and/or its metabolites do not appear to undergo any significant sequestration.

The metabolite profile for urine included 3 compounds identified as parent compound (25.9-62.0% of the administered dose), N-methyl-2-(methylsulphinyl)acetamide (15.5-35.1% of administered dose), and O-desmethylated omethoate (4.4-8.5% of administered dose). Fecal excretion represented only a minor route for the excretory products of omethoate metabolism with only 2.1-4.2% of the administered dose recovered in feces at 48 hrs post-dosing. The compounds identified in feces were omethoate (0.21% of the administered radioactivity), N–methyl-2-(methylsulphinyl) acetamide (0.07-0.20% of administered dose), and O-desmethylated omethoate (0.7-2.0% of administered dose). Omethoate appeared to be metabolized to a greater extent in males than in females as evidenced by higher percentages of parent compound remaining in urine from females and a higher percentage of omethoate metabolites in urine of males.

3.2 Other Animal Metabolism Data

In ruminants and poultry, as with the rat, dimethoate is metabolized via hydrolytic and oxidative pathways (based on tissue analyses). A principal pathway involves conversion of dimethoate to its oxygen analog, omethoate, and cleavage of the P-S bond, resulting in the phosphorylation of natural products. Another involves cleavage of the C-N bond to yield dimethoate carboxylic acid.

3.3 Plant Metabolism Data

Dimethoate is readily taken up by roots or leaf surfaces, and translocated throughout treated plants. Dimethoate is rapidly metabolized in plants by competing hydrolytic and oxidative processes. Evidence indicates that the metabolism of dimethoate among plants is highly variable.

Oxidative desulfuration converts dimethoate to its oxygen analog, omethoate, a potent ChE inhibitor. Available residue chemistry data suggested that under favorable conditions levels of omethoate may exceed levels of dimethoate. This potential was evidenced by available PDP monitoring data.

Oxidative N-demethylation of dimethoate or omethoate results in the formation of N-hydroxymethylated and N-demethylated derivatives of dimethoate and omethoate which are potent ChE inhibitors. Conjugates of N-hydroxymethylated derivatives of dimethoate and omethoate are also formed. Levels of these metabolites are expected to be low compared to levels of dimethoate and/or omethoate but may, under favorable conditions, reach levels of significance.

Hydrolysis of amide or phosphate ester bonds of dimethoate, and its potent ChE inhibiting metabolites discussed above, results in the formation of O-demethylated, carboxylated (cleavage of the C-N bond), and O-demethylated/carboxylated derivatives which are less potent ChE inhibitors.

3.4 Environmental Degradation

The environmental fate and transport of dimethoate is fairly well understood based on submitted data (*RDavid Jones, 2005*). Dimethoate is a mobile, yet relatively non-persistent OP insecticide. The primary route of dissipation appears to be microbially-mediated hydrolytic and oxidative degradation in aerobic soil, particularly under moist conditions, with an estimated half-life of 2.30 days. The major degradate was CO_2, accounting for approximately 62% of the applied amount after 14 days. Two non-volatile degradates, *des*-methyl dimethoate and dimethylthio-phosphoric acid, were identified but were present at levels less than 2% during the study. Dimethoate does not photodegrade. It hydrolyzes very slowly at 25° C in sterile buffered solutions at pH's 5 and 7 with half-lives of 156 and 68 days respectively. However, under alkaline conditions, it degrades rapidly to desmethyl dimethoate and dimethylthiophosphoric acid with a half-life of 4.4 days at pH 9. (Note that the hydrolysis study is a 30-day study so there is increased uncertainty in the estimates at pH's 5 and 7.) Under anaerobic soil

conditions, dimethoate does degrade, though not as rapidly as under aerobic conditions. The anaerobic half-life was found to be approximately 25.7 days, with the major non-volatile degradate being *des*-methyl dimethoate. Although dimethoate does not photodegrade on soil (the degradation rates and products were essentially the same for the light-exposed and dark control), the study did provide information on the degradation of dimethoate on a thin layer of somewhat dry soil. Dimethoate dissipates rapidly on foliage, though not so rapidly as in soil with a mean half-life of 5.1 days for EC formulations and half-life of 7.1 days for a wettable powder formulation. Under these conditions, the soil degradates (dimethylphosphoric acid and dimethylthiophosphoric acid) accumulated and persisted to a much greater extent than in the aerobic soil metabolism study. Therefore, in the field, these degradates may persist under dry conditions at the soil surface.

Dimethoate is highly mobile in soil. In a soil column leaching study, 72-100% of the applied radioactivity was eluted from the columns (loam, silt loam, sandy loam, and sand). Calculated K_d values based on these column studies ranged from 0.06 for the sand to 0.74 for the loam. Degradate mobility has not been well defined; however based on the aged leaching data as well as the metabolism data, degradates are not expected to persist and move through the soil profile.

A study measuring the volatility of dimethoate from the soil surface showed this not to be a significant route of dissipation. After 30 days, only 2.7% of the applied radioactivity had volatilized; 0.7% of which was CO_2. The majority of the radioactivity (83%) was extracted from the soil and most of this (93.2%) was dimethoate. It should be noted that the rate of degradation in this laboratory volatility study, compared with the aerobic soil metabolism study, was particularly slow. The slower rate in the volatility study may again be explained by comparing soil moisture content in the two studies, as dimethoate metabolism appears to be very sensitive to soil moisture.

Under field conditions, omethoate was found although it hadn't been detected in the laboratory studies. The presence of omethoate has been established in insects, plants, and mammals (WHO, (1989). In the dimethoate field dissipation studies, the only degradate analyzed for was omethoate. The other degradates were not identified in the laboratory studies.

3.5 Metabolites in the Risk Assessment

The former HED Metabolism Assessment Review Committee (MARC) reaffirmed that the tolerance expression and risk assessments for dimethoate should include residues of dimethoate and omethoate. The toxicity of the more potent omethoate was addressed in the risk assessment by establishing a TAF for omethoate relative to dimethoate (section 4.3.8). See *Dimethoate (035001): Results of the HED Metabolism Assessment Review Committee (MARC) Meeting Held on 19 February 2002. Bonnie Cropp-Kohlligian. March 20, 2002*.

The HED MARC recommended that the following ChE inhibiting metabolites identified in the FIFRA Section 6(a)(2) notification (letter dated 03/09/01 from Diane Allemang) should be included in the

dietary (food) risk assessments for dimethoate but not the tolerance expression: O-desmethyl omethoate, O-desmethyl omethoate carboxylic acid, and O-desmethyl isodimethoate. In addition, the Committee also recommended that the following potentially ChE inhibiting metabolites should be included in the dietary (food) risk assessments for dimethoate but not the tolerance expression: hydroxy dimethoate and its conjugate, hydroxy omethoate and its conjugate, N-desmethyl dimethoate, N-desmethyl omethoate, O-desmethyl dimethoate, and dimethoate carboxylic acid. *See MARC memo for chemical structures*.

HED's concerns for these 11 dimethoate metabolites (in addition to omethoate) were based on their unverified potential to be ChE inhibiting, as well as based on some data that show residues of these metabolites on crops. Specifically, in a special comparative toxicity study (MRID# 45507001), acute ChE inhibitory potential was tested for dimethoate, omethoate, and four other metabolites. Following a single oral dose of 30 mg/kg in rats, the RBC ChE inhibitory potential of O-desmethyl omethoate, O-desmethyl omethoate carboxylic acid, and O-desmethyl isodimethoate were approximately 50% *less* than that of dimethoate, the parent compound, at 2.5 hours (*Chin, 2002*). In comparison, omethoate showed 840% *more* ChE inhibiting potential than dimethoate. At 30 mg/kg, O-desmethyl N-desmethyl omethoate *did not affect* ChE activity and is not one of the metabolites of concern. Therefore, three metabolites that are structurally similar to omethoate; O-desmethyl omethoate, O-desmethyl omethoate carboxylic acid, and O-desmethyl N-desmethyl omethoate, have less ChE inhibiting potential than dimethoate. More recently, a submitted acute LD_{50} study (MRID# 46548501) in rats administered o-desmethyl dimethoate orally showed an LD_{50} of > 2000 mg/kg, compared to 387 mg/kg for dimethoate. No ChE data were submitted with the study. Based on the results of the comparative ChE study, it is unlikely that the remaining metabolites of concern, will be more potent ChE inhibitors than dimethoate. HED does have some metabolism/residue data showing the abundance of these metabolites on various crops but measurements for all the metabolites are lacking. In some cases, no parent (dimethoate) was found but some of the metabolites were found at low levels [*Dimethoate (035001): Dietary exposure estimates for dimethoate metabolites of concern (excluding omethoate) in food crops. Bonnie Cropp-Kohlligian. July 1, 2002*]. Based on the available data, it is unlikely that exposure to these metabolites of dimethoate (other than omethoate) will make a significant contribution to potential risk. Therefore, they are not quantitatively included in the risk assessment. However, confirmatory data are needed to both measure the ChE inhibiting potential of each metabolite and to measure the residues of each metabolite on a variety of representative crops.

Unlike the metabolites discussed above, omethoate is known to be a potent ChE inhibitor and measurable residues are found on food crops in monitoring data and it is included in the tolerance expression. Potential risks from exposures to omethoate were quantitatively included in the risk assessment for dimethoate. In addition, as Table 6.1.1 shows, residues of omethoate were included even if they were not detected or analyzed for in the monitoring data.

4.0 HAZARD CHARACTERIZATION/ASSESSMENT

4.1 Hazard and Dose-Response Characterization

The text and tables below were summarized or extracted from the toxicology disciplinary chapter (Chin, March 4,1997) or from the following documents prepared for the FIFRA Scientific Advisory Panel (SAP) held on November 30-December 1, 2004 and/or developed subsequent to comments provided by the SAP.

- ❏ Toxicology Chapter for the Reregistration Eligibility Document on Dimethoate. Paul Chin. March 4, 1997.

- ❏ USEPA (2004). Dimethoate: Issues related to the Hazard and Dose-response assessment. November 2, 2004. Prepared by the Office of Pesticide Programs for the FIFRA Scientific Advisory Panel. Docket No. OPP-2004-0320.

- ❏ FIFRA SAP (2005). Meeting Minutes of the FIFRA Scientific Advisory Panel Held November 30 - December 1, 2004. SAP Minutes No. 2005-01. January 25, 2005.

- ❏ Benchmark Dose Analyses of the Dimethoate 28-day Dermal Toxicity Study and the Omethoate 21-day Inhalation Study. PC Code: 035001. DP Barcode D312626. TXR# 0053125. Philip Villanueva. February 15, 2005.

- ❏ DIMETHOATE POST-SAP ENDPOINT SELECTION: PART 2. Outcome of an Ad Hoc Meeting of the HED Hazard Science Policy Council. PC Code: 035001. DP Barcode D312643. TXR# 0052992. Diana Locke. February 15, 2005.

- ❏ Dimethoate and omethoate: comparative toxicity and determination of toxicity adjustment factors. (Addendum to HED nos. 0050651 and 0050901). TXR #. 0052940. Anna Lowit. April 11, 2005.

- ❏ Chin 2005. Omethoate (PC code: 035002): Reviews of 26 Studies. DP Barcode: D291598. TXR# 0051425. Paul Chin. May 31, 2005.

4.1.1 Database Summary

4.1.1.1 Studies available and acceptable

The database of toxicology studies for the parent active ingredient, dimethoate, and the oxon metabolite, omethoate, are considered sufficient for purposes of risk assessment and tolerance reassessment. There are no additional studies required at this time.

Oral studies evaluating subchronic, chronic, developmental, and reproductive toxicity in laboratory animals are available for both dimethoate and omethoate. In addition, developmental neurotoxicity (DNT), companion comparative cholinesterase, and special cross-fostering studies are available for dimethoate. An acceptable dermal toxicity study in rat is available for dimethoate; an inhalation toxicity study in rat is available for omethoate. Metabolism studies are available in the rat for dimethoate and omethoate.

Table 4.1.1.1 Acute Toxicity of Dimethoate

Guideline No.	Study Type	MRID No.	Results	Toxicity Category
870.1100	Acute Oral - Rat	00164219	LD_{50}= 387 mg/kg	II
870.1200	Acute Dermal - Rabbit	00164220	LD_{50} = > 2.0 g/kg	III
870.1300	Acute Inhalation - Rat	00060719	LC_{50} > 2 mg/L	IV
870.2400	Acute Eye Irritation - Rabbit	00164222	Corneal opacities, iritis, and conjunctivitis; reversible within 7 days.	III
870.2500	Acute Dermal Irritation - Rabbit	00164221	Not a dermal irritant	IV
870.2600	Skin Sensitization - Guinea Pig	254924	Not a skin sensitizer	N/A
870.6100	Acute Delayed Neurotoxicity - Hen	42884401	No clinical signs of acute delayed neurotoxicity and no compound-related histological changes in nerve tissue.	N/A

4.1.1.2 Mode of action, metabolism, toxicokinetic data

Dimethoate is an OP pesticide that requires activation via oxidative desulfuration to the ChE inhibiting oxon metabolite, omethoate. OPs cause neurotoxicity by binding to, and phosphorylation of, the enzyme acetylcholinesterase in the central (brain) and peripheral nervous systems. This inhibition leads to the accumulation of acetylcholine, a continuation of uninterrupted neurotransmission and, potentially expression of a cholinergic response. ChEI is typically measured in studies with the parent compound and the oxon metabolite. Dimethoate and omethoate are both included in the common mechanism group for the OPs and are included in the Revised Cumulative Risk Assessment for this class of pesticides (USEPA, 2002).

Regarding *in vivo* metabolism of dimethoate, in the rat, approximately 5% of dimethoate is converted to omethoate. In the human, < 1% of the dimethoate dose found in urine was omethoate. In the human volunteers, dimethoate and omethoate were no longer detected in urine after 24-28 hours. In rats, omethoate was rapidly excreted, primarily in the urine, within 48 hours following a single exposure or following 14-days of exposure.

4.1.2 Toxicological Effects and Dose-response

Consistent with the mode of action, the critical effect[1] for various exposure durations for most OPs is the inhibition of ChE (in the brain or blood compartment). Using ChEI as the critical endpoint for risk assessment purposes protects for other cholinergic effects such as clinical signs. For this class of pesticide, acute and repeated exposures require separate risk assessments since repeated exposures at the same dose level result in increased levels of inhibition compared to acute exposure. Therefore, the points of departure for chronic exposure are typically lower than those for acute exposures. In the case of dimethoate, both ChEI and pup mortality are critical effects. ChEI in blood and brain compartments is the most sensitive endpoint in numerous studies with adult animals following oral or dermal exposures of dimethoate or omethoate. ChEI was the most sensitive endpoint in an inhalation study with omethoate. Furthermore, following exposure to dimethoate, ChEI was shown in juvenile animals in the special comparative ChE study. Rat is a sensitive species for dimethoate and omethoate exposures; results of rat studies are the focus of the discussion here. Details of the remaining dimethoate studies can be found in toxicology disciplinary chapter (Chin, 1997) and of the omethoate studies in the Data Evaluation Record (DER) (Chin, 2005). Omethoate is the oxon and active ChE inhibiting metabolite of dimethoate. As described further below, humans may be directly exposed to omethoate through dietary exposure or from postapplication occupational activities. Section 4.3.8 provides a description of the relative potency of omethoate and the parent compound, dimethoate. Summary information is provided in Table 4.3.8. Based on two-generation reproductive rat studies and on the rat DNT studies submitted and reviewed to date, pup mortality is a unique finding for OPs, as pup mortality has not been found to be the critical effect or the lowest observed adverse effect for other members of this common mechanism group.

Pup mortality as a critical effect for dimethoate was first observed in a rat DNT gavage study. In this study, there was a statistically significant and dose-related increase in total pup mortality at the 0.5 and 3.0 mg/kg/day dose groups when pups were evaluated as individuals. Similarly, although not statistically evaluated, a dose-related increase in mean pup mortality/litter was observed. No effects on pup mortality were found at 0.1 mg/kg/day. Most of the deaths occurred on post-natal day (PND) 1-4. Although the pup mortality observed at both the 0.5 and 3.0 mg/kg/day dose levels in the DNT study appears to be dose-related, and thus treatment-related, this finding is not supported by other studies that had similar exposure regimes (repeated gavage dosing at similar dose levels). For example, in the comparative ChEI study, no pup mortality was observed at any dose (i.e., 0.1, 0.5 and 3 mg/kg/day). In addition, the range-finding study showed no increased pup mortality at 0.2 or 3.0 mg/kg/day. An increase in pup mortality was observed (total litter loss = 2 of litters) at the highest dose tested (6.0 mg/kg/day) in the range-finding study. In the cross-fostering gavage study of dimethoate, although a slight increase in total number of pup deaths was observed at 3.0 mg/kg/day following either pre-natal only or post-natal only exposure, the results at this level are difficult to interpret. Lastly, pup

[1]A *critical* effect is one considered the most sensitive endpoint from the most appropriate species.

mortality was found at 6 mg/kg/day following pre-natal only, post-natal only, and combined pre- and post-natal exposure in the cross-fostering study.

The rat multi-generation reproductive studies on dimethoate and omethoate are important to evaluate given that exposure extends over the entire period of development up to sexual maturation, and viability is evaluated. Although doses used in the omethoate studies are lower than those used in the dimethoate studies, consistent trends regarding pup survival and ChEI were seen for both chemicals. Both two-generation reproductive toxicity studies on dimethoate are dietary studies; similar high doses were used (approximately 6 mg/kg/day). No clear increase in pup death was seen in either study; however a reduction in live births was seen in one study at the 6 mg/kg/day dose level. In a one-generation range-finding reproductive toxicity study with dimethoate, dose-related changes in reproductive parameters were seen starting at 3.9 mg/kg/day (decreases in implantation rate and litter size at birth, increases in post-implantation loss), and increases in pup mortality were seen at doses of 5.8 and 7.5 mg/kg/day. Two multi-generation reproductive toxicity studies are also available for omethoate. A drinking water study found pup mortality at the highest dose tested (1 mg/kg/day), most notably in the second generation. In a feeding study conducted at doses up to 0.5 mg/kg/day of omethoate, small increases in pup mortality were noted in the second generation (note: significant deficiencies were noted in the study protocol of the feeding study).

The association between pup mortality observed in the DNT study and brain ChEI is unclear. Following treatment with the lowest dose producing pup mortality (0.5 mg/kg/day) in the DNT study, only minimal brain ChEI was found in the gestation day (GD) 20 dams (10%), fetus (10%) and the PND 4 pups (8%) for males. At the next highest dose (3 mg/kg/day), there was more pronounced brain ChEI (dams 60%, fetus 33%). The small amount of brain ChEI (7-13%) in PND 4 pups does not support a link between pup mortality and brain ChE nor a "burst" of exposure to dimethoate via lactation. The association between brain ChEI as a causative factor in the pup deaths is also called into question by the results of the comparative ChE and range finding studies. In the comparative ChE study no pup mortality was observed, but the highest dose tested (3 mg/kg/day) produced pronounced brain ChEI in the dams (60%) and fetuses (33%), albeit, minimal inhibition (13%) was found in the PND 4 pups. In the range-finding study, no pup mortality was found at 3 mg/kg/day of dimethoate although greater than 70% brain ChEI was found in the dams and 22-24% inhibition in the fetus. In addition, no increase in post-natal pup deaths was found in the multi-generation reproductive study with dimethoate, where greater than 60% brain ChEI was found in dams (albeit, little brain ChEI found in PND 4 pups) at the highest dose tested (6 mg/kg/day).

Although the underlying basis of the pup mortality is unclear, maternal toxicity does not appear to be the only determining factor. In some studies where significant maternal brain ChEI was observed, increases in pup mortality were not observed. With the exception of the special observations made in the cross-fostering study, no clinical signs of overt toxicity were observed in dams at any dose even where pup death occurred. Lastly, in the cross fostering study, which was designed to address this issue, no clear correlation could be drawn between maternal behavior and pup death.

In conclusion, several studies (i.e., the main DNT, range-finding study, and cross fostering studies, the one-generation range-finding reproductive toxicity study, and the omethoate reproductive toxicity studies) demonstrate increased pup mortality following maternal exposure. Although the comparative ChEI, range-finding, and cross-fostering studies are not consistent with the findings of pup mortality in the main DNT study, it is concluded that the pup mortality observed at both the 0.5 and 3.0 mg/kg/day dose levels cannot be discounted as treatment related. This conclusion is based on the statistically significant response at both the 0.5 and 3 mg/kg/day doses and the dose-related nature of the response. Additional evidence includes: pups were reported to be cold to the touch and unresponsive; low incidence of total litter loss in performing laboratory; similar effect observed in other studies - although dose levels differed; qualitative increased pup death/litter (although does not reach statistical significance until 3 mg/kg/day); and quantitative increase in pup death when evaluated as individuals. The underlying basis of pup mortality is not understood. The available data do not support maternal toxicity as being the only determinant of pup mortality. These conclusions were supported by the FIFRA SAP (2005).

4.1.3 Dose-response assessment

Dose-response modeling is preferred over the use of NOAEL/LOAELs (i.e., no or low observed adverse effect levels) since NOAELs and LOAELs do not necessarily reflect the relationship between dose and response for a given chemical, but instead reflect dose selection. In order to evaluate the appropriate point of departure (PoD) for ChEI and pup mortality, EPA performed a benchmark dose (BMD) analysis (Appendix 9 of USEPA 2004**,** Appendix 8 of USEPA 2004). ChEI data from the following dimethoate studies in rat were analyzed: comparative ChE study, the reproductive toxicity studies, and 28-day subchronic study. Pup mortality data were extracted from the main DNT study.

The estimated dose at which 10% ChE is observed (BMD_{10}) and the lower 95% confidence intervals ($BMDL_{10}$) were estimated by fitting the ChE data to an exponential dose-response model using generalized nonlinear least squares. The BMD_{10} was selected because it is generally at or near the limit of sensitivity for discerning a statistically significant decrease in ChE activity across the blood and brain compartments and is a response level close to the background ChE level. The exponential model was used in the Preliminary OP Cumulative Risk Assessment (USEPA, 2001) to determine relative potency factors and PoDs. The exponential model and statistical methods used to calculated the BMD_{10}s and $BMDL_{10}$s have been supported by the FIFRA Science Advisory Panel (FIFRA SAP, 2002). Technical description of the statistical methods can be found in the cumulative hazard assessment of the Preliminary OP Cumulative Risk Assessment (USEPA, 2001). Model fits and model parameters specific to this analysis can be found in USEPA (2004). The exponential model used here can be downloaded by the public at http://www.epa.gov/pesticides/cumulative/EPA_approach_methods.htm. As described in detail in the issue paper presented to the FIFRA SAP (USEPA, 2004), BMD_{10} and $BMDL_{10}$ s estimates are similar across age, sex, and method of administration (gavage, feeding, drinking water; Table A9.1 of Appendix 9 of USEPA 2004). Table 4.1.3a provides the BMD results from the comparative ChE study.

Table 4.1.3a. Brain Cholinesterase Activity in Adults, Fetuses, and Offspring of Rats Treated with Dimethoate in Comparative ChEI Study.		
Dose (mg/kg/day)	**Benchmark Doses (mg/kg/day)**	
	BMD_{10}	**$BMDL_{10}$**
Acute Exposures		
Adult Males	2.6	2.0
Adult Females	2.2	1.8
PND 11 Males	1.8	1.5
PND 11 Females	1.5	1.3
Repeated Exposures		
GD 20 Dams (n=8/group)b	0.3	0.3
GD 20 Fetuses (n=8/group)b	0.9	0.7
PND 4 Males (n=14-19/group)c	4.3@	2.3@
PND 4 Females (n=12-16/group)c	4.5@	2.3@
PND 21 Males (n=8/group)d	0.4	0.3
PND 21 Females (n=8/group)d	0.4	0.3
Adult Males (n=8/group)e	0.5	0.2
Adult Females (n=8/group)e	0.4	0.3
Post Exposure		
PND 60 Males	NE	NE
PND 60 Females	NE	NE
[a] Results in parenthesis ( ) are percent inhibition relative to control [b] Animals exposed from gestation day 6 to 20 [c] Animals exposed from gestation day 6 to post-natal day 4 [d] Animals exposed from gestation day 6 to post-natal day 21 [e] Animals exposed for 11 days [f] Animals exposed from gestation day 6 to post-natal day 21 * = p≤ 0.05, **p ≤ 0.01	NE=not evaluated @=poor model fit or values outside dose range [g]See Appendix 8 for details of analysis doses in mg/kg/day	

The BMD analysis of the pup mortality data from the dimethoate DNT study was performed using EPA's Benchmark Dose Software (BMDS). The BMDS software, user's manual, and technical guidance can be obtained at www.epa.gov/ncea/bmds.htm. For the dimethoate DNT study, pup mortality was modeled using the available BMDS nested models: NLogistic, NCTR, and RaiVR. Separate BMD analyses were performed for the two post-natal day (PND) periods: PND 1-4 and PND 5-11. A culling event on PND 4 artificially reduced the sizes of the litters, making the PND 1-4 and PND 5-11 study periods incomparable. Based on the background levels for pup mortality, an increase of 5% above background (i.e. a BMD_5) was considered to be the smallest detectable change from background and therefore an appropriate benchmark response (BMR) for this effect. Additional

support for this selection is provided by several analyses in the literature (Faustman et al, 1994; Allen et al., 1994a; Allen et al. 1994b; Kavlock et al., 1995), which report that the use of a $BMDL_5$ for developmental endpoints results in values similar to available NOAELs within the same studies. Available EPA guidance also indicates that a BMR of 5% has typically been used for developmental studies (USEPA, 2000).

Table 4.1.3b. Benchmark Dose Values for Increased Pup Mortality during PNDs 1-4 in the main DNT study

BMD Level	BMD (mg/kg/day)	
	BMD	**BMDL**
BMD_5	0.47	0.27
BMD_{10}	0.99	0.57

Although no clear association can be made between a specific level of brain ChEI and an increase in pup death, results of the BMD analyses support the conclusion that protection against brain ChEI will also result in protection against increased pup mortality following repeated dosing. No consistent age-related differences were seen in calculated BMD_{10} or $BMDL_{10}$ values for brain ChEI; these values were similar to, or lower than, those calculated for increases in pup mortality from the main DNT study (the most sensitive study for that effect). Although the BMD_{10} /$BMDL_{10}$ is higher for ChEI following a single dose, results of the recent cross-fostering study, particularly the results of the pre-natal only and post-natal only dose groups, support the conclusion that increased mortality is not seen following a single exposure at doses up to 3.0 mg/kg. Thus, use of the acute $BMDL_{10}$ values for brain ChEI (1.3-2.0 mg/kg) is expected to be protective for increased pup mortality which might be seen after a single exposure at doses greater than 3.0 mg/kg (for example, at 6.0 mg/kg/day in the cross-fostering study). The FIFRA SAP supported this BMD analysis and indicated that brain ChE is an appropriate endpoint for estimating risk to dimethoate (FIFRA SAP, 2005).

In conclusion, the current analysis supports the use of brain ChEI as an appropriate endpoint for acute or repeated-dose risk assessment scenarios, based on the following:

- ❑ Brain ChEI occurs at doses similar to, or lower than, those causing ChEI in other compartments (e.g., RBC and plasma);

- ❑ BMD analyses results indicate a very robust dose-response curve for brain ChEI, with similar BMD_{10} values from studies with varying modes of administration (dietary or gavage) and durations (short term for DNT studies and longer term for reproduction studies);

- ❑ BMD analyses results indicate similar dose-response curves at all ages, with no difference in BMD_{10} values for different age groups following similar exposure durations;

- ❑ Comparison of BMR dose levels for brain ChEI and pup mortality following repeated dosing indicates that ChEI occurs at doses similar to those associated with increases in pup mortality;

- ❑ Evaluation of pup mortality data from the cross-fostering study reveals clear increases in mortality only at the highest dose following short-term exposure, indicating that increased mortality at lower doses occurs only with repeated dosing;

- ❑ Comparison of the NOAEL for increased pup mortality from limited dosing with the BMD_{10} for brain ChEI following a single dose, indicates that brain ChEI occurs at doses below those causing a clear increase in pup mortality.

Therefore, regulation of dimethoate exposure at levels below those causing brain ChEI in adults will also protect against brain ChEI and increased mortality in pups. The FIFRA SAP was supportive of the use of the BMDs calculated for brain ChEI as the critical endpoint for purposes of risk estimation (FIFRA SAP, 2005). As brain ChEI is considered the appropriate endpoint for developing PoDs and estimating risk from dimethoate, EPA has elected to use brain ChE data measured in the dimethoate dermal toxicity and omethoate inhalation toxicity studies for these routes of exposure. BMD analysis of these data was also performed using the exponential dose-response model. Details of these analyses can be found in Villanueva (2005).

4.2 FQPA Hazard Considerations

As described in detail above, dimethoate and omethoate are neurotoxic OP pesticides which act through inhibition of ChEI. Developmental studies in rats and rabbits are available for dimethoate and omethoate. Reproductive toxicity studies are available for both chemicals. Prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rat or rabbit fetuses to *in utero* exposure to dimethoate or omethoate. Similarly, there was no indication of increased susceptibility in the offspring as compared to parental animals in the reproduction studies. A developmental neurotoxicity study, a companion comparative ChE study, and special cross-fostering study are available for dimethoate. These are studies are considered acceptable; no additional studies are required at this time. As described above BMD analysis of the ChE data from the comparative ChE study indicates that juvenile animals exhibit similar sensitivity to dimethoate from acute or multiple exposures. Furthermore, BMD analysis indicates that use of the $BMDL_{10}$ for brain ChE is protective for potential pup mortality. Therefore, a special hazard-based FQPA factor is **not** needed.

4.3 Hazard Identification and Toxicity Endpoint Selection

4.3.1 Acute Reference Dose (aRfD) - All Population Subgroups

In an acceptable companion (with DNT) comparative ChEI study in adult and juvenile rats (MRID# 45529702), dimethoate (99.1% a.i.) was administered to groups of Crl:CD® (SD) IGS BR rats by gavage at dose levels of 0.0, 0.1, 0.5 or 3.0 mg/kg/day. Treatment groups consisted of 9 pregnant dams treated from GD 6 through GD 20 and terminated; 10 pregnant dams treated from GD 6 through PND 10 followed by treatment of 1 male and 1 female offspring/litter on PND 11 through PND 21; groups of 8 untreated dams whose offspring were treated on PND 11. In addition, groups of 16 adult male and female rats were treated with dimethoate for 11 days. Although the study investigated the effect of the test material on developmental criteria such as reproductive performance, gestation, fetal viability, etc., the primary purpose was to determine the effect of dimethoate on blood and brain ChE activities in adult male and female rats, pregnant dams, fetuses, and offspring following both acute and repeated exposures.

No significant treatment-related effects were found on any reproductive or developmental parameters. In addition, the test material did not increase mortality, or cause clinical signs of toxicity in adult male and female rats, fetuses or offspring at any dose. No histopathology of the nervous system was seen in five offspring examined after PND 60.

Table 4.1.3a provides the results of the BMD analysis for this study. The dose and endpoint for establishing the aRfD for all population subgroups is the $BMDL_{10}$ = 1.3 mg/kg for PND 11 female pups. The endpoint of concern (ChEI) was seen after a single oral dose and thus is appropriate for the general population and duration of concern. A UF of 100 was applied to account for inter-species extrapolation (10X) and intra-species variability (10X).

Acute RfD for general population: $BMDL_{10}$ = 1.3 mg/kg ÷ UF 100 = 0.013 mg/kg
Acute PAD for general population: aRfD 0.013 mg/kg ÷ FQPA 1X = 0.013 mg/kg

4.3.2 Chronic Reference Dose (cRfD)

In a chronic/carcinogenicity feeding study (MRID# 00164177), Wistar rats (65/sex/group) were fed diets containing 0, 5, 25, or 100 ppm dimethoate (0, 0.25, 1.25 or 5 mg/kg/d) for 2 years. An additional 20 animals/sex were given 1 ppm (0.05 mg/kg/d) in order to determine a NOAEL for ChEI.

BMD analyses for chronic dietary exposure risk assessment were conducted for dimethoate as part of the Revised OP Cumulative Risk Assessment, June 10, 2002 (http://www.epa.gov /pesticides/cumulative/rra-op). These analyses are also appropriate for single-chemical risk assessment. BMD_{10}/$BMDL_{10}$ calculations for female and male brain ChEI from the cumulative assessment using the 2-year rat study are provided in Table 4.3.2.

Table 4.3.2

Dimethoate	Female BMD_{10}	Female $BMDL_{10}$	Male BMD_{10}	Male $BMDL_{10}$
	0.25 mg/kg/d	0.22 mg/kg/d	0.35 mg/kg/d	0.31 mg/kg/d

The dose and endpoint for establishing the cRfD is $BMDL_{10}$ = 0.22 mg/kg/day. This endpoint is appropriate for the route and duration of exposure. A UF of 100 was applied to account for both inter-species extrapolation and intra-species variation.

Chronic RfD: $BMDL_{10}$ = 0.22 mg/kg/day ÷ UF 100 = 0.0022 mg/kg/day
Chronic PAD: cRfD 0.0022 mg/kg/day ÷ FQPA 1X = 0.0022 mg/kg/d

4.3.3 Incidental Oral Exposure (Short and Intermediate Term)

No incidental oral endpoints are need at this time since the registrants are not supporting residential uses [*Federal Register: May 1, 2002 (Volume 67, Number 84, Page 21669 ENVIRONMENTAL PROTECTION AGENCY. OPP-2002-0023; FRL-6834-4. Dimethoate Product Cancellation Order and Label Amendment; Technical Correction*].

4.3.4 Dermal Absorption

Three dermal absorption studies are available. The 1st is a 5-day study in which dermal absorption was not measured at 8 or 10 hours post treatment (10 mg/kg; 0.2 mg/cm^2; 2 mg/animal; MRID# 43964001). The 2nd dermal absorption study **(**MRID# 45530501) used ^{14}C-Dimethoate dissolved in a formulation concentrate, the most widely used product, instead of ^{14}C-Dimethoate technical, but did measure dermal absorption at 10 hours post treatment.

The 3rd study, an *in vitro* dermal penetration study (MRID# 45922602) was submitted in which dimethoate was administered to isolated epidermal membranes from human and rat skin. The study was reviewed and determined to be invalid. The Agency has sufficient experimental information to show that this methodology does not accurately predict human or rat *in vivo* absorption.

At this time, brain ChEI is an appropriate risk assessment endpoint for dimethoate. Thus, the dimethoate 28-day dermal toxicity study in rats is the most appropriate study for estimating dermal risk. Therefore, a dermal absorption factor is not needed (*DIMETHOATE POST-SAP ENDPOINT SELECTION: PART 1. Outcome of an Ad Hoc Meeting of the HED Hazard Science Policy Council. PC Code: 035001. DP Barcode D312106. TXR# 0052988. Diana Locke. January 12, 2005*).

4.3.5 Dermal Exposure (Short- and Intermediate-term)

In a 28-day repeated dose dermal toxicity study (MRID# 44999101), groups of 10 male and 10 female Han Wistar rats were treated with dimethoate 400 g/L EC (Lot No. 70917-00; 38% a.i.) at doses of 0, 10.5, 21.0, 31.5, or 63.0 mg/kg/day. The test article was applied neat in a volume sufficient to achieve the required amount of active ingredient. Animals were treated by dermal occlusion for 6 hours/day, 5 days/week for 4 weeks. All animals survived to study termination. No treatment-related clinical signs, dermal effects, effects on body weight, food consumption, hematology, clinical chemistry, urinalysis, ophthalmology, or organ weight were observed. Parameters assessed by neurobehavioral screening were unaffected by treatment. No gross or microscopic abnormalities were noted at necropsy.

Plasma acetylcholinesterase (AChE) activity for both sexes was similar between the treated and control groups on days 7 and 29. RBC AChE activity for high-dose males was 86% (n.s.) and 80% ($p \leq 0.01$) of the control levels on days 7 and 29, respectively. It should be noted that predose RBC AChE activity in the high-dose males was 88% of the control level. RBC AChE activity in the 10.5, 21.0, and 31.5 males and all treated females was unaffected by treatment.

Brain AChE activity in males and females receiving 21.0, 31.5, and 63.0 mg/kg/day was significantly ($p \leq 0.01$) less than the control value. For the 21 and 31.5 mg/kg/day groups, the activity was marginally reduced to 90-92% of the control levels and was considered to be biologically significant. Brain AChE activity in high-dose males and females was 83% and 85%, respectively of the controls.

Aside from ChEI, no other systemic toxicity and dermal toxicity was found in any treatment groups. BMD values were calculated for only the brain ChEI data from the dimethoate 28-day dermal toxicity study, since brain ChE was determined to be more sensitive than plasma or red blood cell ChE in this study (*Villanueva, 2005*). Based on the BMD values, males are more sensitive than females.

Table 4.3.5 BMD Summary for Brain ChEI form Dimethoate 28-day Dermal Toxicity Study (MRID# 44999101)

Sex	Time	BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)
Male	28D	28.70	18.67
Female	28D	41.87	35.23

The dose and endpoint for short (1-30 days)- and intermediate (1-6 months)-term dermal exposure is $BMDL_{10}$ = 18.67 mg/kg/day. This endpoint is appropriate for the route and duration of exposure. No long-term exposures are expected. A UF of 100 was applied to account for both inter-species extrapolation and intra-species variation.

Short- and Intermediate-term Occupational Dermal Level of Concern (LOC) = 100

4.3.6 Inhalation Exposure (Short- and Intermediate-term)

In a subchronic inhalation toxicity study (MRID# 46358601), Folimat (92.4% a.i.; batch/lot # not reported) was administered to 10 Wistar TNO 74 albino rats/sex /concentration by dynamic (evidently nose only) exposure at concentrations of 0, 0.96, 2.3 or 7.5 mg/m^3 (0.00096, 0.0023 or 0.0075 mg/L, respectively) for 6 hours per day, 5 days/week for a total of 15 days. There were no compound-related effects on mortality, body weight, hematology, urinalysis, clinical signs, organ weight, gross pathology or histopathology. Significant inhibition of ChE activity was observed in the red blood cells (both sexes) at all concentrations. The decreased ChE activity in brain is considered toxicologically significant in males at 0.96 mg/m^3 and in males and females at 2.3 and 7.5 mg/m^3. Inhibition of plasma ChE activity was observed at 2.3 and 7.5 mg/m^3 in males and at 7.5 mg/m^3 in females. For the omethoate 21-day inhalation study, benchmark concentration (BMC) values were calculated for brain ChE at day 15 and red blood cell (RBC) ChE at days 5, 10, and 15 (*Villanueva, 2005*; see Table 4.3.6 below).

Table 4.3.6 BMC Summary for Omethoate 21-Day Inhalation Toxicity Study (MRID# 46358601)

Compartment	Sex	Time	BMC_{10} (mg/m^3)	$BMCL_{10}$ (mg/m^3)
Brain	**Male**	15D	0.51	0.38
	Female	15D	1.09	0.71
RBC	**Male**	5D	0.98	0.79
		10D	3.66	1.77
		15D	0.68	0.52
	Female	5D	2.03	1.64
		10D	0.72	0.57
		15D	0.99	0.72

The dose and endpoint for short (1-30 days)- and intermediate (1-6 months)-term inhalation exposure is $BMCL_{10}$ = 0.38 mg/m^3/day. This endpoint is appropriate for the route and duration of exposure. Since the endpoint was calculated from a study on the more toxic metabolite, omethoate, the selection of this endpoint is both protective and conservative. A UF of 100 was applied to account for both inter-species extrapolation and intra-species variation.

Short- and Intermediate-term Occupational Inhalation Level of Concern (LOC) = 100

4.3.7 Cancer Potential and Classification

In a chronic/carcinogenicity feeding study (MRID# 00164177), Wistar rats (65/sex/group) were fed diets containing 0, 5, 25, or 100 ppm dimethoate (0, 0.25, 1.25 or 5 mg/kg/d) for 2 years. An additional 20 animals/sex were given 1 ppm (0.05 mg/kg/d) in order to determine a NOAEL for ChEI. The NOAEL for systemic toxicity was 1.25 mg/kg/d and the LOAEL was 5 mg/kg/d based on increased mortality (females), decreased body weight gain (males), anemia (males) and increased leukocytes (males and females). The ChE activity NOAEL was 0.05 mg/kg/d and the LOAEL was 0.25 mg/kg/d based on brain and RBC ChEI. Administration of dimethoate was associated with dose related trends for:

(i) spleen hemangiosarcoma;
(ii) combined spleen hemangioma and hemangiosarcoma, and;
(iii) combined spleen hemangioma, hemangiosarcoma and skin hemangiosarcoma.

Furthermore, there were significant differences in pair-wise comparisons between controls and the low dose (0.25 mg/kg) or high dose (5 mg/kg) for spleen (hemangioma/ hemangiosarcoma) and in the combined tumors of spleen and skin hemangiosarcoma and lymph angioma/ angiosarcoma. Although there was no dose response, there were significant pair-wise comparisons at the low and high doses for all tumors combined. The HED Cancer Peer Review Committee (CPRC) agreed that despite no dose response, these tumors were compound related but that the tumor incidences did not indicate much more than a weak effect.

In a chronic/carcinogenicity feeding study (MRID# 00163800; Accession# 265362-265364), B6C3F1 mice (60/sex/group) were fed diets containing 0, 25, 100 or 200 ppm dimethoate (0, 3.75, 15 and 30 mg/kg/d) for 78 weeks. Ten animals of the 60 per sex were used as satellite animals and were sacrificed at 52 weeks. The NOAEL/LOAEL for the systemic toxicity were less than 3.75 mg/kg/d (the lowest dose tested) based on:

(i) the increased incidence of hepatic vacuolation in females at all levels;
(ii) decrease in the relative weights of brain, heart, kidney, and spleen in all treated animals;
(iii) decrease in the absolute and relative weight of the ovaries in all treated animals, and;
(iv) a significant decrease in body weight gain in all males and in high dose females (during the first five weeks of the study).

Absolute liver weights were significantly increased in both sexes of the mid and high dose groups, while relative liver weights were significantly decreased in mid and high dose females. The ChE activity NOAEL/LOAEL were less than 3.75 mg/kg/d based on significant depression ($p<0.01$) of plasma and RBC ChE activities at all dosage levels. Brain ChE was not measured. Administration of dimethoate in the males was associated with a significant dose related increase in:

(i) combined lung adenoma and/or adenocarcinoma;
(ii) for lymphoma, and;
(iii) for the combined group of lymphoma, reticular sarcoma, and leukemia.

A significant difference in the pair-wise comparison of control and the highest dose level (30 mg/kg/d) was found for the combined tumor group of lymphoma, reticular sarcoma, and leukemia. The CPRC agreed that the increased incidence for the combined tumors compared to concurrent controls appeared to be compound-related, but could only classify this incidence as equivocal. Administration of dimethoate in females was associated with a significant dose related increase in liver carcinoma and for combined liver adenoma and/or carcinoma. However, the Committee agreed that not much weight should be put on the combined tumor incidence in female mice because there were no significant pair-wise comparisons. There also was no evidence of precursor lesions to carcinogenicity.

The dosing was adequate in both the rat and the mouse studies for the assessment of the carcinogenic potential of dimethoate. The CPRC has classified dimethoate as a **Group C** carcinogen (possible human carcinogen, final document dated 08/29/1991). The classification is based upon equivocal hemolymphoreticular tumors in male B6C3F1 mice, the compound-related (no dose response) weak effect of combined spleen (hemangioma and hemangiosarcoma), skin (hemangiosarcoma), and lymph (angioma and angiosarcoma) tumors in male Wistar rats, and positive mutagenic activity associated with dimethoate. On June 25, 1992, the FIFRA SAP concurred with the Agency's classification of dimethoate as a Group C carcinogen. For the purposes of cancer risk assessment, a dose-response approach (Q_1*) was not indicated for this chemical, but an RfD approach was considered more appropriate for quantification of potential human risk.

POST-SAP DIMETHOATE ENDPOINTS

DIMETHOATE ENDPOINTS 01/27/2005			
Exposure Scenario	**Dose**	**Effect**	**Study**
Acute Dietary (all populations)	$BMDL_{10}$ = 1.3 mg/kg UF = 100 FQPA SF = 1	Brain ChEI in PND11 females (BMD_{10} = 1.5 mg/kg)	Comparative ChEI study in rats. MRID# 45529702
	Acute RfD = 0.013 mg/kg **Acute PAD = 0.013 mg/kg**		
Chronic Dietary (all populations)	$BMDL_{10}$ = 0.22 mg/kg/d UF = 100 FQPA SF = 1	Brain ChEI in females (BMD_{10} = 0.25 mg/kg/d).	2-Year chronic feeding study in rats. MRID# 00164177; Accession# 00265610

DIMETHOATE ENDPOINTS 01/27/2005			
Exposure Scenario	**Dose**	**Effect**	**Study**
	Chronic RfD = 0.0022 mg/kg/d Chronic PAD = 0.0022 mg/kg/d		
Short- (1-30 days) and Intermediate-term (1-6 months) Occupational Dermal	$BMDL_{10}$ = 18.67 mg/kg/d UF = 100	Brain ChEI in males at 28 days (BMD_{10} = 28.70 mg/kg/d).	28-Day repeated dose dermal toxicity in rats. MRID# 44999101
	Short- and Intermediate-term Occupational Dermal LOC = 100		
Short- (1-30 days) and Intermediate-term (1-6 months) Occupational Inhalation	$BMCL_{10}$ = 0.38 mg/m^3 (approx 0.10 mg/kg/d) UF = 100	Brain ChEI in males at 15 days (BMC_{10} = 0.51 mg/m^3).	Omethoate 21-day repeated dose inhalation study in rats. MRID#46358601.
	Short- and Intermediate-term Occupational Inhalation LOC = 100		
Cancer	Classification: Group C or Possible Human Carcinogen		

UF = Uncertainty Factor (10X for inter-species extrapolation and 10X for intra-species variation)
FQPA SF = Food Quality Protection Act Safety Factor
RfD = Reference Dose
PAD = Population Adjusted Dose (RfD ÷ FQPA SF)
LOC = Level of Concern

4.3.8 Oxon Metabolite (Omethoate) & Toxicity Adjustment Factor

Similar to dimethoate, numerous OPs require activation to more toxic oxon metabolites. USDA analyzes for the oxon metabolites of some OPs in their Pesticide Data Program. PDP tests for pesticides in foods commonly consumed by children such as fruits, vegetables, dairy products, and grains. The appearance of numerous detections indicates that dietary exposure to omethoate through food can potentially occur. In addition, DFR studies on tomatoes, grapes, and apples have detected omethoate, following dimethoate application. The results of the DFR studies show that postapplication occupational exposure to omethoate also occurs. More recently, drinking water treatment data have shown the formation of omethoate and its likelihood to reach consumers.

Therefore, since exposure studies indicate that direct exposure to omethoate through food, drinking water, and/or from occupational activites following applications of dimethoate are possible, toxicity adjustment factors (TAFs) have been calculated to account for the increased toxic potency of omethoate compared to dimethoate. A TAF is the ratio of the toxic potency of a given chemical

relative to another chemical. TAFs are being used to convert exposures of omethoate into exposure equivalents of dimethoate in the dietary and occupational exposure assessments. In the case of dimethoate and omethoate, the TAFs are based on the ratio of BMD_{10} from female brain ChEI from either acute or steady state (i.e., > 21 days of exposure) measurements (Lowit, 2005a). As shown in the OP cumulative risk assessment, for most OPs, ChEI reaches steady state following approximately 21 days of oral exposure. Once steady state is reached, BMD values are generally consistent and do not change with longer exposures.

As described in the OP cumulative risk assessment (USEPA, 2002), comparisons of toxic potency should be made using a uniform basis of comparison, by using to the extent possible a common response derived from a comparable measurement methodology, species, and sex for all the exposure routes of interest. Dose-response modeling is preferred over the use of NOAEL/LOAELs (i.e., no or low observed adverse effect levels) for determining relative toxic potency and calculating TAFs. NOAELs and LOAELs do not necessarily reflect the relationship between dose and response for a given chemical, nor do they reflect a uniform response across different chemicals. In the present analysis, OPP has collaborated with Dr. Woodrow Setzer of EPA's National Health and Environmental Effects Research Laboratory to perform BMD modeling (USEPA, 2000) in the evaluation of the relative toxicity of dimethoate and omethoate. The modeling procedure used in this analysis is very similar to the exponential model and statistical procedures being used to estimate cumulative risk to the OPs which has been supported by the FIFRA SAP (FIFRA SAP; 2002). A technical description of the methods used here along with dose-response curves and information regarding fit can be found in TXR# 0050651.

Two previous memos (TXR#s 0050651 & 0050901) described TAFs being used by EPA to account for the increased toxicity of omethoate compared to dimethoate in the dietary and occupational exposure assessments. The original memo (TXR# 0050651, 04/24/2002) developed acute and steady-state (i.e., intermediate-term and chronic) TAFs based on limited data available to EPA at that time. Additional subchronic and chronic studies were later submitted to EPA which provided additional data for evaluation of the steady state TAF. These additional studies verified the original TAF of **3** for application to residues of omethoate in the chronic dietary and the intermediate-term dermal and inhalation occupational exposure assessments (TXR# 0050901, 07/10/2002).

The pesticide registrant, Cheminova, has submitted an acute neurotoxicity study (MRID# 46167701) and associated range finding studies (MRID#s 46122202, 46122203) with omethoate. The range finding studies do not provide appropriate data for the TAF but the results of the BMD modeling performed by Dr. R. Woodrow Setzer (EPA-ORD-NCCT) and used by HED to develop the revised acute TAF can be found in *Lowit, 2005a*. The ChE data used in the BMD calculations are provided in Appendix 1 of that memo (Lowit, 2005b).

Based on the available toxicity studies for dimethoate and omethoate, omethoate is more potent than dimethoate. Female brain ChEI is a reliable and sensitive endpoint for comparing relative potency.

- ❑ A TAF of **12** should be applied to residues of omethoate in the acute dietary and short-term dermal and inhalation[2] occupational exposure assessments, respectively.

- ❑ A TAF of **3** should be applied to residues of omethoate in the chronic dietary and the intermediate-term dermal and inhalation[2] occupational exposure assessments.

[2]Assumes that no omethoate-specific inhalation studies are available. For this assessment, the omethoate inhalation study was used for risk assessment, where appropriate.

Table 4.3.8. Toxicity Profile of Dimethoate and Omethoate

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
2-Generation Reproductive Toxicity Rat–dietary feeding 1, 15, 65 ppm (0.08, 1.2, 5.46 mg/kg/d)	ChEI NOAEL =0.08 mg/kg/d ChEI LOAEL =1.2 mg/kg/d Parental toxicity NOAEL =0.08 mg/kg/d LOAEL =1.2 mg/kg/d Reproductive toxicity NOAEL = 1.2 mg/kg/d LOAEL = 5.46 mg/kg/d	Plasma, RBC & brain ChEI = 11-48% -dec. in live pups/litter -dec. body weight -dec. fertility index & body wt	2-Generation Reproductive Toxicity Rat–dietary feeding 1, 3, 10 ppm	Reproductive toxicity NOAEL =0.05 mg/kg/d** LOAEL = 0.15 mg/kg/d**	No ChEI measured –reduced body wt gain during lactation –dec. viability of pups 5 days after birth

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
			2-Generation Reproductive Toxicity Rat–drinking water 0.5, 3.0 and 18.0 ppm MRID 45806201 (1992)	Parental toxicity NOAEL ≥1.36-3.16 mg/kg/day	
				Parent ChE NOAEL = not identified. ChE LOAEL=0.04-0.08 mg/kg/day	9-16% inhibition of brain ChE in F_1 adults
				offspring ChE NOAEL= 0.04-0.08 mg/kg/day ChE LOAEL = 0.27-0.57 mg/kg/day	15% inhibition of brain ChE in F_2 female pups
				reproductive toxicity NOAEL= 0.27-0.57 mg/kg/day LOAEL= 1.36-3.16 mg/kg/day	-decreased fertility and conception rates (F_1), - increased precoital interval (F_1) - decrease in the number of F_1 and F_2 pups/litter - lesions of the epididymal epithelium (P and F_1 males) .
				offspring toxicity LOAEL= 1.36-3.16 mg/kg/day NOAEL= 0.22-0.77 mg/kg/day	decrease in body weight and weight gain and reduced survival during lactation

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
Two-Year Chronic Toxicity. Rat–dietary feeding 0, 1, 5, 25 or 100 ppm dimethoate (equiv 0, 0.05, 0.25, 1.25 or 5 mg/kg/d)	ChEI NOAEL =1 ppm (0.05 mg/kg/d)** ChEI LOAEL = 5 ppm (0.25 mg/kg/d)**	20-30% depression of brain and RBC ChE	Two-Year Chronic Toxicity. Rat–dietary feeding 0.3, 1.0, 3.0, and 10.0 ppm for up to 2 years (0, 0.015, 0.05, 0.15, and 0.5 mg/kg/day (MRID 46119402)	Systemic NOAEL ≥10 ppm (0.5 mg/k/d) (LDT) LOAEL= not established ChE NOAEL= 0.05 mg/k/d for male and 0.015 mg/k/d for female ChE LOAEL= 0.15 mg/k/d for male and 0.05 mg/k/d for female	Males 0.15 mg/k/d, 28% brain ChEI (**p ≤0.01) 0.5 mg/k/d, 45% brain ChEI (**p ≤0.01) Females 0.05 mg/k/d, 13% brain ChEI (*p ≤0.05) 0.15 mg/k/d, 18% brain ChEI (*p ≤0.05) 0.5 mg/k/d, 36% brain ChEI (**p ≤0.01)
			32-week study rat–drinking water 0.0, 0.0093, or 0.0271 mg/kg bw/day in males; and 0.0, 0.0109, or 0.0322 mg/kg bw/day in females MRID 46099816	No ChE inhibition at all doses	

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
			1-year ChronicToxicity/carcinogenicity. Rat–drinking water 0, 0.5, 4, or 32 ppm (0, 0.04, 0.30, and 2.92 mg/kg/day for males and 0, 0.05, 0.44, and 3.93 mg/kg/day for females MRID 46126001	ChE NOAEL= less than 0.04 mg/kg/day for males 0.05 mg/kg/day for females ChE LOAEL= 0.04 mg/kg/day for males 0.44 mg/kg/day for females	Males 0.04 mg/k/d, 20-37% RBC ChEI (**p ≤ 0.01) Females 0.44 mg/k/d, 44-47% brain ChEI (**p ≤ 0.01); 67-83% RBC ChEI (**p ≤ 0.01)
One year Chronic Toxicity Dog–dietary feeding 0, 5, 20 & 125 ppm (equivalent to an intake of 0, 0.18, 0.70, & 4.18 mg/kg/d in males & 0, 0.19, 0.76 & 4.31 mg/kg/d in females	Systemic NOAEL = < 0.18 mg/kg/d LOAEL = 0.18 mg/kg/d ChEI NOAEL = < 0.18 mg/kg/d ChEI LOAEL = 0.18 mg/kg/d	Dec. liver wts. in females & presence of a brown, granular pigment in the liver of both sexes. Reduction in brain ChE (7% 10%).	One year Chronic Toxicity Dog–Gavage 0.02, 0.125, or 0.625 mg/kg/d	Invalid due to instability of the omethoate in the study	

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
90-day Toxicity Rat–dietary feeding 0, 2, 8, 32, 50, or 400 ppm (equivalent to an intake of 0.1, 0.4, 1.6, 2.5, & 20 mg/kg/d, respectively)	NOAEL =32 ppm (1.6 mg/kg/d)** LOAEL = 50 ppm (2.5 mg/kg/d)**	-depression of plasma, RBC, & brain ChE (no information on % depression).	90-day Toxicity Rat–dietary feeding 0.5, 1, 2, or 4 ppm	NOAEL =0.05 mg/kg/d**; LOAEL =0.1 mg/kg/d**	-slight depression of RBC ChE at 0.1 mg/kg/d. 30-50% RBC depression at 0.2 mg/kg/d.
			Four Month Toxicity Rat–dietary feeding 2.5, 5, 15, 150 or 150 ppm	Invalid due to instability of the omethoate in the study	
Subchronic Neurotoxicity Rat-Dietary feeding 0, 1, 50, & 125 ppm (0.06, 3.22 & 8.13 mg/kg/d for M & 0.08, 3.78, & 9.88 mg/kg/d for F)	ChEI NOAEL = 1 ppm (0.06 mg/kg/d) ChEI LOAEL = 50 ppm (3.22 mg/kg/d)	-no effects in FOB or locomotor activity -reduction in plasma (24-48%) & RBC (34-60%) ChE at 3.22 & 8.13 mg/kg/d	Subchronic Neurotoxicity Rat Not available for omethoate		
Carcinogenicity Mouse- Dietary feeding 0, 25, 100, 200 ppm (0, 3.75, 15 or 30 mg/kg/d)	Systemic NOAEL/LOAEL < 3.75 mg/kg/d (LDT) ChEI NOAEL/LOAEL < 3.75 mg/kg/d (LDT)	At 15 & 30 m/k/d -dec. absolute & relative ovary wt -inc. absolute & relative liver wts. In all treated animals, (i) inc. incidence of hepatic vacuolation(F), (ii) dec. in relative wts of brain, heart, kidney, & spleen	Two year Toxicity Mouse –dietary feeding 1, 3, 10 ppm	Systemic toxicity NOAEL = 10 ppm (reported as equivalent to 3 mg/kg/d) (HDT)	No ChEI information

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
			Two year Toxicity Mouse–drinking water 0, 0.5, 4 or 32 ppm (equivalent to 0, 0.10, 0.82, or 6.48 mg/kg bw/day for males and 0, 0.11, 0.80, or 6.61 mg/kg bw/day for females) MRID 46126002	ChEI NOAEL = 0.1 mg/kg/day ChE LOAEL= 0.80 mg/kg/day	decreases in plasma, RBC, and brain ChE
Four-week Subchronic Toxicity Mouse–dietary feeding Not available for dimethoate			Four-week Subchronic Toxicity Mouse–dietary feeding 1, 3, 10 ppm (0.15, 0.45, 1.5 mg/kg/d)**	ChE NOAEL= 0.15 mg/kg/d** ChE LOAEL =0.45 mg/kg/d**	-at termination, 1.5 mg/kg/d**, ♂♀brain ChEI = 60%, plasma ChEI =20-39% -0.45 mg/kg/d**,♂♀ brain ChEI=up to 30%
90-day Subchronic Toxicity Dog–dietary feeding	ChEI NOAEL = 0.05 mg/kg/d ChEI LOAEL = 0.25 mg/kg/d Systemic NOAEL = 1.25 mg/kg/d LOAEL = 37.5 mg/kg/d	-depression of RBC ChE at 0.25 mg/kg/d & above (no information on % depression). -tremors & dec. food consumption	90-day Subchronic Toxicity Dog–in water 0 or 0.0125 mg/kg/day for 13 weeks. MRID 46099814 (1991)	No ChE inhibition at 0.0125 mg/kg/day (only dose tested)	

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
Developmental Toxicity Rat 0, 3, 6, or 18 mg/kg/d on gestation days 6 through 15, inclusive	Maternal toxicity NOAEL = 3 mg/kg/d LOAEL = 6 mg/kg/d Developmental NOAEL > 18 mg/kg/d (HDT) LOAEL = not established.	-small pellet like feces at 6 & 18 mg/kg/d -body wt decrement at 18 mg/kg/d. ChEI not measured	Developmental Toxicity Rat 0, 0.3, 1, 3 mg/kg/d	Maternal toxicity NOAEL = 1 mg/kg/d LOAEL = 3 mg/kg/d (reduced wt gain) Developmental NOAEL = 1 mg/kg/d LOAEL = 3 mg/kg/d No ChEI measured	-resorption & reduced fetal body wt -no malformation found
			Developmental Toxicity - Rat 0, 0.3, 1, 3 mg/kg/d	Maternal toxicity NOAEL = 1 mg/kg/d LOAEL = 3 mg/kg/d (reduced wt gain)	-no skeletal variation or malformation found -no ChEI measured
Developmental Toxicity Rabbit 0, 10, 20, or 40 mg/kg	Maternal toxicity NOAEL = 10 mg/kg/d LOAEL = 20 mg/kg/d Developmental toxicity NOAEL = 20 mg/kg/d LOAEL = 40 mg/kg/d ChEI not measured	-body wt gain decrement at 20 & 40 mg/kg/d -reduction in fetal wt.	Developmental Toxicity Rabbit 0, 0.1, 0.3, 1 mg/kg/d	ChEI LOAEL= 1 mg/kg/d (HDT) Developmental NOAEL = 1 mg/kg/d (HDT)	-blood ChEI =27% -no malformation found
			Developmental Toxicity - Rabbit 0, 0.2, 1, 5 mg/kg/d	ChEI NOAEL= 0.2 mg/kg/d ChEI LOAEL= 1 mg/kg/d	-brain and RBC ChEI -not teratogenic

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
Developmental Neurotoxicity Rat 0, 0.1, 0.5, or 3.0 mg/kg/d	Maternal toxicity* NOAEL = 3 mg/kg/d (HDT) LOAEL = not identified Offspring NOAEL= 0.1 mg/kg/d offspring LOAEL = 0.5 mg/kg/d	-increased pup death & increased motor activity at 0.5 mg/kg/d (LOAEL).	Developmental Neurotoxicity Rat Not available for omethoate		
3 -Week Subchronic Toxicity Rat–inhalation Not available for dimethoate			Three-Week Subchronic Toxicity Rat–inhalation 1, 2.3, & 7.5 ug/L	NOAEL = 1 ug/L LOAEL = 2.3 ug/L	-Only brain ChEI =up to 58% RBC & plasma (no ChEI info)
21-Day Subchronic Toxicity Rabbit–dermal 0, 100, 300, or 1000 mg/kg/d for 6 hrs/day	NOAEL dermal irritation & systemic toxicity = 1000 mg/kg/d (HDT) LOAEL not determined ChEI - Not measured	Unacceptable study due to several technical deficiencies	21-Day Subchronic Toxicity Rabbit–dermal 0, 2.5 or 20 mg/kg/d for 7 hrs/day MRID 46099804 (1979)	ChEI NOAEL = 2.5 mg/kg/d ChEI LOAEL = 20 mg/kg/d ChEI NOAEL = Not identified ChEI LOAEL = 2.5 mg/kg/d	Unacceptable study due to several technical deficiencies male brain ChE (36% inhibiton) female brain ChE (27% inhibiton)

Dimethoate			Omethoate*		
Study	**NOAEL/ LOAEL**	**Effects**	**Study**	**NOAEL/ LOAEL**	**Effects**
28-Day Subchronic Toxicity Rat–dermal 0, 10.5, 21.0, 31.5, or 63.0 mg/kg/d	NOAEL = 10.5 mg/kg/d LOAEL = 21.0 mg/kg/d	Reduced ChE activity in brains of males & females.	21-Day Subchronic Toxicity Rat–dermal Not available for omethoate		

* Data were extracted from MRID# 44636803 (pp 66-107)

** Default values

5.0 Public Health Data

5.1 Incident Reports

For a review of the pesticide poisoning incident data for dimethoate, HED consulted the following data bases: (1) OPP Incident Data System; (2) Poison Control Centers; (3) California Department of Pesticide Regulation; and (4) National Pesticide Telecommunications Network.

A review of the published incident data indicates that in outdoor agricultural uses, the primary source of occupational exposures associated with poisoning are postapplication field residues and spray drift (*Dobozy, 1996; Blondell, 1999*). Risks to handlers appear to be somewhat lower than with other insecticides. Compared to other OPs used in residential settings (many OPs are classified "restricted use" chemicals), dimethoate has the highest reported incidence of poisonings (none life-threatening). Residential uses are not being supported for reregistration and this is expected to mitigate any concerns for future residential exposures.

6.0 EXPOSURE ASSESSMENT AND CHARACTERIZATION

6.1 Dietary Exposure Pathway

6.1.1 Residue Profile

Dimethoate Use
Tolerances for dimethoate residues in/on plant and animal commodities [40 CFR §180.204 (a), (b), and (c)] are currently expressed in terms of the total residues of dimethoate [O,O-dimethyl S-(N-methylcarbamoylmethyl) phosphorodithioate] and its oxygen analog, omethoate [O,O-dimethyl S-(N-methylcarbamoylmethyl) phosphorothioate].

Currently dimethoate has both permanent and time-limited tolerances. All animal commodity tolerances are established at 0.02 ppm (except for milk at 0.002 ppm), while plant commodity tolerances range from 0.04 ppm to 5 ppm. Adequate methods are available for the enforcement of the established tolerances. The tolerance reassessment may be found in Appendix H.

The HED Metabolism Assessment Review Committee (MARC) concluded (*D280775, Bonnie Cropp-Kohlligian, 03/20/2002*) that the tolerance expression and risk assessments for dimethoate should include residues of dimethoate and omethoate. The Committee further concluded that the following ChE-inhibiting metabolites should be included in the risk assessments for dimethoate but *not the tolerance expression*: O-desmethyl omethoate, O-desmethyl omethoate carboxylic acid, O-desmethyl isodimethoate, hydroxy dimethoate and its conjugate, hydroxy omethoate and its conjugate, N-desmethyl dimethoate, N-desmethyl omethoate, O-desmethyl dimethoate, and dimethoate carboxylic

acid. (*Cropp-Kohlligian, Bonnie, DP Barcode D 283888, 07/01/2002*). However, based on the available data, it is unlikely that exposure to these metabolites of dimethoate (other than omethoate) will make a significant contribution to potential risk. Therefore, they are not quantitatively included in the risk assessment. Confirmatory data are needed to both measure the ChE inhibiting potential of each metabolite and to measure the residues of each metabolite on a variety of representative crops.

Residue Databases

Extensive monitoring data for dimethoate and omethoate from the USDA PDP and the FDA Surveillance Monitoring Program are available. Updated anticipated residues based on recent PDP and FDA data, and dimethoate use information from BEAD are included in this analysis. The voluntary cancellation of the following crops from their dimethoate technical registration are reflected (i.e. not included): apples, grapes, cabbage, collards, spinach, and head lettuce (leaf lettuces are retained). Other uses, not listed on the technical label, but were also voluntarily cancelled include: broccoli raab, fennel, tomatillo, lespedeza, and trefoil *[Federal Register: September 10, 2003 (volume 68, number 175) Environmental Protection Agency (OPP-2003-0263; FRL-7321-2) pp 53371-53374]*.

Generally, PDP data from years 2000 or more recent, where enough data existed to make necessary residue distribution files and calculations, were extracted to represent the different commodities (see *Hrdy, 2005a)*.

Methodology for Combining Residues of Dimethoate with Omethoate

The monitoring programs (PDP and FDA) analyze for both dimethoate (parent compound) and omethoate (metabolite) on each sample collected. Since the tolerance expression includes both dimethoate and omethoate, the residues of parent and its metabolite had to be summed for use in the dietary risk assessment. Furthermore, since it was determined that omethoate was 12 times more toxic than dimethoate in acute dietary exposure and 3 times more toxic than dimethoate in chronic dietary exposure, residues of omethoate [including limit of detection (LOD) values] in/on the same sample were multiplied by a factor of 12 in the acute and by a factor of 3 in the chronic dietary risk assessment before addition to dimethoate residues. Different scenarios were possible (e.g. a tomato sample may be analyzed for one compound but not for the other or it may have a detected residue of one and not the other). Procedures in the following table were used in determining the detected residue values to be inserted in the dietary exposure analyses.

Table 6.1.1 - Procedure used for adding dimethoate and omethoate residues on samples with detected residues of at least one of those compounds.

Dimethoate Value Reported	Omethoate Value Reported	Treatment
Detect	Detect	Dimethoate detect + (12 X omethoate Detect)
Detect	Non-Detect	Dimethoate Detect + (12X½ LOD for Omethoate for that sample)
Non-Detect	Detect	1/2 LOD for Dimethoate for that sample + (12XOmethoate Detect)
Detect	Not analyzed	Detect for Dimethoate + [12XDetect (same value) for Omethoate]
Not Analyzed	Detect	12X Detect for Omethoate + Detect (same value) for Dimethoate

A sample with a detected residue was considered as one that had detected residues of either dimethoate or omethoate or both. Residue Distribution Files (RDFs), used in the acute dietary risk assessment, were comprised of detected residues, ½ LOD's and zeroes. The value of ½ LOD in an RDF was the sum of ½ LOD values due to dimethoate and omethoate. The calculation was as follows for each commodity:

½ LOD in RDF = Combined ½ LOD = (weighted average ½ LOD) + 12X (weighted average ½ LOD)

The total number of ½ LOD values in an RDF was calculated based on the treated portion of the crop (Percent crop treated; %CT) reported by BEAD (*Alsadek, 2004*).

In the chronic dietary risk assessment, point estimates, instead of RDFs were used for all commodities. A chronic point estimate is the average value of another set (different than an RDF) of detected residues, ½ LODs and zeros. The detected residues and ½ LOD values reflected a 3X adjustment for omethoate residues (instead of 12X in the acute). Furthermore, the weighted average %CT value (instead of the maximum %CT used in acute assessment) was used to adjust for the number of ½ LODs and zeros.

Translation of Data
When monitoring data were not available for a particular commodity (e.g, honeydew melon or watermelon), but available for a similar commodity (e.g., cantaloupe), if the use patterns were the same or very similar, monitoring data from the latter crop (source crop) were translated to the former. The Agency's SOP 99.3 was followed in the translation of the data. PDP and FDA data were translated from representative crops. Acute dietary risks from exposure to food alone would exceed the aPAD if fresh green beans from PDP were used to represent all green beans consumed. However, when canned and frozen data were included, the risks were substantially decreased.

Level of Refinement
Residue data incorporated into the probabilistic assessment include field trial data and monitoring data from USDA and FDA data. Monitoring data, including translating from representative crops, were available for all the most significant contributors to exposure. There were no significant contributors that did not have highly refined monitoring data.

Processing Factors
Processing studies that were submitted and accepted by the Agency (*Bonnie Cropp-Kohlligian, DP Barcode Nos: D205591, D206804, D206555, and D213099, 11/06/1995*) include citrus (orange juice, dried citrus pulp), field corn, cottonseed, grapes, potatoes, soybeans, tomatoes, and wheat. The processing factor(s) that were used for these commodities in this assessment are listed below:

Citrus (Orange): juice (0.2X)

Corn: grits (0.4X), meal (0.4X), flour (0.4X), refined oil-all types (0.3 X)

Cottonseed: meal (1.3X), refined oil (0.6X)

For all other commodities the DEEM default processing factors were used.

The Agency identified several studies in the open literature that investigated the effect of kitchen-processing on concentrations of dimethoate residues in foods. (*DeVito, 1999*). Based on the results of these studies, a cooking factor of 0.7 (i.e., 30% reduction of residues by cooking) for any cooked form of vegetables and fruits, and a cooking factor of 0.8 (i.e., 20% reduction of residues by cooking) for any cooked forms of grains were applied in the calculation of the assessment. Since most residue data for vegetables and fruits used in this assessment were from PDP monitoring data, and these type of data are obtained from washed and peeled (where appropriate) fruits and vegetables, no washing or peeling reduction factors were generally used in this risk assessment. No cooking studies for dimethoate in meat were found. A cooking study of several other organophosphate pesticides in meat was found, and showed that cooking causes decomposition of the substances tested. Based on the results of this study, a cooking factor of 0.7 (i.e., 30% reduction of residues by cooking) for any cooked form of meat was applied in the calculation of the assessment.

Percent Crop Treated
Usage data was available for most crops and translations from some crops were made to other crops. The differences in %CT for processed vs. fresh produce were not clarified but may have affected the outcome of this assessment. Imported commodities were handled the same as domestic samples with respect to %CT assumptions.

Sensitivity Analyses
The exposure from food is being driven by the detectable residues and the non-detects so that the assessment is not sensitive to the LOD values.

6.1.2 Drinking Water Exposure

Ready to drink, treated drinking water data for dimethoate, or "at the tap" water data, are not available. Dimethoate is not regulated under the Safe Drinking Water Act and the Agency's OW has not established an MCL for dimethoate or omethoate in water, nor is it included on the OW's Unregulated Contaminant Monitoring List. In other words, public drinking water supply systems are not required to analyze for dimethoate. EFED relies on both limited monitoring data and simulation models to estimate the occurrence of pesticides in drinking water.

Table 6.1.2a EFED's Recommended EDWECs for surface water and ground water based on the maximum use rate on FL citrus. The surface water EDWECs include TAFs to account for the conversion to omethoate during drinking water treatment.		
Source	**Acute EDWEC**	**Chronic EDWEC**
	---------- µg L^{-1} dimethoate equivalents ----------	
Surface Water	1654	73.0
Ground Water	0.044	0.044

Surface water

The revised EDWEC's in surface water were updated to account for the toxic degradate of dimethoate, omethoate, to account for subsequent updates in the Tier 2 models used (PRZM and EXAMS), and changes in the scenarios used for drinking water assessments. The revised assessment uses a time series from the index reservoir scenario for applications of dimethoate to Florida and California citrus. EFED's revised assessment has been adjusted for the Regional Percent Cropped Area (PCA) for the Southeast and California respectively, and for a TAF of 12, assuming 100% conversion to omethoate during drinking water treatment. The TAF has only been applied to surface water, as shallow vulnerable ground water wells are likely to be private and not chlorinated (*RDavid Jones, 2005*). Chlorination is responsible for the conversion of dimethoate to omethoate during drinking water treatment. The chronic EDWECs were estimated using the chronic TAF of 3. EDWEC's were calculated for 7 crops which include those which are the major use sites for the chemical, and some other sites which are representative of a group of other crops on which the pesticide is used (*RDavid Jones, 2005*). Florida and California citrus were chosen for risk assessment purposes because this use pattern often is of particular concern for surface water contamination due to high use rates.

Table 6.1.2b EDWECs for the maximum use patterns for dimethoate on selected agricultural crops. Acute EDWEC were adjusted by a TAF of 12 to account for expected conversion to omethoate during drinking water treatment. Chronic and cancer EDWECs were adjusted by a TAF of 3.		
Crop	Acute EDWEC	Chronic EDWEC
	---------- µg L^{-1} dimethoate equivalents ----------	
Broccoli/Cauliflower	685	34.4
Citrus (FL)	1654	73.0
Citrus (CA)	660	33.3
Corn	197	8.2
Cotton	99.2	9.5
Lettuce	317	28.0
Wheat	446	18.6

Surface water monitoring data from a number of sources are available but are limited in their scope (few years and infrequent sampling), are not nationally representative, and did not analyze for omethoate (*RDavid Jones, 2005*). One monitoring study, sampling over several years, and conducted by CalDPR, found the highest concentration of dimethoate, 2.4 µg/L, in the San Joaquin River basin. Given the sampling pattern and frequency within the study, it is uncertain whether higher concentrations (peak) exist (review; *RDavid Jones, 2004*). Omethoate was not looked for in the study.

The particular concern regarding the toxic metabolite omethoate is that if parent dimethoate reaches a drinking water intake, there is a strong possibility that it could be converted to omethoate by chlorination. Because dimethoate is very mobile and has little binding potential, coagulation and flocculation are not expected to remove it from water. Direct data on omethoate formation during drinking water treatment are available but are limited in scope due to unresolved analytical chemistry issues. Treatment data on other organodithiophosphates such as diazinon and azinphos methyl show that they convert nearly completely to their corresponding oxons during chlorination. Furthermore, once the oxon has formed, it appears to be sufficiently persistent, perhaps due to the presence of chlorine, to travel through the distribution system. Omethoate was found to persist 72 hours after initial treatment in the study, long enough for water to be transported through the distribution system to homeowners' taps. The available dimethoate-specific treatment data (chlorination) indicate, that under some conditions, conversion to omethoate may be as low as 20% (*RDavid Jones, 2005*). However, since these data are limited, 100% conversion of dimethoate to omethoate during drinking water treatment of surface waters has been assumed as a protective measure for this assessment. More data are needed. Without actual drinking water monitoring data (at-the-tap), it is difficult to draw any conclusions about actual residues in drinking water of dimethoate, omethoate, or any other metabolites.

Ground water

The ground water EDWEC was re-estimated using the SCI-GROW model, version 2.3. The Tier 1 SCI-GROW estimate was not adjusted for omethoate formation because the concern for omethoate formation is mostly restricted to surface water. Public drinking water supplies from ground water sources often do chlorinate, but they usually use deep wells and the vulnerability of deep wells to dimethoate contamination is small given the rapid degradation rate of dimethoate. Private wells are often much more shallow and can be much more vulnerable to contamination with pesticides, but chlorination is seldom done on private well water. A single SCI-GROW EDWEC is used for estimating acute and chronic risks due to drinking water exposure.

Laboratory fate data and terrestrial field data indicate that in most cases, dimethoate degrades very rapidly, on the order of days. Data from the Pesticides in Ground Water Database, that were collected from a number of states, show that dimethoate has occasionally been found in ground water at concentrations of up to 1 µg/L. These higher concentrations were found in samples collected from Georgia. Though the occurrence of dimethoate in ground water is consistent with the fate data, the concentrations are not. Many of the highest concentrations in ground water are of low reliability due to the nature of the analytical methods used (in Georgia). While the monitoring data do show that dimethoate can reach ground water, at least occasionally, the uncertainties due to the analytical chemistry

methods make it difficult to reach useful conclusions. Omethoate was not looked for in any ground water samples.

6.2 Dietary Risks and Characterization

Acute and chronic dietary risk assessments for dimethoate/omethoate were conducted using the DEEM-FCID™, Versions 2.02/2.03, which uses food consumption data from the USDA's CSFII from 1994-1996 and 1998. Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the Reference Dose (RfD) divided by the special FQPA Safety Factor. For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: "Available Information on Assessing Exposure from Pesticides, A User's Guide," 06/21/2000, web link: see SOP 99.6 (08/20/1999) or http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf.

6.2.1 Acute Dietary Exposure and Risk

Dimethoate acute dietary exposure assessment was conducted using the DEEM-FCID™, Version 2.02, which incorporates consumption data from USDA's CSFII, 1994-1996 and 1998. For acute exposure assessments, individual one-day food consumption data are used on an individual-by- individual basis. The reported consumption amounts of each food item were "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the acute PAD (aPAD) on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. Sets of highly refined residue inputs were used in estimating the dietary exposures to dimethoate/omethoate. Included in the refinement of anticipated residues are monitoring data from PDP or FDA, % CT information, and processing/cooking factors, where applicable. A highly refined, probabilistic analysis was performed. The results of the DEEM-FCID™ analyses can be found in Table 6.2. The overall acute dietary risk from residues in foods (no water included) at the 99.9th percentile is 16% of the aPAD for the US general population, 14% aPAD for females of child bearing age, and 32% aPAD for the most highly exposed population subgroup, children 1-2 years of age (see *Hrdy, 2005b*). The estimated potential acute dietary risks, based on exposure to food alone, are not of concern for any population subgroup.

6.2.2 Chronic Dietary Exposure and Risk

For the chronic dietary risk estimate, again, sets of highly refined residue inputs were used in estimating the dietary exposures. For chronic dietary exposure, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average

daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. The results of the DEEM-FCID™ analyses can be found in table 6.2. The overall chronic dietary risk from residues in foods (no water included) is 1% chronic PAD (cPAD) for the US general population, 0.8% cPAD for females of child bearing age, and 5% cPAD for the most highly exposed population subgroup, children 1-2 years of age (see *Hrdy, 2005b*). The estimated potential chronic dietary risks, based on exposure to food alone, are not of concern for any population subgroup.

Table 6.2. Summary of Dietary Exposure and Risk for Dimethoate for food alone

Population Subgroup*	Acute Dietary (99.9th Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.002134	16.42	0.000028	1.3
All Infants < 1 year old	0.001958	15.06	0.000042	1.9
Children 1-2 years old	0.004160	**32.00**	0.000111	**5.1**
Children 3-5 years old	0.003145	24.20	0.000076	3.4
Children 6-12 years old	0.002853	21.95	0.000045	2.1
Youth 13-19 years old	0.001569	12.07	0.000023	1.0
Adults 20-49 years old	0.001789	13.76	0.000018	0.8
Adults 50+ years old	0.001954	15.03	0.000019	0.9
Females 13-49 years old	0.001850	14.23	0.000018	0.8

* %PADs reported to 2 significant figures.

* *The values for the highest exposed population are bolded.

6.3 Residential (Non-Occupational) Exposure/Risk Pathway

Based on the available information, products containing dimethoate are currently intended for both the residential and occupational markets. However, since the registrants have indicated that they will not support residential (i.e., home, schools, playgrounds, or other recreational) use patterns during the reregistration process, no residential exposure and risk assessment is included in this document.

6.3.1 Home Uses

The registrants have indicated that they will not support residential use patterns during the reregistration process, no residential exposure and risk assessment is included in this document.

6.3.2 Recreational Uses

The registrants have indicated that they will not support residential or recreational use patterns during the reregistration process, no recreational exposure and risk assessment is included in this document.

6.3.3 Other (Spray Drift, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for dimethoate. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

7.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATIONS

7.1 Overview

Due to the availability of acceptable oral, dermal, and inhalation studies using dimethoate, or omethoate, the dietary, dermal, and inhalation risk assessments were conducted using route-specific endpoints. The acute and chronic dietary, and short-, and intermediate-term dermal, and inhalation endpoints are all based on a common toxic effect, inhibition of brain ChE, observed in animals following acute, subchronic or chronic exposure.

In assessing aggregate risks, HED generally considers exposures from dietary (food and drinking water) and non-dietary (dermal and inhalation) pathways. For residential and other non-dietary exposure pathways relevant incidental oral, dermal, and inhalation (if applicable) exposures are included to calculate short-, intermediate, and long-term aggregate risks. For dimethoate, however,

there are no supported residential or other non-dietary (turf/golf courses) uses. Therefore, the aggregate assessment was conducted for the dietary (food and water) pathway only. For the dietary pathway, food exposure estimates come from the dietary exposure analysis discussed above (Section 6.1). Generally, when there are insufficient water monitoring data available to quantitatively include in the aggregate risk assessment as a means of assessing whether or not aggregate exposures to a chemical and its metabolites are likely to exceed levels of concern, EFED provides estimated drinking water concentrations.

7.2 Aggregate Acute Risk Assessment

The aggregate acute risk estimate includes the contribution of risk from dietary (food + drinking water) sources only. The acute risk estimates from exposures to food alone, associated with the use of dimethoate do not exceed the Agency's level of concern at the 99.9th exposure percentile for any population subgroup. The highest risk is to children 1-2 years of age at 32% aPAD. When combined with drinking water, aggregate acute risk estimates from exposures to food plus water, associated with the use of dimethoate exceed HED's level of concern for all population subgroups (see *Hrdy, 2005b*).

Though some chemical-specific water monitoring data are available, they are not comprehensive, nor nationally representative, and not at-the-tap data. Hence, EDWECs were calculated from models, for risk assessment purposes, based on maximum application rates to Florida and California citrus. The probabilistic EDWECs were combined directly with the acute dietary exposure assessment for all population subgroups to calculate aggregate dietary (food + water) risk. The advantage of this approach is that the actual individual body weight and water consumption data from the CSFII are used, rather than assumed weights and consumption for broad age groups. Surface water EDWECs were combined with estimated food exposure for aggregate risk assessment purposes since the calculated surface water estimates exceed the calculated ground water estimates and therefore, are more conservative. The estimates include 100% conversion to omethoate and the acute TAF of 12X.

Table 7.2 - Results of Aggregate Acute Dietary Exposure Analysis Using DEEM FCID for food and drinking water from surface water modeling distributions from PRZM-EXAM estimates representing FL and CA. FL is the top value and CA is the bottom value.

Population	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
US Population	0.009329	72	0.026446	203	0.068247	525
	0.009399	72	0.019479	150	0.044907	345
All Infants <1 year old	0.032166	247	0.97284	748	0.230466	1773
	0.35193	271	0.070523	542	0.131455	1011

Table 7.2 - Results of Aggregate Acute Dietary Exposure Analysis Using DEEM FCID for food and drinking water from surface water modeling distributions from PRZM-EXAM estimates representing FL and CA. FL is the top value and CA is the bottom value.

Population	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Children 1-2 years old	0.014369	111	0.041061	316	0.100254	771
	0.014836	114	0.030314	233	0.060674	467
Children 3-5 years old	0.013273	102	0.037484	288	0.090321	695
	0.013505	104	0.027410	211	0.053430	411
Children 6-12 years old	0.009082	70	0.026073	201	0.062902	484
	0.009285	71	0.019042	146	0.038924	299
Youth 13-19 years old	0.006640	51	0.020181	155	0.053356	410
	0.007016	54	0.015198	117	0.033054	254
Adults 20-49 years old	0.008762	67	0.024678	190	0.060418	465
	0.008815	68	0.017853	137	0.037123	286
Adults 50+ years old	0.009517	73	0.024330	187	0.052643	405
	0.009071	70	0.016456	127	0.029395	226
Females 13-49 years old	0.008733	67	0.024810	191	0.059999	462
	0.008871	68	0.017959	138	0.036571	281

[a] These crops were cancelled by Cheminova (Cheminova/Diane Allemang to EPA/Dan Kenny, July 8 th, 2000; FR Notice published 05/04/2005): apples, grapes, cabbage, collards, spinach, head lettuce (all other lettuces are retained), and some other very minor crops (broccoli raab, fennel, tomatillo, lespedeza, and trefoil).

Limited monitoring data from CA indicate that concentrations of dimethoate may be 2.4 µg/L, or more (peak unknown). Assuming 100% conversion to omethoate during drinking water treatment, aggregate acute risk estimates from exposures to food plus measured water, also exceed HED's level of concern for some population subgroups (*Hrdy, 2005b*).

7.3 Aggregate Short- and Intermediate-term Risk

Aggregate short- and intermediate-term risk includes the contribution of risk from dietary (food + water) and residential sources to the total risk. Since residential uses are not being supported, exposures from these uses were not included in the risk assessment.

7.4 Aggregate Chronic Risk

Aggregate chronic (noncancer) risk estimates include the contribution of risk from dietary sources (food + water) and residential sources; however, as mentioned above, no residential uses are being supported. Chronic risk estimates from exposures to dimethoate and omethoate in food alone, do not exceed HED's level of concern for the U.S. general population and all population subgroups. When combined with drinking water from surface water, aggregate chronic risk estimates from exposures to food plus water, associated with the use of dimethoate exceed HED's level of concern for infants and children, when EDWECs from applications to Florida citrus are included.

As in the aggregate acute assessment, EDWECs were calculated by EFED to estimate the potential contribution to the chronic exposure from drinking water, and the EDWECs were incorporated directly into DEEM-FCID. The water residue estimates for surface water were calculated by EFED using the PRZM/EXAMS simulation model that uses conservative assumptions regarding the pesticide transport from the point of application to surface and ground water, and were supplemented with limited monitoring data. The estimates also included 100% conversion to omethoate and the chronic TAF of 3X. Again, as noted above, based on dimethoate-specific treatment data and limited data from drinking water treatment facilities, EFED believes that dimethoate is readily converted to omethoate during treatment.

Table 7.4 - Chronic Aggregate Dietary Exposure Estimates and Risk (food and water)[a]

Population	Exposure (mg/kg/day)	% cPAD
US Population	0.001566	71
All Infants <1 year old	0.005086	**231**
Children 1-2 years old	0.002396	**109**
Children 3-5 years old	0.002215	**101**
Children 6-12 years old	0.001521	69
Youth 13-19 years old	0.001135	52
Adults 20-49 years old	0.001455	66
Adults 50+ years old	0.001531	70
Females 13-49 years old	0.001449	66

[a] These crops were cancelled by Cheminova (Cheminova/Diane Allemang, Hand-Delivered Package Addressed to EPA/Dan Kenny, July 8 th, 2003; FR Notice 05/04/2005): apples, grapes, cabbage, collards, spinach, head lettuce (all other lettuces are retained), and some other very minor crops (broccoli raab, fennel, tomatillo, lespedeza, and trefoil).

8.0 CUMULATIVE RISK

The Agency has completed a revised cumulative risk assessment for OPs, (*USEPA, 2002*) which can be found on the Agency's web site http://www.epa.gov/pesticides/cumulative/rra-op/. It assesses the cumulative effects of exposure to multiple OPs, including dimethoate.

9.0 OCCUPATIONAL EXPOSURE/RISK PATHWAY

Dimethoate is an OP insecticide/acaricide/miticide that is used to control a wide variety of target pests including insects and related organisms. Some examples of the pests that dimethoate is intended to control include aphids, citrus thrips, grasshoppers, leafminers, spider mites, and whiteflies. Manufacturing products contain between 95 and 96% active ingredient. Formulated end-use products include: ECs that range in concentration from 8-57% dimethoate, and several WP products that each contain 25% dimethoate. Historically, several other types of formulated products have contained dimethoate, such as dusts and granulars, and a ready-to-use formulation that contains 30.5% dimethoate. It is the understanding of EPA, however, that none of these other formulation types are being supported in the reregistration process. This summary is based on the *Label Use Information System (LUIS)* report for dimethoate, a review of the dimethoate file (November, 1997) in the *Reference Files System*, and was updated to reflect recent voluntary cancellations (*FR May, 4, 2005 vol. 70 number 85*).

An analysis of the current labeling and available use information (e.g., LUIS) was completed. In addition, information was received from the main registrants about use-patterns likely to be supported for reregistration. The information indicates that dimethoate currently is available in a WP formulation for a variety of uses; however, this formulation type will be supported during reregistration for use only on pears, potatoes, and noncrop areas adjacent to vineyards. The information from the registrants also indicates that dimethoate currently is available in a ready-to-use formulation; however, this formulation type will not be supported during reregistration.

The information indicates that dimethoate can potentially be used on the following sites and that these sites are definitely being supported during reregistration:

- *Food/Feed/Fiber Crops*: alfalfa, asparagus, beans (excluding cowpeas), broccoli, Brussels sprouts, cauliflower, celery, cherries, corn, cotton, endive (escarole), grapefruit, grass, leaf lettuce, kale, lemons, lentils, limes, melons, mustard greens, oranges, pears, peas, pecans, peppers, potatoes, safflower, sainfoin, sorghum, soybeans, Swiss chard, tangerines, tangelos, tomatoes, triticale, turnips, watermelons, and wheat

- *Ornamental Crops:* arborvitae, azalea, birch, boxwood, camellia, carnation, cedar, Christmas trees, citrus trees (non-bearing nursery stock), cypress, daylilies, Douglas fir, Elaeagnus, elm,

Euonymous, Ficus nitida, gardenia, gerbera, gladiolus, hemlock, holly (American, English) iris, juniper, oak, pine, pinyon pine, poinsettia, pyracantha, roses, taxus (yew), viburnum

- *Forestry Uses:* conifer seed orchards and cottonwoods grown for pulp

- *Uses on non-crop land adjacent to vineyards:* currently registered only in California

The information indicates that, currently, dimethoate can be potentially used on the following sites; however, these uses are not supported during reregistration and will be removed from labels:

- *Food/Feed/Fiber Crops:* apples, broccoli raab, cabbage, collards, fennel, grapes, head lettuce, lespedeza, spinach, tomatillo, and trefoil

- *Ornamental Uses:* hackberry, honeysuckle

- *Forestry Uses:* all except conifer seed orchards and cottonwoods grown for pulp

- *Uses in and around Residences or Recreation Areas:* including households/domestic dwellings, pet living and sleeping quarters

- *Uses in and around Animal/Livestock Quarters*

- *Uses on Meat or Dairy Animals*

- *Uses in Outdoor Commercial/Institutional/Industrial Premises:* including loading docks, and warehouses

- *Uses on Outdoor Refuse or Solid Waste:* including refuse areas, manure piles, and garbage dumps

- *Uses for Sewage Systems*

In addition to reviewing and summarizing the use information available from within the Agency (e.g., LUIS and labels), EPA also reviewed the following two submissions that document the use patterns for dimethoate:

- *Dimethoate Use Information:* Authored by Blane Dahl of Jellinek, Schwartz, and Connolly (05/21/1997); and

- *Dimethoate Usage Report:* Authored by P. Leanne Pruett (05/30/1996).

Other use-information was received from USDA, various grower organizations, and registrants. EPA records, along with these documents, serve as the basis for the handler exposure/risk assessment presented in this document. Much of the unique information included in these documents was not required for the handler exposure assessment.

9.1 Short/Intermediate/Long-Term Handler Exposure and Risk

9.1.1 Handler Exposure

9.1.1.1 Handler Exposure Scenarios and Assumptions

HED has determined that exposure to pesticide handlers is likely during the use of dimethoate in occupational settings. The anticipated use patterns and current labeling indicate several major occupational exposure scenarios based on the types of equipment that potentially can be used to make dimethoate applications. These scenarios serve as the basis for the quantitative exposure/risk assessment developed for handlers in the occupational setting. These include the following:

(1a) mixing/loading liquids for aerial application;
(1b) mixing/loading liquids for chemigation;
(1c) mixing/loading liquids for groundboom application;
(1d) mixing/loading liquids for airblast sprayer application;
(2a) mixing/loading wettable powders for aerial application;
(2b) mixing/loading wettable powders for chemigation;
(2c) mixing/loading wettable powders for groundboom application;
(2d) mixing/loading wettable powders for airblast sprayer application;
(2e) mixing/loading wettable powders for rights-of-way sprayer application to non-cropland adjacent to vineyards;
(3) applying sprays with aircraft;
(4) applying sprays using a groundboom sprayer;
(5) applying sprays using an airblast sprayer;
(6) applying sprays using a rights-of-way sprayer on non-cropland adjacent to vineyards;
(7) flagging during aerial spray application;
(8) mixing/loading/applying liquid formulations using a low pressure handwand sprayer (PHED);
(9) mixing/loading/applying liquid formulations using a low pressure handwand sprayer (ORETF); and
(10) mixing/loading/applying liquid formulations using a high pressure handwand sprayer.

The following assumptions and factors were used in order to complete this exposure assessment:

- Average body weight of an adult handler is 70 kg. This body weight is used in the short- and intermediate-term assessments, since the endpoint of concern is not gender-specific.

- The number of acres treated or volume of spray solution applied per day are specific to each equipment type addressed in the exposure assessment and are representative of the amount that can be treated/applied in a single 8 hour workday for each exposure scenario.

- Daily areas and volumes (as appropriate) to be treated in each occupational exposure scenario include: 1200 acres for aerial applications to high-acre crops (i.e., alfalfa, corn, cotton, safflower, sorghum, soybeans, and wheat); 350 acres for aerial applications to other crops; 350 acres for chemigation applications to most crops; 200 acres for groundboom applications to high-acre crops; 80 acres for groundboom applications to other crops; 40 acres for airblast applications to all crops, except conifer seed nurseries; 20 acres for airblast/mistblower applications in conifer seed nurseries; 10 acres for applications to noncrop areas adjacent to vineyards; 1000 gallons for high pressure handwand applications; and 40 gallons for low pressure handwand applications. No data or volumes were estimated for the soil drench method or soil injection method, because scenario-specific exposure data are not available and use information describing these techniques in sufficient detail were not available.

- The following are the maximum use rates being supported for reregistration by at least one registrant:

  - At 8.3 lb/A EC formulation: Douglas fir seed orchards in Oregon and Washington
  - At 4.0 lb/A EC formulation: cottonwood grown for pulp
  - At 2.0 lb/A EC formulation: citrus, seed farms, woody ornamentals , Christmas tree plantations, conifer seed orchards (other than Douglas fir seed orchards in OR and WA), and forestry nurseries
  - At 1.0 lb/A wettable powder formulation: pears
  - At 1.0 lb/A EC formulation: Brussels sprouts, cherries, citrus (foliar & soil drench), pears
  - At 0.75 lb/A EC formulation: pears
  - At 0.67 lb/A EC formulation: pecans, wheat
  - At 0.5 lb/A wettable powder formulation: pears
  - At 0.5 lb/A EC formulation: pears, citrus
  - At 0.5 lb/A wettable powder formulation: potatoes
  - At 0.5 lb/A EC formulation: alfalfa, asparagus, beans (excluding cowpeas), broccoli, cauliflower, celery, corn (field and pop), cotton, grass grown for seed, lentils, melons, potatoes, safflower, sorghum, soybeans, tomatoes, watermelons, and herbaceous ornamentals
  - At 0.33 lb/A EC formulation: peppers
  - At 0.25 lb/A EC formulation: endive (escarole), leaf lettuce, kale, mustard greens, Swiss chard, and turnips
  - At 0.16 lb/A EC formulation: peas

- Calculations are completed at the maximum application rates for a variety of crops recommended by the available dimethoate labels to bracket risk levels associated with the various use patterns.

- Due to a lack of scenario-specific data, HED sometimes calculates unit exposure values using generic protection factors that are applied to represent various risk mitigation options; i.e., the use of personal protective equipment (PPE) and engineering controls. PPE protection factors include those representing double layers of clothing (50%) and respiratory protection (90%). Engineering controls are generally assigned a protection factor of 90% or higher. Engineering controls may include closed mixing/loading systems and enclosed cabs and enclosed cockpits.

9.1.1.2 Handler Exposure Assessment

As no chemical-specific handler exposure data were submitted in support of the reregistration of dimethoate, an exposure assessment for each use scenario was developed using surrogate values calculated using the *Pesticide Handlers Exposure Database (V 1.1)*.

Occupational handler exposure assessments are completed by the HED using a baseline exposure scenario and, if required, increasing levels of risk mitigation (PPE and engineering controls) to achieve an appropriate margin of exposure or cancer risk. The baseline clothing/PPE ensemble for occupational exposure scenarios represents an individual wearing long pants, a long-sleeved shirt, no chemical-resistant gloves, and no respirator.

The exposure/risk assessment that has been completed for the occupational handler scenarios is presented in Appendices A through D. Occupational handler scenarios were assessed using the short- and intermediate-term endpoint for dermal and inhalation exposures. The short- and intermediate-term dermal endpoint is a $BMDL_{10}$ of 18.67 mg/kg/day, based on a 28-day repeated dose dermal toxicity study on dimethoate using rats. The short- and intermediate-term inhalation endpoint is 0.1 mg/kg/day, derived from an inhalation concentration level of 0.38 mg/m^3 ($BMCL_{10}$) from a 28-day repeated dose inhalation study of omethoate using rats. No dermal absorption adjustment is required since the dermal endpoint is based on a dermal study. No inhalation absorption adjustment is required, since the inhalation endpoint is based on an inhalation study. The UF for both dermal and inhalation endpoints is 100 (10X for intraspecies variability and 10X for interspecies extrapolation).

HED anticipates that most occupational dimethoate exposures will occur in a short-term pattern, since HED defines short-term exposures for this chemical as the use of the chemical up to 30 days. HED anticipates there may be intermediate-term exposures in some handler exposure scenarios, particularly those involving applications by commercial applicators to large-acreage crops (e.g., field corn, wheat, alfalfa, cotton). However, HED notes that since the intermediate-term endpoint is the same as the short-term endpoint, the MOEs for intermediate-term exposures are the same as those calculated using the short-term endpoint. HED does not anticipate that occupational exposures will be long-term or

chronic, because HED defines long-term or chronic exposures as the use of the chemical more than several months a year and it is anticipated that handlers will not be exposed to dimethoate that frequently.

The calculation of baseline total daily dose levels (mg/kg/day), that include dermal and inhalation exposures, are presented in Appendix A for all occupational handler exposure scenarios. The baseline dermal and inhalation daily doses presented in Appendix A were then used to calculate *Margins of Exposure (MOEs)* for baseline attire using the short- and intermediate-term toxicological endpoints for dermal and inhalation, respectively. In Appendix B, MOEs were calculated using PPE in addition to baseline attire. In Appendix C, MOEs were calculated using engineering controls. Appendix D summarizes the caveats and parameters specific to the surrogate data used for each exposure scenario and corresponding exposure/risk assessment. These caveats include the source of the data and an assessment of the overall quality of the data. The assessment of data quality is based on the number of observations and the available quality control data. The quality control data are assessed based on a grading criteria established by the PHED task force. Additionally, it should be noted that all calculations were completed based on current HED policies pertaining to the completion of occupational exposure/risk assessments (e.g., rounding and acceptable data sources).

9.1.1.3 Calculating Dose from Dermal and Inhalation Exposure

The methods used to calculate daily dose (mg/kg/day) resulting from dermal and inhalation exposures to dimethoate handlers are presented below.

Daily dermal dose is calculated using the following formula [Note: The same formula is applied regardless of the risk mitigation level. Only the unit exposure levels vary with different levels of risk mitigation.]:

$$D_{Daily\ Dermal} = [UE \times AR \times A \times (DA/100)] / BW$$

Where:

$D_{Daily\ Dermal}$	=	Daily absorbed dose (mg/kg/day) resulting from dermal exposure;
UE	=	Unit exposure (mg/lb ai handled) excerpted from PHED surrogate exposure table;
AR	=	Application rate (pounds active ingredient per acre or pounds active ingredient per gallon of dilute pesticide mixture) excerpted from available use information and labels;
A	=	Area treated (acres/day or gallons of dilute pesticide mixture applied per day) based on the application equipment type;
DA	=	Dermal absorption factor (%), if appropriate; and

BW	=	Body weight (kg) based on the body weight of an average adult, since the endpoint is non-sex-specific.

Daily inhalation dose is calculated using the following formula [Note: The same formula is applied regardless of the risk mitigation level. Only the unit exposure levels vary with different levels of risk mitigation.]:

$$D_{Daily\ Inhalation} = [UE \times (1\ mg/1000\ \mu g) \times AR \times A \times (IA/100)] / BW$$

Where:

$D_{Daily\ Inhalation}$	=	Daily absorbed dose (mg/kg/day) resulting from inhalation exposure;
UE	=	Unit exposure (µg/lb ai handled) excerpted from PHED surrogate exposure table,
AR	=	Application rate (pounds active ingredient per acre or pounds active ingredient per gallon of dilute pesticide mixture) excerpted from available use information and labels;
A	=	Area treated (acres/day or gallons of dilute pesticide mixture applied per day) based on the application equipment type;
IA	=	Inhalation absorption factor (%); and
BW	=	Body weight (kg) based on the body weight of an average adult, since the endpoint is non-sex-specific.

9.1.2 Handler Risk

9.1.2.1 Handler Risk Calculations

The calculations of the daily dermal and inhalation dose of dimethoate received by handlers are used to assess the dermal and inhalation risks to those handlers. Short- and intermediate-term MOEs, regardless of the exposure scenario, were calculated using the following formula:

$$MOE = NOAEL\ (mg/kg/day) / Dose_{Dermal\ or\ Inhalation}\ (mg/kg/day)$$

In addition, since the endpoints of concern for dermal and inhalation routes were based on identical adverse effects (i.e., ChEI), the risks are aggregated. For short- and intermediate-term risks, the UF for both dermal and inhalation risk is 100. The total risk can be calculated as follows:

$$Total\ MOE = \{1 \setminus [(1/dermal\ MOE) + (1/inhalation\ MOE)]\}$$

The calculations used to estimate *Daily Dose* and *MOE* for the postapplication scenarios are similar. The only significant difference for postapplication scenarios is the manner in which the *Daily Dose* will

be calculated using a transfer coefficient, transferable residue levels, and accounting for the dissipation of dimethoate over time. *Daily Dose* and *MOE* values are calculated for each postapplication day until a restricted-entry interval (REI) is achieved based on the MOE value in occupational settings (i.e., REIs are based on MOE values ≥ 100).

9.1.2.2 General Risk Characterization Considerations

Several issues must be considered when interpreting the occupational risk assessment. These include:

- No chemical-specific data for handlers were used. As a result, all analyses were completed using surrogate data from sources such as PHED and ORETF. All exposures and risk assessments were completed based on the active ingredient in the end-use product as formulated.

- Some handler assessments were completed using "low quality" PHED data due to the lack of a more acceptable data set (see Appendix D for further details).

- A 50 generic protection factor for double-layer body protection was used to calculate handler exposures for several scenarios. A 90% generic protection factor for the use of a dust/mist respirator was used to calculate handler exposures for several scenarios.

- Various exposure factors used in the calculations (e.g., acres treated or gallons handled per day for each application method) are based on the best professional judgement of HED due to a lack of extensive pertinent data.

- Exposure descriptors have not been assigned to every scenario that has been assessed, because the data to describe distributions for each exposure factor are not available. The PHED surrogate exposure values can be described, however, as values that are generally between the geometric mean and the median of the data set used for calculation of the value. Calculations were completed for a variety of maximum application rates that varied based on crop type for each handler/equipment scenario assessed. No specific data were available pertaining to typical rates. However, an assessment was completed *de facto* because of the large range of application rates assessed for each scenario. Additionally, as indicated above, the area treated values were based on the best-professional judgement of HED. These values, however, are believed to represent typical to high-end acreages and volumes.

Refinement of the HED exposure and risk assessment calculations presented in this chapter is possible if the issues presented above are addressed by the registrant or if more refined approaches and data become available to HED.

9.1.2.3 Total Risks to Handlers

Dermal, inhalation, and total risks for occupational handlers were assessed using the short-and intermediate-term toxicological endpoints. Results from the assessment are presented below. A chronic risk assessment was not completed as HED believes that dimethoate use patterns do not lend themselves to chronic exposure scenarios.

HED identified exposure scenarios based on available labels and other use information, such as the LUIS report. As indicated earlier, surrogate data were used to develop the exposure risk assessment for occupational handlers. In some cases, appropriate surrogate data were not available to serve as the basis for an assessment. The scenarios for which no appropriate data are available:

- Application via soil injection for ornamental cultivation purposes and

- Soil drench application.

9.1.2.4 Short-and Intermediate-term Occupational Handler Risks

HED anticipates that most occupational dimethoate exposures will occur in a short-term pattern, since HED defines short-term exposures for this chemical as the use of the chemical up to 30 days. HED anticipates there may be intermediate-term exposures in some handler exposure scenarios, particularly those involving applications by commercial applicators to large-acreage crops (e.g., field corn, wheat, alfalfa, cotton). However, HED notes that since the intermediate-term endpoint is the same as the short-term endpoint, the MOEs for intermediate-term exposures are the same as those calculated for short-term exposures.

The calculations of short- and intermediate-term total risks to handlers indicate that most occupational handler risks are below HED's level of concern (i.e., MOEs are greater than 100) at some level of risk mitigation. MOEs are a concern (i.e., the MOEs are below 100), even with engineering controls, for:

- mixing/loading liquid formulations to support aerial and chemigation applications to **citrus** at the 2 pounds active ingredient per acre application rate;

- mixing/loading wettable powder formulations to support aerial and chemigation applications to **pears** at the 1 and 0.75 pounds active ingredient per acre application rate;
- mixing/loading liquid formulations to support aerial applications to **wheat** at the 0.67 pounds active ingredient per acre application rate;

- applying sprays with aircraft to **wheat** at the 0.67 pounds active ingredient per acre application rate;

- mixing/loading liquid formulations to support aerial applications to **alfalfa, alfalfa grown for seed, cotton, field corn, pop corn, grass grown for seed, safflower, sorghum, and soybeans** at the 0.5 pounds active ingredient per acre application rate;

- mixing/loading liquid formulations to support aerial and chemigation applications to **woody ornamentals, Christmas tree farms, and conifer seed orchards (other than Douglas firs in OR and WA)** at the 2 pounds active ingredient per acre application rate;
- mixing/loading/applying with high pressure handwand sprayers to **woody ornamentals, Christmas tree farms, and conifer seed orchards (other than Douglas firs in OR and WA)** at the 0.08, 0.06, and 0.01 pounds active ingredient per gallon application rate;
- mixing/loading liquid formulations to support aerial and chemigation applications to **cottonwood grown for pulp** at the 4 pounds active ingredient per acre application rate;

- applying sprays with aircraft to **cottonwood grown for pulp** at the 4 pounds active ingredient per acre application rate; and

- applying sprays with airblast equipment to **Douglas fir seed orchards in OR and WA** at the 8.3 pounds active ingredient per acre application rate.

The following table summarizes the risks to handlers by crop type and application rate.

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP

Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
Noncrop Land Associated with Vineyards					
Non-crop land adjacent to vineyards (using rights-of-way type equipment)	Mixing/loading wettable powders for non-crop land	2.0 lb ai/A & 10 A	5.6	70 (g, dl, 90%r)	1200 (g)
	Applying to non-crop land (uses rights-of-way data)		32	140 (g, 90%r)	Not feasible
Tree Fruit and Nuts					
Citrus	Mixing/loading liquids for aerial and chemigation applications	2.0 lb ai/A & 350 A	0.6	47 (g, dl, 90%r)	**77 (g)**
	Aerial spray applications		No data	No data	110
	Flagging for aerial spray		24	110 (dl, 90%r)	1200

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
	Mixing/loading liquids for airblast	2.0 lb ai/A & 40 A	5.2	360 (g, 90%r)	680 (g)
	Airblast application		14	64 (g, dl, hg 90%r)	160
	Mixing/loading liquids for aerial and chemigation applications	1.0 lb ai/A & 350 A	1.2	95 (g, dl, 90%r)	150 (g)
	Aerial spray applications		No data	No data	210
	Flagging for aerial spray		49	230 (dl, 90%r)	2400
	Mixing/loading liquids for airblast	1.0 lb ai/A & 40 A	10	130 (g)	1400 (g)
	Airblast application		27	100 (g, 90%r)	320
	Mixing/loading liquid for aerial and chemigation applications	0.5 lb ai/A & 350 A	2.4	160 (g, 90%r)	310 (g)
	Aerial spray applications		No data	No data	420
	Flagging for aerial spray		98	450 (dl, 90%r)	4900
	Mixing/loading liquids for airblast	0.5 lb ai/A & 40 A	21	260 (g)	2700 (g)
	Airblast application		54	200 (g, 90%r)	630
Pears	Mixing/loading liquids for aerial and chemigation applications	1.0 lb ai/A & 350 A	1.2	95 (g, dl, 90%r)	150 (g)
	Mixing/loading wettable powders for aerial and chemigation applications		0.32	4 (g, dl, 90%r)	**68 (g)**
	Aerial spray applications		No data	No data	210
	Flagging for aerial spray		49	230 (dl, 90%r)	2400
Pears (cont.)	Mixing/loading liquids for airblast	1.0 lb ai/A & 40 A	10	130 (g)	1400 (g)
	Mixing/loading wettable powders for airblast application		2.8	35 (g, dl, hg 90%r)	600 (g)
	Airblast application		27	100 (g, 90%r)	320

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
	Mixing/loading liquids for aerial and chemigation applications	0.75 lb ai/A & 350 A	1.6	110 (g, 90%r)	210 (g)
	Mixing/loading wettable powders for aerial and chemigation applications		0.42	5.3 (g, dl, 90%r)	**91 (g)**
	Aerial spray applications		No data	No data	280
	Flagging for aerial spray		65	300 (dl, 90%r)	3300
	Mixing/loading liquids for airblast	0.75 lb ai/A & 40 A	14	180 (g)	1800 (g)
	Mixing/loading wettable powders for airblast application		3.7	47 (g, dl, 90%r)	800 (g)
	Airblast application		36	140 (g, 90%r)	420
	Mixing/loading liquids for aerial and chemigation applications	0.5 lb ai/A & 350 A	2.4	160 (g, 90%r)	310 (g)
	Mixing/loading wettable powders for aerial and chemigation applications		0.64	8 (g, dl, 90%r)	140 (g)
	Aerial spray applications		No data	No data	420
	Flagging for aerial spray		98	450 (dl, 90%r)	4900
	Mixing/loading liquids for airblast	0.5 lb ai/A & 40 A	21	260 (g)	2700 (g)
	Mixing/loading wettable powders for airblast application		5.6	70 (g, dl, 90%r)	1200 (g)
	Airblast application		54	200 (g, 90%r)	630
Cherries	Mixing/loading liquids for aerial and chemigation applications	1.0 lb ai/A & 350 A	1.2	95 (g, dl, 90%r)	150 (g)
	Aerial spray applications		No data	No data	210
	Flagging for aerial spray		49	230 (dl, 90%r)	2400

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
Cherries (cont.)	Mixing/loading liquids for airblast	1.0 lb ai/A & 40 A	10	130 (g)	1400 (g)
	Airblast application		27	100 (g, 90%r)	320
	Mixing/loading liquids for aerial and chemigation applications	0.33 lb ai/A & 350 A	3.6	250 (g, 90%r)	470 (g)
	Aerial spray applications		No data	No data	640
	Flagging for aerial spray		150	150 (dl)	7400
	Mixing/loading liquids for airblast	0.33 lb ai/A & 40 A	32	400 (g)	4100 (g)
	Airblast application		82	310 (g, 90%r)	960
Pecans	Mixing/loading liquids for aerial and chemigation applications	0.67 lb ai/A & 350 A	1.8	120 (g, 90%r)	230 (g)
	Aerial spray applications		No data	No data	310
	Flagging for aerial spray		73	340 (dl, 90%r)	3600
	Mixing/loading liquids for airblast	0.67 lb ai/A & 40 A	16	200 (g)	2000 (g)
	Airblast application		41	150 (g, 90%r)	470
	Mixing/loading liquids for aerial and chemigation applications	0.33 lb ai/A & 350 A	3.6	250 (g, 90%r)	470 (g)
	Aerial spray applications		No data	No data	640
	Flagging for aerial spray		150	150 (dl)	7400
	Mixing/loading liquids for airblast	0.33 lb ai/A & 40 A	32	400 (g)	4100 (g)
	Airblast application		82	310 (g, 90%r)	960
Vegetable Crop					
Brussel sprouts	Mixing/loading liquids for aerial and chemigation applications	1 lb ai/A & 350 A	1.2	95 (g, dl, 90%r)	150 (g)
	Aerial spray applications		No data	No data	210
	Flagging for aerial spray		49	230 (dl, 90%r)	2400
	Mixing/loading liquids for groundboom	1 lb ai/A & 80 A	5.2	360 (g, 90%r)	680 (g)

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
	Groundboom application		110	110 (g)	1300
Asparagus, beans, broccoli, cauliflower, celery, lentils, melons, potatoes, and tomatoes	Mixing/loading liquids for aerial and chemigation applications	0.5 lb ai/A & 350 A	2.4	160 (g, 90%r)	310 (g)
	Aerial spray applications		No data	No data	420
	Flagging for aerial spray		98	450 (dl, 90%r)	4900
	Mixing/loading liquids for groundboom	0.5 lb ai/A & 80 A	10	130 (g)	1400 (g)
	Groundboom application		210	210 (g)	2500
Potatoes (wettable powder formulations, see above for liquid formulations)	Mixing/loading wettable powders for aerial and chemigation applications	0.5 lb ai/A & 350 A	0.64	8 (g, dl, 90%r)	140 (g)
	Aerial spray applications		No data	No data	420
	Flagging for aerial spray		98	450 (dl, 90%r)	4900
	Mixing/loading wettable powders for groundboom	0.5 lb ai/A & 80 A	2.8	35 (dl, 90%r)	600 (g)
	Groundboom application		210	210 (g)	2500
Peppers	Mixing/loading liquids for aerial/chemigation	0.33 lb ai/A & 350 A	3.6	250 (g, 90%r)	470 (g)
	Aerial spray applications		No data	No data	640
	Flagging for aerial spray		150	150 (dl)	7400
	Mixing/loading liquids for groundboom	0.33 lb ai/A & 80 A	16	200 (g)	2100 (g)
	Groundboom application		330	330 (g)	3800
Kale, mustard greens, endive (escarole), leaf lettuce, Swiss chard, and turnips	Mixing/loading liquids for aerial and chemigation applications	0.25 lb ai/A & 350 A	4.8	330 (g, 90%r)	620 (g)
	Aerial spray applications		No data	No data	840
	Flagging for aerial spray		200	200 (dl)	9800
	Mixing/loading liquids for groundboom	0.25 lb ai/A & 80 A	21	260 (g)	2700 (g)
	Groundboom application		430	430 (g)	5000

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
Peas	Mixing/loading liquids for aerial and chemigation applications	0.16 lb ai/A & 350 A	7.5	510 (g, 90%r)	970 (g)
	Aerial spray applications		No data	No data	1300
	Flagging for aerial spray		310	310 (dl)	15000
	Mixing/loading liquids for groundboom	0.16 lb ai/A & 80 A	33	410 (g)	4200 (g)
	Groundboom application		670	670 (g)	7800
Field and Fiber Crops					
Wheat	Mixing/loading liquids for aerial applications	0.67 lb ai/A & 1200 A/day	0.52	41 (g, dl, 90%r)	**67 (g)**
	Aerial spray applications		No data	No data	**92**
	Flagging for aerial spray	0.67 lb ai/A & 350 A/day	73	340 (dl, 90%r)	3600
	Mixing/loading/applying liquids for chemigation applications		1.8	120 (g, 90%r)	230 (g)
	Mixing/loading liquids for groundboom	0.67 lb ai/A & 200 A/day	3.1	210 (g, 90%r)	400 (g)
	Groundboom application		64	350 (g, 90%r)	750
Alfalfa, alfalfa grown for seed, cotton, field corn, pop corn, grass grown for seed, safflower, sorghum, and soybeans	Mixing/loading liquids for aerial applications	0.5 lb ai/A & 1200 acres/day	0.7	55 (g, dl, 90%r)	**90 (g)**
	Aerial spray applications		No data	No data	120
	Flagging for aerial spray	0.5 lb ai/A & 350 acres/day	98	450 (dl, 90%r)	4900
	Mixing/loading/applying liquids for chemigation applications		2.4	160 (g, 90%r)	310 (g)
	Mixing/loading liquids for groundboom	0.5 lb ai/A & 200 acres/day	4.2	290 (g, 90%r)	540
	Groundboom application		86	470 (g, 90%r)	1000
Ornamentals and Specialty Crops					
Herbaceous ornamentals	Mixing/loading liquids for groundboom	0.5 lb ai/A & 40 A	21	260 (g)	2700 (g)

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
		0.5 lb ai/A & 10 A	84	110 (g)	11000 (g)
	Groundboom application	0.5 lb ai/A & 40 A	430	430 (g)	5000
		0.5 lb ai/A & 10 A	1700	1700 (g)	20000
	Mixing/loading/applying liquids with low pressure handwand sprayers (ORETF)	0.0025 lb ai/gal & 40 gal	840	16000 (g)	Not feasible
	Mixing/loading/applying with high pressure sprayers	0.0025 lb ai/gal & 1000 gal	No data - dermal 23 - inhalation	110 (g, 90%r)	Not feasible
Woody ornamentals, Christmas tree farms, and conifer seed orchards (other than Douglas firs in OR and WA)	Mixing/loading liquids for aerial and chemigation applications	2.0 lb ai/A & 350 A	0.6	47 (g, dl, 90%r)	**77 (g)**
	Aerial spray applications		No data	No data	110
	Flagging for aerial spray		24	110 (dl, 90%r)	1200
	Mixing/loading liquids for groundboom	2.0 lb ai/A & 80 A	2.6	180 (g, 90%r)	340 (g)
	Groundboom application		54	290 (g, 90%r)	630
	Mixing/loading liquids for airblast	2.0 lb ai/A & 40 A	5.2	360 (g, 90%r)	680 (g)
	Airblast application		14	64 (g, dl, hg 90%r)	160
	Mixing/loading/applying liquids with low pressure handwand sprayers (ORETF)	0.08 lb ai/gal & 40 gal	26	490 (g)	Not feasible
		0.06 lb ai/gal & 40 gal	35	650 (g)	

Table 9.1.2.4 SUMMARY OF HANDLER RISKS FOR DIMETHOATE BY CROP					
Crop	Handler Scenario	Application Rate	Short- and Intermediate-Term Total MOE (Uncertainty Factor =100)		
			Baseline Total MOE	Additional PPE Total MOE	Engineering Controls Total MOE
		0.01 lb ai/gal & 40 gal	210	3900 (g)	
	Mixing/loading/applying with high pressure handwand sprayers	0.08 lb ai/gal & 1000 gal	No data - dermal; 0.73 - inhalation	**4.3 (g, dl, 90%r)**	Not feasible
		0.06 lb ai/gal & 1000 gal	No data - dermal 0.97 - inhalation	**5.7 (g, dl, 90%r)**	
		0.01 lb ai/gal & 1000 gal	No data - dermal (5.8 - inhalation	**34 (g, dl, 90%r)**	
Seed Farms	Mixing/loading liquids for groundboom	2.0 lb ai/A & 80 A	2.6	180 (g, 90%r)	340 (g)
	Groundboom application		54	290 (g, 90%r)	630
Cottonwood grown for pulp	Mixing/loading liquids for aerial and chemigation applications	4.0 lb ai/A & 350 A	0.3	24 (g, dl, 90%r)	**39 (g)**
	Aerial spray applications		No data	No data	**53**
	Flagging for aerial spray		12	56 (dl, 90%r)	610
Douglas fir seed orchards in OR and WA	Mixing/loading liquids for airblast/mistblower applications	8.3 lb ai/A & 20 A	2.5	170 (g, 90%r)	330 (g)
	Applying with airblast/ mistblower sprayers	8.3 lb ai/A & 20 A	3.3	31 (g, dl, hg, 90%r)	**76**

Note:
g indicates a gloved hand scenario,
dl indicates addition of a double layer of protective clothing,
hg indicates addition of chemical-resistant head gear,
90%r indicates use of a half-face or full-face respirator with a dust/mist filter (not a quarter-face dust/mist mask)
No Data indicates an exposure scenario was identified, but there are no acceptable data to complete assessment.
Not Feasible indicates that no engineering controls are known for this exposure scenario.

9.2 Postapplication Exposure and Risk

9.2.1 Postapplication Exposure

9.2.1.1 Postapplication Exposure Scenarios and Assumptions

HED has determined that postapplication exposure is likely following applications of dimethoate to fruit, vegetable, grain, fiber, feed, cottonwood, conifer seed nursery, and ornamental crops, as well as other sites during typical postapplication activities such as harvesting, irrigating, scouting, pruning, thinning, and transplanting. The postapplication risk is based on the short- and intermediate-term dermal toxicity endpoint. In most short- and intermediate-term postapplication scenarios, the residue levels were below the limit of quantification when the target margin of exposure (MOE 100) was obtained. For this risk assessment, HED is characterizing risk to (1) postapplication workers by the required duration of the REI, and (2) crop advisors/scouts by the duration of the postapplication period during which PPE must be used.

Postapplication risks are mitigated for workers using an REI. In general, the REI is established based on the number of days following application that must elapse before the pesticide residues dissipate to a level where estimated worker MOE's equal or exceed 100 while wearing baseline attire (i.e., long-sleeve shirt, long pants, shoes, and socks). Under the Worker Protection Standard for Agricultural Pesticides (WPS) -- 40 CFR Part 170, entry to perform routine hand labor tasks is prohibited during the REI and PPE can not be considered as a risk reduction measure in establishing the REI.

Postapplication risks are mitigated for crop advisors/scouts using entry restrictions, not restricted-entry intervals. Since under the WPS for Agricultural Pesticides -- 40 CFR Part 170, crop advisors/scouts are defined as handlers, HED can permit such persons to enter treated areas to perform scouting tasks, provided they are using required PPE. In general, the entry restriction is established based on the number of days following application that must elapse before the pesticide residues dissipate to a level where estimated scout/crop advisor MOE's equal or exceed 100 while wearing baseline attire (i.e., long-sleeve shirt, long pants, shoes, and socks).

For the purpose of conducting this assessment, indicator crop groups/activities, and assumptions regarding application rates and dermal transfer coefficients for these crop groups, were selected that are likely to be representative of postapplication exposures to dimethoate. Transfer coefficients (Tc) are used to relate the DFR values to activity patterns (e.g., harvesting, thinning, scouting, irrigating) to estimate potential human exposure. All postapplication activities are assessed in this RED using surrogate Tc values to estimate potential exposure levels for all crops so as to determine the number of days following application when target MOEs (i.e., 100) are reached, since no dermal exposure levels were monitored concurrently with the DFR levels in registrant-submitted studies. Many of the transfer coefficients used are listed in the revised policy issued by the Science Advisory Council for Exposure adopted by HED in August, 2000. The transfer coefficients that differ from those in the policy are

from studies submitted by HED's Agricultural Reentry Task Force (ARTF) and are currently undergoing peer review. In some instances, the transfer coefficients obtained from these newly submitted studies are more crop- and activity-specific than the transfer coefficients in HED's policy and, therefore, may provide more crop/activity-specific estimates of postapplication exposure. In such instances, the transfer coefficients from the ARTF data were used in this postapplication assessment.

Since a multitude of crops are treated with dimethoate, it is necessary to assess the exposure potential resulting from a variety of crop types and postapplication activities. These surrogate transfer coefficients are believed to represent a reasonable and reliable estimate of potential postapplication exposures. The following is a summary of transfer coefficients and use-rates by crop used in the postapplication assessment:

Application Rate	**Crop/Transfer Coefficient**
0.16 lb ai/A	Peas: Tc=2500 for hand harvest Tc=1500 for scout & irrigate
0.25 lb ai/A	Endive, escarole, leaf lettuce, kale, mustard greens, Swiss chard, turnips: Tc=2500 for hand harvest & thin Tc=1500 for scout & irrigate
0.33 lb/A	Cherries (old rate): Tc=3000 for harvest & prune Tc=1000 for scout & irrigate, & hand weed Pecans (old rate): Tc=500 for prune & scout Peppers: Tc=1000 for harvest, stake, tie 700 scout, irrigate
0.5 lb ai/A	Alfalfa, safflower, soybeans: Tc=1500 for scout & irrigate Pears: Tc=3000 for harvest, prune, train, tie Tc=1000 for scout & irrigate, hand weed Asparagus: Tc=500 for scout & irrigate

Beans (excluding cowpeas), lentils:
Tc=2500 for hand harvest
Tc=1500 for scout & irrigate

Broccoli, cauliflower:
Tc=5000 for harvest, irrigate, prune, thin & tie

Celery:
Tc=2500 for hand harvest
Tc=1500 for scout & irrigate

Citrus (foliar applications-old rate):
Tc=3000 for prune
Tc=1000 for scout, irrigate, & hand weed

Corn (field & pop):
Tc=17000 for detasselling
Tc= 1000 scout, irrigate, & hand weed

Cotton:
Tc=1500 for irrigate, scout & weed

Melons, watermelons:
Tc=2500 for hand harvest, prune, thin
Tc=1500 for scout, irrigate, & hand weed

Ornamentals - herbaceous:
Tc=400 for all tasks related to nursery crops, except cut flowers or foliage
Tc=500 for tasks related to cutting foliage or flowers, except cut roses or cut carnations
TC=2600 for tasks related to cutting roses or carnations;

Potatoes:
Tc=1500 for scout & irrigate

Sorghum:
Tc=1000 for scout & irrigate

Tomatoes:
Tc=1000 for hand harvest, prune, stake, thin, tie, train
Tc=700 for scout & irrigate

0.67 lb ai/A	Pecans (new rate): Tc=500 for prune & scout
	Wheat: Tc=1000 for scout & irrigate
0.75 lb ai/A	Pears (proposed new rate): Tc=3000 for harvest, prune, train, tie Tc=1000 for scout & irrigate, hand weed
1.0 lb ai/A	Pears (proposed new rate): Tc=3000 for harvest, prune, train, tie Tc=1000 for scout & irrigate, hand weed
	Citrus (foliar applications- (proposed new rate): Tc=3000 for prune Tc=1000 for scout, irrigate & hand weed
	Brussels sprouts: Tc=5000 for harvest, irrigate, prune, thin & tie
	Cherries (proposed new rate): Tc=3000 for hand harvest & prune Tc= 1000 for scout, irrigate & hand weed
2.0 lb ai/A	Citrus (foliar applications- (proposed new rate): Tc=3000 for hand harvest & hand prune Tc=1000 for scout, irrigate & hand weed
	Woody ornamentals, forestry nurseries, and Christmas trees plantations: Tc=3000 for prune & thin Tc=1500 all hand harvest
	Conifer seed orchards (except Douglas fir seed orchards in OR and WA) and forestry nurseries: Tc=1000 for scout, irrigate & weed
4.0 lb ai/A	Cottonwoods grown for pulp: Tc=1000 for scout, irrigate & weed
8.3 lb ai/A	Douglas fir seed orchards in OR and WA: Tc=1000 for scout, irrigate & weed

9.2.1.2 Data Sources and Assumptions for Scenarios Considered

Postapplication exposure data were required for dimethoate during the data-call-in (DCI) in support of the reregistration process, since, at that time, one or more toxicological criteria had been triggered. The following DFR studies were submitted by the registrant and used in this revised assessment:

- *MRID# 446903-02. Bookbinder, M.G. Dissipation of Dislodgeable Foliar Residues of Dimethoate (O,O-dimethyl S-[N-[methylcarbamoyl]methyl] phosphorodithioate) and its Metabolite Omethoate (O,O-dimethyl S-[2-(methylamino)-2-oxoethyl] phorphorothioate) after Application of CLEAN CROP® DIMETHOATE 400 Insecticide to Tomato Plants. October, 1998.*

  The study was conducted in three geographical locations: near Porterville in Tulare County, California; near Hobe Sound, Martin County, Florida; and near Germansville in Lehigh County, Pennsylvania. According to the 1998 Agricultural Statistics Handbook (NASS, USDA), as cited in the study report, the test states and adjacent states produced 78 percent of the 1997 U.S. tomato acreage. At each of the test sites, two plots were established. One plot, located upwind from the other, was left untreated and served as a control. The other plot was divided into 3 subplots. Sampling rows were selected to minimize edge effects and spray overlap. During the field trial, test plots were maintained according to normal regional practice for tomato culture. The test plots received 2 applications, 7 or 8 days apart, of CLEAN CROP® DIMETHOATE 400 insecticide. As prescribed on the label, the dimethoate was formulated as a 42.9 percent EC containing 4 lbs active ingredient (ai) per gallon. The dimethoate was applied at the maximum registered application rate for tomatoes of 0.5 lb ai/acre, using CO_2 powered backpack boom equipment at the Florida site, and tractor-mounted PTO-powered groundboom equipment at the California and Pennsylvania sites. The California test plots received furrow irrigation totaling 22 inches during the trial period, but no rainfall. The Florida sites received drip irrigation totaling 2.16 inches and rain on days 4, 11, 12, and 13 after the second application. No irrigation was applied to the Pennsylvania site, but rain was recorded on days 3, 4, 5, 6, 10, 11, 12, and 14 after the second application -- with a one-day high rainfall event of 2.2 inches on day 6 after the second application. Tomato DFR leaf-punch samples of approximately 400 cm^2 of surface (two-sided) were collected using a 1-inch diameter Birkestrand leaf punch sampler plots prior to each application, as soon as the spray had dried (Day 0), and on days 1, 2, 3, 5, 7, 10, 14, 21, 28, and 35 after the second application. Samples collected after 14 days after the second application were not analyzed, because residues had dropped to below the limit of quantification (LOQ) by that time. In summary, the study met most of the requirements of the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines. The following major issue was

noted: residue values were calculated even for samples with concentrations below the LOQ, which may have affected the half life calculations.

- *MRID# 446903-01. Bookbinder, M. G. Dissipation of Dislodgeable Foliar Residues of Dimethoate (O,O-dimethyl S-[N-[methylcarbamoyl]methyl] phosphorodithioate) and its Metabolite Omethoate (O,O-dimethyl S-[2-(methylamino)-2-oxoethyl] phorphorothioate) after Application of CLEAN CROP® DIMETHOATE 400 Insecticide to Leaf Lettuce. October, 1998.*

  The study was conducted in three geographical locations: near Porterville in Tulare County, California; near Hobe Sound in Martin County, Florida; and near Germansville in Lehigh County, Pennsylvania. According to the 1998 Agricultural Statistics Handbook (NASS, USDA), as cited in the study report, the test states and adjacent states produced 100 percent of the 1997 U.S. leaf lettuce crop. At each of the test sites, two plots were established. One plot was left untreated and served as a control. The other plot was divided into 3 subplots for leaf disc collection. Sampling rows were selected to minimize edge effects and spray overlap. The test plots received 2 applications, 7 or 8 days apart, of CLEAN CROP® DIMETHOATE 400 insecticide. The dimethoate was formulated as a 42.9 percent EC containing 4 lbs active ingredient (ai) per gallon. The dimethoate was applied at the maximum registered application rate of 0.25 lb ai/acre, using CO_2 powered backpack boom equipment at the Florida site, and tractor-mounted PTO-powered groundboom equipment at the California and Pennsylvania sites. Application equipment was calibrated prior to application. Leaf disk samples of approximately 400 cm^2 of surface (two-sided) were collected from both the control and test plots prior to each application, as soon as the spray had dried (Day 0), and on 1, 2, 3, 5, 7, 10, 14, 21, 28, and 35 days after the second application. Samples collected subsequent to 14 days after the second application were not analyzed, because residues had dropped to below the limit of quantification (LOQ) by that time. Daily rainfall data were obtained onsite. Rainfall at the Florida and Pennsylvania sites during the sampling period totaled approximately 160 and 130% respectively of the 10 year regional precipitation avenge for the trial period. The California site received no rainfall during the study period. In summary, this DFR study met most of the requirements of the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines. In addition, some discrepancy and minor issues were noted in this review.

- *MRID# 448276-01. Prochaska, Lee M. Dissipation of Dimethoate and its Metabolite Omethoate Dislodgeable Foliar Residues on Apples Treated with CLEAN CROP® DIMETHOATE 400 - Phase I: Field Investigation and Phase 2: Analytical. May 4, 1999.*

  Clean Crop® Dimethoate 400 was applied using airblast sprayers twice during the growing season in August to apple trees in three locations. An application rate of 1.0 lb. active

ingredient/ Acre (a.i./A) was employed. Application equipment was calibrated prior to application. Foliage samples were collected as soon as sprays had dried (e.g., no later than 4 hours postapplication), 12 hours, 1, 2, 3, 5, 7, 10, 14, 21, 28, and 35 days after the last application. The first study site was in Ottawa County, near Marne, Michigan; the second was in upstate New York, in Wayne County near Alton, NY; and the third site was in the Washington State central valley, in Grant County, near Ephrata, WA. In 1997, the top three U.S. apple-producing states were Washington, Michigan, and New York; these states together produced 69 percent of the total U.S. crop (USDA, Agricultural Statistics, 1997). Historical meteorological conditions at the three sites seem to indicate nearly normal conditions in these areas at the time of the study. There was no rainfall within 24 hours before or after application. Irrigation was applied to the plots in Washington State on the fifth day after application. Cheminova analyzed the dissipation data using a nonlinear regression fit to a first order decay equation. Residues were still detectable 35 days after the application at all locations. The study met most of the requirements of the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines. The major deviation was that the study was conducted using an application rate of 1.0 lb ai/acre as opposed to the label specified maximum application rate of 0.5 lb ai/acre.

- *MRID # 447882-01. Prochaska, Lee M. Dissipation of Dimethoate and its Metabolite Omethoate Dislodgeable Foliar Residues on Grapes Treated with Clean Crop® Dimethoate 400, Phase I Field Investigation & Phase II Analytical, March, 1999.*

  The study was conducted in three geographical locations: in the California Central Valley, near Porterville, in Tulare County; in upstate New York, near Dundee, in Yates County; and in the Washington State central valley, 8 miles south of Quincy, in Grant County. At each of the test sites, two plots were established. One plot was left untreated and served as a control. The other plot was divided into 3 subplots for leaf disc collection. Sampling rows were selected to minimize edge effects and spray overlap. Clean Crop® Dimethoate 400 was applied to the vineyards twice during the growing season from a few days to a month after "veraison," which is the point at which the grape enters the ripening period (i.e., "green" to mature fruit). Both applications were applied at 1 lb ai/A, not the label permitted maximum rate of 2 lbs ai/A. Airblast sprayers were used at all test sites. No rain events are noted in California; irrigation occurred three times (4 inches each time); these did not coincide with pesticide applications. In New York, there were 16 rain events; these did not coincide with pesticide applications. In Washington, there were 10 rain events and two irrigation events; these did not coincide with pesticide applications. Foliage samples were collected as soon as sprays had dried (e.g., no later than 4 hours postapplication), 12 hours, 1, 2, 3, 5, 7, 10, 14, 21, 28, and 35 days after the last application. This study met most of the OPPTS Series 875 Group B Occupational and Residential Exposure Test Guidelines. The most important deviation was that the study was not conducted at the maximum application rate.

9.2.1.3 Postapplication Exposures for Other Crops

HED had no dimethoate-specific data for crops other than lettuce, grapes, tomatoes, and apples. Therefore, a surrogate postapplication exposure risk assessment was conducted for the those crops, using three of the four studies submitted. Data from the grape study (MRID 447882-01) were not used in the postapplication assessment since grape crops are in the process of cancellation.

Data from the apple study were used in the postapplication assessment for all tree fruit and nut crops, cottonwoods grown for pulp, conifer seed nurseries, and woody ornamentals. The apple data (MRID# 448276-01) represent DFR levels obtained at an application rate of 1.0 lb ai/acre. The DFR levels ($\mu g/cm^2$) were normalized to account for a potential increase in residues when dimethoate is applied at the application rates of 2.0, 4.0. and 8.3 lb ai/acre, and for a potential decrease in residues when dimethoate is applied at the application rates of 0.33 lb ai/acre and 0.5 lb ai/acre. These data were used to assess postapplication risks (see Appendix E) from contact with:

- Cherries and pecans at the former application rate of 0.33 lb ai/acre;
- Citrus (foliar applications) and pears at the former application rate of 0.5 lb ai/acre;
- Pecans at the proposed application rate of 0.67 lb ai/acre;
- Pears at the proposed application rate of 0.75 lb ai/acre;
- Cherries, citrus (foliar applications), and pears at the proposed application rate of 1.0 lb ai/acre;
- Woody ornamentals, Christmas tree plantations, conifer seed orchards (other than Douglas fir seed orchards in OR and WA), at an application rate of 2.0 lb ai/acre;
- Cottonwoods grown for pulp at an application rate of 4.0 lb ai/acre; and
- Douglas fir trees grown for seed cone production in Oregon and Washington at an application rate of 8.3 lb ai/acre.

Data from the tomato study (MRID# 446903-02) were used for crops with an application rate ranging from 0.33 lb ai/acre and higher (except tree and woody crops), since the data represent non-woody plants and DFR levels were obtained at an application rate of 0.5 lb ai/acre. For application rates other than 0.5 lb ai/acre, the DFR levels ($\mu g/cm^2$) were normalized to account for a potential increase/decrease in residues when dimethoate is applied at application rates ranging from 0.33 lb ai/acre to 1 lb ai/acre. These data were used to assess postapplication risks (see Appendix F) from contact with:

- Peppers at an application rate of 0.33 lb ai/acre;
- Alfalfa, asparagus, beans (excluding cowpeas), broccoli, cauliflower, celery, corn (field & pop), cotton, lentils, melons, potatoes, safflower, sorghum, soybeans, tomatoes, and watermelons at an application rate of 0.5 lb/acre
- Wheat at an application rate of 0.67 lb/acre; and
- Brussels sprouts at an application rate of 1.0 lb ai/acre.

Data from the lettuce study (MRID# 446903-01) were used for crops with an application rate of 0.25 lb ai/acre and less, since the data represent DFR levels obtained at an application rate of 0.25 lb ai/acre. For applications to peas, the actual DFR levels ($\mu g/cm^2$) were normalized to account for a potential decrease in residues when dimethoate is applied at the application rate of 0.16 lb ai/acre. These data were used to assess postapplication risks (see Appendix G) from contact with:

- Peas at an application rate of 0.16 lb ai/acre; and
- Endive (escarole), leaf lettuce, kale, mustard greens, Swiss chard, and turnips at an application rate of 0.25 lb ai/acre.

9.2.1.4 Postapplication Residential Exposures

Residential uses are no longer being supported. However, based on available information, HED remains concerned about residential risks from dimethoate spray drift. The potential for these non-occupational exposures to individuals living in or near agricultural areas, e.g. potential exposure from spray drift, where dimethoate is being used, was not assessed but will be addressed at a later time when methodologies to perform such assessments are in place.

9.2.2 Postapplication Risk

9.2.2.1 Postapplication Risk Calculations

The postapplication risks were assessed using the four dimethoate DFR studies submitted in support of the reregistration. Each of the studies measured the amount of dimethoate residues remaining on treated leaves following applications and also measured, when present, omethoate residues. Omethoate is a degradate of dimethoate that is twelve times more toxicologically potent than dimethoate. Typically, when omethoate was present in the studies, it peaked in quantity a few days after the application and then gradually dissipated over time. Dimethoate residues peaked immediately after application and dissipated over time thereafter. Due to the differences in the dissipation of dimethoate and omethoate and to the increased toxic potency of omethoate, the risks from each were assessed separately and then the risks were aggregated to determine the total risk resulting from exposures to workers following dimethoate applications. In those studies where omethoate was not found, the postapplication risks were assessed using just the dimethoate residues.

The study data were separated into dimethoate residues and omethoate residues. When the application rate of the crops being assessed for postapplication risk differed from the application rate used in the surrogate crop DFR study, the dimethoate residues and omethoate residues were normalized using the following formula:

$$DFR_{(norm)} = DFR_{(study)} * (Application\ rate_{(norm)} \setminus Application\ rate_{(study)})$$

Whenever feasible, HED prefers to use the actual data reported in a chemical-specific study, rather than using a regression analysis to predict residue levels. The actual DFR data can be found in the HED review of the respective studies. Typically, postapplication studies initially collect data daily (i.e., days 0, 1, 2, and 3) and thereafter collect data at intervals (i.e., days 5, 7, 10, 14, 21, 28, 35). If residues dissipate below HED's level of concern during the time period when data are collected, HED prefers to use the actual data reported in a chemical-specific study to assess postapplication risks. However, if residues remain a concern beyond the period of data collection, HED uses a regression analysis to predict residue levels for those days where data are not collected. No regression analysis was conducted for the lettuce and tomato studies, since residues were not a concern beyond the point where residue data were being gathered. For the California data in these studies, HED "zeroed out" the data two days beyond the day when more than half the data were below the LOQ (as described below). In the postapplication risk assessment, a regression analysis was conducted for the apple study since residues were of concern for the apple study beyond the point where residue data were being gathered. The regression analysis was conducted using the natural log-transformed DFR data from each test site using the following equation:

$$y = mx + b$$

where:

x	=	days postapplication;
m	=	slope of the regression line;
b	=	constant; and
y	=	residue on day x.

For the use-patterns where risks remained a concern beyond the days encompassed by the study, HED used a regression analysis to complete the risk assessment. The dimethoate and omethoate residue values were log-transformed and a separate linear regression was performed on each. Since omethoate residues increase over the first few days after application and then dissipate, the regression was started on the day where average omethoate values were at their peak.

If the dimethoate or omethoate residues reached the limit of quantification (LOQ) in the study on a given day, then HED assumed that the residues were one-half the LOQ on the following day and that the residues approached zero for the day following that. Therefore, once the LOQ was reached for either of the residue types, the residues were assumed to have "zeroed out" within two days of that measurement.

In general, omethoate was a significant factor in arid areas (i.e., areas where the average annual rainfall is less than 25 inches per year). In risk assessments using the apple study data, in general, both dimethoate and omethoate residues were still present up until the target MOE was reached. In the lettuce study, omethoate was not found in either of the nonarid study sites – Florida or Pennsylvania.

Since dissipation rates at the arid sites were significantly different from those at the nonarid sites, the results are reported separately for all study sites.

The calculation of daily exposure to dimethoate by persons entering the treated area after application is used to assess the risk to those persons. The average daily dermal dose is calculated using the following formula:

*Dermal Dose (mg/kg/day) = [DFR(mg/cm^2) * Tc (cm^2/hr) * Abs (0.28) * ED (8hrs/day)] \ BW (60 kg)*

Since omethoate is 12X more potent that dimethoate, the omethoate dermal dose was adjusted by a TAF of twelve, using the following formula:

*Omethoate Dermal Dose (mg/kg/day) = Dermal Dose (mg/kg/day) * TAF (12)*

The postapplication risk, assessed through MOE, is calculated using the following formula:

Total MOE = NOAEL (mg/kg/day) \ Average Daily Dermal Dose (mg/kg/day)

where the short- and intermediate-term dermal NOAEL is 18.67 mg/kg/day and the UF is 100.

9.2.2.2 Risk from Postapplication Exposures

Postapplication occupational exposure is likely following applications of dimethoate to fruit, vegetable, grain, fiber, feed, conifer seed nursery, cottonwood grown for pulp, ornamental, and other crops and sites during typical postapplication activities such as harvesting, irrigating, scouting, pruning, thinning, and transplanting. The results of the risk assessment for postapplication exposures indicate that the location and/or the environmental conditions near the time of application influence the length of time following application until risks are below HED's level of concern (i.e., MOEs are greater than or equal to 100) as does the type of plant to which the application is directed.

For most crops, the risk assessment indicates that following applications in arid areas (i.e., outdoor areas where average annual rainfall is less than 25 inches), residues persist longer than in non-arid areas. Consequently, EPA could potentially establish different entry restrictions for arid areas versus nonarid areas. Since the apple, lettuce, and tomato studies each contained two sites in nonarid areas (i.e., New York and Michigan for apples and Pennsylvania and Florida for lettuce and tomatoes), the results are averaged to obtain a single entry restriction for nonarid areas per use-pattern.

Table 9.2.2.2 Summary of Postapplication Risk Assessment for Dimethoate Using Lettuce or Tomato or Apple Study Data																
Crop Group	Maximum Single App. Rate	Key Tasks					Secondary Tasks					Tasks of Special Concern				
		Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Secondary Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Task-Specific Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)			
			Non-Arid			Arid		Non-Arid			Arid		Non-Arid			Arid
Lettuce Study																
			PA	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**
Endive, Escarole, Kale, Leaf lettuce, Mustard Greens, Swiss chard, Turnips	0.25 lb ai/A	2500 harvest, thin	12 hrs	12 hrs	12 hrs	1	1500 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA				
Peas	0.16 lb ai/A	2500 harvest	12 hrs	12 hrs	12 hrs	12 hrs	1500 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA				
Tomato Study																
			PA	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**
Brussels Sprouts	1 lb ai/A	5000 harvest, irrigate, prune, thin & tie	2	4	3	9	NA					NA				
Wheat	0.67 lb ai/A	1000 scout, irrigate	12 hrs	1	1	12 hrs	NA					NA				
Beans, Lentils, Celery	0.5 lb ai/A	2500 harvest	1	1	1	2	1500 scout, irrigate	12 hrs	1	1	12 hrs	NA				
Tomato Study																

Table 9.2.2.2 Summary of Postapplication Risk Assessment for Dimethoate Using Lettuce or Tomato or Apple Study Data																
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		Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Secondary Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Task-Specific Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)			
			Non-Arid			Arid		Non-Arid			Arid		Non-Arid			Arid
			PA	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**
Melons, Watermelons	0.5 lb ai/A	2500 harvest, prune, thin	1	1	1	2	1500 scout, irrigate, & hand weed	12 hrs	1	1	12 hrs	NA				
Celery	0.5 lb ai/A	2500 harvest	1	1	1	2	1500 scout, irrigate	12 hrs	1	1	12 hrs	NA				
Potatoes	0.5 lb ai/A	1500 scout, irrigate	12 hrs	1	1	12 hrs	NA					NA				
Tomatoes	0.5 lb ai/A	1000 harvest, prune, stake, thin, tie, train	12 hrs	12 hrs	12 hrs	12 hrs	700 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA				
Asparagus	0.5 lb ai/A	500 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA					NA				
Broccoli, Cauliflower	0.5 lb ai/A	5000 harvest, irrigate, prune, thin & tie	1	2	2	5	NA					NA				
Tomato Study																
			PA	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**		**PA**	**FL**	**Avg**	**CA**

Table 9.2.2.2 Summary of Postapplication Risk Assessment for Dimethoate Using Lettuce or Tomato or Apple Study Data																
Crop Group	Maximum Single App. Rate	Key Tasks					Secondary Tasks					Tasks of Special Concern				
		Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Secondary Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Task-Specific Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)			
			Non-Arid			Arid		Non-Arid			Arid		Non-Arid			Arid
Alfalfa, Alfalfa grown for seed, Soybeans, Safflower	0.5 lb ai/A	1500 scout & irrigate	12 hrs	1	1	12 hrs	NA					NA				
Cotton	0.5 lb ai/A	1500 scout, irrigate, weed	12 hrs	1	1	12 hrs	NA					NA				
Field corn, popcorn	0.5 lb ai/A	1000 scout, irrigate, hand weed	12 hrs	12 hrs	12 hrs	12 hrs	NA					17,000 detassel corn	3	4	4	15
Grain Sorghum	0.5 lb ai/A	1000 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA					NA				
Herbaceous Ornamentals	0.5 lb ai/A	500 tasks related to cut flowers & foliage, except roses & carnations	12 hrs	12 hrs	12 hrs	12 hrs	400 tasks related to nursery crops, except cut flowers or foliage	12 hrs	12 hrs	12 hrs	12 hrs	2600 tasks related to cutting carnations & roses	1	1	1	2
Peppers	0.33 lb ai/A	1000 harvest, stake, tie	12 hrs	12 hrs	12 hrs	12 hrs	700 scout, irrigate	12 hrs	12 hrs	12 hrs	12 hrs	NA				
Apple Study																
			NY	**MI**	**Avg**	**WA**		**NY**	**MI**	**Avg**	**WA**		**NY**	**MI**	**Avg**	**WA**

Table 9.2.2.2 Summary of Postapplication Risk Assessment for Dimethoate Using Lettuce or Tomato or Apple Study Data																
Crop Group	Maximum Single App. Rate	Key Tasks					Secondary Tasks					Tasks of Special Concern				
		Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Secondary Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Task-Specific Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)			
			Non-Arid			Arid		Non-Arid			Arid		Non-Arid			Arid
Douglas Fir Seed Orchards in OR and WA	8.3 lb ai/A	1000 scout, irrigate & weed	27	17	22	39	NA					NA				
Cottonwoods grown for pulp	4.0 lb ai/A	1000 scout, irrigate & weed	18	10	14	24	NA					NA				
Conifer seed orchards (except Douglas fir seed orchards in OR and WA)	2.0 lb ai/A	1000 scout, irrigate & weed	7	6	7	14	NA					NA				
Woody Ornamentals and Christmas tree plantations	2.0 lb ai/A	3000 prune & thin	24	14	19	36	1500 harvest	13	7	10	14	NA				
Pecans	0.67 lb ai/A	500 prune & scout	12 hrs	12 hrs	12 hrs	12 hrs	NA					NA				
	0.33 lb ai/A		12 hrs	12 hrs	12 hrs	12 hrs										
Apple Study																
			NY	**MI**	**Avg**	**WA**		**NY**	**MI**	**Avg**	**WA**		**NY**	**MI**	**Avg**	**WA**

Table 9.2.2.2 Summary of Postapplication Risk Assessment for Dimethoate Using Lettuce or Tomato or Apple Study Data														
Crop Group	Maximum Single App. Rate	Key Tasks					Secondary Tasks					Tasks of Special Concern		
		Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Secondary Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)				Task-Specific Transfer Coefficient	Time Following Application until MOEs ≥100 (days, unless specified)	
			Non-Arid			Arid		Non-Arid			Arid		Non-Arid	Arid
Pears	1.0 lb ai/A	3000 harvest, prune, train & tie	13	7	10	14	1000 scout, irrigate, hand weed	2	1	2	4	NA		
	0.75 lb ai/A		9	6	8	12		2	12 hrs	1	2			
	0.5 lb ai/A		6	3	5	9		12 hrs	12 hrs	12 hrs	12 hrs			
Citrus	2.0 lb ai/A	3000 prune	24	14	19	36	1000 scout, irrigate, hand weed	7	6	7	11			
	1.0 lb ai/A		13	7	10	14		2	1	2	4			
	0.5 lb ai/A		6	3	5	9		12 hrs	12 hrs	12 hrs	12 hrs			
Cherries	1.0 lb ai/A	3000 harvest & prune	13	7	10	14	1000 scout, irrigate, hand weed	2	1	2	4			
	0.33 lb ai/A		2	12 hrs	2	4		12 hrs	12 hrs	12 hrs	12 hrs			

10.0 DATA NEEDS/LABEL REQUIREMENTS

10.1 Toxicology

To more accurately characterize the ChE inhibiting potential of the metabolites of concern, a comparative repeated dose ChEI study in rats is needed.

10.2 Residue Chemistry

Magnitude of residue data on alfalfa seed are required to support the use of dimethoate on alfalfa grown for seed.

Storage stability data depicting the stability of dimethoate residues of concern in meat, milk, poultry, and eggs are required. Data should adequately reflect test sample storage intervals and conditions from available animal magnitude of the residue data. In addition, test sample storage intervals/conditions information is required to validate existing cattle magnitude of the residue data. This information remains outstanding and is considered confirmatory.

The reregistration requirements for the magnitude of residue in plants have not been fulfilled for bean forage and bean hay. The deficiencies for the commodities of beans can be resolved by either label amendments and appropriate tolerance proposals based on available data or the submission of new magnitude of the residue data to support the currently registered use rate.

The reregistration requirements for the magnitude of residue in plants have been fulfilled for pea vines and pea hay. The registrant must either petition the Agency for the establishment of tolerances for the total residues of dimethoate and omethoate in/on pea vines and pea hay or amend product labels to restrict the use of dimethoate to peas (not including field peas).

As a result of changes in the Livestock Feeds Table (Table 1, July 1996), magnitude of residue data are currently required by the Agency for cotton gin byproducts.

In order to more accurately characterize the abundance of the residues of the metabolites of concern, magnitude of the residue data are needed.

10.3 Occupational Exposure

Short- and intermediate-term dermal and inhalation exposure assessments were made using PHED Version 1.1 surrogate data since no acceptable chemical-specific handler data were submitted. Dimethoate-specific handler studies may be required pending the outcome of recommended discussions with the registrants and others on handler risk and risk mitigation.

Postapplication exposure is likely following applications of dimethoate to fruit, vegetable, grain, fiber, feed, ornamental, and other crops and sites during typical post-application activities such as harvesting, scouting, pruning, transplanting, etc. Additional chemical-specific data, from which to estimate postapplication exposure to dimethoate and its degradates, may be required pending the outcome of discussions with registrants and others on postapplication risk and risk mitigation.

11.0 ATTACHMENTS

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Appendix H. Tolerance Reassessment Summary.

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Lowit, 2005a. Dimethoate and omethoate: comparative toxicity and determination of toxicity adjustment factors. (Addendum to HED TXR#s 0050651 and 0050901). PC 035001 &035002. D291600. TXR# 0052940. Anna Lowit. April 11, 2005.

Lowit, 2005b. TAF_D291600.appendix1. Spreadsheet for TAF assessment (Lowit, 2005a).

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